P1-0044

Helping Cancer Patients Quit Smoking Using Brief Risk Communication and Motivational Counseling: A Randomized Controlled Trial

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Introduction and Project Objectives: Smoking cessation after cancer diagnosis can lower the risk of disease advancement, minimize adverse treatment-related effects and improve the prognosis and quality of life of patients. We examined the effectiveness of a smoking cessation intervention using a risk communication approach with motivational counseling.

Methods: This was a randomized controlled trial, in which 528 smoking cancer patients (average age 58.9 years, 455 male) were allocated either into an intervention group (n=268) or a control group (n= 260). About 72.9% of the subjects were pre-contemplating quitting. Subjects' mean daily tobacco consumption was 12.5 cigarettes, they had been smoking for over 42 years on average, and were moderately nicotine dependent. The intervention group received 15-30 min individual risk communication and counseling by a nurse counselor while the control group received standard care. Smoking status in both groups was checked at follow-ups at 1 week and at 1, 3, 6, 9, and 12 months

Results: The primary outcome was self-reported point-prevalence 7-day abstinence at 6 months. No significant differences were found between the intervention and control groups (15.7% vs 16.5%; OR 0.94, 95% CI 0.59-1.50). The secondary outcome, the rate of at least 50% self-reported reduction of smoking at 6 months, was higher in the intervention group than in the control group (16.8% vs 12.3%; OR 1.43, 95% CI 0.88-2.35). The biochemically validated quit rate at the 6-month follow-up was higher in the intervention group than in the control group (5.2% vs 3.8%; OR 1.38, 95% CI 0.60-3.16).

Conclusions: The risk communication intervention was not effective for quitting but improved the rate of smoking reduction among smoking cancer patients.

Project Number: 09100991

P2-0156

A Randomized Controlled Trial of a Tailored Intervention Compared to Usual Care to Promote Smoking Cessation and Improve Glycaemic Control on Type 2 Diabetic Patients Who Smoked

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Background: Tobacco smoking not only leads to adverse health problems but also undesirable complications for smokers with diabetes mellitus (DM). Providing brief smoking cessation advices to diabetic smokers should be a part of standard care. More rigorous empirical evidence of its effectiveness is required. This study aimed to investigate the effect of a brief stage-matched smoking cessation intervention in enhancing glycemic control and smoking abstinence for type 2 DM smokers in Hong Kong.

Methods: This was a large randomized controlled trial with 557 type 2 DM smokers randomized into an intervention group (n=283) to receive brief individualized face-to-face stage-matched smoking cessation counseling (around 20 minutes) by a trained smoking cessation nurse counsellor and a diabetes-specific smoking cessation leaflet, or a control group (n=274) who received usual care. Subjects were then followed up at 1 week, 1 month, 3 months, 6 months, and 12 months by telephone and assessed for smoking status.

Results: Above 70% of the subjects were in the pre-contemplation stage of quitting smoking. On average, they smoked 14 cigaretes per day for over 37 years. By intention to treat analysis, both intervention and control groups had similar 7-day point-prevalence smoking abstinence (9.2% vs. 13.9%, p = 0.08), biochemically validated quit rates (3.2% vs. 5.1%, p = 0.25), and HbA1c level (7.95% [63 mmol/mol] vs. 8.05% [64 mmol/mol], p = 0.49) at 12 months. Although the control group had a statistically significantly higher rate of self-reported smoking reduction by at least 50% than the intervention group at 3 months (excluding quitters in numerator: 16.8% vs. 10.2%, p = 0.02; excluding quitters in both numerator and denominator: 18.5% vs. 11.1%, p = 0.02), no significant differences were observed between the two groups at the 6- (excluding quitters in numerator: 13.4% vs. 14.2%, p = 0.78; excluding quitters in both numerator and denominator 16.1% vs. 15.1%, p = 0.77) and 12-month follow-ups (excluding quitters in numerator : 14.8% vs. 14.6%, p = 0.94; excluding quitters in both numerator and denominator: 17.0% vs. 16.3%, p = 0.84).

Conclusion: The results showed that a brief stage-matched smoking cessation intervention was not effective in increasing the rates of quitting or smoking reduction in DM patients who smoked. The intervention was also not effective in improving glycemic control. The quit rate was very low, suggesting that most of these patients were hardcore smokers. More RCTs on more intensive interventions are needed to motivate DM patients to quit smoking.

Project Number: 08091061

P3-0173

Effectiveness of an Individual, Telephone-delivered Acceptance and Commitment Therapy for Smoking Cessation in Adults Recruited in Primary Health Care Settings: A Randomized Controlled Trial

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Introduction: This study aimed to examine the effectiveness of delivering an individual, telephone-delivered Acceptance and Commitment Therapy (ACT) for smoking cessation among a Chinese population.

Method: This is a two-arm randomized controlled trial with assessment at baseline and via telephone follow-ups at 3, 6, and 12 months. Subjects were proactively recruited from primary healthcare centers. Participants were randomized to the intervention (ACT) group (n=70) and control group (n=74) respectively. Both groups received self-help materials on smoking cessation. Those in the ACT group also underwent an initial face-to-face session and two telephone ACT sessions at 1 week and 1 month following the first session. The primary outcome was self-reported 7-day point-prevalence abstinence at the 12-month follow-up. Other outcomes include biochemical measures, smoking characteristics, quitting attempts, intention to quit, self-perception of quitting, and psychological flexibility.

Results: There was no significant difference in the 7-day point prevalence quit rate at the 12-month follow-up between the intervention group (26.1%) and the control group (24.3%) (p=.704). Significant outcomes from baseline to the 12-month follow-up including a forward progression in the participants' readiness to quit smoking (p=.014), increased confidence in quitting smoking (p=.043), and increased psychological flexibility (p=.006) were found in the intervention group

when compared with the control group.

Conclusions: Overall, the results suggested that face-to-face delivery of Acceptance and Commitment Therapy in primary health care settings and by phone within the Chinese population was effective in contributing to improvements in various cognitive processes. More intensive interventions may help to translate these cognitive changes into behavioral change, that is, smoking abstinence.

This study provides the first evidence of a randomized-controlled trial on the adoption of an individual, Acceptance and Commitment Therapy (ACT) for smoking cessation, delivered initially in primary health care settings and subsequently by telephone within a Chinese population. ACT was promising in terms of bringing about cognitive changes, including greater psychological flexibility, greater readiness to quit, and more confidence about quitting, when compared to the use of self-help materials only among the general population. ACT was delivered in a less intensive and briefer format in this study as compared to previous studies, thereby making it a potentially more cost-effective intervention program.

Project Number: 09101421

P4-0019

Physicochemical and Toxicological Assessment of Passenger Daily Exposure to Air Pollutants in Various Public Transport Systems in Hong Kong

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Introduction: Adverse health effects were noted with exposure to airborne particulate matter (PM). Complexity of PM components increase with temperature, relative humidity, etcetera and as well as on source and spatial apportionment. In a densely-populated city like Hong Kong, where majority of people commutes through public transport (mass transit railways (MTR), Bus) and few others on private vehicles, causing different levels of size segregated PM exposure.

Objectives: This project investigated the pollutant concentrations of $PM_{2.5}$, black carbon (BC), ultrafine particles (UFP) and carbonmonoxide (CO) in real-time to determine heterogeneity of passenger exposure in transit microenvironments. A time-integrated filter sampling was carried out to find out surrogates of cellular oxidative stress by determining role of transition metals, ions, BC and polyaromatic hydrocarbons (PAHs).

Methods: A trolley case that housed numerous portable air monitors was used in real-time detection of pollutants in transit microenvironments, classified as 1) busy and secondary roadside bus stops, 2) open and closed termini, and 3) above- (AG) and under-ground (UG) MTR platforms. The chemical properties at these microenvironments were determined by collecting filter samples of coarse (2.5-10μm) and fine (<2.5μm) PM. In addition, a sensitive macrophage-based reactive oxygen species (ROS) activity was determined, on a time and dose dependent manner to assess the health implications of these PM exposures.

Results: Real-time measurements demonstrated highest average particle concentrations at busy roadside and enclosed bus termini compared to MTR platforms. The BC, UFP and CO resulted in large variations than $PM_{2.5}$ at these microenvironments. While BC and UFP concentrations were found high in diesel-run bus cabins, CO was noted to be in greater concentrations in LPG-run bus cabins. The time-integrated sampling, focussed mainly on AG-, UG MTR and bus routes, demonstrated $PM_{2.5}$ concentrations of 47.9, 86.8 and 43.8 $\mu g/m^3$, respectively. The PM-induced cell-toxicity at these microenvironments was analyzed in-vitro and compared with urban ambient environments. Strong positive associations were observed for ROS with water-soluble metals (Cr, Cu, Fe, Mn, Ni, V, Mo; R>0.70) and OCEC (R>0.85) for UG and AG routes. Also, PAHs, n-alkanes, hopanes and steranes were found abundantly in $PM_{2.5}$ fraction of AG MTR route.

Conclusion: The findings strongly suggest the PM mass concentration alone may not be the best surrogate of dose and toxicity while assessing the public exposure. The PM-induced cellular-ROS for these microenvironments were 50-fold lesser than the typical ambient sites, implying very limited oxidative potential of PM in daily commuter exposure in public transport routes.

Project Number: 10112061

P5-0077

PM_{10} Composition and Emergency Hospital Admissions for Cardiovascular and Respiratory Diseases in Hong Kong

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Introduction: Particulate matter (PM) air pollution is a complex mixture of numerous chemical components, however, the overall epidemiologic evidence associating specific PM chemical components with health outcomes has been mixed.

Project Objectives: We aimed to estimate the associations between exposures to 18 chemical components of PM_{10} and daily emergency cardiorespiratory hospitalizations in Hong Kong, China.

Methods: PM_{10} chemical components data were collected from 6 general air quality monitoring stations between January 1, 2001, and December 31, 2007 in Hong Kong. We applied generalized additive models with autoregressive terms to estimate associations between PM_{10} chemical components and cause-specific emergency hospital admissions. Distributed lag models were used to estimate the cumulative effect over several lag days.

Results: After adjustment for time-varying confounders and gaseous copollutants, a 3.4 $\mu g/m^3$ increment in 2-day moving average of same-day and previous-day nitrate concentrations was associated with the largest increase of 1.03% (95% confidence interval: 0.38, 1.67) in cardiovascular hospitalizations, followed by sodium ion, chloride ion, magnesium, and nickel; elevation in magnesium level (0.2 $\mu g/m^3$) was linked to a 0.63% (95% confidence interval: 0.21, 1.04) increase in respiratory hospitalizations, together with sodium ion and aluminium. Cumulative effects distributed over 0-3 lag days showed consistent results with greater effect estimates and wider confidence intervals.

Conclusions: We found evidence that combustion-related particles (i.e., nitrate and nickel), sea salt-related particles (i.e., sodium ion, chloride ion, and magnesium), and particles related to soil/road dust (i.e., aluminium) were significantly associated with cause-specific emergency hospital admissions in Hong Kong in the presence of gaseous copollutants. This study lends support to the growing body of literature concerning the adverse effects of particulate matter chemical composition and guides the further direction in mechanism research.

Project Number: 11120311

P6-0082

A Case-Control Study of Prostate Cancer and Environmental Exposures in Hong Kong Men: with Special Reference to Bisphenol A Exposure

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Introduction and Project Objectives: Environmental Bisphenol A (BPA) is widespread but its evidence on carcinogenesis in human is lacking. Influence of environmental exposures on prostate cancer etiology remains largely unclear.We aim to document the associations between environmental risk factors and prostate cancer in Hong Kong population, with special reference to bisphenol A (BPA).

Methods: This was a hospital-based case-control study. We consecutively interviewed 431 incident prostate cancer cases and 402 controls who had complete information on BPA exposure. A variety of information including smoking, dietary habits, night shift work, and family cancer history were collected using a standard questionnaire. A new assessment tool of environmental BPA exposure was constructed, while a novel cumulative BPA exposure index (CBPAI) was further developed using a semi-quantitative approach. Multiple logistic regression analysis was performed to examine odds ratio (OR) and 95% confidence interval (95% CI) for the association with a novel cumulative BPA exposure index (CBPAI) and other environmental risk factors.

Results: Family history of prostate cancer was more common in cases (9.5%) than controls (3.0%), showing an adjusted OR of 3.68 (95% CI: 1.85-7.34). Weekly consumption of deep fried food and picked vegetable was associated with an excessive prostate cancer risk by 85% (95% CI: 15%-195%) and 87% (7%-228%). Night shift work was hazardous (OR=1.76, 95% CI: 1.07-2.89) but habitual green tea drinking was protective (OR=0.56, 95% CI: 0.34-0.91). A positive exposure-response relationship with CPBAI and prostate cancer was indicated, with a relatively strong gradient in men aged below 70 years.

Conclusions: This study demonstrated an overall picture of environmental exposures to prostate cancer among Chinese men in Hong Kong. Furthermore, this study provided the first epidemiological evidence on carcinogenicity of BPA on human prostate thus added breakthrough data into the literature. This project highlights public health importance on removal toxicant BPA at source to ameliorate prostate cancer through implementing necessary policies. Personalized intervention on reducing fried or preserved food intake and optimizing working schedule should be promoted.

Project Number: 11121091

P7-0121

Characterisation of Benefit:risk Ratios of Seafood Items Commonly Consumed by High-risk Populations in HK

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Introduction and Project Objectives: Dietary fish contain many nutrients, e.g. selenium (Se) and omega-3 long-chain polyunsaturated fatty acids (ω-3 LCPUFA), as well as methylmercury (MeHg) which is an environmental toxicant. Se and ω-3 LCPUFA have been suggested to be able to partially antagonize the adverse effects of MeHg exposure. Understanding the nutritional values of locally available fish would help further improve the risk assessments regarding fish consumption. Se-Health Benefit Values (Se-HBV) has been suggested to be a useful index of risk:benefit ratio to be used; if positive it is considered of greater health benefit than harm.

Methods: A territory-wide survey (n=2917) was undertaken to identify the most commonly consumed fish and seafood items by Hong Kong preschool children and their mothers. The Se and ω-3 LCPUFA content of fish and seafood items were measured, and the Se-Health Benefit Values (Se-HBV) of each fish species was calculated. Nail samples were collected from a subgroup of mother-child pairs (n=307) for Se analysis; fish consumption details for the subgroup were recorded by using a 14-day food dairy. Their Se and ω-3 LCPUFA intake was estimated.

Results: 29 most frequently consumed fish and seafood items from 13 wet markets and supermarkets throughout Hong Kong were collected. The mean ω-3 LCPUFA and Se concentrations were 0.24±0.28g/100g and 0.48±0.21ppm. The Se-HBV for the majority of fish is positive, which means the expected health benefit would be greater than the harm. The mean estimated ω-3 LCPUFA intake for children and mothers were 75.2mg/d and 105.8mg/d. The mean estimated Se intakes were 10.6ug/d for children and 13.7ug/d for mothers respectively.

Conclusion: Fish commonly consumed by Hong Kong high risk populations (i.e. young children and women of childbearing age) are apparently safe for usual consumption. Hong Kong preschool children and mothers should be advised to consume more fish and seafood with positive Se-HBV and high ω- 3 LCPUFA levels in order to minimize the risk of MeHg toxicity while also reaching the RNI for ω- 3 LCPUFA.

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Project Number: 11120641

P8-0122

Identification of Genetic Susceptibilities to Low-dose Mercury Exposure in Children

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Introduction and Project Objectives: Individual variability in methylmercury (MeHg) metabolism and accumulation is well-recognized. Genetic variations in glutathione (GSH)-related and metallothioneins (MTs) genes, which are involved in producing enzymes in the MeHg metabolism pathway were proposed as important contributors to inter-individual differences in Hg metabolism.

To investigate the impact of genetic variations in MTs and GSH-related genes on the association between fish consumption and body MeHg burden, as measured by hair Hg concentrations.

Methods: A total of 189 children and 165 mothers with either high or low fish consumption were recruited. Their hair total Hg (tHg) and

MeHg levels and genotypes for GCLC, GCLM, GPx1, GSTA1, GSTP1, MT1A, MT2A, and MT4 were determined. Based on their 14-day food records, their amounts of fish consumed and their MeHg intakes were estimated. The impact of genetic variations on hair Hg concentrations was examined by using independent t tests and multivariate linear regressions.

Results: The mean hair MeHg and tHg levels were 0.58μg/g and 1.0μg/g for children, and 0.61μg/g and 1.03μg/g for mothers, respectively. The presence of variant alleles of GPx1, GCLC-129, GSTA1-52, GSTP1-105, and MT1M (rs2270836 and rs9936741) were associated with significant differences in hair Hg levels among children and mothers in the independent t tests. After adjustment for fish consumption and other confounding factors, mothers who carried a variant allele of GCLC-129, MT1M (rs9936741), and GPx1 have lower hair Hg levels whereas those with GSTP1-105 variant allele have higher hair Hg levels.

Conclusions: Our results showed that genetic variations in GSH-related and MTs gene have significant effects on body burden of Hg. These genetic variations might have a significant influence on MeHg metabolism and thus affect the accumulation of Hg in our body. Understanding the genetic influence on body burden of Hg could facilitate the identification of people who are highly susceptible to MeHg exposure and improve the accuracy of current risk assessment.

Acknowledgements: Food and Health Bureau of Hong Kong, Health and Medical Research Fund (ref no.: 11120601); study title: Identification of genetic susceptibilities to low-dose mercury exposure in children; Research Grants Council General Research Fund of Hong Kong (ref no.: 468111); study title: Factors affecting mercury concentration in commercially available seafood in Hong Kong.

Project Number: 11120601

P9-0182

The Respiratory Health Effects of Using Household Cleaning Products in Hong Kong School Children

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Introduction and Project Objectives: Household cleaning products are widely used to keep our home sparkling and sweet-smelling. But the chemicals in these cleaners may also contribute to indoor air pollution, and can be harmful if inhaled or touched, especially by children. The present study is to investigate the health effects of using household cleaning products at home in Hong Kong school children.

Methods: This is a prospective cohort study including 2,400 primary school children recruited between 2013 and 2014. At the baseline survey, each student received anthropometric parameters measurement and spirometry test including forced vital capacity (FVC), forced expiratory volume in the first second (FEV_1), maximum mid-expiratory flow (MMEF), and expiratory peak flow (PEF). Parents were required to complete a detailed questionnaire covering a wide range of topics, such as respiratory health, socio-economic status, lifestyle, and disease history. Information on the usage of a total of 14 types of chemical cleaning products was also collected using a questionnaire. The 2,400 students were invited to participate in the follow-up survey after one year. Multiple linear regression and logistic regression were used to assess the relationships between various health outcomes and the usage of cleaning products.

Results:

1. Health effects on pulmonary function: Using chlorine bleach >3 times/week was significantly associated with lower PEF (beta: -72.40, 95% CI: -132.29, -12.50) and MEFE (beta: -43.12, 95% CI: -85.32, -0.921), comparing to those with <1 time/week; similarly, using scented air-fresheners>3 times/week was significantly associated with lower PEF (beta: -76.50, 95% CI: -142.00, -10.99), MFEF (beta: -49.97, 95% CI: -95.96, -3.99) and FEV1/FVC (beta: -0.008, 95% CI: -0.013, -0.002).
2. Health effects on rhinitis: Every 10-hours/week increase in the duration of using cleaners was associated with an increase in the odds of occasional rhinitis (OR, 1.21; 95% CI, 1.05-1.41), frequent rhinitis (OR, 1.36; 95% CI, 1.13-1.60), and persistent rhinitis (OR, 1.12; 95% CI, 1.01-1.56) after adjusting for potential confounders. Compared with children within the lowest tertile of duration of using cleaners, the adjusted OR of occasional, frequent, and persistent rhinitis in children within the highest tertile was 1.29 (95% CI, 1.01-1.65), 1.97 (95% CI, 1.40-2.76), and 1.67 (95% CI, 1.10-2.54), respectively

Conclusions: Frequent use of household cleaning products is associated with poorer pulmonary function; frequent use of household cleaning products increases the risk of rhinitis, especially frequent and persistent rhinitis, which are the more serious patterns.

Project Number: 11121101

P10-0068

Effect of Nasal Continuous Positive Airway Pressure in Uncontrolled Nocturnal Asthmatic Patients with Moderate to Severe Obstructive Sleep Apnea Syndrome

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Background: Unrecognized obstructive sleep apnea syndrome (OSAS) may lead to poor asthma control despite optimal therapy.

Aims and Objectives: To assess (1) the prevalence of OSAS among patients with nocturnal symptoms and poor controlled asthma, (2) asthma control, airway responsiveness, daytime sleepiness and health status at baseline and at 3 months after CPAP treatment among asthma patients with nocturnal symptoms and OSAS; (3) the acceptance and compliance of CPAP treatment.

Study Design: Prospective, randomized control trial

Methods: Patients with nocturnal asthma symptoms despite receiving at least moderate dose inhaled corticosteroid and long acting bronchodilators underwent a limited sleep study using “Embletta” portable diagnostic system (Medcare, Iceland). Patients with significant OSAS (apnea hypopnea index (AHI) ≥10/hr) were randomized to receive either CPAP or conventional treatment for 3 months. Assessments included asthma control test (ACT) score, asthma related quality of life (AQLQ), peak expiratory flow rate, spirometry and bronchial responsiveness.

Results [mean (SD) unless stated otherwise]: Among 145 patients recruited, 122 patients underwent sleep study with 41 patients (33.6%) having AHI ≥10/hour. Patients with OSAS had higher BMI (27.4 (5.1) vs 25.1(4.5) kg/m2, p=0.016), bigger neck circumference (36.6(3.1) vs 34.8(3.6) cm, p=0.006) and lower minimum SaO2 (80.7(6.6) vs 87.2(3.9) %, p <0.001). Using intention-to-treat analysis among 37 patients with AHI ≥10/hour [CPAP group (n=17) vs control group (n= 20)), there was no significant difference in ACT score [CPAP 3.2(2.7) vs control 2.4(5.7), p=0.066) but CPAP group had lower Epworth Sleepiness Score (ESS) (-3.0(4.5) vs 0.5(3.8), p=0.014), better AQLQ (0.6(0.8) vs 0.02(0.7), p=0.022) and improved in the vitality domain in the SF-36 questionnaire (14.7(16.8) vs 0.3(16.2), p=0.012) after 3 months. There was no significant change in spirometry, bronchial challenge test and

cognitive function between two groups. CPAP usage was 5.0(2.1) hrs/d at 1 month and 5.2 (1.8) hrs/d at 3 months. The Berlin Questionnaire had limited role as a screening tool for OSA (AUC 0.677, 95%CI 0.570, 0.784).

Conclusions: High prevalence of OSAS was found among patients with nocturnal asthma despite treatment with at least moderate dose inhaled corticosteroid and long acting bronchodilators. CPAP therapy for 3 months did not improve asthma control but alleviated daytime sleepiness, improved asthma related quality of life and vitality. The Berlin Questionnaire was unreliable as a screening test for OSAS.

Project Number: 10110801

P11-0154

A Randomized Controlled Study Assessing the Role of an Ambulatory Approach versus the Conventional Approach in Managing Suspected Obstructive Sleep Apnoea Syndrome

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Introduction & Project Objectives: Comparisons of home-based versus hospital-based approach in managing patients with suspected obstructive sleep apnoea syndrome(OSAS).

Methods: A prospective, controlled CPAP parallel study of new referrals with suspected OSAS randomized into group A) home-based or B) hospital-based approach. Following detection of apnoea-hyponoea index (AHI)≥15/hr by Embletta sleep study at home (group A) or polysomnography in hospital (group B), patients received CPAP for 3 months after an overnight autoCPAP titration at home or in hospital respectively.

Results: Modified intention-to-treat analysis of those with AHI≥15/hr on CPAP (n=86 vs 86) showed no difference in Epworth sleepiness score, the primary endpoint, but greater improvement in Sleep-Apnoea-Quality-of-Life-Index [difference 0.3,(95%CI 0.02, 0.6), p=0.033] at 3 months in group A. The mean costs for the patients in group A and group B were HK$8479(989) and HK$22,248(2407) respectively. The mean difference between groups was HK$-13,769(USD 1770 equivalent) per patient with 95% CI. (-14324, -13213), p<0.001. The waiting time of patients with AHI≥15/hr who were started on CPAP treatment from the first clinic consultation to the diagnostic sleep test, autoCPAP titration, and CPAP treatment was 189.6, 148.8 and 145.0 days shorter in group A than group B respectively.

Conclusions: Home-based approach is non-inferior to hospital-based approach in managing patients with suspected OSAS, with shorter waiting time, and substantial cost savings. (**Hui DS**, Ng SS, To KW, Ko FW, Ngai J, Chan KK, Yip WH, Chan TO, Yiu K, Tam WW. **Sci Rep**. 2017 Apr 4;8:45901. doi: 10.1038/srep45901).

Project Number: 10110811

P12-0185

The Effects of Home-based Dichoptic Video Game Training on Visual Acuity, Fixation Stability and Stereopsis in Mild Amblyopes

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Purpose: Contrast balanced dichoptic videogame training has been found to improve visual acuity and stereopsis in adults and children with amblyopia. However, its effects in cases of mild amblyopia is unknown. The aim of this study was to assess the effects of dichoptic videogame training on distance visual acuity (DVA), fixation stability and stereopsis in mild amblyopia.

Methods: Participants (aged 7 or above) with DVA ≤ 0.28 log Minimum Angle of Resolution (MAR) in the amblyopic eye and an interocular acuity difference ≥ 0.2 log MAR were recruited. Participants were assigned to a treatment or placebo group in a block sequence. An anaglyphic, contrast balanced dichoptic video game was provided to the treatment group for 6 weeks of home-based training (one hour per day). The placebo consisted of the same iPod game with no contrast difference between two eyes. DVA was measured using an Electronic Visual Acuity Tester; fixation stability quantified as a bivariate contour ellipse area (BCEA) was measured with a Nidek MP-1 micro-perimeter, and stereopsis was measured using the Titmus stereo test before and after treatment.

Results: Twelve participants (mean age 26 ± 16 years) with amblyopic eye DVA 0.21 ± 0.06 logMAR and eleven participants (mean age 26 ±10 years) with amblyopic eye DVA 0.18 ± 0.06 logMAR were recruited in the treatment and placebo groups respectively. Participants played for an average of 37 ± 10 and 33 ± 10 hours over six weeks in the treatment and placebo groups respectively. There were statistically significant improvements in the amblyopic eye DVA in the treatment group (-0.09 ± 0.05 log MAR, t11 = 6.44, p < 0.001) and in the placebo group (-0.03 ± 0.04 log MAR, t10=2.33, p<0.05). The treatment group improvement was significantly larger than that of the placebo group (t10= -3.24, p<0.01). There were no changes in BCEA for the treatment (t11 = -0.72, p = 0.48) and placebo (t10 = -0.61, p = 0.56) groups. Finally, there was a significant improvement in the median Titmus stereopsis -0.40 (IQR 0.65) log arc seconds (Z = -2.50, p < 0.01) in the treatment group but not the placebo group (Z = -1.20, p = 0.23).

Conclusion: With good compliance, dichoptic videogame training could be an effective means to improve DVA, stereopsis but not fixation stability in mild amblyopia.

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Project Number: 11122991

P13-0008

The Effectiveness of a Multidisciplinary Approach to Geriatric Hip Fractures on Improving Clinical Outcomes and Cost of Care

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Introduction: Geriatric hip fracture is one of the most common fragility fractures seen in orthopaedic wards nowadays due to general increase in life expectancy in Hong Kong and the active life style in our geriatric population. A multidisciplinary geriatric hip fracture clinical pathway (GHFCP) program was implemented since 2007 to meet the increasing demand.

Project Objective: To compare the clinical outcomes and cost of manpower of before and after the program.

Methods: The hip fracture data from 2006 was compared with the data of 4 consecutive years since 2008. Basic information of demographics was collected. Efficiency of the program is reflected in the pre-operative length of stay and total length of stay in acute and convalescence hospital. The clinical outcomes include short-term and long-term mortality rates, and complication rates. Cost of manpower was also

estimated and analysed.

Results: After the implementation of the program, the pre-operative length of stay shortened significantly from 5.76 days in 2006 to 1.32 days (p<0.001) in 2011. The total length of stay in both acute and convalescence hospitals were also shortened by 6.05 days and 14.24 days respectively (p<0.001) from 2006 to 2011. The post-operative pneumonia rate also decreased from 1.25% to 0.25%. The in-patient mortality, 30-day mortality and 1-year mortality also showed a general improvement from 2006 to 2011. The 30-day mortality dropped from 5.36% in 2006 to 1.7% (p<0.001). The 1-year mortality rate dropped from 23.93% to 13.8% (p<0.001). Despite the allied health manpower is increased to meet the increasing workload, the shortened length of stay contributes a marked decrease in cost of manpower per hip fracture case. The average manpower cost in Queen Mary hospital is $23907 in 2006 and it decreased to $16448 in 2011. The manpower cost in Fung Yiu King convalescent hospital decreased from $15325 in 2006 to $12936 in 2011.

Conclusion: This study proves that the GHFCP can shorten the geriatric hip fracture patients' length of stay and improve the clinical outcomes. It is also shown to be cost-effective which means that better care is less costly.

Project Number: 11122031

P14-0012

A Randomized Clinical Trial of Electroacupuncture versus Fast-track Perioperative Program for Reducing Duration of Postoperative Ileus and Hospital Stay after Laparoscopic Colorectal Surgery

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Introduction and Project Objective: Ample evidence suggested that 'fast-track' (FT) perioperative program can reduce surgical stress and accelerate postoperative recovery after colorectal surgery. Our recent study also demonstrated that electroacupuncture (EA) at Zusanli, Sanyinjiao, Hegu, and Zhigou can enhance recovery after laparoscopic colorectal surgery. This prospective, randomized, noninferiority trial aimed to compare the efficacy of EA and FT program in reducing the duration of postoperative ileus and hospital stay after laparoscopic colorectal surgery.

Methods: Between January 2014 and March 2016, 164 patients undergoing elective laparoscopic resection of colonic and upper rectal cancer without conversion were randomized to receive either EA or FT program (82 per group). The primary outcome was time to defecation. Secondary outcomes were hospital stay, 30-day morbidity and readmission rates, and overall cost. Data were analyzed by intention-to-treat principle.

Results: The demographic data of the two groups were comparable. The overall protocol compliance rate in the FT group was 85%. The mean time to defecation in the EA and FT groups was 79.0 ± 42.2 hours and 72.9 ± 30.0 hours (difference = 6.1 hours; 95% confidence interval [CI], -5.2 hours to 17.5 hours), respectively (P = 0.286). Noninferiority was demonstrated as the upper limit of 95% CI for the difference was within the prespecified noninferiority margin of 24 hours. There was a trend towards shorter mean total postoperative hospital stay in the EA group (5.8 ± 2.9 days vs. 6.8 ± 5.3 days, P = 0.119). The overall 30-day morbidity rate in the EA and FT groups was similar (13.4% vs. 22.0%, P = 0.152). There was no difference in readmission rates between the two groups. The implementation cost of EA was significantly lower than the cost of implementation of the FT program (HK$999 ± 361 vs. HK$3,971 ± 98, P <0.001). The total direct cost was also lower in the EA group than in the FT group (HK$118,496 ± 24,679 vs. HK$132,642 ± 59,755, P = 0.049).

Conclusions: EA is noninferior to FT program in reducing the duration of postoperative ileus after laparoscopic colorectal surgery. Postoperative hospital stay and overall morbidity rate are also similar between the two perioperative management strategies. EA may be the preferred perioperative therapy for laparoscopic colorectal surgery because it is simpler to implement, less labor intensive, and less expensive than the FT program. (ClinicalTrials.gov number, NCT02059603)

Project Number: 11120121

P15-0061

Comparison of Serum Thromboxane B2 and Platelet Function Testing with the Multiplate® Device as Measures of Aspirin Resistance in Hong Kong Chinese Patients with Increased Cardiovascular Risk with Stable Coronary Heart Disease or Peripheral Artery Disease

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Introduction and Project Objectives: Aspirin resistance is thought to occur in a proportion of patients on long-term aspirin treatment and may increase the risk of cardiovascular morbidity and mortality. Methods to identify aspirin resistance produce conflicting results and there is no single standard method. In this study we examined the response to chronic aspirin treatment by measuring serum thromboxane B2 and platelet function testing using the Multiplate® analyser.

Methods: Chinese patients with stable coronary artery disease or peripheral artery disease who were taking long-term low dose aspirin without any other anti-platelet drug were identified from databases. Eligible patients were invited to attend for the study. They were requested to take their dose of aspirin 80 mg in the morning for 7 days including the day before attending for the blood tests and blood samples were taken 24 hours after the last dose. An oral dose of aspirin 80 mg was then administered and blood samples were taken again 1 hour later.

Results: In 266 patients, who attended for the study, the mean (±SD) age was 66.6 ± 10.7 years, the mean body mass index was 25.1 ± 3.5 kg/m2, 17% were female and 55% were current or previous smokers. The serum thromboxane B2 levels and the measures of platelet aggregation induced by arachidonic acid using the Multiplate® impedance platelet aggregometry (ASPI) were all significantly higher in the samples 24 hours post dose compared to the samples 1 hour after the dose. There were weak but significant (p <0.01) correlations between the serum thromboxane B2 levels and the ASPI measure of platelet aggregation before and after the dose (r = 0.199 and 0.150, respectively). From the baseline demographic factors, those associated with increased aggregation on the ASPI measurement 24 hours post dose were white blood count, haematocrit, platelet count and smoking history. On the ASPI measurement 1 hour post dose only the white blood count and smoking history were significantly associated. Having diabetes was not associated with reduced platelet response to aspirin in these patients.

Conclusions: The anti-platelet response to aspirin declines by 24 hours post dose and becomes insufficient in some patients. This may be best identified by the Multiplate® analyser ASPI measurement. Patients who are smokers and those with higher white blood counts appear to be at increased risk of aspirin resistance. Such patients may benefit from alternative aspirin regimens such as twice daily dosing.

Project Number: 12130981

P16-0064

Cost-effectiveness of Phacoemulsification versus Combined Phacotrabeculectomy for treating Primary Angle Closure Glaucoma

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Aim: To compare the cost effectiveness of phacoemulsification and combined phacotrabeculectomy for lowering intraocular pressure (IOP) in primary angle closure glaucoma (PACG) eyes with coexisting cataract.

Methods: Real-life data of two previous randomized control trials that involved 51 medically-uncontrolled PACG eyes and 72 medically-controlled PACG eyes were utilized to calculate the direct cost of treatment. Cost of pre-operative assessments, surgical interventions, additional procedures for managing complications and maintenance of filtration, post-operative follow-up, and cost of medications were considered. Cost data of three different regions (United State, People's Republic of China, and Hong Kong) were implemented to the scenario.

Results: The corresponding average cost for treating one eye with newly diagnosed PACG by phacoemulsification alone and combined phacotrabeculectomy were United States (US) $3479 and $2439 in the United State, US$1051 and $861 in China, and $6856 and $12087 in Hong Kong; surgical and medications cost were the two key contributors. Combined phacotrabeculectomy is more cost-effective for IOP reduction when calculating with the US and China cost data, but not when calculating with the Hong Kong cost data. Furthermore, for the medically-uncontrolled PACG group, phacoemulsification alone became more cost-effective when the cost of medication was reduced by more than 75%. The cost-effectiveness was insensitive to the cost of follow-up visit and investigations, cost of surgical operation, and cost of post-operative procedures, but sensitive to the cost fluctuation of medications.

Conclusions: Combined phacotrabeculectomy is a more cost-effective option when aiming at maintaining IOP of ≤21mmHg for PACG eyes with co-existing cataract, over a 2-year follow-up period. This might change if there is a drastic reduction of the cost of medication.

Project Number: 11122971

P17-0072

Cross-cultural Adaptation of the Tinnitus Functional Index for Measuring Chronic Tinnitus in Hong Kong Chinese

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Introduction and Project Objectives: Tinnitus is fundamentally a self-report phenomenon which is not readily apparent to others except through the complaints of the sufferer. Thus subjective psychometric measures are essential in assessing the severity and impacts of tinnitus, and determining the effectiveness of intervention. The most commonly employed tinnitus assessment and monitoring device for both research and clinical purposes, consists of a tinnitus questionnaire. The Tinnitus Functional Index (TFI) was developed by a group of experts including audiologists, otologists, hearing scientists and other health researchers. The TFI has been validated both for scaling the severity and negative impact of tinnitus for use in intake assessment and for measuring treatment responsiveness. The objective of this study was to translate the TFI into Chinese and then validate its use in Chinese Hong Kong patients who are suffering from chronic tinnitus.

Methods: The Chinese version of Tinnitus Functional Index (TFI-CH) was administered to 124 patients with chronic tinnitus in the Audiology clinic in a hospital setting. Statistical analysis was performed to determine the psychometric properties of the questionnaire.

Results: The TFI-CH showed good internal consistency reliability (α = 0.97) and test-retest reliability (ICC = 0.84). Confirmatory factor analysis revealed that the TFI-CH has eight factors which are exactly the same as the original version. The TFI-CH has good convergent and divergent validity as supported by the strong correlation of the overall scale with other tinnitus-related distress measures ($r = 0.86$, $P < 0.01$) and weaker correlation with the general health status measures. Moderate to strong effect sizes obtained 3 months after initial visit indicated that the TFI-CH is responsive in detecting change in tinnitus suffering.

Conclusions: The results of this study demonstrate that the TFI-CH is a reliable and valid measure which should be useful in both clinical and research settings for intake assessment and for measuring treatment-related changes in tinnitus.

Project Number: 11120221

P18-0086

Hong Kong Preference-based Health Index - EQ-5D-5L HK

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Introduction and Project Objectives: Health outcomes are often centered on the mortality and morbidity; however, there is increasing interest in and reliance on other metrics that emphasize on patient self-reported health outcome – preference-based instrument. These characterizations allow us to compare health-related quality of life (HRQoL) of people in general, or subgroups by specific disease or different health care interventions and polices. EQ-5D is one of the most widely using utility-based instruments for the assessment of self-reported HRQoL. The validation and valuation study of establishing health state utility value using EQ-5D-5L has been undergoing in different jurisdictions. However, there is no local population of value set of health states offered in Hong Kong (HK) using EQ-5D-5L. This study aimed to have health related quality of life (HRQol) as well as health state utility value using EQ-5D-5L.

Methods: The EQ-5D-5L HK was firstly translated and validated through cross-cultural adaptation. The study design of valuation followed the standard protocol of EuroQol Group. A stratified sampling with quotas by age, gender, education level and geographical district was used to respect the HK population structure. Each respondent was randomly assigned to value 10 health states with a composite time trade-off (C-TTO) approach and complete 9 discrete choice (DEC) tasks. The

face-to-face interviews were conducted by a team of well trained and experienced interviewers with the aid of computer-assisted personal interview software – EuroQol Valuation Technology (EQ-VT). A hybrid modelling was used to maximise the usage of data collected that combines both C-TTO and DCE data to derive health index algorithm of EQ-5D-5L HK; and to estimate the potential value set in Hong Kong.

Results: A validated Hong Kong Chinese version "EQ-5D-5L HK" was developed. The health index algorithm was derived where all the coefficients of the final model were statistically significant and logically consistent. The dimension of mobility was the most important factor in Health-related Quality of Life. The utility value in different segment of gender, age and education was generated. The norm of HRQol in Hong Kong population was 0.9186.

Conclusions: This study elicits health preferences of Hong Kong population using EQ-5D-5L and this local social value set offers an alternative tool to describe the health of HK population in term of HRQol. It can also contribute to the cost-effectiveness analysis of health care intervention/policies so as to provide important information on the policy making and resource allocation.

Project Number: 11120491

P19-0118

The Predictive Biomarkers for EGFR Tyrosine Kinase Inhibitors Treatment in Patients with Advanced Non-small-cell Lung Cancer: A Systematic Review and Meta-analysis of Randomized Controlled Trials

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Introduction: Epidermal growth factor receptor tyrosine kinase inhibitors (EGFR TKIs) have been approved for treating advanced non-small cell lung cancer (NSCLC) for years. However, the treatment is effective in only a subset of patients. It is important to identify the predictors of treatment effects.

Objectives: To identify the predictive biomarkers for EGFR TKIs treatment in patients with advanced NSCLC, with a focus on EGFR mutations, EGFR gene copy number gain, EGFR protein expression and KRAS mutations.

Methods: The study design is systematic review and meta-analysis. Randomized trials evaluating the efficacy of EGFR TKIs in terms of progression-free survival, overall survival, and/or objective response with subgroup analyses according to status of the abovementioned four biomarkers were identified. Interaction between treatment and biomarkers on the outcomes was tested to assess predictive value.

Results: Twenty-eight studies were included. There was interaction between EGFR TKIs treatment and EGFR mutations (on all outcomes), EGFR gene copy number gain (on progression-free survival) and KRAS mutations (on progression-free survival and overall survival). In general, the results on EGFR gene copy number gain and KRAS mutations were less certain than those on EGFR mutations in terms of statistical significance and consistency.

Conclusions: EGFR mutations, EGFR gene copy number gain, and KRAS mutations are predictive of the treatment effects of EGFR TKIs in advanced NSCLC, with EGFR mutations being the most powerful predictor. However, it is not clear whether the predictive roles of EGFR gene copy number gain and KRAS mutations are independent or obtained through their relation with EGFR mutations. There is no convincing evidence to support the predictive value of EGFR protein expression.

Implications: EGFR mutation status should be tested prior to treatment of advanced NSCLC. Patients harboring EGFR mutations are more likely to benefit from EGFR TKIs, while those with wild-type EGFR are recommended to receive chemotherapy.

Project Number: 11120971

P20-0141

Voice Improvement In Unilateral Cord Palsy Patients After Hyaluronic Acid Injection

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Introduction and Project Objectives: Injection laryngoplasty using hyaluronic acid for patients of unilateral cord palsy (UCP) is becoming more common in Hong Kong. The present investigation attempted to explore the efficacy of the procedure by studying videostroboscopic information, patients' quality of life (QOL), and vocal characteristics obtained before and after injection laryngoplasty.

Method: Visual, perceptual and acoustic data were collected from 11 UCP patients during their visits before, one week, one month, and three months after injection laryngoplasty. During each visit, the UVFP patients underwent videostroboscopic examination. They were also instructed to maximally sustain the vowels /i, a, u/ and to read aloud a short passage. Fundamental frequency values, perceptual voice quality ratings, and Voice Handicap Index (VHI-30) scores were obtained. Data obtained before and after the surgery were compared.

Results: Videostroboscopic examination showed a significant improvement in glottal closure over time. VHI-30 indicated that the voice-related QOL was improved. GRBAS scores also showed significant improvement in perceived vocal quality. However, no significant difference was found in fundamental frequency before and after the procedure.

Conclusions: Injection laryngoplasty is effective in helping UCP patients achieve better voice quality and improved QOL. The procedure also appears to show immediate and sustainable effect to up to three months post-surgery.

Project Number: 09101191

P21-0116

A Study to Compare the "Ergo-motor" Intervention Program to Conventional Physiotherapy Treatment in Managing Work-related Neck-shoulder Disorders: A Randomized Controlled Trial

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Introduction: Work-related neck and shoulder problem (WRNSP) are common problems in the working populations. Past occupational research has focused on ergonomic interventions such as adjusting the workstation while physiotherapists have traditionally focused on teaching exercises to improve posture and movement control in the clinical setting. The current study aimed to integrate these two approaches and evaluate the immediate and long-term effects of such interventions.

Method: A total of 101 patients diagnosed with WRNSP were randomized into 2 groups: Control (CO) group (n=50) and Ergo-motor (EM) group (n=51). Each group received a 12-week intervention. Participants in the Control Group received treatment for pain relief and general exercises of their necks while participants in the EM Group received an active program with individualized motor control training integrated with advice of ergonomic modifications at their workplaces. They were evaluated using a numerical pain score (0-10), as well as the functional outcome measures of Neck Disability Index (NDI) and the Disability of Arm, Shoulder and Hand (DASH) at pre- and post-intervention, as well as at 1-year follow-up. A biomechnaical evaluation using surface electromyography and 3D motion analysis system was performed at pre- and post- intervention for both groups.

Result: Both intervention groups achieved significant reductions in neck pain at post-intervention and at 1-year follow-up ($p<0.05$), while EM group showed significantly better improvement of functional ability at 1-year follow-up compared to pre-intervention. At post-intervention, upper trapezius muscle activity was significantly reduced during active neck movements as well as in functional tasks of lifting a weighted cylinder upward. Other muscles also demonstrated an improved activation pattern but these were not statistically significant. EM Group showed significantly improved velocity and acceleration during cervical flexion/extension compared to CO Group. The present results showed that ergo-motor interventions produced better outcomes in terms of improved motor control and functional outcome compared to conventional physiotherapy.

Conclusions: The current study has demonstrated the effectiveness of ergo-motor intervention in terms of improving the motor control pattern of individuals who suffer WRNSP, and this may have a greater impact on addressing the fundamental mechanisms that contributed to the development of these disorders. This result has important implications for future development of effective intervention programs for this group of individuals.

Project Number: 10111841

P22-0147
Evaluation of Dietary Intervention Models for Management of Stage I Hypertensive Patients in a Primary Care Setting: Randomized Controlled Clinical Trial

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Background: The Dietary Approaches to Stop Hypertension (DASH) has been widely recognized as a dietary model of choice for management of hypertension. However, it is not clear whether DASH is effective for Chinese hypertensive patients in primary care settings, and whether a one-off counseling service is sufficient. Therefore, this study evaluated the effectiveness of one dietary counseling based on DASH in reducing cardiovascular risk factors among Chinese Grade 1 hypertensive patients in primary care.

Method: A multi-center, parallel-group, randomized controlled trial (ChiCTR-TRC-13003014) in primary care settings was conducted in Hong Kong among patients (1) aged 40-70 years old, (2) newly diagnosed with Grade 1 hypertension, and (3) currently not taking anti-hypertensive medications. Subjects were allocated into 2 groups with an allocation ratio of 1 to 1 according to random numbers generated by computer. Finally, 275 received usual care (standard education, control), and 281 received usual care plus DASH-based dietary counseling offered by a registered dietitian (intervention). The study endpoints included blood pressure (BP), lipid profile (level of TC, TG, LDL-C and HDL-C), and body mass index (BMI) at 6- and 12-months.
Result: Outcome data were obtained from 504 (90.6%) and 485 (87.2%) patients at 6 and 12 months, respectively. Blood pressure levels reduced in both groups at follow-ups. However, the intervention group did not show a significantly greater reduction in either systolic BP (-0.7 mmHg, 95%CI -3.0-1.5 at 6-month; -0.1 mmHg, 95%CI -2.4-2.2 at 12-month) or diastolic BP (-1.0 mmHg, 95%CI -2.7-0.7 at 6-month; -1.1 mmHg, 95%CI -2.9-0.6 at 12-month), compared to the control group. The improvements in BMI and lipid profile such as TG and HDL-C levels were shown among all subjects at both follow-ups. However, TC and LDL-C were reduced at 6 months only. And no significant differences were detected between intervention and control groups.

Conclusion: The DASH diet by one-off dietitian counseling resembling real-life primary care practice might bring no added long-term benefits in optimizing cardiovascular risk factors. These findings do not support routine referral of all grade-I hypertensive patients for one-off dietitian counseling, and this bears substantial implications on healthcare services. Future research is needed to explore dietary interventions that could effectively modify patient behavior.

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Project Number: 09100701

P23-0140
Long Term Assessment of Functional Outcome in Patients Sustaining Moderate and Major Trauma: A 4-year Prospective Cohort Study

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Introduction: Trauma care systems aim to reduce death and to improve quality of life and functional outcome in trauma patients. It is well documented that trauma systems result in improved survival after injury, yet there is little data on post-trauma functional outcome. Such evaluation of functional recovery is important as this will allow comparison with other settings, evaluate the impact and effectiveness of trauma systems as a whole, and may provide prognostic information for healthcare workers and patients. The aim of this study was to evaluate the baseline, discharge, six-month and 1, 2, 3 and 4 year post-trauma functional outcome and predictors of optimal functional outcome in Hong Kong.

Participants and methods: From 1st January to 30th September 2010, patients were recruited into a prospective multi-centre cohort study of trauma patients and then followed up for four years. The study was conducted in three trauma centres in Hong Kong. Adult patients aged ≥18 years with ISS≥9, entered into the trauma registry, and who survived the first 48 hours of injury were included. The main outcome measures included the extended Glasgow Outcome Scale (GOSE) and SF36.

Results: 400 patients (mean age 53.3 years; range 18-106; 69.5%

male) were recruited. There were no statistically significant differences in baseline characteristics between responders (N=143) and surviving non-responders (N=179). Only 81/400 (20.3%) cases reported a GOSE≥7. If non-responders had similar outcomes to responders, then the percentages for GOSE≥7 would rise from 20.3% to 45.6%. Univariate analysis showed that poor functional outcome at 48 months was significantly associated with admission to ICU (OR 2.267), ISS 26-40 (OR 3.231), baseline PCS on SF36 testing (OR 0.940), one month PCS (OR 0.933), 6-month PCS (OR 0.904) and 6-month MCS on SF36 testing (OR 0.96).

Conclusions: At 48 months after injury, 45% of patients sustaining moderate or major trauma in Hong Kong had an excellent recovery. Admission to ICU, ISS 26-40, baseline PCS, one-month PCS, 6-month PCS and 6- month MCS predict 4-year functional outcome.

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Project Number: 10110251

P24-0170

Prenatal Exposure to Dioxins and Subsequent Neurocognitive and Developmental Function in Hong Kong Chinese Children

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Introduction and Project Objectives: In-utero exposure to dioxins and related compounds have been associated with adverse neurocognitive development in infants. It is not clear whether prenatal dioxin exposure related deficits in neurocognitive function persist from infancy to childhood. This study assessed the association of prenatal dioxin exposure with neurocognitive function in 11 years old children in Hong Kong, and tested whether the association was modified by the duration of breastfeeding.

Methods: In this prospective study of 161 children born in Hong Kong in 2002, prenatal dioxin exposure was proxied by the dioxin content in breast milk collected in early postnatal period determined by bioassay. We used multivariate linear regression analyses to assess the association of prenatal dioxin exposure with the performance in the Wechsler Intelligence Scale for Children Fourth Edition (Hong Kong), the Hong Kong List Learning Test, the Tests for Everyday Attention for Children and the Grooved Pegboard Test, adjusting for child's sex, mother's place of birth, mother's habitual seafood consumption, mother's age at delivery and socioeconomic position.

Results: Prenatal dioxin exposure was not associated with measures of neurocognitive and intellectual function, including full-scale IQ, fine motor coordination verbal and non-verbal reasoning, learning ability and attention at 11 years old, with no difference in the association by breastfeeding duration.

Conclusions: Prenatal dioxin exposure to background levels of dioxins in 2002 in Hong Kong was not associated with neurocognitive function in 11 years old children. Although this negative association is reassuring, it is recognised that growing foetuses are vulnerable to the harmful effects of environmental pollutants and breastfed infants receive dioxin levels above the tolerable daily intake for adults. Continued efforts should be directed towards identifying and controlling environmental sources of these substances in Hong Kong and Mainland China.

Project Number: 10111201

P25-0145

Measuring Avoidable Hospital Readmissions in Hong Kong using the Ambulatory Care Sensitive Conditions

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Introduction and Project Objectives: Rising healthcare needs of aging populations increase the pressure on hospital beds and result in premature discharges from acute hospitals, reduced quality of hospital care and high readmission rates. While it is important to reduce avoidable hospitalizations, the use of medical record reviews for their identification is resource intensive. International studies have used Ambulatory Care Sensitive Conditions (ACSCs) to define potentially avoidable hospitalizations using routine hospital database. The objective is to (a) identify and develop a List of ACSC for Hong Kong (HK-specific ACSCs) through a Delphi Survey; (b) monitor the trend, scale and volume of avoidable hospital readmissions in Hospital Authority (HA) using the HK-specific ACSCs; and (c) identify the factors associated with avoidable readmissions.

Methods: A 5-step approach was utilized to develop the HK-specific ACSCs which includes the establishment of an Expert Panel for local context and a Delphi Survey among local senior clinicians to identify an HK-specific ACSCs List. This List was then used to measure potentially avoidable unplanned readmissions using 2003-2012 HA inpatient data, as defined by the same HK-specific ACSCs admission and readmissions within 30 days.

Results: Three rounds of Delphi Survey were conducted in the 5-step approach. Twenty-four ACSCs accounting for 78 individual International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnostic codes were identified as the HK-specific ACSCs. Among unplanned readmissions in 2003-2012, 23% (121,975 episodes) were identified as potentially avoidable readmissions in accordance with the HK-specific ACSCs List (HK-ACSCs AR). Chronic Obstructive Pulmonary Disease (41.4%), Pneumonia (18.3%) and Chronic Heart Failure (13.5%) accounted for the highest proportion of HK-ACSCs AR. Age-adjusted standardized HK-ACSCs AR rates was lowest in 2003 (0.73 per 1,000 persons), peaked in 2005 and declined to 1.07 in 2012. Those who were male, older, receiving financial assistance, were transferred to other hospitals and had a shorter total length of stay in the index episode were more likely to have HK-specific ACSCs AR.

Conclusions: This is the first attempt to utilize a systematic approach to identify a HK-specific ACSCs List. Our study added value by using HK-specific ACSCs to measure potentially avoidable readmissions. These HK-specific ACSCs may serve as indicators of avoidable hospitalizations. The factors identified may be used to set priority for interventions, service planning and research.

Project Number: 09100651

P26-0171

Does Formula-feeding Increase the Risks of Type 2 Diabetes among Hong Kong Adolescents?

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Introduction and Project Objectives: Hong Kong has experienced an epidemic of type 2 diabetes making this a major public health concern. Increasing evidence suggests modifiable early life factors, including

infant nutrition, could be targeted for possible interventions. This study tested the hypothesis that formula-feeding was associated with type 2 diabetes risk factors in Hong Kong adolescents and examined whether any associations was mediated by infant growth rate.

Methods: This is a prospective birth cohort study Hong Kong "Children of 1997". In 2630 birth cohort participants, we clinically assessed type 2 diabetes risk factors, i.e., markers of glucose metabolism (fasting HbA1c, glucose, insulin and HOMA insulin resistance) and other health markers, including body composition (BMI, % body fat, waist-to-height ratio, total muscle mass and hand grip strength), fasting lipid profile and high sensitive C-reactive protein at 17 years. Multivariable linear regression, with multiple imputation and inverse probability weighting, was used to examine the adjusted associations of early infant feeding at 0-3 months (exclusively breastfed, mixed feeding or always formula-fed, collected in infancy) and duration of regular formula milk use (0-2 years, 3-5 years and until 6 years, recalled by mothers at follow-up) with risk factors, adjusted for sex, birth weight, gestational weeks, parity, pregnancy characteristics, highest parents' education attainment, mother's place of birth, age and pubertal stages at follow-up.

Results: Compared with exclusively breastfeeding at 0-3 months (7%), always formula-feeding (52%) was associated with higher total cholesterol, LDL cholesterol and triglycerides but not with socio-economic position or any measure of body composition, insulin resistance or low grade inflammation at 17 years, with no indication of interaction by sex or infant growth rate in the first year of life. However there was a graded association of breastfeeding exclusivity in the first three months of life with lower fasting insulin and HOMA-IR (p-for-trend <0.05). The association of infant feeding with lipids was not mediated by infant growth, although accelerated infant growth was associated with greater height, BMI, % body fat and lean mass. Duration of formula milk was not associated with any health markers at 17 years.

Conclusions: In Hong Kong where there was little social patterning of breastfeeding, formula feeding was associated with a poorer lipid profile in adolescence but not body composition, suggesting infant nutrition may affect long-term health and disease risks independent of adiposity. Exclusively breastfeeding for three months may be associated with lower insulin resistance in late adolescence.

Project Number: 10111491

P27-0032

The Barriers and Facilitators to Undertaking Continuing Professional Education among Private Non-specialist Primary Care Physicians in Hong Kong

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Background: Strengthening primary care is seen as an effective strategy to ensure financial sustainability of the current public healthcare system. It is also an achievable measure to alleviate disease burden within the community. In Hong Kong, private primary care physicians (PCPs) play a key role in meeting 70% of the primary care needs. They are encouraged to undertake continuing professional education (CPE) that helps upkeep their medical standards and enhance quality of care.

Aims and Objectives: To understand the attitudes, barriers, facilitators and effects of undertaking CPE among the private non-specialist PCPs in Hong Kong, and to suggest policy implications that facilitate greater participation.

Study Design and Methods: A combined qualitative and quantitative approach was adopted. Eight focus group interviews were conducted with a purposive sample of 36 private PCPs. The qualitative findings informed the construction of the cross-sectional survey with a questionnaire which was then mailed to a stratified random sample of 2,567 private non-specialist PCPs.

Results: Among the qualitative interviews and 134 valid questionnaire returns, CME lecture (>75%) was reported to be the most frequently engaged format of CPE, followed by online searching for information (65%). Apart from learning and enhancing standards of medical care, attending CME lectures also served as means of socializing and network building. Age was a significant factor associated with the formats of CPE. While older PCPs tended to attend CME lectures more often, their younger counterparts were keener to engage in online search and learning. Certain barriers and facilitators identified were context-specific to private healthcare sector in Hong Kong, such as long clinic hours, high operation costs and organisation of small learning groups. The latter, though the least frequently attended CPE activity among survey respondents, was positively rated on account of its intensity and interactive knowledge exchange along with active support from specialists. Online access to CME learning materials and more opportunities to participate in public sector CPE activities would be welcomed by private PCPs.

Conclusions: Despite similar findings from oversea studies, certain barriers and facilitators identified in the present study were context-specific to private non-specialist PCPs in Hong Kong. Implementation of more adaptive measures, such as emphasis on self-directed and practice-based learning and support from public authorities to facilitate CPE learning for the private PCPs, may in turn help reduce the healthcare costs in Hong Kong.

Project Number: 11121631

P28-0148

Evaluation of the Introduction of the Reference Framework for Diabetes among Primary Care Physicians in Primary Care Settings

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Background: Primary Care Physicians (PCPs) are in a privileged position to provide first-contact and continuous care. A Reference Framework for Diabetes Care (RF-DM) for Adults produced by the Primary Care Office (PCO) aims to provide PCPs a common reference to guide and coordinate care for diabetes patients. We evaluated the adoption levels of RF-DM among PCPs in Hong Kong, and examined the facilitators and barriers associated with its adoption.

Methods: The focus group interviews were performed with five main types of PCPs in Hong Kong, including those working in (1) group practice in private health maintenance organizations; (2) solo practice in the private sector; (3) general out-patient clinics; (4) family medicine specialist clinics; and (5) PCPs who obtained fellowships of family medicine and participated in teaching medical students for medical schools. Their perceived facilitators and barriers to adopt the RF-DM were explored. The interviews were audio-taped, transcribed verbatim, and analysed to identify the predictors. We also conducted a cross-sectional questionnaire by sending invitations to PCPs in Hong Kong. The factors independently associated with adoption of the RF-DM were studied by binary-logistic regression models.

Results: The qualitative study reported several barriers of implementation, including: 1) issues on the updatedness of the RF-DM; 2) inadequate allied health support for diabetes patients and the limited consultation time; 3) low affordability on diabetes treatment/screening among patients; 4) difficulties on prescriptions; 5) patients' compliance with recommendations in the RF-DM recommendations; 6) clinicians' common practice based on their own experience or other guidelines. On the other hand, raising its awareness and familiarity were facilitators for its adoption. For the PCPs' survey, we collected 414 completed questionnaires. The average adoption score was 3.29/4 (S.D.=0.51). Approximately 70% of the PCPs highly adopted this RF-DM as their routine practice. Binary logistic regression analysis showed that the PCPs' perception of including sufficient local information (adjusted odds ratio, aOR=4.75, 95% CI 1.60-14.12, p=0.005) was the strongest factor associated with their adoption levels in daily practices.

Conclusions: The adoption level of RF-DM was high for adult diabetes in primary care settings among the PCPs. The facilitators and barriers for its adoption were identified, and they should be addressed in its continuous updates. Future studies on strategies to enhance adoption and implementation capacity should be conducted.

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Project Number: 10110601

P29-0125

Evaluation of the Adoption of the Reference Framework for Hypertension in Primary Care: a Mixed Qualitative and Quantitative Study

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Background: The Reference Framework for Hypertension Care for Adults (RF-HT) was produced by the Primary Care Office of the Hong Kong Government in 2010, aiming to provide evidence-based recommendations for management of hypertensive patients in the community. This study evaluated the adoption level of the RF-HT among primary care physicians (PCPs) in Hong Kong, and explored the potential factors associated with its adoption.

Method: A mixed methodology approach consisting of a qualitative and quantitative study was adopted. Eight focus groups and four in-depth face-to-face interviews were conducted with PCPs recruited from: 1) Solo practice in the private sector; 2) General out-patient clinics; 3) Family medicine specialist clinics; 4) Group practice in Health Maintenance Organizations and 5) PCPs who obtained fellowships of family medicine and participated in teaching medical students for medical schools. The potential factors influencing the adoption of RF-HT were explored by qualitative analysis. All interviews were transcribed verbatim we used a framework approach to analyze the data using NVivo 10 software. Self-administered surveys were sent via postal mails, e-mails and on-site invitations in medical seminars. The sampling frame of the survey consists of 2,297 PCPs whose contact information was retrieved from multiple sources. Factors associated with RF-HT adoption were evaluated by multivariate logistic regression analysis.

Result: The major enablers of RF-HT adoption included the perceived feasibility and usefulness in educating patients and the standardized recommendations for local practice. Barriers associated with its adoption consist of the unclear development process of the RF-HT; concerns over patient affordability of certain medications; the presence of competing guidelines; and limited resources. From self-administered surveys, the average adoption level of the RF-HT by the PCPs was 3.43/4.0 (SD=0.314), and it was found that 92.4% of PCPs frequently adopted this framework in their daily consultations. Several factors were found to be significantly associated with high levels of adoption: (1) Female practitioners (adjusted odds ratio [aOR]=3.19, 95% C.I. 1.10-9.26, p=0.032); (2) Easy access to the electronic patient version of the RF-HT (aOR=2.78, 95% C.I. 1.15-6.72, p=0.023); (3). The capability of the RF-HT to be integrated into clinical setting (aOR=7.19, 95% C.I. 2.8-18.5, p<0.001); and (4) PCPs' perception of limited resources in their clinics (aOR=4.08, 95% C.I. 1.62-10.3, p=0.003).

Conclusion: The RF-HT was of high quality and widely adopted by PCPs in Hong Kong. The present findings also identified several areas where the RF-HT could be further tailored-made to enhance its adoption in primary care settings.

Project Number: 12131241

P30-0138

Cost-effectiveness Analysis of Patient Empowerment Programme on Diabetes Mellitus

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Introduction and project objectives: The Hospital Authority has introduced a Patient Empowerment Programme (PEP) for Diabetes Mellitus (DM) patients in 2010 to enhance their disease-specific knowledge and self-management skills, and thus their self-efficacy and lifestyle modifications. The aim of this study was to evaluate the cost-effectiveness of PEP among DM patients who had also enrolled to the Risk Assessment and Management Programme (RAMP-DM) by modelling cost-effectiveness over the five years and programme expansion to identify cost-drivers and areas of uncertainty.

Methods: A cohort study was conducted with primary outcomes being the first occurrence of a macrovascular or microvascular complication or mortality of any cause during the follow-up period in the PEP and non-PEP groups. The programme costs were estimated from the societal perspective which included the provider's costs of setting up and running PEP, the costs to the community, and the costs to the subjects attending PEP. These data were incorporated into an individual-based Markov state-transition model to simulate lifetime costs and outcomes for DM patients with or without PEP. Incremental cost-effectiveness ratio (ICER) was calculated as cost per quality-adjusted life years (QALY) gained, assuming a 5-year programme effect with future cost and QALY discounted at 3.5% per year. Probabilistic sensitivity analysis was conducted with results presented as a cost-effectiveness acceptability curve.

Results: There was a significantly lower cumulative incidence of all deaths (2.9% vs 4.6%, p<0.001); any DM complications (9.5% vs 10.8%, p=0.001); and cardiovascular disease events (6.8% vs 7.6%, p=0.018) in the PEP group than those in the non-PEP group. The programme cost was a 1-time cost and the societal cost per subject for PEP was HK$1,929. In the long term model, the ICER was HK$23,358 per QALY gained at 2013 cost and was highly cost-effective when compared to a willingness-to-pay threshold of HK$240,000 per QALY. Probabilistic sensitivity analysis showed that PEP was 65% likelihood to be cost-effective compared with non-PEP when willingness-to-pay for a QALY was HK$200,000 or above.

Conclusion: The extra amount allocated for running PEP was just under HK$2,000 and appeared to be compensated for to a large extent by improved health of the subjects. Given the carefully measured cost of PEP and the potential benefits in addition to RAMP-DM, we found

PEP could be highly cost-effective.

Project Number: EPC-HKU-1A & 1B

P31-0028

A Community-based Advance Care Planning Programme to Improve End-of-Life Care in Patients with Advanced Disease: A Mixed-method Approach

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Introduction and Project Objectives: Advance care planning (ACP) is defined as an ongoing communication process that aims to empower patients to plan for their future care and promote a shared understanding among patient, family and health care team on their end-of-life care preferences. This project aimed to evaluate the effects of a community-based ACP programme in Chinese patients with advanced disease.

Methods: A randomized controlled trial was conducted in the medical department of a local convalescent hospital between 2014 and 2016. Adult patients were eligible to the study if they were home-dwelling and met the triggers in the Gold Standard Framework. A structured ACP programme, which included personal reflection and a facilitated discussion, was delivered by a trained nurse to the experimental group through three home visits. The outcomes were whether the patients' EoL care preferences were known, patients' level of certainty about EoL care decision, documentation of EoL care decision and healthcare utilization. Outcomes were measured at baseline (T0), one month (T1) and six months (T2). In-depth interviews were conducted with a purposive sample of 20 participants in the experimental group. All statistical analyses were performed based on intention-to-treat principle. Interviews were transcribed verbatim for qualitative content analysis.

Results: A total of 239 dyads agreed to participate in the study, giving a participation rate at 70.9%. Characteristics of participants between the experimental and control groups did not differ statistically at baseline. No significant difference was noted between completers and non-completers. The mean age of patients was 77.7 (SD 9.1) years and with non-cancer diagnoses. At T2, the patient's level of certainty and the dyadic agreement between patients and family member regarding EoL care decision of the experimental group were significantly higher than those of the control group (p ranged from 0.001-0.035). Likewise, documentation of care decisions were significantly higher in the experimental group than the control group. No significant differences were noted in the health care utilization. Qualitative findings also showed that participants felt empowered and relieved following the ACP process.

Conclusions: This is the first published study using a randomized controlled trial design to test the effects of ACP in the Chinese population. The findings supported that ACP can significantly improve the dyadic agreement on EoL care preferencesand thus should be integrated into the care practice in a timely manner. The findings also revealed the importance of developing a more conducive and supportive environment for ACP.

Project Number: 11120861

P32-0007

A Randomized Controlled Trial Evaluating Efficacy of Promoting Home-based HIV Testing with Online Counseling on Increasing HIV Testing among Men Who Have Sex with Men

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Introduction and Project Objectives: HIV testing is an important but under-utilized, recommended global strategy for HIV prevention among men who have sex with men (MSM). We developed an innovative home-based HIV self-testing (HIVST) services that include mailing of a free HIVST kit and providing online real-time instructions and pre-test/post-test counseling (HIVST-OIC) to testers, and evaluated its efficacy in increasing prevalence of HIV testing of any type within a 6-month period among MSM in Hong Kong.

Methods: In 2015, a parallel-group and non-blinded randomized controlled trial was conducted, with a follow-up evaluative telephone survey administered six months afterwards. Participants were adult MSM who have access to online live-chat applications. Exclusion criteria included HIV positive status and HIV testing within the last six months. With verbal informed consent, 430 participants were randomized evenly into the intervention group and the control group. Based on two constructs of the Health Belief Model (e.g., perceived benefit and perceived barrier), health promotion materials were designed by an expert panel. The control group watched an online video that promoted HIV testing in general. In addition to the video watched by the control group, the intervention group watched an online video promoting HIVST-OIC, received motivational interviewing over phone, and were mailed a free HIVST kit. By appointment, participants took up HIVST with real-time instructions/counseling/support provided by an experienced nurse through online live-chat applications. Intention-to-treat analysis was used.

Results: The baseline background characteristics of the intervention and control groups showed no statistically significant differences. At Month 6, as compared to the control group, the intervention group reported significantly higher prevalence of HIV testing of any types (89.8% versus 50.7%; Relative risk reduction (RR): 1.77; p<0.001); 87.9% of the intervention group has taken up HICST-OIC. Among those who have taken up any HIV testing in the last six months as measured at Month 6, significant between-group difference was found in multiple male sex partnerships (34.2% versus 47.7%, RR: 0.72; p=0.021). The HIVST-OIC was assessed positively in the process evaluation.

Conclusion: HIVST-OIC has a strong potential in increasing prevalence of HIV testing and reducing sexual risk behaviors among MSM. Implementation research is warranted.

Project Number: 11120791

P33-0017

Adoption of Health Promoting Lifestyle Among Chinese Breast And Colorectal Cancer Survivors During The First 5 Years After Completion of Treatment

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Introduction and Project Objectives: As a result of advances in early detection and treatment, the number of cancer survivors (CSs) is increasing. Healthcare providers are focusing more on their health needs and quality of life instead of morbidity and mortality. Lifestyle is considered to be a significant modifiable factor in cancer development. Most studies on health promoting lifestyle (HPL) and influencing factors were conducted in Western countries. The cultural, social and

situational influences on HPL among Chinese cancer survivors are largely unexplored. It is the objective of this study to explore CSs' experience of adopting health-promoting lifestyle (HPL) behaviors and the factors influencing the adoption of such behaviors.

Methods: Thirty-two Chinese breast and colorectal CSs who were in their first 5 years after treatment were recruited from an oncology outpatient clinic of a hospital in Hong Kong. Eight focus groups were conducted. Qualitative content analysis was adopted in data analysis.

Results: Diet, exercise, sleep and rest, maintaining psychological well-being, using traditional Chinese medicine and health products, and attending health consultations and follow-up visits were HPL behaviors adopted by participants with the goals of improving general health, controlling cancer, and managing health problems. In the process of adopting HPL, participants 'chose among HPL strategies', 'maintained the HPL' and finally 'integrated the HPL' into their daily routine. Prior HPL, the need for information, coping, motivation and determination, competing demands, support for the cancer survivor (CS), and the Chinese belief in minimizing social disturbance and engaging in collaborative control were factors influencing the process of adopting HPL.

Conclusions: CSs adopted a range of HPL. However, they encountered problems in choosing, maintaining and integrating them into their daily life. Health care professionals can play a significant role in supporting CSs in self-management. Suggested strategies to enable CSs to adopt HPL included clarification of queries about conflicting information, development plan collaboratively with CSs, provision of detailed guidelines on HPL, and reinforcement or modification of HPL plan after completion of treatment so as to address their evolving needs.

Project Number: 11122401

P34-0029

Projection of All-cause Mortality and Life Expectancy in Hong Kong to 2040 by Socio-economic Status: A Population-based Retrospective Cohort Study

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Introduction and Project Objectives: A major shortcoming of the conventional calculation of life expectancy is that it accounts only for the current health status of the population, but not for how long an individual is expected to live. This study aimed to identify relative contribution of macro-environmental risk factors to all-cause mortality and life expectancy, and forecast what may happen to Hong Kong's population health by sex and socio-economic status.

Methods: This study utilized a retrospective cohort design with an age-period-cohort (APC) modeling method. Poisson APC models were used to decompose all-cause mortality into the contributions of age, period and cohort effects. A Bayesian approach was adopted for the projection of mortality. We then applied the projected mortality rates to forecast life expectancy using abridged life tables. Potential years of life lost (PYLL) were also estimated for the burden of disease.

Results: Overall mortality rates would continue to decline and correspondingly life expectancy in every age group to increase in Hong Kong to 2040 for both sexes, regardless of the SES. Age-standardized mortality rate and life expectancy tended to favour men of higher SES, while they were more similar for women of lower and higher SES. PYLL was projected to see an upward rising trend towards the future.

Conclusions: Despite declining overall mortality rates and increasing life expectancy in Hong Kong, the long life span may not be sustainable, especially when the cohorts are exposed to socio-economic development over generations. There may also be presence of sex-specific effects of socio-economic standing on population health. There may be window of opportunity in Hong Kong and similar populations now to put policies into place to prevent diseases of affluence emerging over the future generations.

Project Number: 11121121

P35-0033

The Consequences of In-utero Exposure to Gestational Diabetes on Metabolic Health in Adolescence: Does Breastfeeding Make a Difference?

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Introduction and Project Objectives: There is a biologically plausible mechanism by which early exposures may programme metabolism for life. It has been suggested that short-term breastfeeding from mothers with gestational diabetes (GDM) may increase diabetes risk in offspring. We examined 1) the association of in-utero exposure to GDM with metabolic health in adolescents, proxied by body mass index (BMI), waist-to-height ratio and blood pressure, and 2) whether the association of in-utero exposure to GDM with metabolic health was modified by breastfeeding during the early postpartum period.

Methods: We used multivariate linear regression with multiple imputation in the prospective birth cohort study "Children of 1997" in Hong Kong with 7342 participants (88% follow-up rate), to assess the associations of in utero exposure to GDM with age- and sex-specific BMI z-score and sex-specific waist-to-height ratio z-score at 14 years old and age-, sex- and height- specific blood pressure z-score at 11 and 13 years old, adusted for sex, maternal age and birth place, other pregnancy conditions, mother's current BMI and family socio-economic position. We tested whether the associations varied by mode of feeding during the first two weeks and three months of life (always formula-fed, mixed, always breastfed) from the significance of interaction terms. We also used generalised estimated equations with multiple imputation to assess the associations of in utero exposure to GDM with sex-specific BMI z-score during infancy (0-2 years), childhood (2-8 years) and adolescence (8-16 years).

Results: Adolescents with in utero exposure to GDM (7.5%) had greater BMI and waist-to-height ratio z-scores but not higher blood pressure z-scores, with no difference by sex or mode of feeding. They however had lower BMI during infancy, suggesting GDM related adiposity in children emerged only in childhood, and manifested in adolescence. Short exclusive breastfeeding of two weeks or three months from mothers with GDM was unrelated to adiposity or blood pressure in adolescence and did not change associations of in utero exposure to GDM with subsequent adiposity and blood pressure.

Conclusions: Children with in utero exposure to GDM had greater adiposity during childhood and adolescence. Exclusive breastfeeding in early infancy from mothers with GDM was not associated with greater adiposity or higher blood pressure and thus should not be discouraged. However the impact of being breastfed from mothers with postpartum hyperglycaemia requires further studies to clarify. Promoting maternal health provides early life intervention opportunities to combat obesity and type 2 diabetes.

Project Number: 12132731

P36-0042

Prediction of Cardiovascular Disease Risk in a Cohort of Older Chinese Adults in Hong Kong

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Introduction: Risk prediction models for cardiovascular disease (CVD) derived from Western cohorts allow stratification of CVD risk based on an individual's risk factors and the population's CVD risk. Chinese have relatively low rates of ischaemic heart disease. The predictive performance of such tools in Chinese populations should be evaluated before application.

Project Objectives: We compared the predictive performance of the widely used Framingham Risk Score (FRS) and Globorisk, a new risk prediction model, for adults aged ≥65 years in the Hong Kong Department of Health's Elderly Health Service (EHS) cohort.

Methods: The cohort consisted of 66,820 adults aged ≥65 years enrolled from 1998 to 2001. We tracked CVD deaths prospectively through linkage with death registration until 2012, and assumed a ratio of 8:1 for nonfatal to fatal events. We assessed the discrimination and calibration of the FRS and Globorisk among participants without CVD at baseline. Discrimination was measured using the C-statistic, with 0.5 equating to chance and 1 indicating perfect discrimination. Calibration was measured by the Hosmer-Lemeshow test, with X^2<20 indicating good calibration. We used a random sample of 20,671 participants to generate a new Globorisk function based on mean risk factor levels and CVD death rates in our cohort, and validated this function in the remaining participants.

Results: The FRS overestimated fatal and nonfatal CVD events at 10 years by 7.5% points in men (predicted risk 38.5% vs. observed risk 31.0%; X^2 367.6) and 3.0% points in women (predicted risk 21.6% vs. observed risk 18.6%; X^2 258.6). Recalibration using EHS cohort data improved its performance slightly in men (predicted risk 36.1%; X^2 218.6), but not women (predicted risk 22.2%; X^2 303.0). The calibration of Globorisk using EHS data overestimated CVD deaths at 10 years by 0.4% point in men (predicted risk 4.5% vs. observed risk 4.1%; X^2 34.2) and 1.1% point in women (predicted risk 4.0% vs. observed risk 2.9%; X^2 187.7). The new Globorisk function improved the calibration (X^2 21.1 in men, 61.1 in women) with moderate discrimination (C-statistic 0.668 in men, 0.700 in women).

Conclusions: The FRS and Globorisk overestimated CVD risk by 16% to 19% and 4% to 38% relatively in this cohort of older Hong Kong Chinese despite recalibration. Because our cohort included survivors and case-fatality ratios are decreasing, these models should be used with precaution. New models for CVD with incidence data are needed for CVD prevention and disease burden estimation.

Project Number: 12133051

P37-0045

Adventure-Based Training to Promote Physical Activity, Reduce Fatigue, and Enhance Quality of Life among Hong Kong Chinese Childhood Cancer Survivors: A Phase 3 Randomised Controlled Trial

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Introduction and Project Objectives: Despite evidence that regular physical activity can attenuate cancer-related fatigue, many childhood cancer survivors are reluctant to engage in regular physical activity. Although adventure-based training may be effective in promoting physical activity among childhood cancer survivors, large-scale or robust evidence of its effectiveness is scarce. In addition, it is unclear if adventure-based training can help attenuate cancer-related fatigue. This study examined the effectiveness of an adventure-based training programme in promoting physical activity, reducing fatigue, and enhancing self-efficacy and quality of life (QoL) among Hong Kong Chinese childhood cancer survivors.

Methods: We conducted a prospective, phase 3 randomised controlled trial. Hong Kong Chinese childhood cancer survivors aged 9-16 years were recruited via an outpatient clinic, the Children's Cancer Foundation, and the Sunshine Group. The primary outcome was fatigue. Secondary outcomes were physical activity levels, self-efficacy, hand grip strength, and QoL, which were assessed at baseline, and 3, 6, 9, and 12 months after starting the intervention. Intention-to-treat analysis was used. The study is closed and was registered at ClinicalTrial.gov (NCT02703935).

Results: Between Jan 6, 2014, and June 8, 2015, we randomly assigned 222 eligible childhood cancer survivors to either the experimental group (n=117) to receive a 4-day adventure-based training programme or the control group (n=105) to receive placebo intervention. The experimental group reported statistically significantly lower levels of cancer-related fatigue, higher levels of self-efficacy and physical activity, greater right- and left-hand grip strength, and better QoL than the control group.

Conclusions: This study provides evidence that adventure-based training is effective in promoting physical activity, reducing cancer-related fatigue, and enhancing self-efficacy and QoL among Hong Kong Chinese childhood cancer survivors.

Project Number: 11121461

P38-0047

Unravelling Secular Trends of Blood Pressure in Children and Adolescents in Hong Kong: Information for Action

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Project Objectives: To describe changes in blood pressure (BP) and body mass index (BMI) for children and adolescents in Hong Kong over the past two decades.

Introduction: Secular trends of blood pressure (BP) and body mass index (BMI) during childhood and adolescence are important cardiovascular health surveillance indicators. Trends in early life BP and BMI could underlie and presage the cardiovascular disease burden in the next generation, making context-specific evidence particularly relevant to inform actions for prevention.

Methods: We delineated trends in BP (ages 9-18 years from 1999 to 2014) and BMI (ages 6-18 years from 1996 to 2014) in Hong Kong among the Student Health Service attendees.

Results: Overall, mean systolic BP decreased slightly during 2002-2005 and increased very modestly to 2014; a similar pattern was observed for mean diastolic BP with earlier decrease during 1999-2005. Conversely, mean BMI increased during 1997-2009 and decreased slightly to 2014. Compared with the 2007 WHO growth reference, in girls BP fell to below the reference, whilst BMI rose to the reference, but in boys systolic BP and BMI rose above the reference.

Conclusions: BP declined modestly whereas BMI rose before a recent levelling-off among children and adolescents in Hong Kong during the past two decades. Such divergent trends warrant dual actions in tackling rising BMI, and identifying factors contributed to BP beyond BMI, particularly in boys.

Project Number: 11121371

P39-0076

Dietary Information Processing and Decision Making among Chinese Breast Cancer Survivors

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Introduction and Project Objectives: Chinese breast cancer (BCA) survivors face different and sometimes contradicting dietary information. To ensure smooth cancer care delivery and promote long-term healthy eating in this population, we need more in-depth understanding of how they process dietary information and make dietary decisions over time.

Methods: 39 BCA survivors were followed from immediately post-surgery to six months after completion of adjunct treatments. In-depth interviews were conducted to explore factors influencing their dietary information processing and decision-making during the different time points. All interviews were recorded and transcribed verbatim for analysis. Grounded theory approach was used.

Results: BCA survivors reported to be actively seeking dietary information and making dietary changes immediately after receiving their diagnosis. They were motivated to avoid foods that were believed to have contributed to their cancer, such as chicken, and foods that would interfere with recovery, such as beef and seafood. During and after adjunct therapies, survivors were motivated to try new foods that were believed to be cancer preventing, such as asparagus. This is followed by the gradual re-introduction of previously eliminated foods such as beef and seafood, and sometimes even organic chicken. Survivors' diets were likely to remain the same from this point onwards as active information seeking stopped and things other than health took priorities in life. However, most survivors continued to be receptive to passive information from social media and their social circle. Throughout the process, survivors expressed desire for reassurance from healthcare professionals about their dietary choices, but were unlikely to relax their initial diet restrictions if information contradicts commonly held beliefs.

Conclusions: Survivors were increasingly reliant on social media for health and dietary information. The initial complete elimination of foods can be problematic if patients do not replace with other protein sources during treatment period. Their desire for reassurance from healthcare professionals provides opportunities to guide them to relevant and credible resources. However, recommendations should address and align with commonly held beliefs.

Project Number: 12132571

P40-0080

Effects of Peer Education Intervention Program on Children Healthy Eating in Local Elementary Schools

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Introduction and Objectives: This study aims to develop a peer-mentoring intervention program to promote healthy-eating guidelines and practice among elementary school children in 2012-2014. Evaluation of the impacts on the healthy-eating knowledge and practice in intervals amd upon program completion.

Methods: A single cohort with RCT design study involved 362 children (intervention) and 341 children (control), whilst sub-groups are formed with grade 1-3 children as mentees and grade 4-5 children as mentors. In control group, children were given standard lessons with education resources about daily healthy eating as baseline. Subjects are encouraged to exchange healthy-eating knowledge and experience during the study period. In intervention group, a peer-mentoring program is adopted to impart and reinfore healthy-eating guidelines and skills throughout the intervention period with 10 peer-mentoring lunch meetings. Mentors were involved peers sharing knowledge and attitudes on healthy eating and food choice, and supports mentees' towards desirable eating behaviours during lunch meetings. The primary outcome measures are the anthropometric measures and secondary measures include knowledge and attitude of healthy eating and a 7-day food diary.

Results: The matched and completed data sets were collected for data analysis.

Anthropometric Measures: Intervention group children have significant larger in waist circumference and body mass index than the control group. However, control group children have higher increments on the percentage of body fat.

Effects on healthy-eating knowledge & attitudes: Significant improvement on knowledge of intake of healthy food types and fluid were observed in intervention group. A significant intervention effect was found at the post-intervention point on daily intake of healthy food types and fluids. Majority of children in both groups selected healthy food types as snacks, whilst many children realized that breakfast and lunch were important to them. Around 70% of students intend to skip breakfast and 30% of students prefer lunch if allowed.

Effects on actual dietary intake: Based on the mentees' 7-day food diaries recorded from 24-hour recall on dietary intakes throughout intervention period, significant positive time trends were observed for daily intake of grains and fluid while negative time trends were noted for fruits and milk after intervention completion.

Conclusions: This is the first local study to evaluate the peer education intervention on healthy eating among elementary school children. The concerted efforts in the community shall involve both teachers and parents who have nt roles on childhood eating practice. The results suggest further study to investigate the role of these parties in developing children's healthy eating.

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Project Number: 10111811

P41-0085

Physical Activity and Fundamental Movement Skills in Children with Developmental Coordination Disorder

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Introduction: Children with developmental coordination disorder (DCD) have lower levels of physical activity (PA) and higher risks for obesity than typically developing children. PA and fundamental movement skills (FMS) are associated so interventions that promote FMS of children with DCD potentially are to be recommended.

Project Objectives: We examined (1) the relationship between FMS and PA, and 2) the immediate, shorter- and longer-term effects of FMS training on motor functions and PA using ICF-CY as a theoretical framework.

Methods: It was a multi-method project consisting of a cross-sectional study (Study 1) and randomized controlled trial (RCT) (Study 2). In Study 1, 188 children aged 6-10 years with DCD and with typical development (TD) were involved to examine the FMS-PA relationship. In Study 2, 131 children were allocated to FMS training groups (FMS-DCD n=35, FMS-TD n=29) who received FMS training (eight weekly 40-min sessions) or control groups (C-DCD n=34, C-TD n=33) who had their conventional physical education lessons. Outcome variables including accelerometer-assessed PA, motor functions, self-perceived competence and enjoyment were measured at baseline, 1-week, 3-month, and 12-month after the intervention.

Results: In Study 1, FMS was associated with PA, but such association was stronger in children with TD. In Study 2, FMS training was effective in improving FMS proficiency, facilitating active behaviour, and promoting enjoyment in participation during leisure time in children with DCD. Some effects were evident for both short- and long-terms.

Conclusions: FMS has an important role in the lives of children with DCD. FMS training reflects improvement in motor skills proficiency and translates to activity accrual and enjoyment. Based on the ICF-CY model and the errorless motor learning model, the implementation of a school-based FMS training program has the potential in promoting physical and psychological health in children with DCD in the long run.

Project Number: 11120781

P42-0144

The Characteristics of Students Who Influence Their School Peers' Health Risk Behaviors

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Introduction and Project Objectives: Peer pressure has been identified as a decisive factor in the involvement of adolescents in various risky behaviors. The aim of this study were to explore the relationship between peer pressure and the health risk behaviors of secondary school students, and the characteristics of influential peers and the influence mechanism.

Methods: This study was divided into two phases.
The first is a cross-sectional study. Form 3 students were invited to complete a self-completed questionnaire on their perceptions of peer pressure employing the Peer Pressure Inventory and their involvement in risk behaviors using a modified global school-based student health survey. Students were also asked to nominate peers whom they considered influential in an anonymous ballot.

The second phase of this study involved in-depth interviews of the nominated influential students to explore the characteristics of such influential peers and the mechanism by which they exert their influence on their peers.

Results: Six schools participated in phase 1 of the study. A total of 840 Year-3 secondary students completed the questionnaires. Having friends who are involved in the same risk behaviors is the single most important factor associated with the participation of secondary students in those specific risk behaviors. A high proportion of secondary students involved in risk behaviors were affiliated with peers who were involved in the same activities: smoking (48.9%), drinking alcohol (86.5%), using drugs (18.2%), engaged in sexual activity (34.5%), and bullying (82.6%).

Only three out of these six schools granted access of their students who were nominated by their peers as influential. A total of six focus group interviews (average of seven participants) were conducted. Students considered friendliness (91.0%), being a buddy (88.5%), and entertaining /humor (86.8%) as the top three characteristics of influential peers. The influential peers believed that their power to influence came about through their helpfulness, accommodation, and the closeness of their relationships. Their influence was manifested in both positive and negative ways on the academic pursuits and health-risk behaviors of their peers.

Conclusions: The results of this study provide a better understanding of the association between peer pressure and the adoption of health behaviors, and the characteristics of influential adolescents and the mechanism of peer influence. This will facilitate the identifications of influential students to function as school health ambassadors in peer-led health promotion programs to reduce the uptake of health risk behaviors of adolescents.

Project Number: 10111871

P43-0023

Can Achieving Sustained DAS Remission Prevent Progression of Subclinical Atherosclerosis? A Prospective Cohort Study in Early Rheumatoid Arthritis (ERA)

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Introduction: Patients with rheumatoid arthritis(RA) have higher incidence of cardiovascular disease(CVD) and prevalence of arterial stiffness(AS) due to underlying inflammation. Effective immunosuppression using anti-TNF was shown to improve AS in early RA(ERA) patients. Whether it is a specific effect by blocking the TNFα pathway or suppression of inflammation remains uncertain. While achieving Disease Activity Score in 28 joints(DAS) remission was associated with significant benefits in articular disease, its effect on co-morbidities such as CVD risk is uncertain.

Objectives: To investigate the effect of achieving sustained DAS remission on AS.

Methods: This randomized control trial investigates the effect of 2 tight-

control treatment strategies aiming at 1.Simplified disease activity index remission[SDAI≤3.3] or 2.minimal disease activity[DAS<2.6] on AS in ERA patients. 120 patients with active disease(DAS>=3.2), symptoms onset <2 years and bDMARD-naive were recruited and received 1-year treatment. Treatment were adjusted based on standardized protocol every 3 months aiming at either 1 of the targets. AS was measured by branchial-ankle pulse wave velocity(baPWV) using a dedicated tonometry system(Omron VP-2000).

Results: In the interim analysis, results of 100 patients [male(23.0%);52.8±13 years] who completed 1 year follow-up were analyzed. No significant differences were observed between groups in clinical features, DMARD use and baPWV at month12 (M12) yet significant disease activity improvement was found in both groups. Hence, results from the 2 groups were combined to ascertain if achieving sustained DAS remission can prevent AS progression. The disease activity improved significantly [DAS:4.8(4.2, 5.6) at baseline (BL) vs 2.38(1.6,3.0) at M12, p<0.001]. 57% patients achieved DAS remission at M12 and 36% patients achieved DAS remission over 3 consecutive visits (sustained remission). No significant differences were found in disease activity, cardiovascular risk factors (CRF) and baPWV at BL between groups who can(CA) or cannot achieve(NA) sustained remission. At M12, no significant differences in CRF and baPWV were found between groups. However, the change in baPWV was significantly different between CA and NA group [-65.5(-147.25,44.0)cm/s vs 39(-65.25,124.75)cm/s, p=0.005]. The differences remained significant in the %change of baPWV [-4.4(-9.67,-2.84)% vs 2.51(-4.34,-10.28)%, p=0.006]. In univariate analysis, assocation of change in baPWV and potential predictors included BL baPWV, blood pressure(systolic&diastolic) and sustained DAS remission. By multivariate analysis, achieving sustained DAS remission was an independent predictor for baPWV reduction.

Conclusion: Effective suppression of inflammation by achieving sustained DAS remission may prevent progression of arterial stiffness in patients with ERA.

Acknowledgements: This study was supported by the Health and Medical Research Fund.

Project Number: 10110071

P44-0011

Longitudinal Course of Insomnia Disorder: Bidirectional Association with Depression and Roles of Biomarkers

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Aims: To: 1) examine whether there is a bidirectional association between insomnia disorder and depressive disorder diagnosed by clinical diagnostic interview; 2) identify the biomarkers (including serial salivary cortisol, objective sleep duration, and objective physical activity) that may predict the longitudinal course of insomnia disorder and MDD; 3) investigate the potential roles of these biomarkers in the bidirectional associations between insomnia and MDD.

Methods: The current study was a prospective study of the Hong Kong family-based cohort of insomnia, which was established in 2009-2011. The diagnoses of insomnia disorder and depression were determined by Structured Clinical Interview. Objective and subjective sleep parameters were measured by 3-day actigraphy and sleep diary at baseline and 7-day actigraphy and sleep diary at follow-up. Serial salivary samples were collected to estimate the HPA axis activity at both baseline and follow-up.

Results: A total of 490 out of 798 individuals (61.4%) at baseline were recruited in the follow-up study (31.3 ± 16.3 years old at baseline, 53.3% females). Individuals with baseline insomnia had a higher incidence rate of major depressive disorder (MDD) than those individuals without baseline insomnia (8.8% vs. 3.5%, adjusted OR (95%CI) = 2.55 (1.08-6.07), $p < 0.05$). On the other hand, individuals with baseline MDD had a higher incidence rate of insomnia disorder than those individuals without baseline MDD (18.4 vs. 8.4%, $p < 0.05$). However, this association was not statistically significant after controlling for age and sex in the Generalized Estimating Equation (GEE) model (adjusted OR (95%CI) = 2.01 (0.75-5.36). The bidirectional association between insomnia symptoms and depressive symptoms was, however, confirmed by using cross-lagged analysis. Individuals with new incidence of insomnia had a higher cortisol awakening response reference to ground (AUC_g) than persistent good sleepers (13.1 vs. 11.6, difference = 1.56 ± 0.77, $p < 0.05$). Individuals with new incidence of depression also had a higher cortisol awakening response reference to ground (AUC_g) than persistent good sleepers (13.2 vs. 11.4, difference ± se = 1.80 ± 0.91, $p < 0.05$).

Conclusions: There is a bidirectional association between insomnia and depression at symptoms level and likely at disorder level too. Increased HPA axis activity plays a critical role in the new incidence of both insomnia and depression, which may serve as a common pathway underlying insomnia and depression. Objective sleep duration as measured by actigraphy is not likely to be associated with longitudinal course of insomnia and depression.

Project Number: 11120811

P45-0113

A Brief Integrated Sleep-focused Treatment for Persistent Sleep Disturbances in Residual Depression: An Assessor-blind, Parallel Group, Randomized Controlled Study

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Introduction and Project Objectives: Major depressive disorder (MDD) is a debilitating and recurrent illness with grave consequences. Whilst the ultimate treatment goal is a sustained resolution of the symptomatology with the remission of MDD, a substantial portion of depressed patients continue to experience residual symptoms, particularly sleep disturbances, despite the optimised antidepressant treatment. The current project aimed to examine the efficacy of a brief sleep-focused psychological treatment for patients with treatment resistant depression and comorbid sleep disturbances, including frequent insomnia and nightmares.

Methods: The current study is a single centre, randomized, assessor-blind, parallel-group trial. Recruited depressed patients were randomly allocated to receiving either six sessions of sleep-focused treatment (cognitive behavioural therapy for insomnia, imagery rehearsal therapy for nightmares) added to standard care (intervention group) or standard care alone (control group), and were followed up at one week, two months, six months and 12 months after the treatment. Depressive symptoms were assessed by the Hamilton Rating Scale for Depression (HRSD17). Sleep symptoms were measured by the Insomnia Severity Index and Pittsburgh Sleep Quality Index (PSQI).

Results: A total of 79 patients (50.8 ± 9.2 years, 66% female) were

recruited. Sixty-six patients (83.5%) completed at least one follow-up assessment and were included into the statistical analyses by using the last observation carried forward (LOCF) method. Sleep-focused treatment added to standard care produced significant improvements of sleep symptoms (one-week post-treatment follow-up: p<.05 for both ISI and PSQI) and depressive symptoms (one-week post-treatment follow-up: p < 0.001 and at 12-month follow-up: p = 0.003). Whilst insomnia symptoms were improved over time for both groups (ISI score at 12-mont follow-up: interaction p = 0.20), sleep-focused treatment added to standard care produced a higher remission rate of depression relative to standard care alone at post-treatment one-week and at 12-month follow-up (24.2% vs. 6.1%, p = 0.039).

Conclusions: A brief integrated sleep-focused treatment is effective in improving both depression and comorbid sleep symptoms as evidenced by a higher remission rate and a better clinical outcome. Our findings underscore the need for providing integrated sleep-focused therapy in the clinical management of treatment-resistant depression and comorbid sleep symptoms.

Project Number: 10110341

P46-0130

Internet-based Mindfulness Programme for the Promotion of Public Mental Health: Randomised Controlled Trial

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Background: Access to mental health services is often restricted to face-to-face settings. The high penetration of the Internet offers a unique avenue for mental health promotion. In recent decades, mindfulness training has demonstrated to be efficacious in treating physical and psychological conditions. However, delivering mindfulness virtually is nascent, with preliminary studies showing its potential and effectiveness.

Aims and Objectives: Our aim is to examine the effectiveness of Internet-based mindfulness training (iMIND) in comparison with the well-supported Internet-based cognitive-behavioural training (iCBT) in promoting well-being. The mechanism of change in well-being through mindfulness skills cultivated in iMIND was also examined.

Study Design and Methods: This study was a two-arm, randomised, open-label, positive-control trial comparing iMIND with iCBT. Our study target population was college students and young working adults. Individuals who were aged 18 or above, able to understand Chinese, computer literate, and had consistent access to the Internet were eligible for the study. The sample included 1,255 participants who were randomised and had completed a pre-survey. Participants in the iMIND (n=604) and the iCBT (n=651) received eight sessions with information and exercises related to mindfulness practice and cognitive-behavioural principles, respectively. Randomisation was computer-generated. Primary outcomes included indicators of mental and physical well-being assessed at pre-programme, post-programme, and 3-month follow-up.

Results: Among the 1,255 study participants, 213 and 127 completed the post- and 3-month follow-up assessment, respectively. Missing data were treated using multiple imputation. Both iMIND and iCBT were effective in improving mental (Fs > 5.46, ps<.008) and physical well-being (Fs>8.76, ps<.001), except pain. The hypothesis that iMIND increased well-being through enhancing mindfulness skills was not supported.

Conclusion and Implications: Internet-based mental health programmes showed potential in improving well-being. The high attrition rate in the present study suggests the need for refinement in future technology-based psychological programmes. Mental health professionals need to team up with experts in information technology to increase personalisation of online interventions to enhance adherence.

Project Number: 09100711

P47-0143

Vocational And Clinical Outcomes of Integrated Supported Employment (ISE) Plus Cognitive Remediation Training (CRT) for People with Schizophrenia

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Introduction and Project Objectives: Previous studies have separately shown the benefits of cognitive remediation training (CRT) and Integrated Supported Employment (ISE) on the employment of individuals with severe mental illness (SMI). The present study aims to investigate the synergistic effects CRT on ISE which blends individual placement support service with work-related social skills training for Chinese people suffering from schizophrenia or schizoaffective disorder.

Method: The present study was conducted among 90 participants with schizophrenia or schizoaffective disorders. The participants were recruited from two psychiatric outpatient services in Hong Kong under the network of United Christian Hospital and randomly assigned to either the ISE + CRT group (n= 45) or the ISE group (n= 45). Blinded assessments on vocational, clinical, psychological, and neurocognitive outcomes were conducted by independent assessors. The two groups were followed up at 7 and 11 months.

Results: Participants of both the ISE + CRT and the ISE groups showed improvements in vocational, clinical, psychological, and neurocognitive outcomes based on the assessment immediately after the interventions and at 7 and 11month follow-ups. While no significant group differences were found, significant positive trends over time in vocational, clinical and cognitive outcomes consistently favored the ISE + CRT condition.

Conclusion: Both ISE + CRT and ISE programs demonstrated effectiveness in improving vocational, clinical, psychological, and neurocognitive outcomes, but the present study did not support that cognitive remediation facilitated further improvement in these domains beyond gains associated with ISE alone. It is important to understand which individuals experience a maximal benefit from the specific rehabilitation program components. Hence, further investigation is needed to fully exploit the synergistic potential of ISE combined with CRT.

Project Number: 08091201

P48-0041

Treatment Resistance Following the First-episode Schizophrenia-spectrum Disorder: A Retrospective Case-control Study

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Introduction: Studies have suggested 20-30% of patients with schizophrenia do not respond to antipsychotic medication are considered as treatment-resistant (TR) with poorer functional and clinical outcomes. Identifying predictive factors associate with the development of treatment-resistant schizophrenia is a crucial step in evaluating the possible underlying mechanism. The main challenge of studying prospectively is that the median duration of developing of TRS is 10 years.

Objectives: This is a retrospective case-control study aim to determine the prevalence and patterns of treatment-resistant schizophrenia following the initial onset and explore the predictive factors associating with the development of treatment resistance using a large cohort of first-episode psychosis patients with more than 10 years of illness duration.

Methods: Eligible TR patients and non-TR patient controls were identified from a cohort of first-episode psychosis patients (N=1400) presented to the territory-wide psychiatric service between Jan-1998 until Aug-2003. A detailed screening of clozapine history of all patients was conducted using Clinical Management System (CMS) of Hospital Authority and clinical records. Control group was identified randomly from this cohort matched with the diagnosis of patients with clozapine in a 1:2 ratios. Operational definitions were used to confirm the treatment-resistant status with and without clozapine. Information was obtained from both face-to-face interview and clinical notes review for the whole duration of the illness.

Results: There were 160 patients who have ever been prescribed with clozapine, 146 patients were considered as TR group, 19 were TR group without clozapine and 290 were Non-TR control group. The weighted prevalence of TR schizophrenia was 13.1%. The average delay of clozapine prescription was 7.56 months. The model with age of onset, years of education, the number of relapse in the first three years, duration of the first episode, CGIp at the end of the first month, substance abuse history and PAS adult significantly predicted TR status ($p<0.0001$). The model accounted up to 21.4% of the variance of TR. The model with same variables was significant in predicting the time to TR ($p=<0.0001$).

Conclusion: The delay in clozapine prescription suggesting the importance on strengthening the clinical intervention guideline of treatment-resistant schizophrenia. The results of regression model supported that both neurodevelopmental and early treatment outcomes might be related to the development of TR status. The importance of early treatment outcomes including the number of relapse and duration of the first episode indicated the specific importance of clinical care during the first episode psychosis.

Project Number: 11121721

P49-0043

Psychotic-like Experience (PLEs) in the General Population of Hong Kong: A Two-year Prospective Follow Up Study

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Introduction: Psychotic disorders have a prevalence of 3% with a major global burden to society. It has been argued that psychiatric morbidity in a population may be seen as a shift of a continuous phenotype to a higher value. Although the existence of subclinical psychotic-like experiences (PLEs) in the general population and the phenotypic continuum of psychosis have been widely studied, few were in the Chinese population and few studied the longitudinal outcomes of PLEs.

Objectives: This prospective case-control study of individuals with PLEs identified through the first local population-based epidemiological study, Hong Kong Mental Morbidity Survey 2010 (HKMMS) aim to identify the 2-year trajectories of PLEs, explore the associated environmental factors of the outcomes of PLEs and compare the neurocognitive functions of individuals with persistent PLEs and normal controls.

Methods: PLEs was assessed with Psychosis Screening Questionnaire (PSQ). Positive PLEs was defined as endorse of one or more items on PSQ. 174 subjects (3.04%) fulfilled the inclusion criteria as PLEs positive. Control subjects were identified from the HKMMS sample without a history of psychotic disorder and were negative for PLEs with 1:1 matched on the age, gender and years of education of the PLEs subjects. Face-to-face interviews were conducted for eligible subjects. Information including basic demographics, environmental factors, psychiatric symptoms, neurocognitive tests and PLEs were assessed.

Results: Among the successfully interviewed (70.69%), 58 subjects (47.2%) had persistent PLEs (pPLE) defined as endorsed one or more items of the PSQ; one had prodrome (0.8%) and one was diagnosed to have psychosis (0.8%). Among the successfully interviewed control subjects, four (3.25%) were identified as PLE positive. The regression model was statistically significant ($p=0.001$) in explaining 22.09% of the variance in pPLEs. Gender ($p=0.03$) and religious belief ($p=0.01$) were significant predictors. At follow-up, the pPLE group had significantly poorer quality of life, more physical complaints and psychiatric symptoms. PLE groups had poorer cognitive functions than the Controls.

Conclusions: This is the first study reporting the trajectories of PLEs in non-help-seeking Chinese population in Hong Kong. Subjects with PLEs were found to have poorer social support, social functioning, and quality of life, more stressful life events, more psychiatric symptoms, higher suicidality, more physical symptoms, more family history of psychiatric disorders and impairment of cognitive functions. This suggested that PLEs could be a transdiagnostic symptom groups indicated more severe functioning impairment and psychiatric morbidity with the persistent of PLEs reflected the severity of the psychiatric morbidity.

Project Number: 11121531

P50-0146

Barriers and Enablers of Help-Seeking among the Psychologically Distressed in Primary Care Setting of Hong Kong

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Introduction and Project Objectives: Most of the previous studies on help seeking for psychological distress were derived from Western countries. This project investigated the barriers and enablers to help-seeking for psychological distress among Chinese primary care attenders in Hong Kong.

Methods: Nine focus groups and 6 individual interviews were conducted among Chinese primary care attenders with/without known distress, patients' significant others and the general public. The identified barriers and enablers were investigated in a questionnaire survey with data from 1626 primary care attenders (response rate of 72.3%) recruited from 13 private clinics and 6 public clinics.

Results: Worries about side effects of drugs (79.9%) and drug

dependency (74.7%) were rated as the top barriers in the survey. Qualitative interviews found both worries and actual experience of the side effects of drugs, which weakened patients' trust in the treatment. Factor analysis on all barrier items suggested three factors: 1) worries of treatment, 2) uncertainties on primary care doctors' capacity, 3) public's limited knowledge on distress and sources of help. Distress level, education level and age were associated with factor 1, whereas distress level and healthcare setting were associated with the other two factors. Qualitative interviews revealed that not having a regular primary care doctor in the public setting discouraged disclosure of psychological problems. The top five enablers perceived by the survey respondents who had ever sought professional help for distress (n= 231) were crisis caused by distress (94.2%), distress affecting daily life (92.9%), wanting to treat associated physical symptoms (90.6%), having trust in doctor (90.1%) and encouragement by family/friends to seek help (88.3%). Qualitative interviews found that the patients often somatised their psychological problems. Family members were highly involved in help seeking whereas the doctors were the authoritative figures to convince the patients for treatment.

Conclusions: Relevant public education in a Chinese context should target at reducing patients' worries of drug treatment and strengthening the image of primary care doctors as a feasible source of help. In line with Western findings, crisis and interference in daily life due to distress are the top enablers of Chinese patients in Hong Kong to seeking help. Other three key enablers including treating psychosomatic symptoms, doctors' authority and strong family involvement are likely to be influenced by Chinese culture.

Project Number: 10111371

P51-0049

A Randomized, Controlled Clinical Trial: The Effects of Mindfulness-Based Cognitive Therapy on Chronic Insomnia among Chinese Patients in the Community

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Background: Mindfulness-Based Cognitive Therapy (MBCT) is a potential treatment for chronic insomnia. We evaluated the efficacy of MBCT for insomnia (MBCT-I) by comparing it with a sleep psycho-education with exercise control group (PEEC).

Methods: Adults with chronic primary insomnia (n = 216) were randomly allocated to MBCT-I or PEEC group. The MBCT-I included mindfulness and psycho-education with cognitive and behavioural components under cognitive behavioural therapy for insomnia (CBT-I). PEEC included psycho-education of sleep hygiene and stimulus control, and exercises. Any change in insomnia severity was measured by the Insomnia Severity Index (ISI). Secondary outcomes included sleep parameters measured by sleep diary, health service utilisation, absence from work and mindfulness measured by the Five Facet Mindfulness Questionnaire (FFMQ).

Results: The ISI score significantly decreased in the MBCT-I group compared with the PEEC group at 2 months (i.e. post intervention) (p = 0.023, effect size (95% confidence interval) = -0.360 (-0.675, -0.046)) but not at 5 or 8 months. Treatment response rates and remission rates based on the ISI cut-off scores were not significantly different between groups. Wake time after sleep onset (WASO) was less in the MBCT-I group at 2 and 5 months. At 8 months, both groups showed a reduced ISI score, sleep onset latency and WASO and increased sleep efficiency and total sleep time, however, no group differences were seen. Other outcome measures did not significantly improve in either group.

Conclusions: Long-term benefits were not seen in MBCT-I when compared with PEEC, although short-term benefits were seen.

Project Number: 09100611

P52-0062

Experience of Post-discharge Community Life of Patients with Mental Illness from the Integrated Community Centre for Mental Wellness (ICCMW): A Qualitative Exploration

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Introduction and Project Objectives: A literature review of findings by different research methods for integrated community mental health service (ICMHS) indicated a lack of clear and deeper understanding regarding the process, outcomes, and experience of patients after the multi-disciplinary teamwork of ICMHS, e.g. the Integrated Community Centre for Mental Wellness (ICCMW). The aim of this study was to explore patient's experience of community life after discharge from this type of service. The objectives are

1. to investigate, from the perspectives of patients, staff and their family members, the experience in quality of post-ICCMW community life of the patients after discharge from the ICCMW; and
2. to study patient's perceptions, after discharge, about the care and service they received from ICCMW.

Methods: The qualitative approach of interpretive description that founded on the naturalistic perspective of scientific inquiry was utilized for this study. Purposive sample for data collection through individual open-ended and semi-structured interviews were conducted with a total of 37 interviewees. These included 16 mental health patients discharged from an ICCMW and their respectively relevant family members, plus five staff members. Digitally recorded interviews were transcribed verbatim and analyzed with the conventional content analysis which was aided by NVivo.

Results: The findings indicate that patients discharged from ICCMW continue to walk their community life of recovery in which the presence of family members is requisite, and achieving better self-efficacy and self-management of care (main theme 'ambling with the illness'). Their social network is also expanded. For some patients and their family members, 'letting go' is essential for their walk of community life. Home visits of ICCMW staff are the most integral professional support that fits into the juncture when patients and their families demand the most of breaking through from being lack of more comprehensive help and withdrawal to community life (theme 'seizing the juncture'). Home visits are regular before patient discharge and may continue as necessary after patients are discharged from the ICCMW.

Conclusions: In addition to the current outcome-based and empirical studies, this study contributes to better and deeper understanding of the life of patients in community after ICMHS. The findings generate new and more comprehensive knowledge, and provide better insights, and clearer directions of service improvement for patient-centered care from the perspectives of patients, family members, and staff of the ICCMW.

Project Number: 12131631

P53-0088

Self-determination Theory-based Exercise Programmes for the Enhancement of Exercise Adherence and Well-being among People with Depression: Randomised Controlled Trial

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Background: Ample evidence shows the facilitation effects of physical exercise on mood and physical fitness among people with depression. However, the low retention and adherence rate in exercise programs remains a barrier to maximize the benefits of exercise intervention. Given intrinsic motivation plays a pivotal role in the extent to which individuals initiate and sustain their health-promoting behaviours, people with depression's motivation toward exercise needs to be effectively promoted.

Aims and Objectives: The present study used a randomised controlled trial design to test the efficacy of an exercise programme that is enhanced by principles of the self-determination theory (SDTE) in promoting intrinsic motivation, physical activity, mental well-being, and physical fitness among people with depression, compared with a standard exercise program (SE).

Study Design and Methods: One hundred and thirty-eight participants were randomly assigned to either conditions: (1) Self-Determination Theory-based Exercise (SDTE) programme and (2) standard exercise (SE) programme. All participants attended two 1-hour exercise sessions every week for 8 weeks. The SDTE provides an interpersonal climate promoting the fulfilment of psychological needs of autonomy, competence, and interpersonal relatedness, whereas the SE was not facilitative of psychological need support. We hypothesised that the SDTE, relative to the SE, can enhance greater intrinsic motivation and more physical activity, and thus promote better mental and physical health, than SE.

Results: Both SDTE and SE groups were found to be efficacious in improving intrinsic motivation, amount of vigorous physical activity, mental health (less depressive symptoms, more positive mental health, better quality of life), and some physical fitness parameters (level of resistance and flexibility) at post-intervention, and the effect was maintained at 3-month follow-up (except for intrinsic motivation and quality of life). However, no significant differences in actual number of steps walked, aerobic fitness, and body composition were found in both groups.

Conclusion and Implications: Engaging regularly in group-based physical exercise programme itself can facilitate people with depression's intrinsic motivation to exercise, engagement in more vigorous physical activity, and improvement in their mental health and physical fitness. Adjunct to formal medical and psychological interventions, people with depression should be encouraged to participate in regular exercises to engage in physical activity in their everyday lives, which is conducive to their intrinsic motivation and overall well-being.

Project Number: 11120951

P54-0097

Mobile Self-compassionate Programme For The Promotion Of Public Mental Health: Randomised Controlled Trial

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Introduction and Project Objectives: In the recent decade, self-compassion has garnered much evidence in its salutary effects on mental health, while smartphone and mobile technology has been increasingly applied in promoting and maintaining health in the general public. The present study adopted the increasingly popular means of smartphone and mobile technology to cultivate self-compassion and promote mental health in the young adult population. Using the randomised controlled trial design, the efficacy of a self-compassion programme in improving self-compassion, emotion regulation, mental health, and psychological distress among young adults, in comparison with a cognitive behavioural psychoeducation control was investigated.

Methods: The present study was a two-arm randomised controlled trial involving self-compassion (SCP) and cognitive behavioural psychoeducation (CBP). 1,543 participants were randomised into either one of the two conditions (SCP, N=748; CBP, N=795), followed by the pre-programme survey assessment. Throughout the 4-week, 28-session programme, participants spent 10 minutes daily in reviewing the course content and practicing various related exercises. Post-assessment and 3-month follow-up surveys were administered to measure changes over time.

Results: Both conditions were found to be efficacious in improving mental well-being, self-compassion, emotion regulation, and reducing psychological distress. No significant differences between groups regarding usage and users' satisfaction were found between the two conditions. High attrition rate was noted in both conditions.

Conclusion: Both self-compassion and cognitive behavioural psychoeducation mobile applications showed promising results in promoting mental health among young adults in Hong Kong. Future app-based psychological training programmes should consider gamification and personalisation of content or feedback to enhance engagement and mitigate the high attrition rate that are common in app-based health promotion programmes.

Project Number: 11121081

P55-0124

Poor Sleep Quality in Adolescence: A Pathway to Depressive Disorders through Inhibitory Control

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Objectives: Although sleep disturbances were found to be a prospective predictor of future depression, the underlying mechanisms have not been established. Given that restricted sleep and the physiology of sleep were associated with altered activation in the prefrontal cortex as well as impaired inhibitory control, we examined whether sleep disturbances relate to depressive disorders through its influence on reducing inhibitory control ability.

Methods and Materials: Participants (n=166, 17-24 years, 66% female) were followed longitudinally and completed the Structured clinical interview for DSM-IV disorders, Affective go/no-go task for inhibitory control ability, the Pittsburgh Sleep Quality Index, and wore an actigraph-watch for 7 days at baseline and at the follow-up assessment 12 months later. Structural equation modeling was used to determine whether poor sleep quality predicted depressive disorders and the mediating role of inhibitory control ability.

Results: Results from structural equation modeling showed that after adjusting for the effect of depressive disorders at the first assessment, poor sleep quality (PSQI>5) had a significant direct effect on the development of depressive disorders at follow-up, OR=4.60, estimate=1.54, standard error=.62, p=.019, and also indirectly predicted depressive disorders through lower inhibitory control ability, OR =1.14, estimate=1.14, standard error=.11, p=.038, and the model achieved good fit index, $\chi^2(4)=27.32$, p=.0006.

Conclusion: Both sleep problems and depressive disorders are prevalent among adolescents and young adults, whose prefrontal cortex is still in development. Here, we provide the empirical evidence that poor sleep is contributory to depressive disorders through its effects on inhibitory control ability. The present study highlights the importance of sleep health for the development of a strong inhibitory control ability and the prevention of depressive disorders in adolescence and young adulthood.

Acknowledgement: This study was funded by the Health and Medical Research Fund (#11122051), Food and Health Bureau, HKSAR

Project Number: 11122051

P56-0172

The Experience of Tobacco Use among Chinese Individuals with Schizophrenia in Community-based Residential Settings: A Qualitative Study

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Introduction: Although there is a high prevalence of smoking among individuals with schizophrenia, no previous attempt has been made to explore experiences of tobacco use and cessation within a Chinese sample of this population.

Methods: This paper reports the findings of a study with an interpretive description design based on individual and semi-structured interviews that explored the experiences of tobacco use and quitting in a sample Chinese population with schizophrenia. Twenty-three eligible participants were recruited from three community residential mental health service settings.

Findings: Four main themes representing the experiences of the participants were uncovered in this study: (1) smoking rationale; (2) environment and culture; (3) rationalization for smoking; and (4) beliefs about cessation methods. The findings indicated that the participants perceived many benefits to smoking. Although some thought of quitting at times, most gave up the idea or failed to quit due to a lack of cessation support. The data also provided important insights, namely, that the smokers believed that smoking brings a sense of freedom, relieves negative symptoms, and is a means of preventing a relapse of their illness. It also shed light on how they viewed the regulations and culture in hospitals and rehabilitation settings as facilitating or hampering their smoking behaviors.

Conclusions: The most notable finding concerns the use of avoidance coping by the participants, who relied on smoking to fulfill their need for comfort. Future smoking cessation treatments should address the internal barriers to quitting and the psychological needs of individuals with schizophrenia.

Project Number: 10111861

P57-0006

Prevention and Treatment of Gastrodia-Uncaria Water Extract Tolerated with Intravascular Administration of Recombinant Tissue Plasminogen Activator in Experimental Cerebral Ischemia

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Introduction and Project Objective: Stroke is the third cause of death in worldwide and also leads to disability. The recombinant tissue plasminogen activator (tPA) is the only approved drug to treat acute ischemic stroke. However, limited patients are received treatment due to its narrow therapeutic window and increase risk of hemorrhagic transformation. Gastrodia Rhizome (GE) and Uncaria Ramulus (UR) are the two main components in the Tianma-Guoteng decoction for stroke treatment in China. Thus, in this project, we aim to study neuroprotective effect of Gastrodia-Uncaria water extract (GUW) with or without tPA in pre- or post- onset of ischemia.

Methods: Embolus induced middle cerebral artery occlusion (MCAO) on rat model was applied to this study. Neurological deficits scoring, behavioral rearing test and brain infarct volume were assessed for the effect of GUW in focal cerebral ischemic rat. The efficacy of GUW and tPA and their drug interaction were evaluated via in vivo molecular imaging, histology, immunohistochemistry and gene expression.

Results: Pretreatment of GUW improved infarct volume of the brain and the motor behavior recovery significantly and maintained tissue integrity in histology. It also increased the efficacy of tPA treatment against embolic induced cerebral ischemia in terms of reduction of infarct volume and neurological deficit score and enhancement of motor behavior recovery. Interestingly, Pretreatment of GUW suppressed tPA induced MMP activity significantly. Additionally, GUW increased anti-oxidative enzyme catalase activity while tPA treatment did not involve regulation of anti-oxidative enzymes. Moreover, pretreatment of GUW induced gene expression of neutrophins BDNF, GDNF, NGF and MBP which involve neuroprotection and neuronal differentiation in recovery. However, tPA treatment inhibited gene expression of NGF and MBP.
Similar to GUW pretreament, post-stroke GUW treatment reduced brain infarct volume and improved the motor behavior recovery significantly. Furthermore, it enhanced efficacy of tPA against embolic induced cerebral ischemia and suppressed tPA induced MMP activity. Post-treatment of GUW upregulated gene expression of BDNF, GDNF, NGF and MBP is up-regulated and overcame downregulation of NGF and MBP induced by tPA.

Conclusion: Thus, our result demonstrated the preventive and treatment potential of GUW on transient (with tPA treatment) or permanent (without tPA) cerebral ischemia. It also showed intravascular administration of tPA is well tolerated with oral administration of Gastrodia-Uncaria water extract, and even reduced risk of tPA induced intracranial haemorrhage. It also shed light on integrative therapy of traditional Chinese medicine together with western drug.

Project Number: 11120381

P58-0013

Three Courses of Tianjiu Therapy in Sanfu Days for Chronic Asthma: A Clinic Efficacy Observation Trial

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Objective: This study was aimed to compare the efficacy among

chronic asthma patients who received 1 course treatment, 2 courses treatment and 3 courses treatment of Tianjiu Therapy in Sanfu Days.

Methods: Comparing efficiency with 3 courses of Tianjiu Therapy for asthma in 91 chronic asthma patients. For each course, patients received 3 times treatment, pretreatment assessment and posttreatment assessment.

Results: 91 asthma participants completed at least 3 courses of Tianjiu Therapy in Sanfu Days. (1) Days for asthma attacked, the frequency for asthma attacked and incidence of admitting to clinic (Integrated Chinese medicine & Western Medicine Clinic) when asthma attack during the last 12 months; times of admitting to clinic; times of solving by persistent medicine and times of solving by own medicine when asthma attack during the last 12 months; and symptoms associated with Chinese medicine of waking by asthma symptoms, lack of strength, lassitude, rapid or difficult breathing were improved at the 1st course, the 2nd course and the 3rd course compared with baseline (All P<0.05); (2) the incidence of admitting to In-patient Hospital and solving by persistent prescription when asthma attacked; the frequency of Chinese Herbal Medicine used during Tianjiu Therapy; the status of asthma under controlled and no improved by self-evaluation were similarly improved at the 2nd course and the 3rd course (All P<0.05);(3) incidence of admitting to A&E for asthma attacked during the last 12 months, and other treatments except Western Medicine, Chinese Herbal Medicine, and Acupuncture & Moxibution during the last 12 months were improvement at the 3rd course (All P<0.05);(4) symptoms associated with Chinese medicine of spontaneous sweating and reduction of exercise were improved at the 1st course (P<0.05); (5) symptom of diarrhea after intake of oil food was became a little bad at the 2nd course and the 3rd course (P<0.05); (6) The frequency of bronchodilator used when asthma attack was reduced in the 1st course and the 2nd course (All P<0.05); (7) Lung function of FEV1 and FEV1/FVC(×100) were a little improvement, but have no significant statistical difference (P>0.05); (8)The total score of ACT at all 3 courses did not improved significantly (All P>0.05).

Conclusion: After Tianjiu Therapy in Sanfu Days participants have achieved good efficiency, and as the course get longer, the efficiency of more symptoms associated with chronic asthma were improved. Suggest patients with chronic asthma continuous receive Tianjiu Therapy in Sanfu Days which will be a feasible treatment.

Project Number: 12133081

P59-0014

Investigation of the Potential Herb-Drug Interactions between Danggui Buxue Tang Decoction and Selective Estrogen Receptor Modulators (Tamoxifen and Raloxifene) Using Established Preclinical Model

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Introduction and Project Objectives: Hormone Replacement Therapy (HRT) has been regarded as the gold standard method for management of postmenopausal symptoms. However, due to the increased risk of reproductive cancer and stroke related to treatment with estrogen, postmenopausal women turn to alternative approach for help. The increasing use of phytoestrogen containing herbal medicine as an alternative to HRT amongst postmenopausal women has aroused the concerns about their safety and the potential interactions with prescription drugs such as selective estrogen receptor modulators (SERMs, e.g. tamoxifen and raloxifene) as many of their effects are mediated by the same estrogen receptors (ERs). Danggui Buxue Tang (DBT) decoction is a commonly prescribed herbal treatment for women in China that is known to contain phytoestrogens. The present study was designed to characterize the estrogenic effects of DBT and its interaction with SERMs on estrogen sensitive tissues.

Methods: Four estrogen sensitive tissues including uterus, breast, brain and bone in both in vivo (mature ovariectomized (OVX) rats) and in vitro models (estrogen sensitive cell lines) were chosen to investigate the estrogenic effects of DBT and its interactions with tamoxifen and raloxifene. Specific estrogen responsive parameters for each tissue were measured.

Results: DBT significantly alleviated estrogen deficiency induced changes in bone, brain and breast without stimulating uterus growth in OVX rats. Moreover, DBT did not significantly alter the actions of SERMs in estrogen sensitive tissues nor induce pathological changes at major organs alone or in combination with SERMs in OVX rats. DBT exerted direct estrogenic effects in the estrogen sensitive cells. Crude DBT at high concentrations, but not metabolized DBT, appeared to enhance or weaken the effects of SERMs in estrogen sensitive cells. However, such concentrations are too high to be achieved in vivo.

Conclusions: DBT exerted estrogenic effects in tissue-selective manner without observable pathological changes in major organs and did not significantly alter the estrogenic actions of SERMs in OVX rats.

Project Number: 11122111

P60-0025

Evaluation of Potential Herb-drug Interactions between Oseltamivir and Commonly Used Anti-influenza Chinese Medicinal Herbs

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Oseltamivir (O) is a potent and selective inhibitor of the neuraminidases glycoprotein. Our preliminary studies suggested that co-administration of YinQiaoSan and SangJuYin with O in rats would inhibit the transformation of O to oseltamivir acid (OA). To clarify if such herb-drug interactions are prevalent between O and commonly used anti-influenza Chinese medicinal herbs, eight herbs and ten marker components from these eight herbs are selected for the screening of potential herb-drug interactions in rats. To screen potential inhibition of herbs/herbal components on O hydrolysis, O was incubated with herbs/herbal components in diluted rat plasma, microsomes and human recombinant carboxylesterase 1 (hCE1) under optimized conditions. MDCK-WT and MDCK-MDR1 cell lines were utilized to identify potential modification of herbs/herbal components on P-gp mediated transport of O. Caco-2 cell monolayer model was used to study the effect of herbs/herbal components on the uptake of O via PEPT1. Modification on OAT3 mediated transport by herbs/herbal components was verified by the uptake of O in HEK293-MOCK/HEK293-OAT3 cells. Our results demonstrated that Fructus Forsythiae and Fructus Arctii could extensively inhibit the hydrolysis of O (>97%). Herbal components including Baicalein, Wogonin and Arctiin also showed significant inhibition on the hydrolysis of O (>50%). In addition, Epigoitrin showed strong inhibition of O hydrolysis in rat liver microsomes and hCE1. Our developed in vitro screening model for transport of O indicated that i) Baicalein, Glycyrrhizic acid and Radix et Rhizoma Glycyrrhizae could inhibit the P-gp mediated efflux of O; ii) no OAT3-mediated transport and limited uptake through PEPT1 transporter were observed for O. Anti-virus effects were evaluated using plaque reduction assay for H1N1 and H3N2 viruses, which found no significant inhibition on the

virus plaque reduction of O by the studied herbal components. Potential in vivo pharmacokinetic and pharmacodynamic interaction between O and the selected herb of Radix Scutellariae (RS) with the most potent impact on the absorption and metabolism of O were carried out in rats. It was found that RS could only inhibit the hydrolysis of O with no influence on its overall anti-virus effects. In summary, the selected commonly used anti-influenza herbs and their marker components could cause potential pharmacokinetic but not pharmacodynamic herb-drug interactions. Further in vivo evaluation on human is warranted for its potential clinical impact.

Project Number: 11120451

P61-0026

Is It Safe to Take Danshen-Gegen Product with Warfarin and Aspirin? A Pilot Study in Human Subject

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Danshen-Gegen (DG) product, containing Salviae Miltiorrhizae Radix et Rhizoma and Puerariae Lobatae Radix, is a Compound Chinese Medicine targeting cardiovascular diseases (CVD). Warfarin and aspirin are commonly used drugs to prevent blood clots. In integrative medicine clinical practice, DG is co-administrated with warfarin or aspirin to reduce the risk of heart attack or stroke. Significantly decreased C_{max}, AUC_{0-t} and the prothrombin time of warfarin were observed in our preliminary animal study, indicating that the co-administration of DG with warfarin could cause significant pharmacokinetic (PK) and pharmacodynamics (PD) herb-drug interactions in rats. To further explore the interaction between DG and warfarin in clinical settings, we proposed the current study to examine whether such PK and PD interaction would happen in healthy male subjects. A multiple dose (5 days), five-session design has been performed, in which 14 healthy subjects received aspirin alone (100 mg once daily for 5 days), DG alone (750 mg twice daily for 5 day), aspirin in combination with DG product, warfarin alone (1 mg once daily for 5 days) and warfarin in combination with DG, respectively. There is a washout period of 2 weeks between sessions. During the combination treatment with DG and aspirin/warfarin, DG was given 2 h post that of aspirin/warfarin. Following first dosing on Day 5, plasma samples were collected at different time intervals till 12 hours (aspirin)/168 hours (warfarin). For the pharmacodynamics measurement, whole blood of each subject was collected at 30 min after DG dosing or at 2.5h after aspirin/warfarin dosing for monitoring of the platelet function and soluble Thrombomodulin (sTM) concentrations. Based on the observed AUC_{0-t} and C_{max} and T_{max} of the studied compounds, DG could moderately increase AUC0-t of aspirin and decrease AUC0-t of 7-hydroxyl warfarin with no impact on that of salicylic acid and warfarin's systemic exposure; Warfarin (rather than aspirin) could greatly increase the systemic exposure of Danshensu, the marker compound of DG; Co-administration of aspirin/warfarin with DG had synergistic effect on TXB2 inhibition by aspirin and offset enhanced sTM by warfarin. Our study indicated that co-administration of DG with aspirin/warfarin could cause potential pharmacokinetic and pharmacodynamic herb–drug interactions in healthy human subjects with no higher risk of bleeding.

Project Number: 10110131

P62-0038

Ginsenoside-Rb1 as an Anti-Cancer Therapeutics in Targeting Wnt/b-catenin and ATP-Binding Cassette G2/P-Glycoprotein Signaling

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Chemotherapy is a major treatment for cancers, but the common recurrence is still the leading cause for its high mortality. Recently, cancer stem/tumor-initiating cells (CSCs), albeit a minor population, have been reported to possess the self-renewal, differentiation, and drug resistance properties that lead to tumorigenesis and chemoresistance. Moreover, this subpopulation is not eliminated by conventional chemotherapy due to distinct molecular signatures. Thus, understanding CSCs biology and targeting CSCs will be a promising approach for therapeutic interventions. Ginsenoside-Rb1, isolated from Panax ginseng, is a notable saponin which is a nonpeptide small molecule that has been shown to exhibit potent cytotoxic effects as chemotherapeutics. Here we show for the first time that ginsenoside-Rb1 and its metabolite compound K exhibit potent cytotoxicity on CSCs and could effectively suppress CSC self-renewal without regrowth. Rb1 and compound K treatment also sensitized the CSCs to clinically relevant doses of the front-line chemotherapeutic agents cisplatin and paclitaxel, suggesting a potential avenue to improve the clinical efficacy. Moreover, we did not observe adverse toxicity to the liver, heart, and kidney. In search of the underlying mechanisms, we found that Rb1 and compound K activated Wnt/b-catenin and ATP-binding cassette G2/P-glycoprotein signaling, a key cancer-associated pathway in this process. These results suggest that Rb1 and compound K should be further exploited as an anti-cancer therapeutics.

Project Number: 11121191

P63-0039

A Double-blind, Randomized, Two-dose Trial of Tumor-shrinking Decoction (TSD), a Chinese Medicine Preparation in Patients with Symptomatic Uterine Fibroids

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Uterine fibroids (UFs) are the most common benign tumors in females in the middle and later reproductive ages
On the basis of empirical evidence and clinical practice, a formula called Tumor-shrinking Decoction (TSD) was developed for the treatment of UFs.

Methods: A total of 78 subjects with symptomatic UFs were recruited. During the study, the subjects received either low or high dose daily TSD for 16 weeks.

The size of the tumor peripheral blood biochemical profile assessed with the clinical instruments, pelvic imaging (MRI) and biochemical analysis, at baseline and end point for the efficacy and safety evaluation.
To ensure the quality of the herbs in TSD, the quality analysis fingerprinting, i.e. (UPLC) and (HPLC) were established for quality tracking.

Results: Of the 78 randomized subjects, 5 patients dropped out. The dropout rate is 6.4%. For the primary outcome, showed that there was no significant difference between two groups in UFS-QoL derived

symptom severity and HRQL score, PBAC and pelvic pain scores (all P> 0.05).

Subjects in Low-dose group had significantly higher reduction of TCM syndrome score at end-point than those in High-dose group (P<0.01). The difference between Low-dose group and High-dose group in reducing TCM syndrome remained significant after adjusted for the covariates of age, duration of illness and co-medication.

Therefore, High-dose group was not more efficacious than Low-dose group in reducing UFS symptoms, blood loss, pelvic pain and improving related quality of life across study time points. But both High-dose and Low-dose group showed thereduction in the fibroids size.

On the safety front, all the tested samples fulfilled the Hong Kong Chinese Materia Medica Standards.

Conclusions: There was no significant difference observed between the high- and low- doses of the herbal formula. But both could improve the UFs-related symptoms and reducing the fibroid size among the patients.

The within-group analysis showed that there was significant difference observed between end point to the baseline in the UFS symptom-related outcomes that the strongest effect was on pelvic pain, followed by UFS-QoL derived symptom severity, PBAC and UFS-QoL derived quality of life.

Herbs in daily-base clinic practice seems to be safe, and no heavy metal and pesticides were detected outside normal range.The result of quality control tests also showed the quality of TSD was verified, stable and safe. Further investigations of the Chinese medicine in treating uterine fibroids can be considered.

Project Number: 11121841

P64-0057

Investigation of the Protective Effects of Herba Cistanche on Statin-Induced Muscle Toxicity

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Statins, commonly prescribed to hypercholesterolemic patients to control cholesterol production, are well known to cause myotoxicity in some patients. Herba Cistanches (HC) is a Chinese herb traditionally used for muscle problems. We recently demonstrated that HC aqueous extract (HCE) could dose-dependently reduce simvastatin-induced muscle toxicity via the caspase 3 pathway, and preventing simvastatin-induced reduction in ATP production in vitro1. The aims of the present in vivo study were to determine whether the combination use of simvastatin with HCE could reduce the muscle toxicity caused by simvastatin, and exert synergistic effects on reducing high-fat diet-induced hypercholesterolemia and elevated liver cholesterol. This study also investigated whether such beneficial effects were due to the chemical marker verbascoside in HCE.

The effect of HCE on simvastatin-induced muscle toxicity was investigated using simvastatin-induced Sprague Dawley rats, which were treated with 640 mg/kg simvastatin and/or HCE (1.1 or 2.2 g/kg) or verbascoside (0.94 or 1.87 mg/kg) for 4 weeks. Blood and muscle were collected for assessment of creatine kinase (CK) activity, reactive oxidant species production, mitochondrial membrane permeability transition and muscle inflammation. The effect of the combined use of HCE and simvastatin on diet-induced metabolic syndrome was determined using high-fat diet-induced C57Bl/6 mice. Mice fed with high-fat diet for 8 weeks were then treated for another 8 weeks with simvastatin (50 mg/kg), or HCE (4.4 g/kg), or verbascoside (3.74 mg/kg) or a combination of HCE (4.4 g/kg) and reduced dose of simvastatin (25 mg/kg). Plasma lipid and insulin levels, liver size and liver lipid levels, as well as adipose tissues weight were determined.

Our results demonstrated that HCE in simvastatin-treated rats could restore muscle weights, reduce simvastatin-induced elevated plasma CK, improve muscle glutathione levels, restore muscle mitochondrial membrane permeability potential, and reduce muscle inflammation, thereby confirming that HCE could prevent simvastatin-induced muscle toxicity *in vivo*, which could partly due to verbascoside. In addition, our results showed that HCE could reduce liver weight, total liver lipid levels, and plasma lipid and insulin levels in mice with diet-induced obesity.

In conclusion, our *in vivo* results provided evidence for the first time that HCE not only has a potential protective effect on simvastatin-induced muscle toxicity, but also exhibited beneficial effect on diet-induced non-alcoholic fatty liver and hyperlipidemia when being used alone or in combination with simvastatin.

Reference: Wat E, ..., Lau CBS (2016). The protective effect of Herba Cistanches on statin-induced myotoxicity *in vitro*. Journal of Ethnopharmacology 190, 68-73.

Project Number: 11120831

P65-0063

Investigation of the Combined Use of Andrographis paniculata and Chemotherapeutics in the Treatment of Metastatic Esophageal Cancer – A Pre-clinical Study

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The incidence and mortality of esophageal cancer (EC) are high in China and eastern Asia, with poor prognosis even after surgical treatment. Cancer metastasis may account for the high postoperative recurrence rate. Adjuvant chemotherapy, radiotherapy or chemoradiotherapy following surgery improved survival but accompanied with side-effects. Alternative adjuvant treatments for metastatic esophageal cancer, such as Chinese herbal medicines, provide another choice for the patients. The water extract of well-known anti-cancer herb Andrographis paniculata (AP) was shown to exhibit anti-tumor and anti-metastatic activities in human esophageal cancer cell-based and animal models in our previous studies.

The present study aimed to further validate the anti-tumor and anti-metastatic activities of AP water extract (APW) combined with EC chemotherapeutics (cisplatin and 5-fluorouracil) in esophageal cancer metastatic mouse models. Besides, the immunomodulatory effect of APW and the gastrointestinal absorption characteristics of APW were also determined.

Intraperitoneal and subcutaneous esophageal tumor xenograft-bearing nude mice models were employed to evaluate the in vivo anti-tumor and anti-metastatic activities of APW alone or in combination with chemotherapeutics. The immunomodulation were studied in

carcinogen-induced esophageal carcinogenesis immune competent C57BL/6 mice. The effects of the absorbed AP components through Caco-2 monolayers were evaluated in human esophageal cancer cells (EC-109) using proliferative assays, migration assays, etc.

Results from intraperitoneal xenograft-bearing mouse model showed that APW alone and combined with chemotherapeutics (cisplatin plus 5-fluorouracil) exhibited anti-tumor and anti-metastatic activities, which may also be responsible for the prolongation of survival of mice. Besides, the combined APW with chemotherapeutics treatment induced apoptosis, exerted anti-proliferative and anti-angiogenic effects in subcutaneous xenografts. In the immune competent mice, combined treatment increased cytotoxic T-lymphocytes and decreased regulatory T cells population. In addition, combined treatments modulated the productions of TNF-alpha, IL-10 and IL-12 by spleen lymphocytes of mice. The components transported through the Caco-2 monolayer (including five diterpenes and two flavonoids) were shown to possess anti-migratory effects on esophageal EC-109 cancer cells.

In conclusion, the present study demonstrated the anti-metastatic effect of APW plus chemotherapeutics (cisplatin & 5-fluorouracil) in metastatic esophageal mouse models. The additional benefits (enhanced anti-tumor effect) of APW plus chemotherapeutics were shown in xenograft-bearing nude mice and immune competent mice. Hence, the adjuvant value of APW in metastatic EC treatment has been confirmed in this preclinical study, and such evidences will support the clinical use of APW alone or in combination with chemotherapeutics in the management of metastatic esophageal cancer.

Project Number: 11120981

P66-0087

Improving Darifenacin-associated Gastrointestinal Adverse Effects by Isoflavone-rich Chinese Herbal Supplements in the Treatment of Detrusor Overactivity

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Aim: The aim of this study was to prove the in vivo efficacy of Gegen on improving detrusor overactivity and its possible synergism with darifenacin (a first-line muscarinic receptor-3 inhibitor) in spontaneously hypertensive rats (SHR), a rat model exhibiting symptoms of detrusor overactivity.

Method: After daily oral administration of Gegen 30 (Gegen, 30 mg/kg); Gegen 300 (Gegen, 300 mg/kg); Low_Dar (darifenacin, 3 mg/kg); High_Dar (darifenacin, 30 mg/kg) Low_Dar+Gegen 30 or High_Dar+Gegen 30 for 3 weeks, bladder detrusor strips of the rats were isolated and assessed with different stimulators for the measurement of tonic and phasic contractile activities (including phasic amplitude and frequency). Modes of stimulation included the use of carbachol, isoprenaline and electrical field stimulation (EFS).

Results: All drug treatments significantly reduced carbachol-stimulated tonic contractile activities, but did not change the phasic amplitude. Meanwhile, the treatments with Gegen 300; Low_Dar; Low_Dar+Gegen 30; and High_Dar+Gegen 30 decreased carbachol-stimulated phasic frequency. Gegen 300 and Low_Dar+Gegen 30 showed stronger potency on lowering EFS-induced responses. Under isoprenaline-induced relaxation, only Gegen 300 significantly enhanced this relaxation by decreasing tonic contraction; Gegen 300; Low_Dar; Low_Dar+Gegen 30; and High_Dar+Gegen 30 increased the reduction of phasic frequency, but all treatment did not alter their phasic amplitude. Combination Index (CI) showed that the combination with Low_Dar and Gegen 30 had very strong synergism (CI < 0.1) on inhibiting EFS-induced contractile response.

Conclusion: Gegen improved detrusor overactivity through neurogenic and anti-muscarinic mechanisms. Gegen and darifenacin together attained synergism for detrusor overactivity treatment via the neurogenic pathway.

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Project Number: 10110411

P67-0090

Protective Effects of the Flavonoid Genistein on the Inflammatory Responses to Cigarette Smoke and Bacterial Lipopolysaccharide in the Airway

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Introduction and Objectives: Chronic obstructive pulmonary disease (COPD) is characterized by chronic airway inflammation and oxidative stress. Exacerbations of the condition occur with bacterial infection, leading to increased mortality and morbidity. The present study examined whether or not genistein, a flavonoid found in the soy diet, is effective in reducing the inflammatory responses caused by cigarette smoke (a major risk factor for COPD), without or with concomitant presence of lipopolysaccharide (LPS, an endotoxin commonly found in Gram-negative bacteria).

Methods: Human bronchial epithelial BEAS-2B cells were incubated with medium containing cigarette smoke (CSM, 4%), without or with LPS [10^{-5} g/ml; to mimic bacterial infection], and in the absence or presence of genistein (10^{-6} M). The cells were also incubated with inhibitors or activators of adenylyl cyclase, phosphodiesterase (PDE) and protein kinase A (PKA). The levels of the inflammatory mediator interleukin (IL)-8 and the oxidative stress markers [8-isoprostane and malondialdehyde (MDA)] were measured, and the activities of antioxidant enzymes [superoxide dismutase (SOD), catalase and glutathione peroxidase] and PKA were determined with enzyme-linked immunosorbent assay (ELISA) or biochemical assays.

Male Sprague Dawley rats (8 weeks old) were given genistein (10^{-5} g/kg) or its vehicle once daily by gavage and exposed to cigarette smoke (4%) or sham air one hour per day for 8 weeks, without or with intratracheal injection of LPS ($2x10^{-4}$ g/kg, by microsprayer on day 29 and day 43). The degree of oxidative stress and inflammatory status in the lungs were examined.

Results: CSM, alone or in combination with LPS, increased IL-8 release. The increases were associated with increased levels of 8-isoprostane and MDA and reduced activities of SOD and catalase. These effects of CSM, without or with LPS, were inhibited by genistein, and by PDE4 inhibitor (rolipram) and PKA activators (8-bromo-cAMPS and 6-bnz-bromo-cAMPS). Genistein increased cyclic adenosine monophosphate (cAMP) level and PKA activity in BEAS-2B cells.

In rats exposed to cigarette smoke, without or with airway LPS exposure, the levels of CINC-1 (equivalent to human IL-8), IL-6 and monocyte-chemotactic protein-1 (MCP-1) in the bronchoalveolar lavage fluid, and of MDA in lung tissues were increased; these increases were reduced in rats treated with genistein.

Conclusions: Genistein produces anti-inflammatory effects in bronchial epithelial cells and in the airway of rats against cigarette smoke

challenge, alone or with LPS exposure. The anti-inflammatory effects of the flavonoid are partly related to reduction of oxidative stress and partly mediated through activation of cAMP/PKA pathway.

Project Number: 11123011

P68-0093

A Study on Synergistic Bone Anabolic Effects of a Combination Use of Alendronate and Herba Epimedii in Treating Osteoporosis of Ovariactomized Rats

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Introduction and Project Objectives: Osteoporosis, a silent disease, is characterized by compromised bone strength predisposing to an increased risk of fractures. A study conducted in Hong Kong Chinese (Hong Kong Osteoporosis Study) reported that the overall incidence of hip fractures for women older than 65 years was 379 per 100,000 person-years. Nowadays, over 200 million people worldwide are affected by this crippling disease. With increasing life expectancy, the number of post-menopause-associated bone loss will escalate exponentially. Current therapeutic strategies using bisphosphonates e.g. Alendronate (the most potent FDA-approved bisphosphonate) are very effective at lowering the risk of spine and hip fractures. Unfortunately, FDA (2011) announced the incidents of a rare but serious problem (fracture of the thigh bone) after long-term uses of bisphosphonates. Herba Epimedii (Yinyanghuo) has been used for thousands of years in China. Oral consumption of Herba Epimedii extract enhances bone healing and reduces the incident of osteoporosis in animals and in human clinical trials without any side effects. In contrast to monotherapy, combination drug therapy utilizes more than one medications with which individual agent is given at the lowest possible therapeutic dosage with synergistic therapeutic outcomes resulted. In this study, we evaluated the synergistic bone anabolic properties of Alendronate plus Herba Epimedii combination to tackle post-menopausal osteoporosis.

Methods: Osteoblasts were harvested from sham and OVX rats, incubated with Alendronate (1 μM) and Herba Epimedii water extract (1 μg/ml), alone or in combination. OVX rats were administered (daily, 3 months) with Alendronate (0.03 μg/100g, s.c.), alone or in combination with Herba Epimedii water extract (oral gavage, 2 mg/100g).

Results: A generalized reduction of the expression of bone anabolic / transcription factors was detected in osteoblasts of OVX rats compared with sham, and Alendronate plus Herba Epimedii water extract elicited a concentration- and time-dependent increase of all bone anabolic biomarkers measured, with a greater magnitude of increase in OVX rats. Consumption of Alendronate plus Herba Epimedii water extract resulted in the restoration of reduced serum Ca2+ levels of OVX rats. Combined drugs consumption increased the failure load / stress and stiffness of femurs, and improved the micro-structure of the L-5 lumbar vertebra of OVX rats. An atrophic structure with a lower insulin expression was detected in sections of the pancreas of OVX rats which were reversed by combined drugs consumption.

Conclusions: Our results illustrate the bone anabolic effects of Alendronate plus Herba Epimedii water extract in treating oestrogen deficiency-associated osteoporosis.

Project Number: 10110371

P69-0112

Evaluation of the Chronic Toxicity of a Commonly Used Chinese Medicinal Herb Siegesbeckiae Herba

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Introduction and Project Objectives: Siegesbeckiae Herba (SH) is traditionally used for treating chronic diseases such as arthritis. It was first recorded as a low-toxicity herb in "Xin Xiu Ben Cao". To reduce its toxicity, SH is traditionally steamed with rice wine. Acute and sub-chronic toxicity studies showed that SH could induce lung toxicity in mice. However, up to now, the chronic toxicity data of this herb are not available. In this study, we aim to evaluate the chronic toxicities of SH and processed-SH (PSH) in rats, and to explore the underlying mechanisms of SH-induced toxicities and the toxicity-reducing effect of processing.

Methods: Rats were randomly divided into seven groups (n=20), and daily intragastrically administered with distilled water (control), SH [5.0 g/kg/day (group-1), 2.5 g/kg/day (group-2), 1.3 g/kg/day (group-3)] or PSH extracts [5.0 g/kg/day (group-4), 2.5 g/kg/day (group-5), 1.3 g/kg/day (group-6)] for 6 months, respectively. Body weights, clinical signs, urinalysis, hematological and biochemical parameters, histopathological observations and organ indices were compared among all groups. Metabolomics analysis of the most severely damaged organ was performed to identify the mechanisms of SH's toxicities and the toxicity-reducing effect of processing.

Results: Intragastric administration of SH resulted in significant body weight loss in rats. The mean leukocyte counts, neutrophil percentage, alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotrasferase (ALT), lactate dehydrogenase (LDH), and the lung and liver indices were significantly increased in SH group. Histopathological damages were observed in the lung and liver tissues of SH-treated rats, and the lung damages were more obvious. While, in PSH group these symptoms were alleviated. Metabolomics analyses showed that fourteen metabolites were significantly altered by the treatment of this herb.

Conclusions: We found that processing with rice wine significantly reduced the chronic toxicities of SH, which supported the traditional Chinese Medicine (TCM) theory "processing can reduce the toxicity of SH". Inhibition of β-catenin signaling might be one of the mechanisms for SH-induced lung toxicity, and free radical scavenging might be responsible for the toxicity-reducing effect of processing. This study provides a scientific justification for the traditional processing theory, and should guide rational and safe clinical applications of SH by helping in optimizing its processing procedure and clinical compatibility.

Project Number: 11122521

P70-0131

Electroacupuncture and Splinting versus Splinting Alone to Treat Carpal Tunnel Syndrome: a Randomized Controlled Trial

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Introduction and Project Objectives: The effectiveness of acupuncture for managing carpal tunnel syndrome is uncertain, particularly in patients already receiving conventional treatments (e.g., splinting). We aimed to assess the effects of electroacupuncture combined with splinting.

Methods: We conducted a randomized parallel-group assessor-blinded 2-arm trial on patients with clinically diagnosed primary carpal tunnel syndrome. The treatment group was offered 13 sessions of electroacupuncture over 17 weeks. The treatment and control groups both received continuous nocturnal wrist splinting.

Results: Of 181 participants randomly assigned to electroacupuncture combined with splinting (n = 90) or splinting alone (n = 91), 174 (96.1%) completed all follow-up. The electroacupuncture group showed greater improvements at 17 weeks in symptoms (primary outcome of Symptom Severity Scale score mean difference [MD] -0.20, 95% confidence interval [CI] -0.36 to -0.03), disability (Disability of Arm, Shoulder and Hand Questionnaire score MD -6.72, 95% CI -10.9 to -2.57), function (Functional Status Scale score MD -0.22, 95% CI -0.38 to -0.05), dexterity (time to complete blinded pick-up test MD -6.13 seconds, 95% CI -10.6 to -1.63) and maximal tip pinch strength (MD 1.17 lb, 95% CI 0.48 to 1.86). Differences between groups were small and clinically unimportant for reduction in pain (numerical rating scale -0.70, 95% CI -1.34 to -0.06), and not significant for sensation (first finger monofilament test -0.08 mm, 95% CI -0.22 to 0.06).

Conclusions: For patients with primary carpal tunnel syndrome, chronic mild to moderate symptoms and no indication for surgery, electroacupuncture produces small changes in symptoms, disability, function, dexterity and pinch strength when added to nocturnal splinting.

Project Number: 09100681

P71-0153
Investigation of the Inhibitory Effects of Metronomic Zoledronate in Combination with Coriolus Versicolor in Cancer Propagation and Bone Metastasis in Breast Tumour Rodent Model

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Breast cancer metastases frequently produce osteolytic bone lesions by activating local osteoclasts to break down existing bone. We previously showed that repeated metronomic dose of zoledronate (anti-resorptive treatment for bone metastases) could reduce tumour burden and exert anti-osteolysis effects in breast cancer-induced osteolysis mouse model. *Coriolus versicolor (CV)*, a medicinal mushroom widely used as adjuvant in cancer patients, was also shown to exhibit anti-tumour and anti-metastatic effects in breast tumour-bearing mice. Hence, the aims of this study were to determine the interaction of metronomic zoledronate (ZOL) and CV aqueous extract in cancer propagation, metastasis and bone destruction using mouse models. The molecular mechanisms of ZOL combined with CV in anti-metastasis and immunomodulation were also delineated using breast cancer cells *in vitro*.

Mice inoculated with human breast cancer cells tagged with a luciferase reporter construct (MDA-MB-231-TXSA) in tibia or mouse breast tumour 4T1 cells in mammary fat pads were treated with CV aqueous extract, metronomic dose of ZOL, or the combination of both. Various parameters in tumour growth, metastasis and immunomodulation were determined after treatments. MDA-MB-231-TXSA and 4T1 cells were subjected to CV and/or ZOL treatments in vitro, and the proliferation, migration as well as protein and mRNA expressions related to these processes were evaluated.

Results showed that combination of CV and ZOL diminished tumour growth without altering the incidence of lung and liver metastasis in intratibial breast cancer model. The combination (CV and ZOL) exhibited significant inhibition in tumour size against ZOL alone and reduced the bone loss in both tumour and non-tumour bearing legs. In the mouse breast tumour metastasis model, the tumour sizes of mice after combined treatment were significantly decreased and were smaller than those after ZOL treatment alone. The proliferative tumour cells and endothelial cells in tumour sections were also reduced in the combined treatment group. Furthermore, mild immunostimulatory effects were observed in mice treated with CV alone. Results from *in vitro* study demonstrated that the anti-tumour and anti-migrating effects of CV and the combined CV and ZOL were likely via PI3K pathway in human breast cancer cells.

In conclusion, our findings suggested that combination of CV and ZOL attenuated breast cancer propagation, protected against breast cancer-induced bone destruction in metastatic breast tumour models. Scientific evidences on the pre-clinical outcome of using CV in combination with metronomic zoledronate in the management of breast cancer and bone metastasis were gained from this study.

Project Number: 10110891

P72-0158
Interactions of Herbs with Statin Drugs and Potential Mediation by Drug Transporters

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Introduction and Project Objectives: Green tea and soy are extensively consumed in daily life. Recent research has shown that green tea catechins and soy isoflavones may influence the activity of drug metabolizing enzymes and drug transporters. We examined whether green tea extract and soy isoflavones might affect the pharmacokinetics of simvastatin and rosuvastatin in healthy subjects and whether these interactions are influenced by polymorphisms in relevant drug transporters, solute carrier organic anion transporter family member 1B1 (SLCO1B1) and ATP-binding cassette sub-family G member 2 (ABCG2).

Methods: The project included two open-label, single-dose, three-phase clinical pharmacokinetic studies. Healthy Chinese male subjects were given a single dose of rosuvatatin 10 mg (Study A) or simvastatin 20 mg (Study B) on 3 occasions: 1. without herbs; 2. with green tea extract; 3. with soy isoflavone extract. The green tea and soy isoflavone extract were given at a dose containing epigallocatechin gallate (EGCG) 800 mg once daily or soy isoflavones ~ 80 mg once daily for 14 days before statin dosing with at least 4-weeks washout period between phases.

Results: In study A (n= 20), intake of green tea extract significantly reduced the systemic exposure to rosuvastatin by nearly one third [geometric mean (% coefficient of variation) area under the plasma concentration-time curve from 0 to 24 hours (AUC_{0-24h}) from 108.7 (28.9) h•g/L to 74.1 (35.3) h•g/L; geometric mean maximum plasma concentration (C_{max}) from 13.1 (32.2) µg/L to 7.9 (38.3) µg/L, $P<0.001$ for all] without affecting the elimination half-life. The ABCG2 421C>A polymorphism had no effect on this interaction. In study B (n= 18), intake of soy isoflavones was associated with reduced systemic exposure to simvastatin acid [geometric mean (% coefficient of variation) AUC_{0-24h} from 16.1 (44.2) h•g/L to 12.1 (54.6) h•g/L, $P<0.05$] but not the lactone. Further analysis showed that the interaction between simvastatin and the soy isoflavones only occurred in subjects with the SLCO1B1 521TT genotype but not in those with the 521C variant allele.

Conclusions: This study showed repeated green tea catechin or soy isoflavonones administration reduced the bioavailability of statins in

healthy volunteers.

Project Number: 09100321

P73-0162

Morbidity and Management Patterns of Traditional Chinese Medicine (TCM) Primary Care in Hong Kong Population

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Background: Primary health care plays an important role to the health of the population by managing more than 90% of the illnesses. There was a lack of information on the morbidity pattern and management process despite 8815 of Chinese Medicine Practitioners (CMP) providing primary care to Hong Kong population.

Aims and Objectives: To determine the morbidity pattern and the management process of CM in primary care in Hong Kong

Methods: A cross-sectional study of prospective recording of all clinical encounters that presented to the participating CMP were collected for four seasons in 2012. All health presenting problems were coded by ICPC-2 and the national classification of disease and Zheng of CM. The prevalence was expressed in percentage distribution.

Results: 55,312 subjects' health encounters were collected from 260 CMP in 2012. Female were more likely to consult CMP than male (67.0%). Most subjects (64.0%) consulted for a chronic problem whom were elderly. By ICPC-2 coding, the respiratory (24.9%, R) and musculoskeletal (22.7%, L) problems were the most common complaints, especially cough (11.7%, R05) and low back symptom/ complaint (6.6%, L03). By national classification of diseases, internal diseases (65.1%) were the most commonly diagnoses. The top 3 diseases were muscle/ tendon-related illnesses (9.4%), flu-related illnesses (8.8%) and cough (6.2%). By national classification of Zheng (i.e. syndrome differentiation), organs and channels-and-collaterals syndromes (40.5%) were the most common Zheng. Chinese herbs were commonly used as management treatment by CMP together with lifestyle advices. For musculoskeletal problem, massage or acupuncture were adopted instead.

Conclusion: This was the first study to investigate the morbidity patterns in Hong Kong managed by CMP with the parallel coding from both ICPC-2 and national classification of diseases and Zheng (i.e. syndrome differentiation) from TCM aspect. Several factors have contributed to the difference of morbidity and management patterns.

Project Number: 09101111

P74-0184

Does Concomitant Use with Chinese Medicines Alter Pharmacokinetic and Toxicological Profiles of Antipsychotic Drugs in Experimental Rats? Implication for Herb-drug Interactions

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Herbal supplements are increasingly used in clinical practice of psychiatry. Our epidemiological study has identified several herbal preparations associated with adverse outcomes of antipsychotic therapy. In this Hong Kong Health Medical Research Fund (HMRF)-supported project, we evaluated the in vitro and in vivo of effects of one herbal mixture called Peony-Glycyrrhiza Decoction (PGD) and the four individual herbal preparations, Radix Rehmanniae (RR, Di-Huang), Fructus Schisandrae (FS, Wu-Wei-Zi), Radix Bupleuri (RB, Chai-Hu), and Fructus Gardeniae (FG, Zhi-Zi) on cytochrome P450s (CYPs) involved in the metabolism of clozapine (CLZ) in human liver microsomes (HLMs), recombinant human cytochrome P450 enzymes (rCYPs) and in rats. N-desmethylclozapine and clozapine N-oxide, two major metabolites of CLZ, were measured using high-performance liquid chromatography (HPLC).

PGD, individual peony and glycyrrhiza preparations, and the two individual preparations in combination reduced production of CLZ metabolites to different extents in HLM. While the known bioactive constituents of PGD play a relatively minor role in the kinetic effects of PGD on P450 activity, PGD as a whole had a weak-to-moderate inhibitory potency toward P450s, in particular CYP1A2 and CYP3A4. FMOs are less actively involved in mediating CLZ metabolism and the PGD inhibition of CLZ.

FG, RR, and RB showed negligible inhibitory effects in both in vitro systems, with estimated half-maximal inhibitory concentrations (IC50) and apparent inhibitory constant values (Ki) greater than 1 mg/mL (raw material). The FS extract affected CYP activity with varying potency; its effect on CYP 3A4-catalyzed clozapine oxidation was relatively strong (Ki: 0.11 mg/mL). In in vivo experiments, Rats were given a single or multiple intraperitoneal injections of 10 mg/kg CLZ, either alone or with individual herbal water extracts administered orally. The formation of both metabolites was reduced, while no significant change was observed in the CLZ pharmacokinetics for any of the herbal extracts. In the chronic treatment, none of the four herbal extracts significantly influenced the pharmacokinetic parameters of CLZ and its metabolites. Our results suggest that, although the inhibitory effects of herbal preparations tested on clozapine metabolism are weak and limited, caution should be paid on the potential herb-drug interaction in clinical practice.

Project Number: 10111381

P99-0002

Potential Use of Patient Specific Induced-Pluriopotent Stem Cell (iPSC) to Define Genetic Lesions Contributing to the Disease Phenotypes of Hirschsprung (HSCR)

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Background & Project objectives: Hirschsprung disease is caused by failure of enteric neural crest cells (ENCCs) to fully colonize the bowel, leading to bowel obstruction and megacolon. Heterozygous mutations in the coding region of the RET gene cause a severe form of Hirschsprung disease (total colonic aganglionosis). However, 80% of HSCR patients have short-segment Hirschsprung disease (S-HSCR), which has not been associated with genetic factors. We sought to identify mutations associated S-HSCR, and used the CRISPR/Cas9 gene editing system to determine how mutations affect ENCC function.

Methods: We created induced pluripotent stem cell (iPSC) lines from 1 patient with total colonic aganglionosis (with the G731del mutation in *RET*) and from 2 patients with S-HSCR (without a *RET* mutation), as well as *RET*+/– and *RET*–/– iPSCs. IMR90-iPSC cells were used as the control cell line. Migration and differentiation capacities of iPSC-derived ENCCs were analyzed in differentiation and migration assays. We searched for mutation(s) associated with S-HSCR by combining genetic and transcriptome data from patient blood- and iPSC-derived ENCCs, respectively. Mutations in the iPSCs were corrected using the CRISPR/Cas9 system.

Results: ENCCs derived from all iPSC lines, but not control iPSCs, had defects in migration and neuronal lineage differentiation. RET mutations were associated with differentiation and migration defects of ENCCs *in vitro*. Genetic and transcriptome analyses associated a mutation in the vinculin gene (*VCL* M209L) with S-HSCR. CRISPR/Cas9 correction of the *RET* G731del and *VCL* M209L mutations in iPSCs restored the differentiation and migration capacities of ENCCs.

Conclusions: We identified mutations in *VCL* associated with S-HSCR. Correction of this mutation in iPSC using CRISPR/Cas9 editing, as well as the RET G731del mutation that causes Hirschsprung disease with total colonic aganglionosis, restored ENCC function. Our study demonstrates how human iPSCs can be used to identify disease-associated mutations and determine how they affect cell functions and contribute to pathogenesis.

Project Number: 01121476

P100-0070

Therapeutic Potentials of Stem Cells in Hirschsprung's Disease

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Stem cells are multipotent cells which can form a multitude of tissues under different conditions, and thus stem cell-based therapy has raised hopes for a variety of diseases. Hirschsprung's disease is a common gut motility disorder in newborns, characterized by a reduction of gut peristaltic movements because of a regional absence or reduction of enteric ganglia in varying lengths of the colon. We hypothesized that stem cells are able to form enteric ganglia when transplanted to the aganglionic colon of patients with Hirschsprung's disease. To test this hypothesis, we used the Dominant megacolon mouse mutant (*Dom*) as the animal model of Hirschsprung's disease, and employed a three-pronged approach to (1) establish and characterize cultures of stem cells from different sources *in vitro*, (2) determine the differentiation abilities of these stem cells with an *ex vivo* gut culture system, and (3) ascertain their therapeutic potentials *in vivo* by transplanting them to aganglionic gut segments of the animal model. Five types of stem cells including vagal and sacral neural crest stem cells, skin-derived stem cells, enteric stem cells and induced pluripotent stem cells (iPSCs) from the mouse model were isolated, expanded *in vitro*, and characterized. Next, four of these five types of stem cells were transplanted to the hindgut explant *ex vivo*. Among these four types of stem cells, vagal neural crest stem cells, skin-derived stem cells and enteric stem cells were found to be able to engraft, migrate and differentiate within the hindgut explant, while mouse iPSCs failed to survive. As the expansion of vagal neural crest stem cells *in vitro* for further transplantation purposes were found to be difficult, only skin-derived stem cells and enteric stem cells were used for transplantation to the descending colon of wild-type and heterozygous Dom postnatal mice *in vitro*. These stem cells survived, engrafted and migrated within one week after transplantation, and some of them underwent morphological differentiation. However, the transplanted cells were no longer found in the colon 2 weeks after transplantation. In conclusion, among the five types of stem cells examined, skin-derived stem cells and enteric stem cells showed the best ability to engraft, migrate and differentiate after transplanted to the hindgut explant *ex vivo* or to the descending colon of the animal model of Hirschsprung's disease *in vivo*. However, the long-term survival of transplanted cells within the recipient gut segment is still an unresolved problem which awaits further investigations.

Project Number: 01120456

P101-0108

Placental Biology of Down Syndrome in Relation to Increased Gene Dosage

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Introduction and Project Objectives: Down syndrome (DS) is the most common congenital abnormality in humans. Trisomy 21 is the major cause accounting for about 95% of DS. The complex and highly variable clinical presentation of DS individuals is well documented. It has been suggested that various phenotypes of DS may be the results of the extra copy of dosage sensitive genes human chromosome 21. The 'gene dosage' effect on phenotype of DS placentas is relatively unexplored. This study aims to investigate the expression levels of DS candidate genes (APP, ETS2, SOD1, and HMGN1) in DS placentas and the impact of their overexpression in trophoblast culture models.

Methods: Expression levels of candidate genes/proteins in tissue samples of normal and DS placentas were evaluated by reverse transcription quantitative PCR (RT-qPCR) and immunohistochemistry. Inducible Tet-on expression systems were established in the model trophoblast cell lines HTR-8/SVneo and BeWo. Cell growth/proliferation/death was monitored by MTT assay, BrdU incorporation assay, flow cytometry and TUNEL. Cell migration and invasion were evaluated by transwell migration/invasion assay. The impact of APP expression on trophoblast differentiation was examined by syncytialization marker α/β-hCG and syncytin expression as well as confocal imaging of syncytia formation upon induction by forskolin.

Results: Among APP, ETS2, SOD1, and HMGN1, both APP and SOD1 were found overexpressed in trisomy 21 placentas at RNA level. On the other hand, ETS2 and HMGN1 were downregulated in DS placentas. The overexpression of APP (amyloid precursor protein) in DS placentas was also confirmed immunohistochemically as assessed by Aperio image analysis. APP induction in HTR-8/SVneo dose-dependently decelerated cell growth, through increasing cells undergoing apoptosis. Moreover, HTR-8/SVneo expressing APP migrated and invaded slower than the control uninduced cells and expressed less Erk1/2. Forskolin treatment induced α/β-hCG and syncytin expression in BeWo but such induction

was inhibited by APP expression. E-cadherin immunofluorescence also showed that there was a decrease in syncytia formation in forskolin treated BeWo expressing APP. hCG secrection was also suppressed in HTR-8/SVneo after APP induction.

Conclusions: APP is likely to be a dosage sensitive gene in DS placentas. APP overexpression observed in DS placentas produced significant impact on trophoblast functions and may contribute to the abnormal phenotypes of DS placentas.

Project Number: 01120936

P102-0005

Drug Transporter Expressions Associate with Drug Resistance and Prognosis in Liver Cancer Patients

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Background: Primary liver cancer accounts for over 700,000 deaths annually worldwide and has been the third leading cause of cancer death in Hong Kong. Curative treatments, which include surgical resection and transplantation, are applicable only for early-stage patients. However, the majority of liver cancer patients are diagnosed at an advanced stage with limited treatment options and systemic therapies have dismal response rates. The research effort should continue to further understand the molecular mechanism of drug resistance to improve treatment strategies.

Aims: The study proposed to characterize the ATP-binding cassette (ABC) drug transporter members for their expression profiles in liver cancer. We aimed to investigate their association with drug resistance and recurrence after curative surgery.

Methods and Results: We have systematically examined the drug transporter expression profiles in liver cancer by real-time quantitative RT-PCR. A panel of drug transporters including ABCB5, ABCF1, ABCA3 were significantly associated with recurrence-free survival. For liver cancer patients who received transarterial chemoembolization (TACE) treatment for recurrences, non-responders demonstrated enhanced ABCF1/ABCB5 expression levels. Furthermore, ABCF1/ABCB5 levels were elevated in chemo-resistant liver cancer cells. ABCF1/ABCB5 suppression enhanced apoptosis induced by chemotherapeutic agents and molecular targeted agent sorafenib.

Conclusion: Drug transporter expression levels were able to provide prognostic information and stratify liver cancer patients according to drug response.

Project Number: 01121566

P103-0010

Molecular Diagnosis for Severe Combined Immunodeficiencies (SCID) using Whole Exome Sequencing

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Primary immunodeficiency disorders (PID) are rare inborn errors of the immune system, mostly with Mendelian mode of inheritance. Severe Combined ImmunoDeficiencies (SCID) are severe forms of PID, characterized by profound defects in T cell development. Making accurate molecular diagnosis for SCID patients impacts on the treatment of the disease and provides informative and useful genetic counselling for the families. Traditional candidate gene testing, using mostly PCR and Sanger sequencing, is inefficient, tedious, and insensitive. Whole exome sequencing (WES) powered by next generation sequencing technology provided a powerful tool to have accurate and efficient molecular diagnosis for the SCID patients.

We have studied 50 samples from 33 families suffering from SCID and identified the causal mutation in 19 families, with a success rate at 57%. This rate is bit higher than that of most other WES studies. The majority of the causal mutations found are mutations reported previously for SCID, including DCLRE1C, IL2RG, TTC37, LIG4, etc. This work provided definitive diagnoses for the patients and families and ensured accurate genetic counselling and prenatal diagnoses. There are also a number of patients for whom we cannot provide definitive molecular diagnosis, probably reflecting the inadequacy of the NGS technologies at their current form and the lack of complete understanding of the genes and the complex disease mechanisms.

Even for the ones we have definitive causal mutations detected, some of the mutations were not predicted from initial phenotype evaluation. The molecular diagnosis sometimes prompted us for re-phenotyping the patients and gave us better understanding on the phenotype-genotype correlations. There are a number of cases that the causal gens were suspected before but missed by previous testing using traditional approaches but achieved molecular diagnosis by WES. This highlights the diagnostic value and the cost effectiveness of WES.

During the process of this project, we have gathered valuable experience in analysing NGS data, and have developed an in-house pipeline and a small database relevant to local population for WES data analysis. We also have reported novel PID genes and explored the value of RNA-seq in helping with molecular diagnosis when WES results are negative. We will also discuss our future plans in using whole genome sequencing and RNA-seq to tackle the negative detections for the SCID cases. We believe our experience is also valuable to making molecular diagnosis for other Mendelian diseases in Hong Kong.

Project Number: 01120846

P104-0058

Clinical Application of an Established Target-enrichment Massively Parallel Sequencing Method for Genetic Screening and Diagnosis of Hereditary Hearing Loss Patients with Normal arrayCGH Result

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This project aimed to demonstrate the feasibility of a local designed targeted-enrichment next generation sequencing system as a comprehensive and robust genetic test for hereditary hearing loss. We also aim to to characterize the frequency of variants in Chinese population, to establish a genotype-phenotype relationship database. In this study, we recruited two cohorts from Chinese population, 1) a cohort of 5800 neonates screened by the universal newborn hearing screening after birth and before discharge from hospital and 2) A hundred patients who were diagnosed with hearing loss from different clinics. First, we established and implemented the SNaPshot genotyping method to investigate the frequency of 15 common mutations in GJB2, SLC26A4 and the mitochondrial genome among the 5800 neonates. 15.9% (923/5,800) of this cohort carried at least one of these 15 mutants, indicating that one of 6.3 babies carried at least one mutant allele of a hearing loss gene. The most prevalent mutated allele was GJB2 c.109G>A with an allele frequency 5.26% (610/11600),

followed by GJB2 c.235delC (0.94%, 109/11600), and SLC26A4 c.919-2A>G (0.84%, 98/11600). In addition, 0.48% newborns (28/5,800) could be genetically diagnosed as hearing loss because of carrying compound or homozygous mutations in GJB2 and SLC26A4. Seven of these 28 newborns failed the universal newborn hearing screening program-OAE test for at least one ear. We have now established the SNaPshot as a genetic test for hereditary hearing loss in our laboratory. To provide more comprehensive genetic diagnosis and management of hereditary hearing loss not associated with the above common hot-spot mutations, we further developed our targeted-enrichment next generation sequencing system to screen 261 genes associated with hearing loss in patients. Read depth ranged from 86X to 352X, with target region coverage between 94.9-98.6%. Our data showed this comprehensive gene panel was able to detect pathogenic or likely pathogenic variants in the 21% of the hearing loss patients. Lately we have successfully obtained funding support from the Innovation and Technology Support Programme to fabricate our target enrichment next generation sequencing system. In summary, apart from beneficial with an early genetic diagnosis, our study can aid initiate early intervention to prevent delayed language acquisition in childhood hearing loss, identification of causative mutations in patients with syndromic hearing loss for prevention or early detection of associated symptoms and in extended family members.

Project Number: 01120256

P105-0107
Cellular Functions and Potential Clinical Application of miR-143 in Cervical Cancer

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Introduction and Project Objectives: The microRNA (miRNA) miR-143 is an anti-oncomir in some human malignancies. Remarkable downregulation of this miRNA in cervical cancer has been documented. Ectopic overexpression of miR-143 in cervical cancer cell lines led to suppression of cell growth and migration. However, the role played by miR-143 in cervical carcinogenesis is unclear. This study aimed to understand the molecular mechanisms of miR-143 mediated cell migration inhibition; to delineate the relationship between HPV infection and miR-143 dysregulation; and to identify miR-143 downstream targets usable as cervical cancer markers.

Methods: Cervical cancer cell lines HeLa, SiHa, and CaSki stably overexpressing miR-143 were established. Cell migration and invasion ability was evaluated by transwell assay. Rac activity was tested by PAK-RBD pulldown assay and the cellular localization of Rac was observed by immunofluorescence confocal microscopy. The spatial expression pattern of miR-143 in normal, precancerous, and cancerous cervices was characterized by in situ hybridization. Target mRNAs of miR-143 were shortlisted by in silico means and then screened by RT-qPCR in HeLa-143/Null. Protein expression of potential targets was examined in cytology samples of cervices by immunocytochemistry.

Results: miR-143 reduced cell mobility and invasiveness of HeLa and SiHa in association with miR-143 mediated reduction in the protein levels of β-pix and p130Cas, two activators of Rac1. Consistently, miR-143 stable expression in HeLa reduced the level of GTP-Rac1, but did not cause significant translocation of Rac1 within the cell. In situ hybridization revealed loss of epithelial miR-143 RNA expression during transformation, and displayed a pattern complementary to that of p16INK4A and MCM7 protein expression. Among the miR-143 targets, TARDBP and PHF6 displayed most significant downregulation by miR-143. A luciferase reporter linked with TARDBP 3'UTR was specifically suppressed by miR-143 supporting a direct role in transcription regulation. Immunocytochemical studies of miR-143 targets TARDBP, PHF6, ERK5, and KRAS showed significantly increased expression of these proteins in squamous cell carcinoma (SCC), high grade squamous intraepithelial lesions (HSIL) than in low grade lesions or normal cervix. They could be used to highlight SCC and HSIL with high sensitivities and specificities.

Conclusions: miR-143 is involved in regulation of cell migration of cervical cancer cells through regulation of Rac activity. Downregulation of miR-143 in cervical cancer is probably related to the action of HR-HPV onco-protein. The targets of miR-143 TARDBP, PHF6, ERK5, and KRAS can be explored as immunocytochemical markers in cervical cancer detection.

Project Number: 01121366

P106-0110
ASPP Family Members and Gestational Trophoblastic Disease (GTD)

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Introduction: ASPP (apoptosis-stimulating protein of p53) family comprises of ASPP1, ASPP2 and iASPP which are modulators on the p53 activities and play essential roles for different cellular functions in cancer cells. Gestational trophoblastic disease (GTD) includes a heterogeneous family of lesions such as hydatidiform moles (HM) and choriocarcinoma with different malignant potential. The understanding on the molecular functions of ASPP members in GTD will shed light on the development and phenotypes of GTD.

Objectives: 1. To study the expression of ASPPs in placentas and GTD and to evaluate the mechanisms regulating ASPPs expression in trophoblast cells; 2. To investigate the effects of ASPPs on trophoblastic activities and possible crosstalk signaling pathways.

Methods: Immunohistochemistry was performed in clinical samples of GTD and normal placentas. Choriocarcinoma cell lines, JEG-3 and JAR, were used and compared with normal trophoblastic cell line, HTR-8/SVneo, on their ASPP expressions. 5-azacytidine and Trichostatin A treatment, bisulfite sequencing and chromatin immunoprecipitation (CHIP) qPCR assay as well as precursor and inhibitor for miR-205 were used to evaluate epigenetic regulation of ASPPs expression. The effects of ASPPs on trophoblast cell growth were evaluated by MTT, clonogenic and BrdU incorporation assays. TUNEL assays, flow cytometry, transwell assay and autophagy evaluation were also performed.

Results: Differential expressions of ASPP members in HM when compared with normal placenta were detected. Lower expression of ASPP1/2 was found in HM, whereas overexpression of iASPP was found in HM when compared to normal placenta. Unlike ASPP1 which was regulated by histone acetylation, ASPP2 level was affected by miR-205. Consistently, choriocarcinoma specimens also expressed higher miR205 level than normal placenta. Transfection of miR-205 further downregulated ASPP2 expression, indicating a regulatory role of miR-205 on ASPP2. Overexpression of ASPP1/2 induced apoptosis as demonstrated by the TUNEL assay, whereas downregulation of iASPP suppressed cell growth through senescence. Moreover, different profile changes in the apoptotic genes were resulted from ASPP1/2 overexpression. MCL1 was downregulated in ASPP1 but not in ASPP2 overexpression. iASPP impeded autophagy in choriocarcinoma cells although downregulation of iASPP had no effects on the sustainability of choriocarcinoma cells in hypoxia. Both ASPP1/2 was also found to inhibit cell motility of choriocarcinoma cells.

Conclusions: Our results indicate that the differential expressions of ASPP family members in GTD are regulated by different mechanisms. They play important roles in regulating apoptosis, cell motility and autophagy and are likely to contribute to the pathogenesis and progress of GTD.

Project Number: 01121336

P107-0114

Functional Annotation of Genes Highly Expressed in Peripheral Blood of Pregnant Women Ending in Preterm Birth

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Introduction and Project Objectives: Preterm birth (delivery of a human fetus before 37 gestational weeks) is a major cause of neonatal mortality and morbidity. To gain insights into this disease systematically, we analyzed the transcriptome, the entire set of RNA transcripts, of maternal blood samples collected from women during their preterm labor which ended in spontaneous preterm birth.

Methods: We systematically analyzed RNA levels of each robustly detectable exon (functional sub-region of a gene transcript). Based on 20 sets of preterm birth-associated blood transcriptome data, a mean percentile rank of the level of each exon in each sample was calculated. Highly-expressed gene transcripts across all 20 datasets were identified and annotated for their functions by controlled vocabularies known as gene ontology (GO) terms. Over-representation of GO-terms among the highly-expressed genes was tested by statistical tools in the PANTHER website.

Results: A total of 11,455 gene exons were robustly detected across the 20 sets of preterm birth-associated blood transcriptome data. The percentile rank in each sample of the top 400 genes ranges from 96.2%-100% (the highly-expressed genes) across the 20 datasets. Compared with the GO-terms for annotating the functions of all genes in the human genome, we observed over-representation of GO-terms in the highly-expressed genes in the preterm birth-associated blood transcriptome. For GO-terms in biological process, immune system process (3.1-fold enriched; adjusted p-value = 7.5E-29), leukocyte degranulation (6.8-fold; p = 1.5E-26) and leukocyte activation (5.0-fold; p, 1.6E-26) were over-represented. For GO-terms in cellular component, vesicle (2.2-fold; p = 4.4E-20), secretory granule (4.5-fold; p = 4.1E-20) and secretory vesicle (4.4-fold; p = 1.8E-21) were over-represented. Since the statistical tests on over-representation were applied on multiple GO-terms, all p-values above were adjusted for multiple testing by the Bonferroni method.

Conclusions: The top 3.8% of the most highly-expressed RNA transcripts in maternal blood samples collected from women ending in preterm birth are over-represented with certain biological processes and cellular components. The functional roles of these genes warrant further investigation. The peripheral blood RNA levels of these genes may be important in the pathological process culminating in preterm birth and useful for predicting the disease.

Project Number: 01120066

P108-0117

Elucidating the Genetic Basis for Early-age Onset Nasopharyngeal Carcinoma in Hong Kong

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Introduction and project objectives: Nasopharyngeal carcinoma (NPC) is an intriguing cancer of special relevance to Hong Kong, where it is also dubbed the "Guangdong tumor" because of its especially high incidence among the Southern Chinese. The peak age for NPC diagnosis is in the upper 40's. In Hong Kong, a small proportion of NPC patients are early-age onset (EAO) pediatric patients, who are diagnosed with this cancer at 20 years of age or less and who have a higher frequency of advanced-stage cancers. Very little is known about these patients. The aim of the study is to utilize the whole-exome sequencing (WES) approach to characterize the germline variants of EAO NPC in Hong Kong in to understand the genetic basis for this rare group of NPC patients.

Methods: A total of 39 EAO NPC patients were sequenced using Illumina TruSeq WES kit. Additional 63 cases from 52 family history-positive (FH+) NPC families and 59 sporadic cases, and controls including 895 non-cancer Southern Chinese were also studied by WES. The selected variant was validated by LightSNiP assay in 2160 cases and 2433 controls. We further examined the candidate gene using a Roche NimbleGen SeqCap targeted sequencing approach in 1224 NPC cases and 1256 non-cancer controls.

Results: Five rare deleterious missense variants at *MST1R* were identified in the EAO cases by WES, but were rare in the controls (EAO cases vs. controls: 17.95% vs. 1.22%, $p=7.94\times10^{-12}$). The gene-based burden test including WES data from a total of 161 NPC cases and 895 controls confirmed the association between *MST1R* and NPC (Variant Test p=0.0009). The validation study including 2160 cases and 2433 controls showed that the *MST1R* variant c.G917A:p.R306H is highly associated with NPC (odds ratio=9.0) [1]. The follow-up validation study for *MST1R* gene-level targeted sequencing further demonstrated that the NPC cases more frequently carried the rare deleterious variants at this gene, especially in the intracellular domain, than the non-cancer controls (p=0.036). Conclusion: Our study highlights the role of *MST1R* as a NPC genetic susceptibility gene. *MST1R*, encoding Macrophage-Stimulating Receptor 1, is predominantly expressed in the tissue-resident macrophages and is critical for innate immunity that protects organs from tissue damage and inflammation. Our data suggest that the deleterious germline variants may impair its function in innate immunity and host defense.

Reference: [1] Dai W, Zheng H, et al. Lung M. WES Identifies MST1R as a Novel Genetic Susceptibility Gene in NPC. ***PNAS***. 2016

Project Number: 01121496

P109-0021

Disruption of Hippocampal-Anterior Cingulate Cortex Synchrony in a Rat Model of Chronic Pancreatic Pain

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Introduction and Objectives: The chronic visceral pain mechanisms are incompletely understood. Our series of publications have demonstrate that the perigenual anterior cingulate cortex (ACC) modulates the sensory and emotional aspects of visceral pain in visceral hypersensitive rats (Gastroenterology 134:535-543, 2008; 136:1732–1740, 2009. J Physiolog. 570 (1):169-184, 2006; Cerebral Cortex i:10.1093/2013; Experimental Neurology 136:74–85 2016). An EEG study suggested that pain in patients with chronic pancreatitis (CP) was associated with cortical reorganization and perigenual neuroplastic changes, we aimed to characterize the dysfunction of ACC neuronal circuitry which was responsible for learning and triggering of pain memories in the CP state.

Methods and Results: A single injection of trinitrobenzene sulfonic acid into the biliopancreatic ducts in rats produces a robust chronic inflammation of the pancreas accompanied by glandular atrophy and loss, severe periductal and intralobular fibrosis, and ductular stenosis with luminal blocking plugs.

Pancreatic pain was assessed by visceromotor response evoked by intraductal injection of trypsin. Markedly increases in pain responses were observed in the awake CP rats. The up-regulation of NR2B-receptor protein in the ACC was verified by Western blot analysis. Reactive astrogliosis was characterized with decreased glutamate transporter expression (EAAT2), and increase in glial fibrillary acidic protein (main intermediate filament protein in astrocytes), and glutamine synthetase in the ACC of rat with CP.

Electrophysiological recording showed increased ACC spontaneous activity and a striking enhanced neuronal discharges induced by intraductal injection of trypsin in CP. Further, injection of selective NMDA 2B receptor antagonists R025-6981 at dose of 10 mM into the ACC significantly suppressed the trypsin-induced pancreatic pain and ACC neuronal responses in CP rats. Multiple-electrode array recordings of local field potential (LFP) showed increases in theta-band power in hippocampus (HPC) and ACC. Spike-field coherence analysis revealed chronic pancreatic pain led to suppression of ACC spike timing and HPC local theta oscillation. Finally, cross-correlation analysis revealed decreases of synchronization of theta oscillation between the HPC and ACC, indicating reduced neuronal communications between these two regions.

Conclusions: We establish a CP rat model with severe pancreatic fibrogenesis, and demonstrated for the first time that enhanced NR2B subunit activation in the ACC was responsible for pain and ACC sensitization in the CP state. The disruption of synchronization of Theta LFP recorded in the ACC-HPC represents a dysfunction of timing relationship that may have important consequences suggesting pain was associated with cortical reorganization. These neuroplastic changes may cause emotional and cognitive dysfunction.

Project Number: 01122006

P110-0022
The Effects of Mirror Therapy with Bilateral Arm Training for Hemiplegic Upper Extremity Motor Functions in Adults with Chronic Stroke

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Introduction and Project Objectives: Mirror Therapy (MT) appeared to have beneficial effects on the recovery of the hemiplegic hand in the evidence recently, however, it is not known whether the clinical benefits in mirror therapy was due to the incongruent visual feedback induced by mirror in bilateral arm training (BAT). The objectives of this study were: to compare the effectiveness of MT and BAT in improving motor and functional performance of hemiplegic upper extremity for adults with chronic stroke; and to examine by means of EEG whether recruitment of the mirror neurons, as reflected in mu rhythm suppression, mediated recognition of the mirror illusion on MT instantly and upon training.

Methods: One hundred and one participants with chronic stroke were recruited by convenience sampling from a convalescent hospital and self-help groups in the community. Participants were randomly assigned to either the MT group (n=51) or BAT group (n=50) and participated in a 6-week customized upper limb training programme which consisted of two 45-minute training sessions per week. Both groups were equivalent to each other except that there was a mirror in the MT group. Main outcome measures were upper extremity motor and functional tests, and grip strength. Participants were evaluated at baseline, post-treatment and 3-months follow-up. Twenty out of 101 participants (11 MT; 9 BAT) were invited to participate in pre/post-intervention EEG analysis, twenty healthy counterparts (mean age=61.3; 12 males, 8 females) were also recruited for EEG comparison.

Results: A significant group-time interaction (F= 3.527; p=0.033) for Fugl-Meyer Assessment (FMA) hand subscores of the participants was found between the two groups. No between-group differences were found in other outcomes. The EEG results in C3/C4 showed that mu suppression was less reduced in both mirror and no mirror task conditions in stroke participants than their healthy counterparts, in the alpha-1 and alpha-2 bands in both contralateral and ipsilateral motor cortices. After practice, significant main effect of training in the mirror task condition was found in both groups in beta bands as well as alpha-2 band in the MT group.

Conclusion: Both MT and BAT were shown to be effective in enhancing hemiplegic arm functions in adults with chronic stroke, with possible benefits of MT to the distal hand functions. The reduced mu suppression reflected that action observation for motor preparation in chronic stroke patients was much reduced, thus affecting their motor learning. After practice, both MT and BAT showed more readiness in lateralized potentials in the motor cortex which provides an evidence for neuroplasticity.

Project Number: 01121966

P111-0034
Therapeutic Potential of Heat Shock Protein 27 on Guillain-Barré Syndrome

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Background: Guillain-Barré syndrome (GBS) is an acute autoimmune peripheral neuropathy in which a person's own immune system damages their peripheral nerves, causing muscle weakness, paralysis, and loss of sensation in lower limb. Ganglioside located primarily on plasma membranes of neurons which is highly abundant in peripheral nerves. The abundance of anti-gangliosides antibodies correlates with severity of disease and also accounts for incomplete functional recovery in patients.

Aims and Objectives: Hsp27 is detected in the cerebrospinal fluid and sera from GBS patients suggested that Hsp27 could play an important role in GBS. We therefore plan to induce GBS in human (h)

Hsp27 overexpressing mice, and examine regeneration and functional recovery after peripheral nerve (PN) injury. This study represents a major effort to provide an insight into a potential therapeutic approach of using Hsp27 to treat GBS.

Methods: Rate of neurite extension was quantified in anti-GD1a/GT1b-2b-treated primary sensory neuron purified from hHsp27 transgenic mice and littermate control. Sensory (pinprick test) and motor (toe spreading test) functional recovery were determined in hHsp27 transgenic mice and age-matched control group after treated with anti-GD1a/GT1b-2b using neurobehavior, electrophysiology and histology approaches.

Results: We cultured primary dorsal root ganglion (DRG) neurons from hHsp27 mice and treated with anti-ganglioside (GD) 1a/GT1b-2b. Forced expression of hHsp27 was able to overcome anti-GD1a/GT1b-2b induced neurite outgrowth inhibition in DRG neurons significantly, as compared to littermate controls. We further extend this to in vivo animal studies and showed that functional recovery was promoted in GBS-induced hHsp27 TG mice. The animal behavior data were confirmed by electrophysiology and histology studies.

Conclusions: Forced expression of hHsp27 specifically in neurons not only overcame the inhibitory effect of anti-GD1a/GT1b-2b in axon growth but also reduced the delay of functional recovery in animal model of GBS.

Project Number: 01122026

P112-0040
Novel Beta-Amyloid Aggregate Inhibitors for Alzheimer's Disease

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Introduction and Project Objectives: Alzheimer's disease (AD) is an irreversible neurodegenerative disorder that causes the loss of cognitive functioning and behavioral abilities. The pathogenesis and disease progression are closely associated with the formation and accumulation of neurotoxic forms of amyloid-β (Aβ) oligomers and aggregates due to the inefficient clearances. The development of potent inhibitors that can prevent neurotoxic oligomeric Aβ formation has been considered as one of therapeutic approaches for AD treatment. Toward this end, a series of novel cyanine-based Aβ peptide aggregation inhibitors has been designed and synthesized for an investigation of their potential to improve cognitive impairment in AD mouse model.

Methods: Novel cyanine derivatives bearing various functionalized heteroaromatic electron-accepting moieties have been synthesized. The aggregation inhibitory effect was investigated by real-time fluorescence microscopy and SDS PAGE and circular dichroism. Cytotoxicity and neuroprotection of the new cyanines on neuronal cells were evaluated by MTT assay. The effect of the cyanine on amyloid-induced ROS toxicity and calcium uploading were also studied. The blood-brain barrier (BBB) permeability and Aβ targeting properties of these cyanines were studied on both normal and transgenic mice. The cognitive test was assessed by Morris water maze test and followed by multiple biochemical analyses of brain slices, including the Western blot analysis, immunohistochemistry and immunofluorescence.

Results: A series of novel effective Aβ oligomerization/ aggregation inhibitors based on donor-acceptor type cyanines has been developed. Some of these newly developed cyanines show desirable biological properties including blood-brain barrier permeability, low toxicity, and neuroprotection against Aβ-induced toxicities. Importantly, triple transgenic mice intraperitoneally treated with one of the developed cyanines for 45 days showed significant cognitive improvement, as assessed by Morris water maze test. Furthermore, biochemical analyses consistently showed that those cyanine-treated mice exhibited a dramatic reduction in both oligomeric Aβ contents and tau proteins particularly in the cerebral hippocampal region which was attributed to the induction of autophagic flux.

Conclusions: Our results demonstrate that multifunctional cyanines capable of inhibiting neurotoxic Aβ aggregates formation and modulating autophagic flux show promising clinical potential for the therapeutic treatment of AD.

Project Number: 01122066

P113-0073
Leucine-Rich Repeat Kinase 2 (LRRK2) Knockin Mouse Model for Pathophysiological Studies of Parkinson's Disease (PD)

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Introduction: Parkinson's disease (PD) is a neurodegenerative disorder characterized by degeneration of dopaminergic neurons in the brain, with motor symptoms including tremor, rigidity, bradykinesia, and postural instability. The disease pathogenesis is unclear with no cure. There is a lack of appropriate in-vivo models which accurately mimic human PD. Most existing models rely on short-term lethal intoxication to induce acute neuronal damages and do not reflect the natural lifelong progression of PD. Knockout (removal of a gene) and transgenic (overexpression of a gene) models do not mimic the human condition due to non-physiological level of gene expression. Developing an appropriate disease model which incorporates the effects of aging, genetics and environmental factors and reproduces the pathogenic processes in human PD will facilitate the identification of biomarkers and therapeutic targets. Mutations in leucine-rich repeat kinase 2 (LRRK2) represents the commonest genetic risk in both familial and sporadic PD. Patients with LRRK2-associated PD demonstrate indistinguishable clinical features from typical idiopathic cases, suggesting similar pathogenic mechanisms. Hence, LRRK2-based genetic models can best represent the wide clinical spectrum of PD.

Project Objectives and Methods: We generated homozygous $LRRK2^{R1441G}$ knockin mutant mice to study their susceptibility to nigrostriatal dopaminergic cell death, and examined for pathological changes in nigrostriatal network, dopamine uptake and locomotor activity. Our $LRRK2^{R1441G}$ knockin mice express mutant LRRK2 at physiological levels, similar to human PD. In contrast to the LRRK2 knockout or transgenic mice, these knockin mice do not show overt motor phenotype but have subtle abnormalities and increased susceptibility to stress-induced locomotor deficits and dopamine depletion.

Results: Striatal synaptosomes from young knockin mice demonstrated lower levels of dopamine uptake with impaired locomotor activity after injection with reserpine (an inhibitor of dopamine uptake into synaptic vesicles) (Liu et al., Ann Clin Transl Neurol. 2014;1:199-208). Mutant mice chronically exposed to low sub-lethal doses of oral rotenone (a natural pesticide) for 50 weeks (~half the mouse's lifespan) resulted in more severe locomotor deficit, compared to their wildtype littermates (Liu et al., Sci Rep. 2017;7:40887).

Conclusions: The combined effects of aging, genetic mutation and environmental stress contribute to disease development. Pre-symptomatic humans with LRRK2 mutation may already harbour subtle abnormalities in the brain, and show greater susceptibility to developing PD as they age and upon chronic exposure to environmental toxins. Our novel experimental model more closely mimics human PD, and will be invaluable in future studies to elucidate early pathogenic processes and

to develop novel therapies.

Project Number: 01120976

P114-0101

REM Sleep Behavior Disorder in Psychiatric Populations- A Prospective Study Searching for Early Neurodegenerative Biomarkers and Clinical Outcome

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Objective: REM sleep behavior disorder (RBD) is a parasomnia affecting older age group and is a precursor of neurodegeneration, particularly synucleinopathy. Growing evidence reveals that RBD is found in patients with psychiatric illness (pRBD) and dopamine dysfunction by neuroimaging had been reported. In this study, we aimed at looking into 1) longitudinal course of RBD in terms of clinical and polysomnographic (PSG) REM-related electromyography (EMG) activities, any new onset of neurodegenerative diseases; 2) neuro-cognitive profile as early neurodegenerative markers; 3) dopaminergic transmission abnormality by neuroimaging technique.

Method: A prospective case control cohort study including a Phase-1 assessment for pRBD and controls subjects from two control arms (pControl- psychiatric illnesses only without RBD symptoms; hControl-healthy control subjects). A sub-set of subjects were recruited to participate in Phase-2 which involved an overnight PSG study, neurocognitive tests and neuroimaging study.

Results: Among 173 subjects in the cohort, 120 completed the follow-up study with a response rate of 69.4%. The mean duration of follow-up was 52.0 ±15.6 months. At follow-up, 2 out of 39 subjects from pRBD developed Parkinson's disease (PD). For 37 subjects who remained free of any neurodegenerative disorder, 31 (83.8%) reported persistent RBD symptoms, and 6 (16.2%) reported no active RBD symptoms over the past 1 year. For the pControl group, 3 subjects developed RBD. For the hControl group, there was no new incidence of RBD or neurodegenerative diseases. The pRBD group was found to have higher score in depressive and anxiety symptoms, motor symptoms by the Unified Parkinson's disease rating scale (UPDRS). PSG result revealed that pRBD group had significantly higher REM-related EMG score at both baseline and follow-up ($F(2,99)=16.088$, $p<0.01$) than the other two groups. For the neurocognitive profile, pRBD group had persistent olfactory dysfunction at both baseline and follow-up. (pRBD 24.1%; pControl 5.9% and hControl 4.7%; $p<0.05$). There was no significant difference between pRBD and pControl group in other neurocognitive batteries. Thirty subjects completed the triple PET neuroimaging study (pRBD = 14, pControl = 6, hControl = 10). There was no significant difference in the dopamine transmission among the three groups.

Conclusion: RBD in patients with psychiatric illnesses could run a persistent course and had a higher chance of developing PD compared with those with psychiatric illnesses only. They had more prominent depressive and anxiety symptoms, showed increased motor symptoms of Parkinsonism, were more likely to have olfactory dysfunction, and had persistent increase in REM-related EMG activities.

Project Number: 01120326

P115-0031

Prevalence of Vitamin D Insufficiency among Healthy Infants in Hong Kong: A Pilot Study

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Background: Vitamin D deficiency has been shown to be associated with many disease conditions in addition to its influence on skeletal health. High prevalence of vitamin D deficiency in children is reported worldwide but local data are scarce.

Objective: To obtain pilot data regarding the prevalence of vitamin D deficiency among healthy infants in Hong Kong.

Methods: It was a pilot cohort study. Healthy full-term Chinese newborns were recruited from the postnatal wards at the Prince of Wales Hospital. Serum 25-hydroxyvitamin D [25(OH)D] levels were measured at 3 months of age. Self-administered questionnaires completed by parents were used to collect information on infant's feeding pattern, use of vitamin D supplement and maternal diet during pregnancy and lactation. In our study, vitamin D sufficiency was defined as serum 25(OH)D ≥50 nmol/L and deficiency was defined as a level lower than 50nmol/L.

Results: One hundred and fifty five healthy local newborns completed the study. The median serum 25(OH)D level at 3 months was 58nmol/L (IQR 32 to 75nmol/L). Fifty two (33.5%) had vitamin D deficiency with 25(OH)D <50nmol/L and 34 (21.9%) had levels <25nmol/L which signified more severe deficiency. Significantly greater proportion of infants was exclusively breastfed in the group with vitamin D deficiency when compared with the group with normal vitamin D levels ($p<0.001$). There was a significant inverse correlation between duration of exclusive breastfeeding and 25(OH)D levels at 3 months of age ($r = -0.605$; $p<0.001$). Positive correlation between serum 25(OH)D and plasma phosphorous concentrations was observed ($r = 0.556$; $p<0.001$). There were no significant correlations between serum 25(OH)D and infant's sunlight exposure, plasma calcium, alkaline phosphatase or growth at 3 months of age.

Conclusions: Vitamin D deficiency is prevalent in local infants. More studies are needed to evaluate the health outcomes related to vitamin D deficiency in infancy.

Project Number: 01120026

P116-0048

Prospective Study of the Association between Childhood Primary Snoring and Cardiovascular Health

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Introduction: Our previous cross-sectional study found that children with primary snoring (PS) had a lower flow-mediated dilation (FMD) of the brachial artery, meaning a poorer endothelial function, compared to non-snoring controls.

Objectives: We aimed to conduct a prospective follow-up study of a

cohort consisting of children with or without PS, in order to investigate the longitudinal association between PS and endothelial function.

Methods: In this prospective cohort study, all subjects underwent overnight polysomnography and FMD measurement at both baseline and follow-up visits. Twenty-four ambulatory blood pressure (ABP) monitoring was also performed at the follow-up visit. The mean±SD length of the follow-up period was 5.1y±1.3.

Results: A total of 96 primary snorers and 111 non-snorers were included in the final analysis. The primary snorers had significantly lower FMD at both baseline (8.2%±1.3 c.f. 8.5%±1.0, p=0.037) and follow-up (8.2%±0.9 c.f. 8.5%±0.8, p=0.002). At follow-up, 76 out of 96 snorers had persistent SDB, while 73 out of 111 non-snorers remained snoring-free. The persistent SDB group tended to have lower FMD at baseline (8.2%±1.2 c.f. 8.6%±0.9, p=0.061) and had significantly lower FMD at follow-up (8.3%±0.9 c.f. 8.6%±0.8, p=0.026). But there was no significant difference in the changes in FMD between two groups (0.0%±0.9 c.f. 0.0%±0.8, p=0.9). Further analysis revealed that incidence of obstructive sleep apnoea (OSA) at follow-up was associated with higher ABP when compared to the PS and control groups.

Conclusions: Childhood PS was not longitudinally associated with deterioration of endothelial function and blood pressure. However, incidence of OSA at follow-up was associated with higher ABP.

Implications: Children with PS was not associated with higher cardiovascular risk longitudinally, but it may progress to OSA which was found to be associated with higher cardiovascular risk. Therefore, children with PS should be followed up regularly to monitor its progression in order to prevent any possible cardiovascular complication.

Project Number: 01120736

P117-0050

Age and Sex Specific Flow-mediated Dilation in Hong Kong Chinese Children and Adolescents - A Community Based Study

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Background: Optimal endothelial function is important in maintaining good cardiac health. Flow-mediated dilation (FMD) is a well-recognised easily obtainable clinical marker of endthelial function. Reference values for FMD in children andadolescents are unavailable in the current literature. This study aimed to established normal FMD values for Chinese children and adolescents.

Methods: Healthy Chinese children and adolescents aged 8-18 years were randomly selected from primary and secondary schools from 4 geographical regions of Hong Kong. The following parameters were recorded from each participant; anthropometric data, level of physical activity, pubertal status and resting blood pressure. Flow-mediated dilation of the brachial artery was measured by the gold standard ultrasound technique. Blood samples were also taken for assessment of cardiovascular risk.

Results: Six primary and 14 secondary schools were recruited and 1637 subjects (829 males) took part in the study. The average FMD across the entrie age range was around 8%. However, no significant correlation could be demonstrated between FMD with weight, waist circumference, BMI and baseline artery diameter. The correlation of FMD and age was (r = 0.060) and height was (r = 0.066). FMD increased with age in both gender, the increase in FMD plateaued after about age 14 years, and this trend was more obvious in girls. FMD was associated with cholesterol (p = 0.012) and triglyceride (p = 0.019) respectively.

Conclusions: Normal FMD values for Chinese children and adolescents were established. FMD was associated with age, gender, height, serum cholesterol and triglyceride levels in this study.

Project Number: 01120406

P118-0091

Functional Analysis and Evaluation of Ultrastructure of Respiratory Cilia in Healthy Chinese Children in Hong Kong

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Introduction: Normal reference range of ciliary structure and beat frequency (CBF) is available in Western population but lacking in the Chinese population for the early diagnosis of Primary Ciliary Dyskinesia (PCD). This study aims to establish a reference of the ciliary structure and beat frequency in a healthy Chinese paediatric and adolescent population.

Project Objectives: Our objective is to establish the normal reference range for respiratory CBF and determine the ciliary ultrastructure in healthy Chinese children in Hong Kong.

Methods: Subjects Nasal epithelial cells were obtained from 162 children (age range 2-17 years) by brushing inferior turbinate.

CBF The movement of cilium was examined using a high speed camera. CBF of each ciliated strip was counted and a maximum of 10 ciliated edges were analyzed per subject. CBF was determined by the number of frames required to complete 10 cycles.

Ultrastructure Ciliary ultrastructures were examined using transmission electron microcopy.

Data analysis: Age were first sub grouped into 2-6, 7-12 and 13-17. The mean for CBF was compared among each age group using ANOVA. Standard deviation, 5th and 95th percentiles, and 95% confidence intervals of whole age group were calculated if there is no significant observed.

Results: Nasal brush samples obtained from 141 healthy children (70 male) were included for CBF and CBP evaluation following the inclusion criteria. The mean CBF for children was 10.4Hz (SD 2.2, 95% CI 10.0 to 10.8). There was also no significant difference in mean CBF between the individual age groups (unpaired t-test, p>0.5). For CBP, circulating beating cilia was found on ciliated strips from a child. Normal CBP was observed in the other samples. One hundred and twenty five samples were sufficient for ultrastructural analysis. Dynein arm defects were not found in the cilia. The mean outer and inner arm counts were 8.5 and 7.8 for children. Microtubular defects were found in 9.2% of cilia counts from children. Other ciliary ultrastructural defects were found in less than 3% of cilia for individual age groups.

Conclusions: The normal reference range of CBF for children was 10.4Hz (SD 2.2, 95% CI 10.0 to 10.8). A further investigation of microtubular defects will be followed.

Project Number: 02133316

P119-0056

Early Detection and Prognosis of Esophageal Squamous Cell Carcinoma (ESCC) Using the Circulating Plasma SAA Protein and the SAA1 Polymorphisms

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Background and aims: Esophageal Squamous Cell Carcinoma (ESCC) is a deadly cancer and its early detection is very difficult. It is essential to identify an early marker and a predictive marker for this disease. We aim to (1) determine whether the *Serum Amyloid A1* (*SAA1*) polymorphisms can be used as a predictive marker in ESCC, and (2) determine whether the circulating SAA and its related circulating proteins are useful in early ESCC detection.

Methods: The association of *SAA1* polymorphisms with ESCC risk and the elevated circulating SAA and the related IL-6, IL-8, and MMP-9 levels in ESCC patients will be investigated. Direct DNA sequencing will be used to genotype the *SAA1* variants and enzyme-linked immunosorbent assay (ELISA) will be used to detect the circulating protein levels.

Results: We found that the plasma SAA alone could show a 100 % sensitivity and specificity for early ESCC detection. The choice of using serum or plasma samples is critical for the circulating SAA detection. The median survival time of patients with *SAA1.3/1.5* genotype was 10.63 months which was much shorter than others (20.41 months; p = 0.004) and that was likely due to the extra high circulating IL-6 concentrations.

Conclusions: The *SAA1* polymorphism can be used as a predictive biomarker to identify poor clinical outcomes of ESCC patients, and the plasma SAA seems to be useful for early ESCC detection. The addition of plasma SAA to the current biomarker system is likely to improve early detection of ESCC and *SAA1* genotyping of ESCC patients can help to predict the worst survival group.

Project Number: 01120886

P120-0066

Effects of iASPP and PLK1 in Ovarian Clear Cell Carcinoma

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Introduction: Ovarian clear cell carcinoma (OCCC) is a histotype of epithelial ovarian cancer with a relatively high prevalence in Asians. OCCC is associated with endometriosis and chemoresistance against platinum-based chemotherapy and thus poor prognosis. Inhibitory member of ASPP family proteins (iASPP) is an inhibitor on p53 activity, whereas Polo-like kinase (PLK)1 is a serine-threonine kinase regulating mitosis and spindle formation. Autophagy can protect cancer cells during challenges from chemical insults or stressful circumstance.

Objective: 1. To investigate the functional roles of iASPP and PLK1 in OCCC cells. 2. To delineate the effects of iASPP, PLK1 and autophagy on the chemoresistance of OCCC cells. 3. To assess the impact of expression of iASPP, PLK1 and autophagy proteins on chemoresistance and survival in patients with OCCC.

Methods: Two OCCC cell lines, OVTOKO and KK, were used in this study. Knockdown of iASPP and PLK1 was carried by shRNAs and siRNAs, respectively. Bafilomycin A1 was used as an autophagy inhibitor. Clonogenic and MTT assays were used to measure cell growth and viability. Flow cytometry was also used to measure the change and apoptosis after knockdown with the presence or absence cisplatin. Immunohistochemistry was performed and the scores were analyzed by Aperio Scan Scope System and correlated with chemosensitivity and survival.

Results: Knockdown of iASPP or PLK1 decreased the cell growth and viability of both OVTOKO and KK cells. Both downregulation resulted in cyclin B1 reduction as well an inactivation of autophagy in OCCC cells. The formation of LC3-II and LC3 puncta were much less in cells with either knockdown, suggesting that autophagic flux was suppressed. Moreover, knockdown of iASPP reduced PLK1 expression, suggesting that PLK1 may be a downstream target of iASPP. Similarly, downregulation of iASPP or PLK1 sensitized OCCC cells in response to cisplatin. More prominent apoptosis was induced in OCCC cells treated with cisplatin and knockdown. Such sensitization may attribute to autophagy inhibition as treating OCCC cells with Bafilomycin A1 and cisplatin resulted in more cell death. High iASPP protein expression was found to correlate with chemoresistance and poorer survival in patients with OCCC while PLK1 expression correlated only with chemoresistance.

Conclusion: Both iASPP and PLK1 affected OCCC cell growth and regulated the chemosensitivity, whereas PLK1 may be the downstream target of iASPP. iASPP and PLK1 are potential biomarkers for chemoresistance and survival.

Project Number: 01121526

P121-0119

Development of PEGylated Recombinant Human Arginase As A Drug To Treat Breast Cancer

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The Hong Kong Polytechnic University

Introduction: Breast cancer is the single most common cancer in women, and accounts for the highest female cancer death. Approximately 207,500 out of the 1,383,500 breast cancer patients worldwide (as of 2008) would be resistant to hormone receptor- or HER2-targeting therapies. Safe and effective treatments against "triple-negative" breast cancer (not expressing estrogen receptor, progesterone receptor and HER2) are greatly in demand. Arginine has been shown to be essential for the growth of a variety of tumors. Depletion of arginine using arginase, an arginine-depleting enzyme, can potentially inhibit the growth of difficult-to-treat breast cancer. We aim to develop PEGylated recombinant human arginase (rhArg-PEG) as an effective agent against breast cancer.

Project Objectives: To test the in vitro efficacy of rhArg-PEG; to study cell death pathways caused by rhArg-PEG; to test whether ornithine transcarbamylase (OTC) expression can induce rhArg-PEG resistance; to study the anti-migratory properties of rhArg-PEG; to study the efficacy of rhArg-PEG in mice.

Methods: This is a proof-of-concept study using breast cancer cell lines. Cell proliferation assay, flow cytometric analyses, Western blotting, confocal microscopy imaging, migration and invasion assays, human breast tumor cell xenograft mouse model, allograft metastasis mouse model, statistical analysis.

Results: rhArg-PEG is highly potent and kills various breast cancer cell lines, including "triple-negative" and highly aggressive metastatic cells, in vitro and in vivo, in a receptor-independent manner. It induces multiple cancer cell death pathways, which are cell-line dependent. It

inhibits mTOR, activates AMPK, and induces a novel type of biphasic autophagic response in cancer cells, leading to autophagic cell death. It kills cancer cells lacking OTC and/or argininosuccinate synthetase (ASS), inhibits more tumors when compared with PEGylated arginine deiminase (ADI-PEG), and is a promising personalized medicine.

Conclusions: As rhArg-PEG is derived from human arginase, it is a safer drug with less immunogenicity problems comparing to the bacterial enzyme arginine deiminase (ADI). It is a promising safe and effective treatment against "triple-negative" or highly metastatic breast cancer, which is greatly in demand. Our findings provide important information that facilitates our next stage of investigation. In the future, human patients (e.g. triple-negative breast cancer patients) will be used in our clinical trial studies.

Acknowledgements: This study was supported by the Health and Medical Research Fund (HMRF: 01121936), Food and Health Bureau, Hong Kong SAR Government.

Project Number: 01121936

P75-PF0001

Developmental and Parenting Program for Parents of Preterm Children

Administering Institution: Department of Paediatrics, The Chinese University of Hong Kong

Co-organisation(s):
1. Neonatal Unit, Prince of Wales Hospital
2. Psychological Studies, The Education University of Hong Kong

Project Team Members:
1. Dr Dorothy FY CHAN (Associate consultant, Department of Paediatrics, Prince of Wales Hospital)
2. Dr Hugh Simon HS LAM (Associate Professor, Department of Paediatrics, The Chinese University of Hong Kong)
3. Ms Billie SY LEE (Nursing consultant, Department of Paediatrics, Prince of Wales Hospital)
4. Dr Simpson WL WONG (Assistant Professor, Department of Psychological Studies, The Education University of Hong Kong)

Project Start Date and End Date: 1 July 2014 to 30 June 2016

Purposes/Objectives:
1. To promote early developmental stimulation to preterm children
2. For early recognition and intervention of high risk preterm infants and children by structured education workshops provided to their parents to empower and enhance their parenting skills and for the train-the-trainer programme (TTT)
3. To promote the awareness of parenting and developmental facilitation in daily practice of health care professionals
4. To encourage trained health care professionals to conduct similar workshops for parents of preterm infants in the future

Activities/Programmes: The programme was well received by both health care professionals and parents of the preterm infants and they enjoyed the interaction during the sessions and participated actively during the programme.

1. *Train- the- trainer programme (TTT)*
   (a) 5 sessions of 3-hour teaching workshops on developmental facilitating skills, parenting skills and techniques for conducting parent workshop for preterm children.
   (b) Age specific educational sessions
   (c) Comprehensive training manual containing all workshop teaching materials
   (d) Coached practical sessions for trained health care professional to participate in delivering parent workshop
2. *Developmental and parenting workshops*
   (a) Four age specific parent workshops which consist of 8 to 12 hours training on developmental stimulation technique and positive parenting for preterm children.
   (b) Pre- and post- assessment: Parental stress, parent-child bonding and parenting competency.
   (c) A 2 hour "Q & A" sessions conducted after each group of training.
   (d) Manual of training materials for parents
3. *Training DVD for health care professionals*
   (a) 100 copies of training DVD consists of training manual and power point for both TTT and parent program
   (b) Deliver to all departments of Paediatrics under public or private hospital, Family health Services and NGOs related

Targets/Recipients:
1. Parents of preterm infant
2. Medical and nursing staffs who were working in the field and interested in participating

Expected and Actual Participation:
Train-the-Trainer Program
Expected: 40 health care professionals in participating
Actual: 41 of nurses or health care professionals participated

Parent workshops:
Expected: 80 families or parents will join the workshop
Actual: 80 parents completed the whole program and 92 parents attended the program

The programme is effective and feasible as indicated by the high attendance rate, significant improvement of bonding and parenting sense of competency, reduction of internalization and problematic behavior of the children. All parents feel comfortable with the flexibility of the programme and its ability to meet their needs. In addition, all participants agreed that the programme should be run on a regular basis.

The train the trainer programme is useful and effective as shown by a figure of over 95% participants satisfying the content of the course and agreeing that the content is appropriate and useful for their daily practice. It also created awareness of the importance of the parents' role in relation in supporting their preterm infants' growth and development, and to strengthen or modify parents' attitudes, beliefs and practices in relation to caring for a preterm infant. Using the train-the-trainer approach, 41 health care professionals were trained for the programme. In total 92 parents joined the programme and 80 of them completed the whole programme.

Benefits Derived:
1. A new comprehensive program for promoting developmental and parenting facilitation and
2. A new training program for health care professional.
3. Continuity of this effective and feasible program can be achieved by developing the training DVD.

Extent of Objective Achieved:
(1) Enhanced the understanding of the importance of developmental and parenting aspects of preterm children will affect their long term development.
(2) Successfully aroused the awareness on this important community social aspect of general health of preterm children in acute hospital and health care professionals.
(3) Established a model for enhancing the post discharge health promotion

Conclusion:
(1) In Hong Kong, more preterm children are becoming long term survivors and experiencing more developmental problems or disabilities;
(2) A new approach or programme which is not only concentrating on acute life-saving therapies, but bridging to the developmental needs and rehabilitation of the child will facilitate their long term coping and diminish the disturbance from their developmental problems or disabilities.
(3) This project changes the pre-existing conception in dealing with preterm children and their parents in acute hospital settings
(4) Continuity of promoting this bridging program by the development of the training DVD for health care professionals.
(5) We expected this workshop will improve the parent-child interaction and parent competent in handling the preterm infants and children. The information of normal development will help the parents in early recognition of sign and symptom of developmental problems. The parent participants can implement early intervention at home, and early referral can be made to appropriate rehabilitation service in Hong Kong will shorten the waiting time for formal training.
(6) The 41 trained nursing staffs are expected to use the learnt materials in their daily practices.

Project Number: 27130664

P76-PF0002

Mobile Application for Risk Understanding By Yourself (RUBY) on Diabetes

Administering Institution: Asia Diabetes Foundation Limited (ADF)

Project Team Members:
1. Prof Juliana Chung-Ngor Chan (Principal Applicant/ Chief Executive Officer, Asia Diabetes Foundation Limited)
2. Dr Risa Ozaki (Honorary Senior Research Associate, Asia Diabetes Foundation Limited)
3. Prof Andrea Luk (Deputy Medical Director, Asia Diabetes Foundation Limited)
4. Ms Harriet Chung (Honorary Nurse Consultant, Asia Diabetes Foundation Limited)
5. Mr Clement Siu (IT Manager, Asia Diabetes Foundation Limited)
6. Ms Vanessa Lau (Operation Manager, Asia Diabetes Foundation Limited)
7. Ms Amy Fu (Assistant Project Manager, Asia Diabetes Foundation Limited)

Project Start Date and End Date: October 2013 to February 2015

Purposes/Objectives: To develop a mobile application of a validated diabetes risk score for raising awareness and detecting high risk subjects for early intervention.

Activities/Programmes: The mobile version and web-based platform of Risk Understanding By Yourself (RUBY) was developed to allow users to evaluate their diabetes risk supplemented with health information and recommendations for follow up actions. The RUBY was promoted through press conference, outreach program, webpage, radio broadcasting, and television program to raise awareness.

Targets/Recipients: All Hong Kong citizens with smart phones, electronic tablets or access to internet, targeting at young to middle-aged group to empower them regarding the common, devastating but preventable nature of diabetes through proactive health management and periodic assessment.

Expected and Actual Participation: The mobile application and website of RUBY developed by ADF was promoted through a series of awareness program. Since its introduction in November 2014, we have reached out to 10,737 subjects using RUBY.

Benefits Derived: Participants can use the mobile application to assess and monitor their risk for diabetes supplemented by definitions of common risk factors and practical advice on how to minimize risk with recommendations on follow up action.

Conclusion: This project is an ongoing campaign to raise awareness, improve health literacy and detect high risk subjects for health protection. The launching of the mobile application and website of RUBY has provided a useful tool to enable users to assess and monitor their risks for diabetes with access to health information and recommendation for follow up action.

Project Number: 05120195

P77-PF0024

Terminating Poor Oral Habits of Preschool-aged Children

Administering Institution: Faculty of Dentistry, The University of Hong Kong

Co-organisation(s): Hong Kong Society for the Protection of Children (HKSPC)

Project Team Members:
1. Dr Yang Yanqi (Clinical Associate Professor, Faculty of Dentistry, The University of Hong Kong)
2. Prof Chu Chun Hung (Clinical Professor, Faculty of Dentistry, The University of Hong Kong)

Project Start Date and End Date: 31 July 2012 to 30 January 2015

Purposes/Objectives: Poor oral habits have considerable influence on children's oral health. Risk of tooth decay raises substantially with poor diet or inadequate oral hygiene habits. The other poor oral habits such as finger sucking are associated with malocclusion. Early intervention to break these poor oral habits can reduce the risk of having tooth decay and prevent the development of malocclusion. This project aims to educate parents and teachers in nurseries and kindergartens to understand the importance of early intervention and to identify dental problems, and to train parents and teachers to help children break poor oral habits, in an attempt to prevent tooth decay and malocclusion.

Activities/Programmes: The 2.5-year project provides 2 rounds of oral examination for the pre-school children, 1 round of education workshop, 1 round of individual consultation, and 3 rounds of questionnaire surveys as well as distribution of educational documents.

Targets/Recipients: Pre-school children aged 2-6 from different kindergartens and their parents and kindergarten school teachers.

Expected and Actual Participation: We worked with a non-governmental organisation, the Hong Kong Society for the Protection of Children (HKSPC). Invitation was sent out to all the 17 nursery schools of HKSPC. Ten of the nursery schools agreed to join this service project. The 10 nursery schools involved are distributed across the three main territories of Hong Kong: Hong Kong Island, Kowloon and the New Territories. All the children aged 2-6 from 10 nursery schools were invited to join this 2.5-year service free of charge. Parents' consent was collected before the project started. As a result, in total 1565 children were covered, with 1024 of them having attended the first dental examination and 1202 of them having attended the second examination. Among them, 661 children attended both of the 2 rounds of dental examination.

Benefits Derived: Firstly, the oral health knowledge of parents had been significantly improved. Secondly, the percentage of children with poor oral habits assessed has significantly decreased. Thirdly, follow-up examination revealed that the condition of children's oral health was under control without any deterioration of tooth decay. Besides, there was a rise in the mean number of filled teeth, which suggests the improved utilization of dental service with parents' improved sense on their children's oral health.

Conclusion: The project was effective in helping children to terminate poor oral habits and improving parents' oral health knowledge. It is highly recommended to implement such oral health programs in other kindergarten schools.

Project Number: 25110524

P78-PF0025

Parent-based Sleep Education Workshop for Children with Autism Spectrum Disorders

Administering Institution: Department of Paediatrics, Prince of Wales Hospital, The Chinese University of Hong Kong

Project Team Members:
1. Yu, Xinting (Postgraduate Student, The Chinese University of Hong Kong)

2. Lam, Hugh Simon (Associate Professor, The Chinese University of Hong Kong)
3. Au, Chun Ting (Research Associate, The Chinese University of Hong Kong)
4. Chan, Hiu Yan Sharon (Research Assistant, The Chinese University of Hong Kong)
5. Chan, Fung Ying Dorothy (Honorary Clinical Associate Professor, The Chinese University of Hong Kong)
6. Li, Albert Martin (Professor, The Chinese University of Hong Kong)

Project Start Date and End Date: 1 October 2012 to 29 September 2013

Purposes/Objectives:
1. To examine the longitudinal effects of parent-based behavioural education on sleep problems and daytime functioning in children with autism spectrum disorders (ASD).
2. To determine whether the education was helpful in improving parental sleep and stress.

Activities/Programmes: Three parent-based sleep behaviour education workshop sessions were conducted over consecutive weeks (week 1-3). Materials covered at the workshop sessions included importance of sleep, strategies to promote healthy sleep habits, medical conditions that could affect sleep. Weekly (week 1-7) telephone interview was conducted by the research nurse to answer queries, provide support and reinforce strategies designed for that particular family. Parents were requested to complete the same set of sleep habit and behavioural checklist questionnaires at baseline and end of the workshop at week 3, week 7, and at a face to face interview at week 11.

Targets/Recipients: Families with children younger than 6 years diagnosed to have ASD and sleep problems as reported by parents.

Expected and Actual Participation: Expected Participation: 100; Actual Participation: 90

Benefits Derived:
1. Children were found to have increased sleep duration, decreased sleep problems and better sleep hygiene.
2. Parents were found to have shorter sleep onset latency, less sleep disturbance and improved daytime function.

Conclusion: Parent-based sleep behavioural education was feasible and effective with sustainable benefits in improving sleep duration and sleep problems in children with ASD.

Project Number: 25110424

P79-PF0026

Increase the Parental Knowledge towards Amblyopia and the Awareness of Importance of the Pre-school Visual Screening Program in Lower Income Class Families Living in Sham Shui Po

Administering Institution: Department of Ophthalmology and Visual Sciences, The Chinese University of Hong Kong (DOVS-THE CHINESE UNIVERSITY OF HONG KONG)

Project Team Members:
1. Dr YAM Jason Cheuk-sing (Assistant Professor, DOVS-THE CHINESE UNIVERSITY OF HONG KONG)
2. Dr JHANJI Vishal (Associate Professor, DOVS-THE CHINESE UNIVERSITY OF HONG KONG)
3. Dr CHEN Lijia (Assistant Professor, DOVS-THE CHINESE UNIVERSITY OF HONG KONG)
4. Dr THAM Clement Chee-yung (Chairman and Professor, DOVS-THE CHINESE UNIVERSITY OF HONG KONG)
5. Ms LEUNG Yuen Yik, Michelle (Project Coordinator, DOVS-THE CHINESE UNIVERSITY OF HONG KONG)

Project Start Date and End Date: 1 July 2015 to 30 December 2016

Purposes/Objectives:
1. To increase the understanding of the disease amblyopia among parents from the lower income class families
2. To increase the awareness of importance of preschool eye screening among lower income class families
3. To increase the uptake of the pre-school screening program offered by MCHC among the lower income class families

Activities/Programmes:
1. Production Education video and pamphlets on children eye care
2. 15 Public Education Talks to reach out 4,360 parents from Sham Shui Po, Yuen Long, Kowloon City, and Kwun Tong District
3. 3 Training workshop for 125 social workers and volunteers of NGOs in Sham Shui Po and Yuen Long
4. 70 Saturday screening days to a total of 2,156 children for comprehensive eye examination

Targets/Recipients:
1. Parents from lower income families
2. Social workers and volunteers of NGOs
3. Children for comprehensive examination

Expected and Actual Participation:
Expected Participation:
(1) 800 Parents of kids aged between 4- 6 from lower income class families in Sham Shui Po District.
(2) 80 Social workers supporting the lower income families in Sham Shui Po District.

Actual Participation:
(1) 421 Parents of kids aged between 4- 6 from lower income class families in Sham Shui Po District attended public education workshop. In total, 4,360 parents from Sham Shui Po, Yuen Long, Kowloon City and Kwun Tong District attended the public talks.
(2) 90 Social workers from Sham Shui Po and 35 Social Workers and Volunteers from Yuen Long has attended Educational workshop respectively.
(3) A total of 2,156 children have received comprehensive screening programme organized by our Department.

Benefits Derived:

Parents of lower income families

95.7% of parents have increased understanding in amblyopia and 100% of them have increased awareness of the importance of the preschool vision screening program and have attended the eye-screening program offered by our Department

Social Workers supporting lower income families

95.6% of social workers understand the underlying reasons causing amblyopia and 100% of them are well aware of the importance of preschool eye screening programme would be willing to help with the promotion after joining the education workshop.

Screening Programme results

35% of them (755 children) suffered from myopia, and examination all were prescribed with spectacles. Detailed education counseling was provided to all families for methods preventing myopia progression, including increasing outdoor activities and restraining the use of electronic devices. Among them, 400 children were offered treatment with low dose atropine eye drops in our THE CHINESE UNIVERSITY OF HONG KONG-Eye Centre with subsidy, with alarmingly success for the myopia control. Furthermore, we found that 40% of them (862 children) have ocular allergy and were offered eye drops for allergic eye disease and behavioral adjustment; 4% of them (87 children) with

lazy eye and patching therapy was offered; 5% of them (107 children) with squint, with further referral and management; and 4% of them (87 children) with color insufficiency and counseling was provided. Children with other eye diseases requiring surgical therapy, such as congenital cataract, congenital ptosis, inherited retinal diseases, was referred promptly to respective cluster of Hospital Authority for further management.

Conclusion: Targeted approach to increase the knowledge and awareness of children eye care of parents and social workers by public health talks and education material distribution is an effective way to increase the attendance of eye screening programme.

Project Number: 28140334

P80-PF0027

Developing an Interactive Social Game Playable on iPhones, iPads and Facebook for Promoting Sexuality Education among Youngsters

Administering Institution: Faculty of Education, The University of Hong Kong

Co-organisation(s):
1. School of Communication and Information, Rutgers, The State University of New Jersey, New Brunswick, USA
2. Institute of Human Performance, The University of Hong Kong
3. FifthWisdom Technology Limited
4. The Family Planning Association of Hong Kong
5. School of Nursing, The University of Hong Kong

Project Team Members:
1. Dr Samuel Chu, Associate Professor, Faculty of Education, The University of Hong Kong
2. Ms Grace Lee, Education Officer In-charge, The Family Planning Association of Hong Kong
3. Mr Alvin Kwan, Lecturer, Division of I&T Studies, The University of Hong Kong
4. Mr Frankie Tam, Director, FifthWisdom Technology Limited
5. Dr Athena Hong, Lecturer, School of Nursing, The University of Hong Kong
6. Mr Charles Lam, Education Officer, The Family Planning Association of Hong Kong

Project Start Date and End Date: 1 April 2012 – 31 December 2014

Purposes/Objectives: A game app "Making Smart Choices" (MSC) was developed to fill the gap of limited easy-to-access resources available on sex education in Hong Kong and to disseminate correct knowledge and positive attitudes towards sex to teenagers using popular platforms such as iPad, Facebook and the web.

Activities/Programmes: We developed "MSC" for use on iPad, the social networking site Facebook, as well as the web to enable wide dissemination of the game through social networking and smart devices commonly used by adolescents.

The game content was designed by experts from the Hong Kong Family Planning Association with experience in developing and disseminating multimedia resources on sex education. Academics with extensive expertise in education and health science were responsible for aligning the game content with targeted learning outcomes. Computer and information science experts provided suggestions on the game framework, game structure and mechanism, thereby contributing to the acceptability and utility of the game. The game was developed with target learning outcomes adopted from the International Technical Guidance on Sexuality Education.

Overall, the information and values embedded into the game messages fall in line with the learning points related to sex education in the curriculum of the Life and Society subject prepared by the Curriculum Development Council in Hong Kong. Advanced graphics in the game were created by a software vendor, Fifthwisdom Technology Limited, specialised in education game development. Usability tests with the target users (adolescents) were conducted during different phrases of game development.

To evaluate the effectiveness and acceptance of the app among teenagers, a series of game sessions in six co-ed schools were conducted. Pre-test and post-test were embedded at the beginning and at the end of the game. Each test consisted of six identical multiple choice questions drawn from a pool of 12 questions related to safer sex knowledge that are covered in the mini-game as part of the game. Students' feedback on the value and effectiveness of the game were collected through questionnaires and focus group interviews.

Targets/Recipients: Secondary school students aged 12-16 years

Expected and Actual Participation: 1,176 secondary school students (ages 12-16) in six co-ed schools participated in the game sessions. A total of 788 sets of pre-test and post-test scores were collected. The total number is smaller than the actual number of students who played the game because data from students who did not submit their consent forms was excluded in the analysis and some students did not complete the post-test at the end of the game.

Benefits Derived: Our work provides preliminary findings that suggest game-based learning, preferably delivered through popular interactive platforms, can be effective in promoting sex education to teenagers.

Conclusion: The game app MSC was developed to fill the gap of limited easy-to-access resources available on sex education in Hong Kong and to disseminate correct knowledge and positive attitudes towards sex to teenagers using popular platforms such as iPad, Facebook and the web. This pioneer Chinese language interactive game on sex education has been well received among Hong Kong adolescents since its introduction. The game-based affordances of this game has led to positive changes in students' safe sex knowledge (particularly in those who repeat gameplay), with student responses indicating a link between gameplay and potential for behavior change. Given that discussions on sex is still taboo in many of the Asian regions and among families with Chinese origins, there is great potential for the "MSC" game in promoting sex education for teenagers in Mainland China, Macau, Taiwan, and other Chinese speaking teenagers worldwide.

Project Number: 04110185

P81-PF0010

踢「酒」智多FUN!

Administering Institution: United Christian Nethersole Community Health Service (UCN)

Project Team Members:
1. Ms Evelyn Lai Yan Lee (Community Nurse Manager, United Christian Nethersole Community Health Service)
2. Dr Joyce Shao Fen Tang (Medical Director, United Christian Nethersole Community Health Service)
3. Ms Afra Nga Wun Wong (Project Coordinator, United Christian Nethersole Community Health Service)

Project Start Date and End Date: 1 April 2015 to 30 June 2016

Purposes/Objectives: This project sought to enhance knowledge and awareness about the harmful effects from alcohol consumption among

primary school students and their parents, emphasize the importance of abstinence and in turn, promote parents to be a role model.

Activities/Programmes: We collaborated with different local primary schools and recruited students and parents to join our tailor-made interventions. Multiple interventions including health talks, student and parents workshops, newsletter and board game card distribution were conducted to achieve the aims.

Targets/Recipients: Primary 5 to 6 students and parents

Expected and Actual Participation: Health talks targeting 1000 primary grade 5 to 6 students and workshops intended for 300 primary grade 6 students and 100 parents were conducted. Newsletters were distributed to all participants and board game cards were given to student who participated in the workshops. By project end, 1262 students had joined the health talks, 314 students and 124 parents had participated in the workshops. Moreover, 2469 newsletters and 534 board game cards had been distributed to the participants.

Benefits Derived: This project successfully raised the awareness of schools on the topic of alcohol consumption among youth and other related health education, such as drug abuse, would be conducted in the future.

Conclusion: Multi-dimensional interventions including health talks, student and parent workshops, newsletters and board game card distribution were effective tools in promoting alcohol harm reduction among primary students.

Project Number: 28140504

P82-PF0018
Love Heart Family (愛「心」之家)

Administering Institution: Care For Your Heart

Co-organisation(s):
1. Prince of Wales Hospital
2. North District Hospital
3. Hong Kong Society for Rehabilitation-Community Rehabilitation Network

Project Team Members:
1. Ms Leung Yim Ching (Former Chairperson, Care for Your Heart)
2. Ms Yau Shuk Man (Former Executive Secretary, Care for Your Heart)
3. Ms Cheung Sin Chun (Former Project Coordinator, Care for your Heart)
4. Ms Cheung Heung Wan (Nurse Consultant, Prince of Wales Hospital)
5. Ms Yiu Sau Ching (Advanced Practising Nurse, North District Hospital)
6. Ms Siu Choi Fong (Social Worker, The Hong Kong Society for Rehabilitation)
7. Ms Kwan Cheuk Yin, Jackie (Social Worker, Hong Kong Society for Rehabilitation -Community Rehabilitation Network)

Project Start Date and End Date: July 2013 to June 2014

Purposes/Objectives:
1. To enhance public and patients' awareness and understanding of Coronary Heart Disease (CHD) and Cardiac Arrhythmias by various rehabilitation programs and public events
2. To encourage the patients with cardiac arrhythmias and their carers to tackle the psychosocial problems and relieve their stress related to their illness
3. To build up a cardiac patients' mutual support group in New Territories
4. To educate public and patients to build up the healthy life style in diet and exercise

Activities/Programmes:
Part 1. Opening Ceremony and Health promotion (開幕典禮及健康教育推廣)
The Opening Ceremony and Health Exhibition launched at the community. Recovered patients participated as volunteers to plan, organize and operate the ceremony.

Part 2. Health Education Talks (健康教育講座)
Health Education Talks with different topics on CHD, Cardiac Arrhythmias and risk factors
launched at Sheung Shui, Tai Po and Shatin districts. The talks were given by cardiologists and related health care professionals. Updated information of the disease delivered to patients and care-takers.

Part 3. Cardiac Rehabilitation Workshop (健康護心坊)
Cardiac Rehabilitation Workshop provided information about the risk factors of CHD & Cardiac Arrhythmias. It helped eliminating incorrect concepts and recommending changes to healthy lifestyle.

Part 4. Diet Training Workshop (護心飲食)
After the Cardiac Rehabilitation Workshop, another session of Diet Training Workshop was provided with information of healthy diet to patients and the carers. The workshops were hosted by project worker and professionals.

Part 5. Exercise Training Workshop (保心運動)
After the Diet Training Workshop, they needed to learn a session of Exercise Training Workshop providing information of regular and suitable exercise. The workshops were hosted by project worker and professionals.

Part 6. Patients Mutual Support Group (病友互助組)
Eleven groups of patients formed Patients Mutual Support Groups after completion of the Cardiac Rehabilitation Workshop, Diet Training Workshops and Exercise Training Workshop. The groups aimed to encourage home-bounded patients to participate in the self-help process. District based support groups were established to gather patients and their care-takers. Potential patients were invited to be group leaders to develop the connection among each other.

Part 7. Education in Community (心繫社區)
Potential patients were invited to be group leaders, volunteers and trainers in the project. Thus, they provided cardiac health service to the community and educated the public.

Part 8. Graduation Ceremony (開心畢業禮)
A Graduation ceremony was in place to celebrate those participants who had completed the basic requirements of the programme and kept the healthy lifestyle in their daily life.

Part 9. Educational Materials (教育資訊)
The patients' kit included a set of educational materials which provided accurate information of the illness and self-check list for patients and carers.

Targets/Recipients: People with CHD and Cardiac Arrhythmias as well as the public in New Territories

Expected and Actual Participation: Expected participants: 5,155 Actual participants: 5,500

Benefits Derived: Participants were educated to be aware of the causes, symptoms, diagnosis, treatment and prevention of the heart diseases and to control risk factors of heart diseases including hypertension, diabetes mellitus and high cholesterol. Also, this project trained a group of people with CHD and Cardiac Arrhythmias to

become trainers to teach other newly diagnosed people with cardiac diseases and to help forming a group supporting each other during their recovery from the sickness. Over the period, they built up an inner bonding relationship like family members within the groups. At the end of the project, participants become promoter of Heart Health in their community and social network.

Conclusion: This project reached 5,500 people. Through the post-function questionnaires, we found that most participants claimed that their stresses were crucial to the heart diseases. They felt less worried about their diseases after chatting with other participants who had similar conditions. Though interviewing with the participants, it was also found that most of them agreed that they had become happier with improved quality of sleep. It is believed that patients' mutual support groups play an important role in cardiac rehabilitation in tacking psychological problems and stress related to their illness. We have positive feedbacks and outcomes from this program.

Project Number: 26120454

P83-PF0019
預防大腸癌妙法，你做左未呀？

Administering Institution: United Christian Nethersole Community Health Service (UCN)

Project Team Members:
1. Ms Evelyn Lai Yan Lee (Community Nurse Manager, United Christian Nethersole Community Health Service)
2. Dr Joyce Shao Fen Tang (Medical Director, United Christian Nethersole Community Health Service)
3. Ms Afra Nga Wun Wong (Project Coordinator, United Christian Nethersole Community Health Service)

Project Start Date and End Date: 1 May 2015 to 31 October 2016

Purposes/Objectives: This project sought to enhance general public (aged between 50 and 75 living in Kowloon East and New Territories East, who have never been screened for colorectal cancer before)'s knowledge on CRC prevention and motivate them to consult their family doctor and undergo CRC screening test.

Activities/Programmes: We collaborated with different local elderly centers and private corporates for eligible participants' recruitment. Multi-dimensional interventions including health talks, demonstration and tasting of seasonal vegetable recipes, distribution of pamphlets including CRC prevention tips and tailor-made simple recipes designed by registered dietitians, and phone follow-ups by trained staff were conducted to achieve the aims.

Targets/Recipients: General public aged between 50 and 75

Expected and Actual Participation: Health talks and cooking demonstration classes targeting 1,000 general public aged between 50 and 75 were targeted. By project end, 1,278 participants had joined the health talks and cooking demonstration classes, Amongst all, 502 participants received 2 follow-up phones calls and short private consultation by trained staff for CRC risk assessment and screening advices. Moreover, 2,000 pamphlets including CRC prevention tips and tailor-made simple recipes had been distributed to the participants/ elderly centres/ corporates.

Benefits Derived: This project has successfully raised the awareness about CRC-related issues among the participants. The Participants did demonstrate positive knowledge enhancement on CRC prevention lifestyles and choices of screening tests.

Conclusion: Multi-dimensional interventions including health talks, demonstration of seasonal vegetable recipes, distribution of pamphlets, and phone follow-ups were effective tools in promoting CRC prevention among general public aged between 50 and 75. Yet, despite the fact that the participants did increase their intention to seek family doctor's advice on undergoing CRC screening, the costs serve as one of the main barriers and current government's policy in subsidizing CRC screening services though, is good but might have to be expanded and cover more groups.

Project Number: 28140494

P84-PF0006
餐餐智慳嚐有營

主辦機構：基督教聯合那打素社康服務(社區營養服務)

計劃成員：
1. 劉碧珊女士(基督教聯合那打素社康服務 社區營養服務 服務經理)
2. 陳紫敏女士(基督教聯合那打素社康服務 社區營養服務 助理服務經理)
3. 莫穎姍女士(基督教聯合那打素社康服務 社區營養服務 社區營養師)
4. 羅曼詩女士(基督教聯合那打素社康服務 社區營養服務 高級社區營養師)
5. 梁素顏女士(基督教聯合那打素社康服務 社區營養服務 前社區營養師)
6. 梁可琪女士(基督教聯合那打素社康服務 社區營養服務 前社區營養推廣主任)
7. 利嘉麗女士(基督教聯合那打素社康服務 社區營養服務 前社區營養推廣主任)

計劃開始及完成日期：2013年4月1日至2015年3月31日

目的/目標：
目標：以新界西區的貧窮率較高而社區營養推廣較缺乏為選區作推廣。透過營養講座、親子小組、家長跟進小組、食譜集及教育海報，增加參加者對營養素(包括優質蛋白質、鈣質和鐵質) 及其食物來源的認識、提升家長安排合乎經濟和營養原則的膳食之能力(budget meal planning ability)，改善學童進食含優質蛋白質、鈣質和鐵質的食物之次數以及增加社區人士對經濟兼含豐富營養的食物之認識。

目的：參與活動後(或至2015年3月31日)，
1. 營養知識：70%參與計劃之學童和家長能正確指出兒童成長的必需營養素
2. 營養知識：70%參與計劃之學童和家長能正確指出含必需營養素的食物來源
3. 飲食技巧：60%參與計劃之家長懂得在有限的預算下（即120至230元以內）編排供四人家庭的均衡營養三餐
4. 飲食習慣：60%參與計劃之家長能每星期最少3天為子女安排含有必需營養素的食物

活動/推行大綱：
1. 聚焦小組：共邀請11名家長及5名學童以了解新界西區內人士的膳食及開支狀況，並參考所提供之意見設計講座及學堂的內容。
2. 學生義工培訓期：向香港大學專業進修學院保良局何鴻燊社區書院(營養及食品管理高級文憑) 的30名學生提供培訓，內容除透過教學模式加強他們對正確營養素的知識外，每名學生義工均參與最少2次親子學堂，讓他們實踐所學。
3. 活動推行期-由註冊營養師：
   - 3.1 主講「小食智慳嚐有營」營養講座予學童，教授有利學童成長的必需營養素，以互動手法鼓勵他們善用金錢去選購健康小食
   - 3.2 舉辦「餐餐智慳嚐有營」親子學堂。第一節(家長及學童組別同時進行各一節)以加強知識及技巧為主，學童組透過遊戲活動帶出重要營養素的訊息及鼓勵善用金錢選購健康小食；家長組透過營養知識教學及食譜創作學習符合經濟及營養原則的膳食編排及技巧，並認識更多區內之「食物銀行」及「平價市場」資源；第二節以實踐及親子為主，除了透過選出家長設計之優異食譜示範及營養師的健康煮食示範，亦安排親子「至慳有營」小食製作，深化學習及實踐健康飲食模式。

4. 家長跟進小組：邀請曾參與學堂之家庭出席作持續推廣。透過三場小組討論，家長表達活動得著、實踐心得及處理困難之技巧；另透過由義工學生帶領營養互動遊戲，讓學童重溫所學，繼續實踐。
5. 社區推廣期：以「智慳營養七大招」海報及「智慳有營煮一餐」食譜作為持續推廣教育工具，除向本計劃30所學校及參與機構派發，另上載至本機構之網頁供下載及傳真至新界西的52個物業管理處及社福機構宣傳，供張貼作持續推廣。

對象/受惠者：新界西區(元朗、天水圍及屯門區)內6000名學童、300名受惠於半數及全數書簿津貼的學童及其家長(各150名)及間接受眾為社區人士8000名(食譜編制及海報推廣)。

預期及實際參與人數：
1. 學生營養講座的受惠人數為5,834人(達預期97.2%)
2. 親子學堂的總受惠人數為166位家長及186位學童，其中：
   2.1 參與了一節學堂受惠人數155位(103%)
   2.2 完成兩節學堂受惠人數130位(86.7%) 。
3. 透過教育小冊子及海報作間接推廣的人次和網頁瀏覽量受惠人次/流為7,027(87.8%)。

效益：
整體成效評估結果：
前後測評估問卷(講座及學堂)、飲食習慣前後測問卷(學堂)、活動滿意度及跟進小組之意見進行分析及評估。
結果：參與計劃的85%學童和82%家長在知識層面均有增長，能正確指出兒童成長必需的營養素；77%學童和83%家長能正確指出優質的食物來源；61%家長提升了飲食技巧，懂得在有限的預算下編排符合均衡營養原則的三餐以供一個四人家庭食用。九成家長表示能協助子女實踐健康飲食，如每星期最少3天為子女安排優質營養的食物。此外，大部分學童(92%)和家長(99%)願意選購健康的食物取代不健康的零食有利學童成長。

總結：
透過工作坊及聚焦小組，有效提升家長及小學生的知識(有助孩子成長並容易被忽略的營養素)、態度(加強對營養的關注，家長能衡量金錢與營養)和行為(知行合一，把知識實踐於生活中)；亦能提升家長掌握以較相宜的價錢選購更健康和合適的食物，增加自我效能去管理子女健康的技巧。資訊若能普及至家中老幼成員，冀能將家庭營養狀況得到改善；或考慮將培訓投放於老師及社會工作者(Train-the-trainer)，讓營養推廣活動得以延伸，與各持份者配合下共同帶出有效的學習。

計劃編號：26120334

P85-PF0008
穿「蔬」工作間 (LOVE VEG at Workplace)

主辦機構: 基督教聯合那打素社康服務(社區營養服務)

計劃成員：
1. 劉碧珊女士(基督教聯合那打素社康服務 社區營養服務 服務經理)
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6. 梁可琪女士(基督教聯合那打素社康服務 社區營養服務 前社區營養推廣主任)
7. 利嘉麗女士(基督教聯合那打素社康服務 社區營養服務 前社區營養推廣主任)

計劃開始及完成日期：2015年4月15日 至 2016年10月14日

目的/目標：
目標：以工作間作為健康推廣平台，透過互動方式旨向在職人士提供有關蔬菜的營養教育及飲食建議，並以"LOVE"為理念冀將個人的健康飲食改變 (Diet Change) 伸延至工作間及家人朋輩中，包括：Learn (學習蔬菜的營養特色如維他命、礦物質及抗氧化元素) 、Open-minded (持開放態度接受不同類型的蔬菜和味道)、Variety (多元化的蔬菜種類包括菜葉、瓜、果、莖、根等)、Enjoyment (以不同的烹調方法提升味道，將進食蔬菜轉化成生活享受)。
目的：在職人士完成了「穿『蔬』工作間」活動後：
1. 蔬菜營養及相關知識及技巧評分(Knowledge and Skill Score)達平均值70%或以上
2. 蔬菜攝取態度及意向評分(Attitude Score)達平均值70%或以上
3. 蔬菜平均每天攝取量飲食習慣評分(Dietary Behavior Score): 七成或以上參加者達每天攝取多於一碗熟菜或類同份量
4. 向工作間朋輩及或家人推廣或鼓勵『每天應攝取足夠蔬菜以預防慢性疾病』: 七成或以上參加者向3人或以上推廣或鼓勵

活動/推行大綱：
計劃鼓勵參與工作間成立工作小組由計劃推行成員於籌備階段到訪每所工作間作實地視察，以了解個別需要作適切修改。每所工作間舉辦三節工作坊及持續推廣活動，包括：
1. 穿『蔬』營養防三高：以專題蔬菜營養講座講解蔬菜攝取與預防慢性疾病的關連，介紹五色蔬菜及其營養素的知識；設有五色沙律菜試食，讓在職人士嘗試不同顏色的蔬菜
2. 穿『蔬』每日『嚐』：透過「蔬菜馬拉松遊戲」鼓勵參加者積極構思如何將蔬菜入饌；邀請農莊/水耕種負責人講解蔬菜種植；以蔬菜作健康禮品並鼓勵多進食蔬菜
3. 穿『蔬』新『煮』意：即場煮食示範教授自家烹調技巧；教授外出飲食和在家煮食時增加蔬菜攝取的策略
4. 穿『蔬』大挑戰持續推廣：鼓勵參加者將自製或外出用膳時之蔬菜或菜式拍照，上載至其工作間內聯網作工作間推廣或上載於計劃的臉書(Facebook)專頁；另提供印有五種蔬菜例子及營養素之蔬菜便條貼以作日常提示及持續推廣

對象/受惠者：
1. 十所工作間及其約30-50名在職人士(直接受惠)
2. 透過參與計劃之在職人士作推廣或鼓勵(間接受惠人士)
3. 營養學系或相關之專上學院學生(提供課堂培訓及協助活動推廣)

預期及實際參與人數：
- 直接受惠人次：[預計]900-1500人次(十所工作間，每所三節工作坊，每節30-50人)：[實際]1,303人次，而每節工作坊的平均參加人數約43人
- 間接受惠人士：[預計] 900-1500人；[實際] 2,099人
- 受培訓的營養學系或相關之專上學院學生：[預計] 30-100人；[實際] 31人

效益：
整體成效評估結果：根據工作坊前後測評估問卷，分析了十所工作間的參加者於知識、態度及行為上改變(前測填寫人數：405人；後測：244人)，均達至預期成效指標，並得出以下結果：
- 知識和態度平均值分別為76.7%和98.6%，行為改變方面，七成五參加者表示每天有攝取多於一碗熟菜或類同份量。
- 經中期報告的檢討及建議方案，各成效指標均有所改善。三大成效指標當中，以知識增長最高，有30.1%增長，而行為改變亦有15.8%增長。參加者對蔬菜攝取的態度及意向於工作坊前已十分正面，超過九成八參加者均同意或非常同意蔬菜的重要性和願意增加蔬菜的攝取，而工作坊後亦維持高於九成八。

持續推廣成效：十所工作間均有為員工提供持續推廣活動，其中兩所舉辦健康蔬菜食譜創作比賽，經本計劃註冊營養師評分及提供評語，再由工作間負責人頒發獎項；另外四所工作間分別於其刊物刊登健康文章及活動分享花絮，並透過定期會議向其他員工推廣進食蔬菜的重要性；三所工作間於內聯網、茶水間和告示板等張貼或上載蔬菜攝取的溫馨提示；亦有一所工作間為員工提供蔬菜。每所工作間均獲發證書以示鼓勵，並獲贈蔬菜營養全書乙本作持續營養推廣。

此外，計劃製作了三千份蔬菜便條貼予參加者作教育資訊品，藉此作個人日常提示及用作向他人推廣之用。每所工作間獲發份量為該參加者人數的3-4倍，約共1,900件，由工作小組向參加者派發並著重向其他3人作健康宣傳之用。同時，工作間獲發索取持續推廣報告及建議概要表格，以了解日後可實行的健康推廣建議及措施。

總結：

1. 增加蔬菜攝取是預防肥胖及多種慢性疾病策略之一。工作坊後，十所工作間的參加者於知識、態度及行為上改變均達至預期成效指標。
2. 營養知識著重五彩蔬菜的認識，其豐富植物元素具抗氧化功能並有助預防或減慢癌症的形成。計劃發現參加者對部份蔬菜如白色、橙黃色和紫藍色蔬菜與其營養素的認知較淺，需加強其認知以擴闊選擇類別及增加攝取量。
3. 計劃結果仍反映員工進食午餐經常欠缺足夠蔬菜，展望未來能由不同持份者加強合作，包括政府健康促進的宣傳，社區非牟利組織繼續推行並與相關推動健康飲食文化的委員會配合，飲食業界的支持（如:主動增加蔬菜供應等），以配合市民所需及營造健康的飲食環境。
4. 參加者除增加蔬菜的知識外，更建立了對蔬菜攝取的正面態度、加強自我管理能力(外出用膳及家中烹調技巧)及營造健康環境(不論於工作間、社交羣組、朋輩同事間)，並推動了同行支援的作用。

未來計劃建議透過健康促進計劃於香港作科學研究，把本計劃的藍本作驗證(validation)並研究不同工作性質的成效分別，持續於不同的工作間推廣，有助將受惠者擴大至更多工作間。

計劃編號 : 28140524

P86-PF0007

DASH A DAY – Community Promotion Program

Administering Institution: Community Nutrition Service, Preventive Medicine & Clinical Services Division, United Christian Nethersole Community Health Service (UCNCHS)

Project Team Members:

1. Ms LAU, Pik Shan Doris (Principle Applicant, United Christian Nethersole Community Health Service)
2. Ms LO, Man Sze, Mancy(Accredited Practising Dietitian, United Christian Nethersole Community Health Service)
3. Ms CHAN, Tze Man, Heidi (Registered Dietitian, United Christian Nethersole Community Health Service)
4. Ms MOK, Wing Shan, Sabrina (Accredited Practising Dietitian, United Christian Nethersole Community Health Service)
5. Ms LEE, Ka Lai, Kelly (Former Program Coordinator, United Christian Nethersole Community Health Service)
6. Ms LEUNG, Ho Ki, Winky (Former Program Coordinator, United Christian Nethersole Community Health Service)

Project Start Date and End Date: 1 April 2013 to 31 March 2015

Purposes/Objectives: To increase the awareness of middle-aged adults and the elderly about diet, hypertension and heart disease and to increase their capability to adapt DASH diet in their daily life.

Activities/Programmes: Each participating Elderly Community Center (ECC) received 1 educational workshop and 2 focus groups, each at 1.5hr. The educational workshop included the education of relationship between diet, hypertension, heart disease, education of low sodium diet & DASH diet. Participants who participated educational workshop and self-willing to join were invited to join focus group 1, which was an in-depth DASH diet mock practice to adapt DASH in daily life. Focus group 2 (~2-3 months after workshop 1) were conducted for the participants and the dietitian-in-charge, to share practical experience, successfulness and difficulties on adaptation of DASH diet in their daily living, in order to sustain long-term compliance.

Targets/Recipients: 50-75 elderly (aged 60 or above), which activities of daily living were independent and/or their middle-aged carers/ adults (aged 30-59) in the community, recruited through ECCs.

Expected and Actual Participation: With the expectation of at least 1100 target to join our program, a total of 1160 direct beneficiaries (75.6% attendance) joined the program. Average knowledge score of participants' DASH diet components raised from 45.0% to 90.3%. Average attitude score of participants towards willingness on adapting DASH diet increased from 80.5% to 95.3%. The average spreading of information of DASH Diet/DASH a DAY educational booklet from participants joined focus group and not joined focus group was 74% and 32.6%, with an average of 1 participant spread to 1.7 people. Also, 82.6% participants, who joined focus group (N=311) ,reported with adapting DASH diet in daily life 4.7 days per week, compared with 32.4% participants, who without joined focus group (N=611), reported with adapting DASH diet in daily life 3.3 days per week.

Benefits Derived: Participants were provided with practical experiences for knowledge attainment and application of DASH diet and thus increase the frequency of practicing DASH diet in their daily lives after this program. Improvement has been shown in obtaining more than 90% in knowledge and attitude scores. Average spreading of DASH diet/information per reporting participant is 1 to 1.7.

Conclusion: This program enhanced participants' knowledge in the components of DASH diet and further improved their attitudes towards willingness to adapt DASH diet in daily lives. As a result, participants were proved to increase their frequency of practicing DASH diet on their own after this program and postulated that in the long run through group education focusing reducing salt intake and adapting the DASH diet would help to prevent development of hypertension in the community.

Project Number: 26120344

P87-PF0009

Food Label Reading for Stylish Eating–Community Promotion Program

Administering Institution: Community Nutrition Service, Preventive Medicine & Clinical Services Division, United Christian Nethersole Community Health Service (UCNCHS)

Project Team Members:

1. Ms LAU, Pik Shan Doris (Principle Applicant, United Christian Nethersole Community Health Service)
2. Ms LO, Man Sze, Mancy (Accredited Practising Dietitian (RD1), United Christian Nethersole Community Health Service)
3. Ms MOK, Wing Shan, Sabrina (Accredited Practising Dietitian (RD2), United Christian Nethersole Community Health Service)
4. Ms CHAN, Tze Man, Heidi (Registered Dietitian, United Christian Nethersole Community Health Service)
5. Mr LO, Ting Wai (Accredited Practising Dietitian, United Christian Nethersole Community Health Service)
6. Ms LEE, Ka Lai, Kelly (Former Program Assistant, United Christian Nethersole Community Health Service)
7. Ms LEUNG, Ho Ki, Winky (Former Program Assistant, United Christian Nethersole Community Health Service)
8. Mr LAU, Tsz Hei (Former Program Assistant, United Christian Nethersole Community Health Service)
9. Miss SO, Yuen Ying (Program Assistant, United Christian Nethersole Community Health Service)

Project Start Date and End Date: 1 April 2015 to 31 December 2016

Purposes/Objectives: To increase food label reading ability of parents, carers, teachers in kindergartens/primary schools; student leaders, teachers in secondary schools and Hong Kong community participants under NGOs.

Activities/Programmes: Each unit received 2 food-labelling workshops. Workshop 1 is food labelling theory and reading practice workshop. Workshop 2 is an in-depth food-labelling reading practical including technique to compare different food/snacks, by a mock supermarket at the participating unit or a real supermarket tour at nearby supermarket.

Each participant received a self-administered questionnaire to evaluate changes in knowledge, attitude and behavior on nutrition labelling.

Targets/Recipients: 30-50 participants in 28 units (kindergartens, primary/secondary schools /NGOs in HK

Expected and Actual Participation: With the expectation of at least 840 targets to join our program, a total of 1001 participants joined the program, with 83.9% attendance and 35.8 participants per unit. Average knowledge score of participants' food-label reading ability increased from 35.8% to 95.1%. Average attitude score of participants towards food-label law enactment, food label & its relation to develop healthy eating behaviour and food-label & its practicability at daily use increased from 89.8% to 93.8%, 89.5% to 93.7% and 87.7 % to 94.0%, respectively. The average spreading of food-label information per participant to at least 1 people increased from 5.6% to 58.6%, with an average of 1 participant spread to 1.8 people. Also, 76.8% participants reported with maintenance or an increase of reading food-labels and the average no. of food-labels per 10 pre-packaged foods that participants read increased from 2.9 to 4.9 before and after the program.

Benefits Derived: Participants were provided with practical learning experiences for knowledge application and thus increase the frequency of reading food-labels after this program. Improvement was shown with more than 90% knowledge score and attitude scores. Average spreading of reading food-labels per person is 1 to 1.8. Average satisfaction rating towards program's practicality of contents and degree of overall satisfaction to our program reached 95.9% and 95.5%, respectively.

Conclusion: The program enhanced participants' food labelling reading skills that is conducive to nutritional's health and provided long term compliance & sustainability to read and compare food labels on their own. We postulated that in the long run interactive group education across different target groups would be an effective strategy to sustain individuals' learning towards reading food labels and practice it at daily life that strengthened community actions towards reducing salt and sugar intake in Hong Kong.

Project Number: 28140534

P88-PF0013

Eat for Fun (識食家"FUN") - A Parenting Workshop to Enhance Parental Skills on Handling Children's Mealtime Behaviours and Making Healthy Food Choices for Young Children in Hong Kong

Administering Institution: Department of Medicine and Therapeutics, The Chinese University of Hong Kong

Co-organisation(s):
1. Centre for Nutritional Studies, The Chinese University of Hong Kong
2. Family Health Service, Department of Health
3. Institute of Human Performance, The University of Hong Kong

Project Team Members:
1. Prof Chan Suk Mei Ruth (Department of Medicine and Therapeutics, The Chinese University of Hong Kong & Centre for Nutritional Studies, The Chinese University of Hong Kong)
2. Prof Woo Jean (Department of Medicine and Therapeutics, The Chinese University of Hong Kong & Centre for Nutritional Studies, The Chinese University of Hong Kong)
3. Prof Sea Man Mei Mandy (Department of Medicine and Therapeutics, The Chinese University of Hong Kong & Centre for Nutritional Studies, The Chinese University of Hong Kong)
4. Dr Luk Wai Yin (Family Health Service, Department of Health)
5. Ms Ip Francis (Family Health Service, Department of Health)
6. Dr Tso Ka Pik Karen (Family Health Service, Department of Health)
7. Prof Sobko Tanja (Institute of Human Performance, The University of Hong Kong)
8. Ms Yip Chun Fan Marianna (Family Health Service, Department of Health)
9. Ms Lai Kit Yu Margaret (Family Health Service, Department of Health)
10. Ms Mak Lai Tim (Family Health Service, Department of Health)

Project Start Date and End Date: 1 April 2014 to 30 September 2015

Purposes/Objectives: The project aimed to develop and disseminate a parenting program entitled "Eat for FUN" that incorporated components on parental skills on handling child's mealtime behaviours and making healthy food choices for the children. The specific objectives were:
1. To increase parents' knowledge of the key age-appropriate food choices for their children
2. To increase parents' knowledge of the developmental characteristics of their children
3. To increase parents' competence in terms of knowledge, attitudes, skills and parents' self-efficacy in applying appropriate feeding practices and managing problems related to feeding and mealtime behaviours for their children.

Activities/Programmes: The "Eat for FUN" parenting program was designed by primary care physicians, Maternal and Child Health Centre (MCHC) nurses, dietitians, nutritionists and clinical psychologists. Two levels of workshops were developed, namely the infant workshops and the toddler workshops. Each workshop consisted of two 2-hour sessions and were delivered on a weekly basis by a nurse and a dietitian. The first session of the infant workshop focused on the feeding behaviors and development of feeding skills of infants, whereas the second session focused on food choices and food preparation skills to meet the nutritional needs of infants of 6 to 12 months old. For the toddler workshop, the first session focused on food choices and skills of planning and sharing a healthy family meal with the toddlers. The second session focused on the feeding behaviors and handling of meal time behaviors of the toddlers. Interactive components were incorporated as part of the workshop activities. These components included sharing sessions, cooking demonstrations, video clip viewing, activity worksheets, and discussion on child feeding practices. Participants completed questionnaires at pre-, post-workshop and one month following the workshop for evaluation of the workshops.

Targets/Recipients: The program targeted for Chinese parents with index child aged under 36 months. Other main caregivers of the index child, such as grandparents were also encouraged to join the program. The infant workshops targeted for parents with children aged between 6-12 months; while the toddler workshops targeted for parents with children aged between 18-36 months. The project team aimed to deliver the program to about 70 to 100 participants for each workshop.

Expected and Actual Participation:
Workshop: Eat for FUN – for infants
There were 10 infant workshops held between July 2014 and May 2015 in nine different MCHCs. A total of 172 parents and other caregivers enrolled in the workshops. Among them, 127 attended the workshop (attendance rate: 74%), with 94 completed both sessions. A total of 85 participants returned both pre- and post-questionnaires. Among them, 53 also submitted the one-month questionnaire.

Workshop: Eat for FUN – for toddlers
There were 13 toddler workshops held between July 2014 and May 2015 in nine different MCHCs and two non-governmental organizations. In total, 185 parents and other caregivers enrolled in the workshops. Among them, 124 attended the workshop (attendance rate: 67%), with 78 completed both sessions. A total of 73 participants returned both pre-and post-questionnaires. Among them, 46 also submitted the one-month questionnaire.

Benefits Derived: The project enhanced the awareness of healthy food choices and the adoption of appropriate feeding practices among parents with young children. Participants of the infant workshops reported that their knowledge in child feeding and child feeding practices were greatly increased and some of their previous negative perceptions on child feeding were improved after the workshops. Similarly, participants of the toddler workshops shared that their knowledge in child feeding and their perceived self-efficacy of various child feeding skills were increased after the workshops. Furthermore, a few of their child feeding practices and their perceptions of child feeding were significantly changed in a favourable direction after the workshops.

Conclusion: The "Eat for FUN" workshops are feasible to increase parents' competence in terms of knowledge, attitudes, skills and parents' self-efficacy in applying appropriate feeding practices and managing problems related to feeding and mealtime behaviours for their children.

Project Number: 27130574

P89-PF0005

Bicycle Helmet Rental Scheme: Promotion of Bicycle Helmet Use among Recreational Riders

Administering Institution: Jockey Club School of Public Health and Primary Care, The Chinese University of Hong Kong

Co-organisation(s):

1. Accident & Emergency Medicine Academic Unit, The Chinese University of Hong Kong
2. Division of Neurosurgery, Department of Surgery, Prince of Wales Hospital / The Chinese University of Hong Kong
3. Department of Orthopaedics, The Chinese University of Hong Kong

Project Team Members:

1. Prof Katrina Tsang (Assistant Professor, SPHPC, The Chinese University of Hong Kong)
2. Dr Kevin KC Hung (Assistant Professor, Accident & Emergency Medicine Academic Unit, The Chinese University of Hong Kong KONG)
3. Prof Colin A Graham (Professor, Accident & Emergency Medicine Academic Unit, The Chinese University of Hong Kong)
4. Prof Emily YY Chan (Professor, SPHPC, The Chinese University of Hong Kong)
5. Prof George KC Wong (Professor, Division of Neurosurgery, The Chinese University of Hong Kong)
6. Prof Timothy H Rainer (Professor, Accident & Emergency Medicine Academic Unit, The Chinese University of Hong Kong)
7. Dr Danny TM Chan (Consultant, Division of Neurosurgery, Prince of Wales Hospital)
8. Dr Raymond CH Cheng (Consultant, Accident & Emergency, Prince of Wales Hospital)
9. Dr Janice HH Yeung (TNC, Accident & Emergency Department, Prince of Wales Hospital)
10. Dr Marco CL Kwan (Associate Consultant, Division of Neurosurgery, Prince of Wales Hospital)
11. Prof PC Ho (Professor, Department of Orthopaedics, The Chinese University of Hong Kong)

Project Start Date and End Date: 1 June 2013 to 30 November 2015

Purposes/Objectives: The goal of this helmet rental project was to increase bicycle helmet use and eventually lead to reduction in bicycle related mortality and morbidity from head injury.

The primary objective was to i) increase the bicycle helmet use for recreational cyclists by providing easier access for to helmets in affordable prices, ii) raise the awareness and acceptance for bicycle helmets use in Hong Kong.

Activities/Programmes:

1. Helmet Rental Scheme
   The helmet rental scheme rolled out to 4 bicycle rental shops (one company is in two locations) in Tai Wai, Shatin bicycle park, Tai Po Waterfront Park and Tai Po Tai Mei Tuk from December 2013 to November 2015, spanning a total duration of 24 months (730 days). A total of 150 bicycle helmets of a combination of adult and children sizes were provided to the rental shops. To promote wearing helmets correctly, banners and pamphlets were displayed and made freely available at the bike shops.
2. Promotional Events
   This project had nine promotional events promoting bike safety and helmet use with games, poster and banner displays and live demonstrations.

Targets/Recipients: Initial target beneficiaries was 20400. Daily rental target was 50 helmets. This project period would include at least two promotional event on helmet use.

Expected and Actual Participation: The total number of beneficiaries from December 2013 to November 2015 was 10450. During this period, 1 shop in 2 locations was closed for refurbishment for two months and another was closed intermittently for two months. Among the 10450 helmet rentals, 3425 (32.78 %) were adult-sized helmets while 7025 (67.22 %) were children-sized helmets. The overall average number of helmet rental was 14.32 per day regardless of rainfall (total 730 days) and regardless of weekday or weekend or holiday.
A total of nine promotional events on community education and outreach were organised and participated. We estimate that these events reached over 150,000 people.

Benefits Derived: The acceptability, satisfaction and feasibility of rental scheme to users were demonstrated by the significant helmet use of 10450 and from questionnaires received. We also found that the bike shops in this scheme are supportive, able and willing to provide helmets to recreational riders. Questionnaires also showed that most helmet users were satisfied with this scheme and majority would return to join the scheme again.

Conclusion: More resources are needed in promoting helmet use and rental schemes as generally, bikers were unaware of the scheme and unaware of the importance to wear helmets to reduce bike related head injuries. This project had resources only sufficient for isolated one-time events. Longer term, regular and continuous promotions such as government promotion producing Announcements for the Public Interest (APIs) or advertisement in television, internet, public transport, are expected to reach more of the general public.

Project Number: 26120044

P90-PF0011

Sport Therapy Enhancement Project (STEP) for Special educational needs children 特殊學習需要學童運動治療改善計劃

Administering Institution: Chinese YMCA of Hong Kong 香港中華基督教青年會

Project Team Members:

1. Miss SHIU Yuen-ling, Coordinating Secretary, Chinese YMCA of Hong Kong
2. Mr Ng King-kit, Service Development Officer, Chinese YMCA of Hong Kong
3. Mr Chung Chun-hung, Project Officer, Chinese YMCA of Hong Kong

Project Start Date and End Date: 1 June 2015 to 31 August 2016

Purposes/Objectives:

Purpose: Sport Therapy Enhancement Project ("STEP Project") for special educational needs children aimed at encouraging students from Primary 1 to 3 with Special Educational Needs (SEN) (especially autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD)) to engage in game play which incorporates physical training, as to enhance their all-round development in health and improvement in cognitive abilities.

Objectives:

1. To stimulate participant's intensity in sports activities
2. To elevate participant's attention skills
3. To improve participant's interpersonal skills, especially in social skills and emotional control

Activities/Programmes:

1. Sports Therapy Enhancement training courses in primary schools (8-12 sessions per school)
2. Education lectures for participants' parents (2 lectures)
3. Teaching workshop for teaching staff from special education units in schools (1 workshop)
4. Certificate programme for sports therapy instructors (6 sessions and 1 practical training)
5. Press Conference

Targets/Recipients:

1. Primary school students from P1-P3, with special education needs as stated above
2. Parents of SEN students
3. Teaching staff from special education units
4. Sports and recreation staff, social worker and tertiary students majoring in sports, rehabilitation and social work

Expected and Actual Participation:

Target	Expected Participation	Actual Participation
Number of SEN students participated:	80	115
Number of parents attended lectures:	60	65
Number of staff from special education units attended teaching workshop:	20	30
Number of Students attended 70% of training sessions or above	56	110

Benefits Derived: The overall effectiveness of STEP programme was examined by 4 sets of pre- and post- testing and questionnaires for participants' parents.

Assessment tasks included single leg balancing, symbol pairing, shuttle run and numbering test, and to evaluate their balancing skills, coordination skills, selective attention as well as sustained attention. A total of 111 SEN (ASD or ADHD) students from P.1-3 were invited to receive training. Compared with pre-treatment condition, the assessment results indicated significant post-treatment improvements in participants' selective attention (68.80%, 75/109 students), sustained attention (57.78%, 63/109 students) and sensitivity (81.31%, 87/107 students) respectively.

Parents of SEN students also observed that the programme positively impacted their children, especially the intensity in sports. Their questionnaires showed an elevation of students' attention skills (56.76%, 63/111 students) and improvement in social skills (86.49%, 96/111 students).

Conclusion:

Students with SEN in mainstream school were more than expected

It was interpreted that there are 12 students with ASD/ADHD per mainstream primary schools in 2013-14. Assumed two-third of them were P.1-P.3, the number of junior students with ASD/ADHD should be around 8. However, the above assumption was not applicable as 2/3 of our partner schools (8 out of 12) had more than 8 of junior students with ASD/ADHD, and their needs should be catered.

Uneven service provision to SEN students

Supporting services to ASD/ADHD students concentrate on language, sensory integration, social and attention skills, whereas these training could not cater their all-round development. Sports are crucial for children's growth while SEN students are usually excluded in physical education lesson because of their physical constraints.

Partner schools welcome diversified teaching method in helping SEN students

STEP Programme is expected to provide services for number of 80 SEN students, and therefore we recruited participants through our existing school network. Surprisingly, 30 primary schools submitted application. After several interviews with particular school, we discovered most of them are willing to seek for diversified teaching method in helping SEN students, no matter for learning abilities or social skills.

High attendance rate of participants

110 out of 115 participants attended 70% or even more for training sessions, it manifested the popularity of STEP Programme. Merge of game and training convinced students completed the course without hardship or feeling bored. For instance, practice of reversing flying disc trained students' thigh muscles, as they were doing squat during the exercise, and hence to improve the ability of balancing and agility.

Significant improvements of students' agilities

The research illustrated sports therapy training enhanced students' attention skills, social skills as well as in physical development, especially for elevating students' agilities. The assessment took in semester 2 showed a great contrast between control group and experimental group; whereas there were no differences in semester 1 before STEP begins. (Agility means the quick movement of particular part of body and ability to alter the direction).

Project Number: 07140055

P91-PF0014
Enhance Public Awareness of Sarcopenia among the Community Elderly

Administering Institution: Department of Orthopaedics and Traumatology, The Chinese University of Hong Kong

Project Team Members:

1. Prof Leung Kwok-Sui (Emeritus Professor, Department of Orthopaedics and Traumatology, The Chinese University of Hong Kong)
2. Prof Cheung Wing-Hoi (Associate Professor, Department of Orthopaedics and Traumatology, The Chinese University of Hong Kong)
3. Dr Dai Lok-Kwan (Consultant, Department of Medicine and Therapeutics, Prince of Wales Hospital)
4. Prof James-Francis Griffith (Professor, Department of Diagnostic Radiology & Organ Imaging, The Chinese University of Hong Kong)
5. Ms Leung Chung-Kwan (Nurse, Department of Orthopaedics and Traumatology, The Chinese University of Hong Kong)
6. Ms Yuen Wai-Fan (Nurse, Department of Orthopaedics and Traumatology, The Chinese University of Hong Kong)

Project Start Date and End Date: 1 April 2014 to 31 March 2016

Purposes/Objectives: The purpose of this project was to enhance public awareness of the impact, consequences and intervention of

retarding sarcopenia among elderly in the community. This project aimed to promote importance of healthy lifestyle including diet and exercise against sarcopenia, to raise public concern about the importance of muscle-bone health and awareness of fall and fracture prevention through education talks and training workshops to elderly and healthcare providers, to assess and evaluate the risk of sarcopenia for community-dwelling elderly.

Activities/Programmes: To enhance the public awareness of sarcopenia and its related problems among the elderly in the community, series of education talks, training workshops, educational events, assessment and booklet distribution events were launched.

1. Education talk in community
   Education talks were held in collaborating community centres to enhance public awareness of sarcopenia. Content of the talk included epidemiology of sarcopenia, consequences, social impact as well as risk factors of sarcopenia among elderly.
2. Sarcopenia prevention booklet
   3000 booklets of diet modification and exercise training targeting on sarcopenia were distributed to community elderly and their carers. Booklets were also placed in different community centres and fragility clinic in Prince of Wales Hospital.
3. Sarcopenia risk assessments
   Participants were assessed for muscle strength and physical performance for the preliminary screening of sarcopenia. Assessments included grip strength and 6-meter walking test (Tests are recommended by ASWG). Participants with high sarcopenia risk were referred to receive dual energy X-ray absorptiometry (DXA) scan to diagnose sarcopenia and osteoporosis.
4. Training sessions for frontline staff, healthcare providers, caregivers and volunteers

Frontline staff, healthcare professionals, caregivers and volunteers serving the elderly were invited to attend training workshops. Professional knowledge and practical assessment skills were provided. The aim of training session was to equip the professionals with knowledge of sarcopenia management and hence promote its importance in long run.

Targets/Recipients: This project was expected to provide education to 1000 elderly, 400 volunteers and healthcare workers within two years.

Expected and Actual Participation: The project was successfully completed. 1285 elderly and 500 volunteers and healthcare workers were benefited from our project. Trained healthcare workers were able to further promote in the community.

Benefits Derived: Over 3000 booklets were distributed.
821 participants received sarcopenia assessment and individual advices on sarcopenia prevention.

80.6 % participants were at high risk of sarcopenia by the definition of the AWGS. It showed that a number of community dwelling elderly are at high risk of sarcopenia.

100 participants with high sarcopenia risk were benefited from DXA scanning to diagnose sarcopenia and osteoporosis. 70% of the participants were diagnosed to have low muscles mass.
63% of participants had osteoporosis along with sarcopenia that may increase the risk of fragility fractures in those individuals.
500 volunteers and healthcare workers from 15 community centres were benefited in Train-the-Trainer workshops. Trainees of the workshop were well-trained on sarcopenia and they were able to spread the message in the community and also for the non-community dwelling elderly.

Conclusion: With increasing elder population in Hong Kong, the burden of fragility fracture to the healthcare system may increase. It is required to conduct education on the causes of fragility fracture, where sarcopenia is one of the key factors that lead to falls and fractures.

Project Number: 06130175

P92-PF0016

Make a Change through Photovoice (MCPv): Engaging Diabetic and Hypertensive Patients in Physical Activity

Administering Institution: School of Nursing, The University of Hong Kong

Co-organisation(s):

1. Hong Kong Sheng Kung Hui Welfare Council Western District Elderly Community Centre
2. Active Health Clinic, Institute of Human Performance, The University of Hong Kong
3. Hong Kong Sheng Kung Hui Western District Elderly Community Centre

Project Team Members:

1. Dr Angela Yee Man LEUNG (Associate Professor, School of Nursing, The Hong Kong Polytechnic University of Hong Kong; Honorary Associate Professor, School of Nursing, The University of Hong Kong)
2. Ms Katherine Kit Ling WONG (ex-District Director, Hong Kong Sheng Kung Hui Western District Elderly Community Centre)
3. Dr Michael TSE (Director, Active Health Clinic, Assistant Director, Institute of Human Performance, The University of Hong Kong)
4. Dr Pui Hing CHAU (Assistant Professor, School of Nursing, The University of Hong Kong)
5. Mr Perick Lai Choi WONG (District Director, Hong Kong Sheng Kung Hui Welfare Council)

Project Start Date and End Date: 31 July 2014 to 31 March 2016

Purposes/Objectives: The project aims to assist community-dwelling older adults with diabetes and/or hypertension to identify facilitators and barriers to physical activity and increase their engagement in physical activity (such as walking within the neighbourhood). Specific objectives of the project are:

1. Increase the participants' level of activity by at least one level
2. Increase their self-efficacy in doing regular physical activity
3. Improve their physical fitness (including body strength, body flexibility)

Activities/Programmes: This project took reference to the photovoice framework proposed by Catalani and Minkler. Several activities were included in the project: Health seminars (HS), health assessment (HA), group meetings (GM) and photo exhibitions. In the HS, the importance of regular physical activity in chronic illness management was introduced and participants for the GM were recruited. HA included physical activity intensity (measured by accelerometers, ACC), self-efficacy for doing physical activity (measured by the 9-item Self-efficacy Scale for Exercise - Chinese version), barriers to exercise (measured by the 23-item Chinese Barriers to Exercise Scale), and physical fitness (measured by Senior Fitness Tests). All these measurements were made at Week 0 and Week 10. Physical activity intensity was measured one more time at Week 6. GMs were weekly 1-hour meetings and were held from Week 1 to Week 6. In the GM, the participants learnt a set of stretching and muscle strengthening exercise, captured photos and walked in the neighbourhood, identified facilitators and barriers to physical activity, brainstormed ways to remove barriers and worked out individualized action plans for physical activity commitment. After the GMs, participants executed their action plans for four weeks. Photo exhibitions were held to arouse general public's awareness of the identified barriers/facilitators.

Targets/Recipients: There were 3 target groups in this project: older

adults (as participants in the GM), centre staff (as supporters in GM and advocators in photovoice) and relatives/friends/general public (as participants in the photo exhibition cum award ceremony). Those who met the following criteria were recruited to participate in the GM: 1) Aged 55 or above; 2) Diagnosed with type 2 diabetes mellitus and/or hypertension; 3) Able to ambulate independently; 4) Able to communicate in Cantonese.

Expected and Actual Participation:
Expected Participation: We expect to recruit 1,000 persons to participate in health seminars and 202 persons to participate in the intervention and health assessments.

Actual Participation: In this 2-year photovoice project, we offered 10 Health Seminars (HS), 18 sessions of Health Assessment (HA), 17 classes of Group Meetings (GM), 4 photo exhibitions (one of which included the closing ceremony), and develop 1,000 copies of user manual. A total of 1,776 persons participated in various activities (506 in HS, 351 in HA, 204 in the GM, 476 in ACC, 5 in staff training and 234 in the last photo exhibition cum closing ceremony). The number of audience of the first 3 photo exhibitions in the three MTR stations (HKU Station, Sai Ying Pun, Kennedy Town) was estimated to be 1,000,000 in the period of 3 months.

Benefits Derived: Majority (75%) of the participants were female and their mean age was 73.3 (SD 7.5). After the 6-week intervention, 14 % of the participants' physical activity intensity level increased by 1 level or more. Three situations were identified as the situations where participants had the least self-efficacy to do exercise: 1) when the participants were bored by the activity, 2) when they had pain, and 3) when they were tired. Participants' lower body strength (mean difference, m.d. = 0.94, p=0.047) and lower limb flexibility (m.d. = 2.04, p=0.017) was significantly improved.

Participants' physical activity intensity and physical fitness were significantly improved after attending this program. A team of 20 volunteers were trained up as health ambassadors in Central and Western District. Their capacity to assist in health assessments was built up. They provided 22 times service for 250 persons. The staffs of the three elderly centres developed confidence to run this program by themselves in future.

Conclusion: The percentage of the participants (13%) with improved physical activity intensity was much higher than the targeted percentage (5%). Participants' lower body strength and flexibility were significantly improved. The MCPv program successfully increased participants' walking level and fitness. Social network support was built and protocols for health promotion through photovoice were planned and implemented.

Project Number: 06130305

P93-PF0004
A Training Workshop for Foreign Domestic Workers Caring for Elderly with Dementia at Home

Administering Institution: Psychogeriatric Team, Kwai Chung Hospital

Project Team Members:
1. Dr H Y Tang, Associate Consultant, Kwai Chung Hospital
2. Dr S K Chu, Resident Specialist, Kwai Chung Hospital
3. Ms W Y Fung, Ward Manager (Psy), Kwai Chung Hospital
4. Ms K K Lau, Ward Manager (Psy), Kwai Chung Hospital
5. Ms W S Chan, Registered Nurse (Psy), Kwai Chung Hospital
6. Mr C K Lee, Occupational Therapist I, Kwai Chung Hospital
7. Mr S W Sham, Physiotherapist I, Kwai Chung Hospital

Project Start Date and End Date: 1 May 2015 to 30 June 2016

Purposes/Objectives:
1. To organize a training workshop for the foreign domestic workers to deal with common behavioural and psychiatric symptoms of dementia (BPSD), aiming to reduce their caring burden and the BPSD of the elderly
2. To evaluate the training workshop in terms of acceptability, feasibility in application and the effectiveness
3. To develop and produce a trilingual caregivers' guide in Chinese, English and Indonesian for common BPSD which can serve as a reference for the foreign domestic workers

Activities/Programmes: To tailor the program specifically to the needs of foreign domestic workers, a focus group formed by 21 members of the Domestic Worker Support Group of the Kwai Chung Hospital was interviewed in the Ha Kwai Chung Psychogeriatric Outpatient Department in May 2015. The Neuropsychiatric Inventory (NPI) was used as the tool to collect the foreign domestic workers' experiences for BPSD. The five most distressing BPSD identified were delusion, aggression, depression, irritability and sleep disorders. The result served as the basis of the content of subsequent workshops and the trilingual caregivers' guide.

Four identical and full-day workshops were held in August of 2015 to February of 2016. The theme of the workshops was "Non-pharmacological management of BPSD of dementia". The speakers of the workshop included psychiatrist, psychiatric nurses, clinical psychologist, occupational therapist and physiotherapist of the psychogeriatric team. The language adopted by the speakers was English and Cantonese. An Indonesian translator was also present during the workshop to provide live translation. The effectiveness of the training program was examined by a modified version of the NPI, to be completed by the participants before and 1 month after the workshops, from which the level of BPSD and carer strain can be evaluated.

The trilingual guide "Caring for an elderly with dementia: a guide to foreign domestic workers" was produced by the project team. Taking into account the language used by most of workers, this was to provide a user-friendly and handy resource for the foreign domestic workers caring for elderly with dementia. It consists of 4 parts, covering the basic knowledge of dementia, skill for caring for elderly with BPSD, caregiver stress and sharing from domestic worker.

Targets/Recipients: Live-in foreign domestic workers caring for elderly with dementia

Expected and Actual Participation: 100 foreign domestic workers were expected to participate in the 4 workshops. The actual no. of workers that participated in the workshops was 113.

Benefits Derived: Majority of the participants (99.1%) passed the written test at the end of the workshops. From the satisfaction survey, the programme was well received by the participants.

Paired sample T-tests was conducted to evaluate the impact of the workshops on the behavioural symptoms of the care-recipients and the caregiver stress. The post-workshop symptom score (mean = 7.66, SD = 8.27) was shown to be significantly lower than the pre-workshop symptom score (mean 17.25, SD = 15.06), $t(112)=9.13$, $p< .001$. The post-workshop carer strain score (mean = 1.97, SD = 2.85) were also shown to be significantly lower than the pre-workshop carer strain score (mean = 8.59, SD = 6.47), $t(112)=13.44$, $p<.001$. The decrease in behavioural symptoms and carer strain score in all five symptom domains were found to be statistically significant.

The trilingual caregiver guide was published in June 2016 with 1000 copies printed. To our knowledge, this was the first trilingual guide on

handling BPSD specifically targeted for foreign domestic helpers in Hong Kong. It was distributed to the users in our unit as well as to the wider public through our community partners. An electronic version has been uploaded to the webpage of the Kwai Chung Hospital.

Conclusion: This project has shown that training workshops for foreign domestic workers was beneficial in reducing BPSD and caregiver strain. Additional resources for carer support service specifically tailored for foreign domestic workers is recommended.

Project Number: 28140014

P94-PF0012

Game Intervention Scheme for Elderly with Cognitive Impairment at Day Care Centres

Administering Institution: Jockey Club Centre for Positive Ageing

Co-organisation(s): Hong Kong Lutheran Social Service, The Lutheran Church-Hong Kong Synod

Project Team Members:

1. Prof Timothy KWOK, Chairman and Director, PA Company Limited, Director, Jockey Club Centre for Positive Ageing, Professor, Department of Medicine & Therapeutics, The Chinese University of Hong Kong
2. Ms YU, Shun Ngo, Service Director, Hong Kong Lutheran Social Service, The Lutheran Church-Hong Kong Synod
3. Ms HO, Kwai Ying Florence, Secretary, PA Company Limited, General Manager, Jockey Club Centre for Positive Ageing

Project Start Date and End Date: 1 May 2015 to 31 October 2016

Purposes/Objectives: To develop a game intervention protocol to help enhance the quality of life of community-dwelling people with dementia, and to promote proper knowledge and positive attitude towards dementia among the community.

Activities/Programmes: The intervention consisted of 20 games and lasted for 24 sessions, two sessions per week, each session one hour. The intervention was delivered at five local day care centres. Public education and sharing sessions were organised for the general public and field professionals.

Targets/Recipients: Community-dwelling people with dementia aged 55 or above were targeted for intervention. General public and field professionals who were interested in cognitive impairment and game intervention were targeted for public education.

Expected and Actual Participation: A total of N=126 participants joined the program. Eight public education and two sharing sessions were conducted to N=1,500 general public and field professionals. Participation expectation is fulfilled.

Benefits Derived: Quality of life (QoL-AD) and cognitive functioning (MMSE) of participants were the expected benefits of the intervention. N=83 completed samples (n=39 intervention group and n=44 control group) was included in analysis. QoL-AD of intervention group increased significantly after intervention ($p < .05$) and had an insignificant increase at follow-up. QoL-AD of control group yielded an insignificant improvement of mean score. Both intervention group and control group had an insignificant improvement in MMSE after intervention. The difference of the change of quality of life and cognitive functioning between intervention group and control group was not significant. As for the evaluation of public education, over 80% of valid samples indicated that they had good knowledge and positive attitude towards dementia after the education talks.

Conclusion: The intervention protocol is effective in improving the quality of life of community-dwelling elderly with dementia. More community-wide public education is needed to introduce to general public proper knowledge and encourage positive attitude towards dementia.

Project Number: 07140245

P95-PF0015

"Youth for care" - Dementia Awareness Promotion Programme

Administering Institution: The Lok Sin Tong Benevolent Society, Kowloon

Co-organisation(s): Jockey Club Centre for Positive Ageing

Project Team Members:

1. Lau Oi Sze, Alice (Chief Executive, The Lok Sin Tong Benevolent Society, Kowloon)
2. Ng Chak Hang, Matthew (Medical Service Manager, The Lok Sin Tong Benevolent Society, Kowloon)
3. Chow Sheung Man, Sherman (Assistant Medical Service officer, The Lok Sin Tong Benevolent Society, Kowloon)
4. Lam Yuk Wai (Project Assistant, The Lok Sin Tong Benevolent Society, Kowloon)

Project Start Date and End Date: October 2015 to September 2016

Purposes/Objectives: The project adopts "train the trainer approach, it aims to raised youth participants' awareness and understandings towards dementia, build up positive attitudes and acquire skills in promoting dementia care towards their family members and elderly in the community through engaging in different workshops and caring activities, through 12-month period.

Activities/Programmes: The implementation of this project is closely collaborated with the Jockey Club Centre for Positive Ageing, with regards to the provision of educational tool kits and professional trainers for the health talks and workshops. The 12-month project included 4 components: 1. School talks and workshops; 2. Caring activity; 3. Health promotion campaign and 4. Publications.

1. School talks and workshops
School talks were held by registered social workers and nurses in order to raise the awareness of the youth towards general mental well-being and suggest the possibility for them to engage in promoting dementia care in the community. On-site workshops has been subsequently offered to those interested students, which served as training session to equip them with evidence-based practical skills on dementia preventive care. They were then expected to design and implement a series of caring activities for the elder upon completion of training.

2. Caring activities
Different types of caring activities have been organized at the district elderly units and being supported by the trained students. The main activity included 'Brain Gym' which focused on improving the cognitive abilities of the elder and gaining better coordination of their whole-body, and mini-game trainings focused on calculating or cognitive aspects. In addition family photo portraits were made by the youth participants for the elders to aid them remembering their family members.

3. Health promotion campaigns
Promotion campaigns were held to raise the public awareness towards dementia and the ways of prevention. Game booths and educational materials such as information boards and promotional pamphlets were set up to disseminate the causes, symptoms, treatments and prevention methods of dementia, as well as the community resources for dementia

care to the community. It also suggested of the benefits in early identification of dementia symptoms by youth, family and community members.

4. Publications
Knowledge on dementia prevention were disseminated through publishing promotional pamphlets and a social media platform. A Facebook page was set up to share dementia care news and information online. The youth participants also helped publishing the memoirs, which recorded the life journey and the worries and hopefulness towards the future of the interviewed elders. The memoirs were then distributed back to the elders for their memories. Throughout the activities the youth participants could understand more about the elders' feelings towards life.

Targets/Recipients: The project targets secondary school students recruited from local schools; general talks and training are given to all participated students, while in-depth training and service opportunities are given to those who are interested to learn more and practice in the community.

Expected and Actual Participation: We expected to train total of 200 students, in which 100 students would attend in-depth training and engaged in service provision for 100 elders and 100 carers. The project had finally recruited 478 students who have attended general training, in which 120 of them had been engaged in in-depth training workshops and provided service for the 120 elders and 104 carers in the community. The number of participants recruited have reached our expected target.

Benefits Derived: The project has successfully reached three concerned target: student, elders and carers. More than 15 educational talks and training workshops have been offered to 478 students, and served over 220 elders and carers in the community. Questionnaire result indicated more than 90% of the participated students agreed the programme have raised their awareness towards dementia and have acquired skills and positive attitudes in organizing preventive care activity for elders. Near 90% of them had developed positive attitude towards holding preventive care activity for elders and being confident in presenting dementia to the public and communicate with the demented patients. While evaluation from elders and carers showed that 93% of them felt satisfied with the outreach services and workshops. The results indicated the 'train the trainer' approach has successfully implemented using school setting as a platform and utilized in health promotion aspect.

Conclusion: The project has successfully achieved its objectives – increase awareness and understandings among youths towards dementia, build up positive attitude on dementia care and promoting it to their families and carers in the community. Thanks to the "train-the-trainer" approach, they were also able to acquire skills in identifying dementia symptoms and utilize dementia care resources in the community throughout the caring activities for the elders. This approach could prove successful in spreading dementia care knowledge among the community. Furthermore it was observed throughout the project that motivating youth participants to delivering health messages in the community could create a warm, and supportive atmosphere, which may act as a cue to empower the elders to strive for a better health.

Project Number: 28140454

P96-PF0017
iPEP (internet-based Psychosis Education Program): Web-based Self-help Psychoeducation Program for Caregivers of Patients with Psychosis

Administering Institution: The University of Hong Kong

Co-organisation(s): Hong Kong Early Psychosis Intervention Society (Fund)

Project Team Members:
1. Dr Chan Kit Wa, Associate Professor, Department of Psychiatry, The University of Hong Kong
2. Prof Chen Yu Hai Eric, Professor, The University of Hong Kong
3. Prof Tse Shu Ki Samson, The University of Hong Kong
4. Dr Chang Wing Chung, Clinical Assistant Professor, The University of Hong Kong
5. Dr Lee Ho Ming Edwin, Clinical Assistant Professor, The University of Hong Kong
6. Dr Hui Lai Ming Christy, Assistant Professor, The University of Hong Kong
7. Dr Wong Hoi Yan Gloria, Assistant Professor, The University of Hong Kong
8. Miss Lai Dik Chee, The University of Hong Kong
9. Miss Tam Man Yee Wendy, The University of Hong Kong
10. Miss Tang Yee Man Jennifer, The University of Hong Kong
11. Miss Kok Joy, Hong Kong Early Psychosis Intervention Society (Fund)

Project Start Date and End Date: 23 September 2013 to 22 September 2015

Purposes/Objectives: To establish a comprehensive and up-to-date online resource center about psychosis and web-based psychoeducation program for caregivers of patients with psychosis. To promote and integrate this program into the existing services. To enhance the awareness of psychosis in general public in order to encourage help seeking behavior and reduce stigma.

Activities/Programmes: iPEP, a user-friendly on-line psychoeducation resource center for caregivers of patients with psychosis was established. Dissemination of this website information to the target group and integrating the iPEP into the current clinical practice has been carried out.

Targets/Recipients: Caregivers of patients with psychosis are the main target group. Other target groups include health care professional, patients and general public.

Expected and Actual Participation: It is expected that the psychoeducation website specific for caregivers will have 800 registered members who are caregivers with 20000 total website page views. It is also expected to provide talks to 500 audiences over two years. The project has achieved the target by recruiting 809 members for the iPEP website with 58333 total page views. Ten talks were delivered with total audience of 569. The evaluation on the use of website and talks has been satisfactory.

Benefits Derived: The website provides comprehensive psychoeducation information for caregivers; it is also a resource center for the care providers. Effort of integrating this website to the existing service could ensure the sustainability of the website.

Conclusion: This is one of the first on-line comprehensive psychoeducation resources center specific for caregivers with psychosis. This will set a platform for future development of on-line basis psychoeducation program for caregivers.

Project Number: 26120264

P97-PF0022

Education and Coping Toolkit for People with Early Psychosis and Their Carers

Administering Institution: Kwai Chung Hospital

Project Team Members:

1. Dr LO Tak-lam William (Hospital Chief Executive, Kwai Chung Hospital)
2. Miss KU Man-wing Betty (General Manager (Nursing), Kwai Chung Hospital)
3. Mr LUK Kwok-leung (Department Operation Manager, Kwai Chung Hospital)
4. Miss KWOK Man-yuk Cordelia (Nurse Specialist, Kwai Chung Hospital)
5. Mr CHAN Pak-ho Arthur (Clinical Psychologist, Kwai Chung Hospital)
6. Dr CHONG Shiu-yin Catherine (Associate Consultant, Kwai Chung Hospital)

Project Start Date and End Date: January 2013 to June 2014

Purposes/Objectives: The Early Intervention Team of Kwai Chung Hospital provides early assessment and treatment service for adolescents and adults suffering from first-episode psychosis. Effective psychoeducation for patients and their caregivers is essential in this client group, as understanding of the illness can enhance treatment adherence, minimize misconceptions about the illness and its treatment, reduce stigma and self-stigma, and ultimately, improve well-being of the sufferers of mental illness and their loved ones. As such, we aimed to develop a supported self-help package for people with early psychosis and their carers, to provide essential information and guidance on the illness and its management, as well as tips to help them to stay well.

Activities/Programmes: A set of guided self-help material was developed for people suffering from first-episode psychosis and their carers. The content was developed by professional staff in the project team, which was subsequently reviewed by some patients and their carers. The final version was produced after consolidation of comments from the service users.

After production of the material, each of our service users gets a set of the Toolkit, which is gone through with the guidance of their respective community Case Managers, who attend monthly case sharing and discussion with the team Associate Consultant and Clinical Psychologist to ensure fidelity of the delivery of the guided self-help materials. A sharing of the materials was also arranged with staff from 7 Integrated Community Centre for Mental Wellness (ICCMW) within the catchment area of Kowloon West Cluster to equip them with updated knowledge and skills in handling their clients suffering from first-episode psychosis in their Centres. More than 100 participants joined the sharing session and visions on betterment of early psychosis services were shared amongst the staff of ICCMW and KCH.

Targets/Recipients: Adolescent and adult clients suffering from first-episode psychosis and their carers

Expected and Actual Participation: We initially expected that the materials were to be distributed to clients under the treatment of the Early Intervention Team and their carers. However, with positive feedbacks from our clients on the usefulness of the self-help materials, we also shared the materials with our community partners, i.e. the Integrated Community Centre for Mental Wellness, as well as fellow providers of early psychosis services, i.e. EASY teams of other clusters of Hospital Authority. Approximately 1000 sets of the Toolkits have been shared with our service users and community partners.

Benefits Derived: Services users and their carers welcomed the use of the self-help materials. They had a better understanding of their illness and managed to appreciate psychosis in both medical and recovery models. They felt more confident in handling issues arising from the mental condition, especially on skills in managing their symptoms and tips in dealing with potential side effects of medications.

Conclusion: The Education and Coping Toolkit for People with Early Psychosis and Their Carers is an effective intervention to empower our service users and their carers in managing their mental condition. We will continue to share the Toolkit with other potential healthcare service providers to generalise the gains to a wider group of service users.

Project Number: 26120204

P98-PF0023

FitMind Exercise for Improving Cognition: A Train-the-trainer Program for Mental Health Caregivers in the Community

Administering Institution: The University of Hong Kong

Co-organisation(s):

1. Hong Kong Early Psychosis Foundation
2. Early Assessment Service for Young People with Psychosis
3. Hong Kong Jockey Club Early Psychosis Project
4. Caritas Hong Kong
5. Mental Health Association of Hong Kong

Project Team Members:

1. Dr Edwin Ho-Ming Lee, Clinical Assistant Professor, Department of Psychiatry, The University of Hong Kong
2. Dr Jingxia Lin, Post-doctoral Fellow, Department of Psychiatry, The University of Hong Kong
3. Dr Michael Tse, Assistant Director, Institute of Human Performance, The University of Hong Kong
4. Dr Christy Lai-Ming Hui, Assistant Professor, Department of Psychiatry, The University of Hong Kong
5. Dr Wing-Chung Chang, Clinical Assistant Professor, Department of Psychiatry, The University of Hong Kong
6. Dr Sherry Kit-Wa Chan, Clinical Assistant Professor, Department of Psychiatry, The University of Hong Kong
7. Prof Eric Yu-Hai Chen, Professor, Department of Psychiatry, The University of Hong Kong

Project Start Date and End Date: 23 September 2013 to 22 September 2015

Purposes/Objectives:

1. Develop a locally relevant training manual for paid staffs and carers of people with psychosis
2. Train paid staffs and carers to utilize the above training manual effectively
3. Provide a systematic exercise intervention program for people with psychosis
4. Promote use of the training manual in the community

Activities/Programmes: The train-the-trainer program was conducted in three phases.

1. Phase I - The research team developed a locally relevant training manual. A tailor-made exercise program for the psychosis population was developed with the expert advice from certified exercise specialists for safety. Elements of exercise coaching were embedded in the training manual so as to carry out the exercise intervention program more efficiently. Advice was sought from exercise coaching professionals. A survey about the exercise experiences was conducted to modify our training manual.
2. Phase II – Twelve workshops for paid staff and carers were held. They were trained to use the tailor-made exercise program for psychosis population and also taught the skills on exercise coaching within

the exercise intervention program by trained professionals from the Department of Psychiatry, the University of Hong Kong. Assessment for the trainers was held 2 times per year.

3. Phase III - People with psychosis were assessed prior to exercise intervention program to assess their physical activity level. A tailor-made exercise program was taught by the trainers, who also monitored their exercise progress to implement a suitable exercise habit.

Targets/Recipients: This was a territory-wide program which is open to all paid staffs and carers in the community. The target groups were identified by two major existing services for people with psychosis including the Early Assessment Service for Young People with Psychosis and the Hong Kong Jockey Club Early Psychosis Project. They provided outpatient and inpatient services for people with psychosis covering all districts in Hong Kong. The program also promoted to non-government organizations in the community providing mental health services for people with psychosis, like the Caritas and Mental Health Association of Hong Kong. Caregivers of people with psychosis receiving above services were introduced about the program and invited for participation.

Expected and Actual Participation: The objectives were all achieved with locally relevant training manual, exercise training DVD and leaflet were developed. A total of 12 workshops were held and trained 261 paid staffs and carers. Free exercise classes for people with psychosis were provided in the community. Two press conferences and one public exercise event were organized to promote the program. The project had reached 796 persons with psychosis and their caregivers.

Benefits Derived: The awareness of benefit of exercise for improving cognition was raised and exercise intervention programs were provided for free to improve the physical and mental health of people with psychosis.

Conclusion: Exercise has beneficial effects on mental and physical health in people with psychosis, as well as normal people. Train-the-trainer program can help to promote exercise habit in people with psychosis in the community.

Project Number: 26120214

P122-0020

Understanding the Small RNA-regulated Dissemination of Emerging Multidrug Resistant Mobile Elements in Hong Kong

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Background: The dissemination of CTX-M gene is commonly achieved through plasmid conjugation. Narrow host-range incFII plasmids play important roles in the dissemination of CTX-M-14. In Hong Kong, CTX-M-carrying plasmid pHK01 and pHK01-like plasmids which belong to incFII group were widely disseminated in hospitals. These plasmids were also found to be highly related to CTX-M plasmids in mainland China and Vietnam. Although extensive studies have been performed on this type of plasmid and most of them focused on drug resistance genes, little is known about the dissemination and bacterial host fitness upon pHK01 acquisition.

Objective: To identify and characterize the novel chromosomal and plasmid-encoded sRNA which involve in the dissemination of the CTX-M-type plasmid, pHK01, among bacteria in Hong Kong, and to determine the global changes of the RNA repertoire of Escherichia coli upon introduction of pHK01

Methods: We performed Next-generation sequencing and qRT-PCR to study transcriptome profile of transconjugant strain Escherichia coli J53 in different growth phases. Novel plasmid-encoded small RNAs (sRNAs) were predicted using bioinformatics methods and validated by Northern Blot. Putative sRNA targets were confirmed using qRT-PCR upon sRNA over-expression.

Results: The transcriptomes and small RNA of Escherichia coli J53 carrying pHK01 and its isogenic strains at mid-log and early stationary phases were sequenced and analysed. The differential gene expression influenced by the carriage of pHK01 at two different growth stages were clustered into their functional pathways. The motility of the bacteria carrying pHK01 was reduced because of the downregulation of flagellar systems. Bacterial growth curve and motility were studied. Numerous plasmid-encoded sRNAs were identified and validated. We showed that overexpression of AS-TraI can shortens the host lag phase merely in the presence of pHK01.

Conclusions: The transcriptional profiling of Escherichia coli J53 upon the acquisition of pHK01 shows altered distribution in RNA repertoire including several key pathways such as nitrogen metabolism and motility, suggesting pHK01 could potentially induce diverse fitness changes in bacterial host. Moreover, the identification of plasmid-encoded sRNAs and their gene regulation of hosts will greatly improve our understanding of the effect of plasmid to host at the post-transcriptional

Project Number: 13121502

P123-0157

Investigation on the Synergists from Vegetable Portulaca Oleracea with Macrolides Against Methicillin-resistant Staphylococcus aureus and Related Mechanism

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Combating against methicillin-resistant Staphylococcus aureus (MRSA) - two fatty acids from Purslane (Portulaca oleracea L.) exhibit synergistic effects with erythromycin

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Introduction and Project Objective: MRSA is a serious global problem. Because of the frequent occurrence of co-resistance pattern, discovering of effective agents are urgently needed. The objective of this study is to identify the active ingredients from Portulaca oleracea L. (PO) that could provide synergism with antibiotics, e.g. erythromycin, against MRSA and their possible mechanisms of combating MRSA.

Methods: High-speed counter-current chromatography (HSCCC) coupled with gas chromatography-mass spectrometry were used to fractionate PO extract. A panel of laboratory MRSA strains were used for checkerboard inhibitory assays. The ethidium bromide efflux inhibitory assays were used in mechanistic studies.

Results: Linoleic and oleic acids were identified from HSCCC fraction 18 of PO with synergistic antibacterial activity when combined with erythromycin against RN4220/pUL5054. Ethidium bromide efflux inhibitory studies revealed that linoleic and oleic acids may interfere the activity of MsrA pump in MRSA strains. By comparing among a panel of linoleic and oleic acids analogues, unsaturated fatty acids in salt form with cis configuration and an increase in number of double bonds were found to further increase the antibacterial activity when used alone or in combination with erythromycin.

Conclusion: This study reported that two active ingredients, namely linoleic and oleic acids, were identified from PO with synergistic antibacterial activity when combined with erythromycin against MRSA RN4220/pUL5054 and possibly act by inhibiting efflux pumps of bacteria cells.

Publication: Ben C.L. Chan et al. Journal of Pharmacy and Pharmacology 67:107-116 (2014).

Project Number: 11100442

P124-0030

Community Study of Nasopharyngeal Colonization and Antimicrobial Resistance of Streptococcus pneumoniae in Hong Kong Children Less Than 2 Years of Age

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Background: In Hong Kong, pneumococcal conjugate vaccine (PCV) has been introduced into the childhood immunisation programme (CIP) since 2009. A local surveillance study is essential to examine changes in pneumococcal carriage.

Objective: This study aimed to assess nasopharyngeal pneumococcal

carriage rate, serotypes and antimicrobial resistance pattern in young children after the introduction of 13-valent PCV (PCV13).

Study Design & Method: A community-based, cross-sectional surveillance study was performed on healthy infants attending eleven Maternal and Child Health Centres across different parts of Hong Kong. Nasopharyngeal swabs were obtained from healthy children aged 2, 12 and 18 months during their visit to the centres for immunization from June 2013 to June 2014. Pneumococcal isolates were serotyped and tested for antimicrobial resistance. Details of the demographics, family composition, vaccination history and medical history was obtained through interview of the guardians.

Results: 1541 children were recruited. The overall carriage rate was 5.5% and the carriage rates at 2, 12 and 18 months old were 2.3%, 7.9% and 5.9% respectively. Children aged 12 and 18 months were more likely to have pneumococcal colonization (12 months OR: 2.88; 95% CI: 1.41-5.87 and 18 months OR: 2.19, 95% CI: 1.05-4.57). Recent respiratory symptoms and presence of siblings younger than 6 years were independently associated with pneumococcal carriage. Eight-four pneumococcal isolates were serotyped. The most prevalent serogroup/types were 15 (15B/C, 16.7%; 15A/F, 9.5%), 6C (15.5%) and 23A (13.1%). Overall, 2.4% of the isolates were heptavalent PCV serotypes, 10.7% were 13-valent PCV (PCV13) serotypes and 89.3% were non-PCV13 serotypes. The proportions of penicillin, cefotaxime and erythromycin non-susceptible isolates were 7.3%, 13.4% and 79.3% respectively.

Conclusion: The rate of pneumococcal carriage was low in young children in Hong Kong and compared to previous local studies. An overall reduction in the carriage rate was observed after the introduction of PCV. Likely serotype replacement was noted with a predominance of non-vaccine serotypes in pneumococcal carriage with the emergence of serogroup/type 15 and 6C.

Implications: Further monitoring and evaluation of the prevalent serotypes among carriage isolates and invasive disease are warranted.

Project Number: 12111852

P125-0152

Relationship of Pst, a High Affinity Phosphate Transporter, Beta-lactam Resistance and Biofilm Formation in Streptococcus pneumoniae

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Introduction: Streptococcus pneumoniae is the leading cause of pneumonia, meningitis and sepsis. Pneumococcal biofilm related infections pose significant clinical problems as the bacteria are difficult to eradicate and are often multi-drug resistant. The PstS, phosphate binding protein, is a subunit of the phosphate transport (Pst) system which plays a key role in phosphate homeostasis and pathology in various bacteria. We herein evaluated the relationship of phosphate, antibiotic resistance and biofilm formation in S. pneumoniae.

Project Objectives: (1) To elucidate the effect of phosphate on β-lactam (cefotaxime) resistance in S. pneumoniae and its effect on pst system and pnpR/pnpS, (2) To elucidate the effect of phosphate on the biofilm formation in S. pneumoniae and its underlying mechanisms, and (3) To characterize the possible relationship between phosphate, antibiotic resistance and biofilm formation based on results obtained in aims 1 and 2, and test whether phosphate repletion is a possible strategy to alleviate antibiotic resistance and biofilm formation in S. pneumoniae.

Methods: Antibiotic susceptibility, biofilm formation capacity and the gene expression of pstS, pstB and pnpS under inorganic phosphate repletion were evaluated. Pneumococcal biofilms were grown on 24-well plates or 8-well chamber slides and quantified by crystal violet staining, colony forming units and by confocal laser scanning microscopy. pstS mutants were constructed to elucidate the role of the Pst system in CTX resistance and biofilm formation. Statistical analyses were performed by Spearman correlation and one-way anova where indicated.

Results: Our results showed that pstS and pstB were overexpressed in resistant strains and correlated with CTX resistance and were down-regulated by high concentrations of phosphate. Phosphate enhanced the bactericidal activities of CTX against S. pneumoniae and inhibited biofilm formation.

Conclusions: The study highlights the importance of PstS in S. pneumoniae β-lactam resistance and biofilm formation. Phosphate supplement sensitized S. pneumoniae cells to CTX and inhibited biofilm formation.The correlation of pst system with β-lactam resistance enhances our understanding of the pst system in S. pneumoniae. Phosphate enhances CTX activities against S. pneumoniae and inhibited biofilm formation.

Project Number: 13120402

P126-0059

A Single DNA Molecule Detection Platform for Pathogen Typing and Identification

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Introduction and Project Objectives: Pathogen identification is a foremost step in epidemiological surveillance. Precise sub-species level classification, known as strain typing, helps in tracing transmission routes and formulates subsequent outbreak control. Current standard methods analyze the lengths or sequences of DNA fragments. Pulse-field electrophoresis (PFGE) captures whole genome information, but does not provide the order information of fragments. In contrast, multilocus sequence typing (MLST) uses only loci of several essential genes, but misses a comprehensive view of the whole genome. Due to the limited resolution, biologically significant features that affect infection outcomes could be missed. Moreover, these methods are time-consuming and require laborious work. We aim to develop a more precise and efficient strain typing method.

Methods: We introduce a strain typing method employing data from a high-throughput platform named optical mapping. Sequence-specific cuts on long single DNA fragments (>150kb) produced by nicking enzyme are labeled with fluorescence and imaged. The molecule lengths and label positions are recorded as optical maps, providing long-range structural information across the whole genome. We have developed novel means to efficiently align, compare and visualize optical mapping data of multiple samples. Optical maps were aligned against NCBI genome references for species identification. Samples are compared by their similarity of signal patterns to study their phylogenetic relationships. Our methods were tested with samples from three types of nosocomial pathogens, with analysis focused on the Acinetobacter baumannii dataset.

Results: By comparing signal patterns of references and samples, we successfully revealed the species identity and reconstructed the phylogenetic relationships among samples. Results are largely consistent with independent MLST results, and show more refined groupings. By multiple alignment of optical maps, we generated a global signal pattern view across genomes of references and samples,

with comparison of genomic structures visualized. While most MLST profiling genes lie on regions with signal patterns conserved in all samples, our analysis offers a global perspective that show complex genomic rearrangements in other regions, which gave further evidence on phylogenetic relationships with functional significance.

Conclusions: We present a strain typing method that provide a global view on genomic structural variations, and demonstrate that this method has a higher resolution power than current standard method. We anticipate our analysis method will facilitate optical mapping in becoming a powerful tool in epidemiological studies.

Project Number: 12110542

P127-0164

Comparative Genome Analyses of Clonally-related Streptococcus pneumoniae with Incremental Resistance to Third-generation Cephalosporins

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Introduction: Streptococcus pneumoniae is a Gram-positive coccus responsible for a range of infections, including life-threatening invasive pneumococcal diseases such as pneumonia, sepsis and meningitis. Serogroup 19 multi-locus sequence type 271 (ST271) was a multidrug-resistant clone belonging to clonal complex 320/271 (CC320/271), which was responsible for increase in resistance to third-generation cephalosporin, cefotaxime, and was characterized by a high cefotaxime MIC of 8 μg/ml.

β-lactam is the major drug of choice in the treatment of respiratory pathogens, and resistance against this class of antibiotics limits the choice and complicates management of such infections. Amino acid substitutions in the active sites of penicillin-binding proteins (PBPs) were identified responsible for β-lactam-resistance. Non-PBP genes were published related to β-lactam non-susceptibility, including proteins involved in cell wall synthesis, stress response, competence, autolysis and quorum-sensing pathways.

Project Objectives:
1. To obtain the draft genomes of ST271 clinical isolates with different MICs to cefotaxime and ciprofloxacin,
2. To compare single-nucleotide polymorphisms (SNPs) between the genomes, especially in published (potential) β-lactam-resistance-determinants,
3. To characterize the role of selected SNPs in β-lactam-resistance.

Methods: Draft genomes of ST271 clinical isolates, namely CU_SPNE1_05 (cefotaxime MIC 1μg/ml, ciprofloxacin MIC 32μg/ml) and CU_SPNE32_06 (cefotaxime MIC 32μg/ml, ciprofloxacin MIC 1μg/ml), were analyzed. Non-synonymous SNPs in predicted open reading frames between the two genomes were studied, focusing on a list of ninety-two (potential) non-PBP β-lactam-resistance-determinants derived from publications from NCBI Pubmed, with search string "Streptococcus pneumoniae AND (penicillin OR cefotaxime OR beta-lactam) AND resistance". Selected SNPs were analyzed by deduced amino acid sequence comparisons, prediction of protein-protein interactions and complementation studies.

Results: Comparative genomics showed that both genome strains carried the same set of non-synonymous SNPs in known β-lactam-resistance-determinants, such as PBPs. CU_SPNE1_05 carried a truncation mutation in a two-component system, histidine kinase, which was not present in CU_SPNE32_06 and other CC320/271 genomes. The SNP was located before the catalytic ATPase domain, and was supposed to fail in activating downstream regulon, including the essential cell division proteins. Complementation of the non-truncated gene to the histidine kinase into CU_SPNE1_05 increased resistance to cefotaxime (from MIC 1μg/ml to 32μg/ml), and surprisingly decreased ciprofloxacin MIC (from MIC 32μg/ml to 1μg/ml).

Conclusions: Besides cell wall synthesis pathway components, mutations in non-PBP genes such as in two-component systems could turn on or off β-lactam-resistance in the same background of SNPs in (potential) β-lactam-resistance-determinants.

Project Number: CU-12-05-02

P128-0178

Antibiotic Resistance Rates and Physician Antibiotic Prescription Patterns of Uncomplicated Urinary Tract Infections

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Uncomplicated urinary tract infections (UTI) are common in primary care. Whilst primary care physicians are called to be antimicrobial stewards, there is limited primary care antibiotic resistance surveillance and physician antibiotic prescription data available in southern Chinese primary care. The study aimed to investigate the antibiotic resistance rate and antibiotic prescription patterns in female patients with uncomplicated UTI. Factors associated with antibiotic resistance and prescription was explored. A prospective cohort study was conducted in 12 primary care group clinics in Hong Kong of patients presenting with symptoms of uncomplicated UTI from January 2012 to December 2013.

A total of 298 patients were included in the study. *E. coli* was detected in 107 (76%) out of the 141 positive urine samples. Antibiotic resistance rates of *E. coli* isolates for ampicillin, co-trimoxazole, ciprofloxacin, amoxicillin and nitrofurantoin were 59.8%, 31.8%, 23.4%, 1.9% and 0.9% respectively. *E. coli* isolates were sensitive to nitrofurantoin (98.1%) followed by amoxicillin (78.5%). The overall physician antibiotic prescription rate was 82.2%. Amoxicillin (39.6%) and nitrofurantoin (28.6%) were the most common prescribed antibiotics. Meanwhile, whilst physicians in public primary care prescribed more amoxicillin (OR: 2.84, 95% CI: 1.67 to 4.85, P<0.001) and nitrofurantoin (OR: 2.01, 95% CI: 1.14 to 3.55, P=0.015), physicians in private clinics prescribed more cefuroxime and ciprofloxacin (P<0.05). Matching of antibiotic prescription and antibiotic sensitivity of *E. coli* isolates occurred in public than private primary care prescriptions (OR: 6.72, 95% CI: 2.07 to 21.80 P=0.001).

In conclusion, nitrofurantoin and amoxicillin should be used as first line antibiotic treatment for uncomplicated UTI. There were significant differences in antibiotic prescription patterns between public and private primary care. Development and dissemination of guidelines for primary care management of uncomplicated UTI as well as continued surveillance of antibiotic resistance and physician antibiotic prescription is recommended.

Project Number: CU-10-03-01

P129-0001

C-terminal Truncated Hepatitis B Virus X Protein Promotes Hepatocellular Carcinogenesis through Induction of Cancer and Stem Cell-Like Properties

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Introduction: Tumor relapse after chemotherapy typifies hepatocellular carcinoma (HCC) and is believed to be attributable to residual cancer stem cells (CSCs) that survive initial treatment. Chronic infection with hepatitis B virus (HBV) has long been linked to the development of HCC. Upon infection, random HBV genome integration can lead to truncation of hepatitis B virus X (HBx) protein at the C-terminus (HBx-ΔC), which has been linked to promote HCC development. However, the mechanism by which this occurs remain understudied.

Project Objectives: To elucidate the functional role of HBx-ΔC in the induction of stemness properties and a CD133 CSC subset in HCC.

Methods: Two naturally occurring truncated HBx mutants (14 and 35 amino acids C-truncation) was investigated. Presence of the HBx-ΔC mutants and its correlation with CD133 were examined. Empty vector or HBx-ΔC mutants were overexpressed in two liver / HCC cell line models. Functional studies to examine their ability to alter cancer and stemness properties were performed. RNA-Seq profiling was also conducted to identify an underlying mechanism by which HBx-ΔC mutants confer cancer stemness properties in HCC.

Results: We found HBx-ΔC to promote the appearance of a CD133 liver CSC subset and confer cancer and stem cell-like features in HCC. HBx-ΔC was exclusively detected in HCC cell lines that were raised from patients presented with a HBV background with concomitant CD133 expression. Stable overexpression of the naturally occurring HBx-ΔC mutants, HBx-Δ14 or HBx-Δ35, in HCC cell lines Huh7 and immortalized normal liver cells MIHA resulted in a significant increase in the cells ability to self-renew, resist chemotherapy and targeted therapy, migrate and induce angiogenesis. MIHA cells with the mutants stably overexpressed also resulted in the induction of CD133, mediated through STAT3 activation. RNA sequencing profiling of MIHA cells with or without HBx-ΔC mutants stably overexpressed identified altered FXR activation. This, together with rescue experiments using a selective FXR inhibitor suggested that C-terminal truncated HBx can mediate cancer stemness via FXR activation.

Conclusions: Collectively, we find C-terminal truncated HBx mutants to confer cancer and stem cell-like features in vitro and to play an important role in driving tumor relapse in HCC.

Project Number: 12110792

P130-0024
Role of Caveolin-1 in Hepatitis B Virus-induced Hepatocarcinogenesis

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Introduction and Project Objectives: Chronic hepatitis B virus (HBV) infection has been well established to be a major risk factor of hepatocellualr carcinoma (HCC). Accumulating evidence have shown that the smallest protein, hepatitis B virus x prtoein (HBx), among the four proteins encoded by HBV plays a crucial role in HCC pathogenesis. HBx has been implicated in various aspects of liver diseases, for instance, chronic hepatitis, cirrhosis and hepatocarcinogenesis. HBV genome integration generates 3'-deletion in HBV X gene and results in C-terminal truncated HBx. Indeed, C-terminal truncated HBx is frequently detected in tumors of HBV-positive patients with HCC. Functionally, truncated HBx possesses more potent oncogenic capacity than full length form. However, the mechanism underlying the actions of truncated HBx in HCC remains unresolved. The overall goal of this study is to investigate the molecular mechanism and functional effect of truncated HBx-mediated caveolin-1 (Cav1) expression in HCC. We hypothesize that truncated HBx protein acts as a positive regulator of Cav1 leading to the acquisition of aggressive behavior of cancer cells.

Methods: The expression of Cav1 and presence of truncated HBx were analyzed and correlated in HCC cell lines and clinical samples. The activation of Cav1 promoter by truncated HBx was studied using luciferase reporter assay. The expression of truncated HBx was induced by doxycycline in SMMC7721 cells and subjected to various functional assays *in vitro* and *in vivo*. The expression and role of downstream effector of Cav1 in truncated HBx overexpressing cells was also investigated.

Results: Higher expression of Cav1 was found to be significantly correlated with the presence of C-terminal truncated HBx in HCC tissues when compared to cases without truncated HBx. Expression of two naturally occurring C-terminal deletion mutants, HBx1-130 and HBx1-119 were able to upregulate the expression and activate the promoter of Cav1. Conversely, knockdown of HBx expression resulted in reduced expression of Cav1. SMMC7721 cells established with doxycycline inducible expression of HBx1-119 displayed augmented cell migration, invasiveness and tumor development. However, such enhancement in growth and motility was abrogated when Cav1 expression was suppressed in HBx1-119 cells. Our findings also revealed that FERM domain containing 5 (FRMD5), acts downstream of Cav1, was also upregulated by HBx1-119. Knockdown of FRMD5 abrogated the oncogenic capacity of HBx1-119.

Conclusions: C-terminal truncated HBx mediates the upregulation of Cav1-FRMD5 resulted in the enhanced aggressiveness of HCC cells. Our findings have deciphered novel molecular pathways contributing to the understanding of HBV-induced hepatocarcinogenesis.

Project Number: 13121302

P131-0054
HBx Oncoprotein Induces Chromosome Instability in Hepatocarcinogenesis via Dysregulation of Putative Tumor Suppressor, TAX1BP2

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Introduction and Project Objective: Chronic hepatitis B virus infection has been implicated in development of hepatocellular carcinoma (HCC). Evidence indicates that the HBV X protein (HBx) is involved in the aberration of centrosomes, which are major microtubule-organizing centres for regulating spindle assembly and bipolarity. It is suggested that cancer is a multi-step accumulation process of genomic instability resulted from centrosome dysfunction. Herein we present a mechanistic study on the roles of HBx in inducing genomic instability through centrosome aberration.

Methods: Two stable expression systems of HBx were achieved in cell-lines. Centrosome dynamics were investigated by various types of microscopy as well as biochemical methods. Genomic instability was evaluated in terms of chromosome number and mitotic aberration. The detailed mechanism of chromosome instability was elucidated in cell-lines as well as on clinical HCC samples using molecular assays.

Result: HBx expression resulted centrosome ultrastructure disorganization as well as centrosome numerical defects. Further investigation suggests that HBx binds to a centrosome protein called TAX1BP2, which was previously shown to be an intrinsic block of centrosome over-duplication and a tumor suppressor being down-regulated in HCC. Restoring TAX1BP2 was found to block the effect of HBx in centrosome aberrations. Moreover, we found that HBx expression resulted in aberrant mitosis and chromosome mis-segregation. Elucidation of the mechanisms revealed that HBx upregulated mitotic gatekeeper pumilio 2 through down-regulation of its upstream inhibitor NORAD. Similar dysregulation of pumilio 2 and NORAD were found in clinical HCC samples.

Conclusion: Taken together, herein we have provided evidence on the mechanism of genomic instability induced by hepatitis B virus X protein via TAX1BP2 and pumilio 2. These findings shed light on potential blockage of genomic instability induced by hepatitis B virus infections.

Project Number: 12110872

P132-0065

Novel Pre-mRNA Splicing of Intronically Integrated HBV Generates Oncogenic Chimera in Hepatocellular Carcinoma

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Background & Aims: Hepatitis B virus (HBV) integration is common in HBV-associated hepatocellular carcinoma (HCC) and may play an important pathogenic role through the production of chimeric HBV-human transcripts. We aimed to screen the transcriptome for HBV integrations in HCCs.

Methods: Transcriptome sequencing was performed on paired HBV-associated HCCs and corresponding non-tumorous liver tissues to identify viral-human chimeric sites. Validation was further performed in an expanded cohort of human HCCs.

Results: Here we report the discovery of a novel pre-mRNA splicing mechanism in generating HBV-human chimeric protein. This mechanism was exemplified by the formation of a recurrent HBV-cyclin A2 (CCNA2) chimeric transcript (A2S), as detected in 12.5% (6 of 48) of HCC patients, but in none of the 22 non-HCC HBV-associated cirrhotic liver samples examined. Upon the integration of HBV into the intron of the CCNA2 gene, the mammalian splicing machinery utilized the foreign splice sites at 282nt. and 458nt. of the HBV genome to generate a pseudo-exon, forming an in-frame chimeric fusion with CCNA2. The A2S chimeric protein gained a non-degradable property and promoted cell cycle progression, demonstrating its potential oncogenic functions.

Conclusions: A pre-mRNA splicing mechanism is involved in the formation of HBV-human chimeric proteins. This represents a novel and possibly common mechanism underlying the formation of HBV-human chimeric transcripts from intronically integrated HBV genome with functional impact.

Lay Summary: HBV is involved in the mammalian pre-mRNA splicing machinery in the generation of potential tumorigenic HBV-human chimeras. This study also provided insight on the impact of intronic HBV integration with the gain of splice sites in the development of HBV-associated HCC.

Project Number: 13120932

P133-0123

Regulation and Function of Histone Demethylase JMJD3 in HBV-induced Hepatocarcinogenesis

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Introduction and Project Objectives: Previous studies have demonstrated that JMJD3 (a jmjd domain containing histone demethylase) played a crucial role in inflammation. We aimed to investigate the functional roles of JMJD3 in hepatocellular carcinoma (HCC).

Methods: Cell proliferation, wound healing, colony formation assays were used to evaluate the roles of JMJD3 in HCC *in vitro*. Anchorage-independent cell growth assay and *in vivo* tumor xenograft mouse model were used to examine the roles of JMJD3 in HCC cell transformation and tumorigenesis. Tissue microarray, western blotting and chromatin immunoprecipitation were performed to delineate the mechanism underlying JMJD3 regulation on its downstream targets.

Results: Our study showed that JMJD3 was significantly down-regulated in HCC cell lines and tissues. Restored expression of JMJD3 inhibited oncogenic phenotypes of HCC cells *in vitro* and tumorigenicity *in vivo*. These suggested a tumor suppressive role of JMJD3 in HCC. DACH1 was identified as one of the JMJD3 downstream targets. Tissue microarray analysis showed a positive correlation between the expression of JMJD3 and DACH1 in HCC. DACH1 promoter was found to be in a high H3K27 tri-methylation (H3K27me3) status which was attenuated by ectopic expression of JMJD3 in HCC cells. This result, suggested that JMJD3 regulated DACH1 expression by histone demethylation. We found that HBx suppressed JMJD3 expression through activation of miR-29a in HCC.

Conclusions: JMJD3 plays tumor suppressive roles in HCC by regulating DACH1 expression.

Project Number: 12110352

P134-0169

Prospective Study on Oral Candidial Infection after Intensity-Modulated Radiation Therapy for Non-Metastatic Nasopharyngeal Carcinoma: Correlation with the Radiation Dose to the Parotids

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Introduction and Project Objectives: Nasopharyngeal carcinoma (NPC) is endemic in Southern China. Intensity-modulated radiation therapy (IMRT) for NPC may damage the salivary glands and lead to xerostomia, providing an ideal environment for opportunistic candidial infections. We prospectively investigated the incidence and factors correlating with oral candidial infection in NPC patients treated with radical IMRT.

Methods: Forty five patients with non-metastatic NPC were prospectively recruited. Saliva and mouthrinse samples were saved at baseline and then two-weekly during IMRT. They all received IMRT with 70Gy in 33 to 35 fractions over 7 weeks concurrent with cisplatin chemotherapy. Besides the gross tumour and positive neck nodes, the parotids, submandibular and sublingual glands were contoured on

Eclipse Treatment Planning System™ for radiation dose calculation. Fungal culture was performed on Sabouraud dextrose agar and CHROMagar™. In addition, API-32C AUX method and species-specific Taqman probes were used for specific identification of Candida species. The study endpoints are predictors of development of oral candidial infection and the incidence and types of candidial infection during IMRT. Anti-fungal sensitivity tests were also performed for any anti-fungal resistance.

Results: Eleven (28.9%) had oral candidial infection at baseline which increased to 25 (55.6%) patients during IMRT for their NPC. Considerable number of patients i.e. 9 (20.0%) and 25 (55.6%) patients had clinical diagnosis of oral candidiasis and positive candidial culture respectively during IMRT. *C. parapsilosis* (24 patients, 53.5%) followed by *C. albicans* (18 patients, 40.0%), *C. guilliermondii* (8 patients, 17.8%), *C. glabrata* (4 patients, 8.9%) and *C. tropicalis* (4 patients, 8.9%) were the most commonly found candida. Mixed fungal growth was observed in 17 patients (37.8%). Grade 2 and 3 xerostomia were noted in 13 (28.9%) and 32 (71.1%) patients respectively. Univariable and multivariable analysis revealed that mean radiation dose to the parotids >=45Gy was the only factor (p=0.045 and p=0.043 respectively) correlating significantly with occurrence of oral candidial infection.
For drug resistance assay by antifungal susceptibility tests for amphotericin B, caspofungin, ketoconazole, itraconazole, voriconazole and fluconazole, it was found that candida species in 11 patients (24.4%) demonstrated drug resistance to 2 antifungal agents, 5 patients (11.1%) with drug resistance to 3 antifungal agents and 3 patients (6.7%) to 4 antifungal agents.

Conclusions: Our study demonstrated that IMRT to the parotids may predispose to oral candidial infections which should be taken into account when managing NPC patients who undergo radiation therapy.

Project Number: 11100722

P135-0078
Human Cytomegalovirus and Human Immunodeficiency Virus Type 1 Co-infection of CD34⁺ Myeloid Progenitor Cells

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Introduction and Project Objectives: Individuals who have been pre-infected by human cytomegalovirus (HCMV) are more prone to AIDS disease progression after subsequent HIV-1 infection but the underlying mechanism remains elusive. HCMV is a ubiquitous DNA virus that commonly establishes lifelong latent infection in CD34⁺ progenitor cells, where latency-specific HCMV genes may modulate host restriction to HIV-1 infection. To test this hypothesis, we studied progenitor cells that are known to resist replicative HIV-1 infection due to the intrinsic expression of host restriction factors.

Methods: Primary CD34⁺ cells isolated from healthy human PBMC were cultured in specialized media. HCMV was used for infection and analyzed for latent viral DNA, latency-associated genes, and phenotypic changes to the cells. Digital PCR, real-time PCR and flow cytometry was used for these assays. Success of latent infection was assessed by reactivation experiments by stimulation or co-culture with permissive fibroblasts. HIV-1 live virus or dual-reporter pseudovirus was used to infect CD34⁺ cells with or without latent HCMV and examined for HIV-1 proviral DNA, LTR transcription, and p24 protein. The presence of HCMV and HIV-1 proteins in the cells was assessed by flow cytometry and confocal microscopy. Transfer of HIV-1 from CD34⁺ cells and CD4⁺ T cells was performed by co-culture.

Results: An enhanced level of HIV-1 proviral DNA and replication was observed in HCMV latently infected CD34⁺ cells and confirmed using dual reporter pseudovirus encoding X4- or R5-tropic envelope and T cell transfer. This phenomenon may be partially explained by the upregulation of HIV-1 entry co-receptors including chemokine receptors CXCR4 and CCR5 but not of the primary receptor CD4. Furthermore, latent HCMV infection downregulated the expression of HIV-1 restriction factors SAMHD1, APOBEC3G, tetherin and Mx2 in CD34⁺ progenitor cells that may confer to enhanced HIV-1 infection. However, this enhancement was abrogated when UV-inactivated HCMV was used for comparison, suggesting that expression of latent HCMV genes is essential for this effect. Importantly, co-infection of CD34⁺ cells can be found by detection of HCMV gB and HIV-1 p24 in the same cell by immunofluorescence and flow cytometry.

Conclusions: We established a primary cell culture model using CD34⁺ cells isolated from healthy human PBMCs for studying the establishment of HCMV latency and HIV-1 co-infection in CD34⁺ cells. Our results indicate that latent HCMV likely leads to host cell gene modulation that favors HIV-1 infection and has implications for future development of anti-HIV therapy in patients with pre-existing latent HCMV.

Project Number: 12111162

P136-0104
Novel Secretory Immunoadhesins for HIV Prevention

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Introduction and Project Objectives: The human immunodeficiency virus (HIV) has led to 39 million deaths since AIDS was discovered in 1981. However, due to the extensive genetic diversity of the virus, an effective vaccine remains elusive. With the development of antibody isolation techniques, numerous broadly neutralising antibodies (bnAbs) have been discovered. We hypothesize that engineering of bnAbs may further increased their potency, breadth and cost-effectiveness. To test this hypothesis, we sought to construct a broadly reactive bi-specific immunoadhesin (BiIA) to achieve a BiIA-based immunoprophylaxis.

Methods: By molecular engineering, we constructed multiple IAs using the genes of existing bnAbs. Following anti-HIV measurement *in vitro*, a synergistic pair of IAs was used for generating a novel single gene encoded BiIA (BiIA-SG). The biological properties of BiIA-SG were characterized by Western blot, ELISA, SPR, FACS and neutralisation assays. The *in vivo* efficacy of BiIA-SG was evaluated in humanised NSG mice challenged by live HIV_{JR-FL}. Viral load, proviral load P24 antigenemia in plasma were measured by Q-PCR and ELISA. Infected cells in blood and spleen were also determined by FACS and immunohistochemistry.

Results: We found that BiIA-SG displayed similar biological properties to parental IAs. Interestingly, however, BiIA-SG was superior to parental IAs with significantly improved anti-HIV activity and breadth. It neutralised 100% HIV-1 pseudotypes and primary isolates tested including all co-circulating subtypes/recombinant forms, transmitted/founder viruses and viral strains naturally resistant to parental IAs and to other bnAbs. Importantly, pre-exposure BiIA-SG conferred complete protection against diverse live HIV-1 challenges in humanized mice. No infected cells were found in all tissue compartments tested. Furthermore,

BiIA-SG also displayed potent activity in control HIV-1 replication when administrated 5 days after HIV-1_{JR-FL} infection in humanized mice.

Conclusion: In this study, we have successfully constructed the novel secretory BiIA-SG, which displays potent anti-HIV activities against a large panel of genetically divergent viral subtypes found in China including Hong Kong. Our results warrant the clinical development of BiIA-SG for HIV-1 prevention and immunotherapy in Hong Kong.

Project Number: 12110952

P137-0079

Epidemiology, Seroprevalence, and Clinical Manifestations of Immunodeficiency due to Autoantibody against Interferon Gamma in Hong Kong.

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Introduction/Project Objectives: Patients with adult-onset immunodeficiency due to autoantibodies against interferon gamma (anti-IFN-γ autoantibodies) may develop disseminated and/or recurrent opportunistic infections, including non-tuberculous mycobacteriosis, non-typhoidal salmonellosis, burkholderiosis, penicilliosis, and herpes zoster. While the condition appears to be especially common among Asians, including Chinese residents in Hong Kong, Taiwan, and mainland China, the seroprevalence rate of anti-IFN-γ autoantibodies among these populations is unknown. Moreover, the full spectrum of infective and non-infective clinical manifestations of this immuondeficiency syndrome is not fully understood. This retrospective case-control analysis aimed to investigate the epidemiology, seroprevalence rate, and clinical manifestations of this emerging immunodeficiency syndrome in Hong Kong.

Methods: This study was approved by the Institutional Review Board of The University of Hong Kong/Hospital Authority Hong Kong West Cluster. Archived serum samples from subjects aged ≥18 years, with or without opportunistic infections, were tested by a screening enzyme immunoassay and an IFN-γ spiking assay for the presence of anti-IFN-γ autoantibodies. The patients' clinical data were retrieved from the Hospital Authority Electronic Patient Record (ePR) system and entered into a predesigned database. Comparisons between patient groups were evaluated by the Chi-square test (categorical variables) and Mann-Whitney U-test (continuous variables). All statistical analyses were performed using SPSS18.0 for Windows. $P<0.05$ was considered statistically significant.

Results: 3198 serum samples from 3198 patients were tested. Overall, anti-IFN-γ autoantibodies were detected in 34 serum samples (34/3198, 1.1%) in the screening enzyme immunoassay. These included 11 patients with opportunistic infections including non-tuberculous mycobacteriosis, penicilliosis, non-typhoidal salmonellosis, burkholderiosis, and/or herpes zoster (11/133, 8.3%), 4 subjects aged >65 years without these opportunistic infections (4/783, 0.5%), 14 patients with autoimmune diseases without these opportunistic infections (14/753, 1.9%), and 5 patients with chronic HBV/HCV infection without these opportunistic infections (5/764, 0.7%). The seroprevalence rate of anti-IFN-γ autoantibodies in subjects without opportunistic infections was ~1%, which was significantly lower than that of patients with opportunistic infections (8.3%, $P<0.001$). Some patients with high-titer serum neutralizing anti-IFN-γ autoantibodies also developed reactive (Sweet's syndrome and lobular panniculitis) and infective dermatoses. Anti-IFN-γ autoantibodies were strongly associated with HLA-DR*15:02/16:02 and HLA-DQ*05:01/05:02 among the affected patients.

Conclusions: These findings helped to optimize the diagnostic and treatment protocols for this emerging immunodeficiency syndrome. Routine screening for anti-IFN-γ autoantibodies in asymptomatic patients is unlikely warranted. A working algorithm for the diagnosis and treatment of patients with dermatoses associated with anti-IFN-γ autoantibodies was established. Our non-laborious screening enzyme immunoassay could be adopted by clinical laboratories.

Project Number: 13121342

P138-0151

Elucidating Virulence Determinants of Streptococcus agalactiae Serotype-III-4 in Toxic Shock-like Syndrome and in Adult Invasive Streptococcal Disease through Comparative Genome Analyses and Ex-vivo Cytokine Stimulation Assays

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Introduction: Invasive diseases of Streptococcus agalactiae or group B streptococcus (GBS) of serotype III subtype 4 (III-4/ST283) are an important cause in non-pregnant adult meningitis and invasive disease, including toxic shock. We hypothesize invasive GBS serotype III-4 carry unique virulence determinants when compared to non-invasive strains.

Project Objectives:

(1) To complete genome sequencing of 4 representative isolates of serotype III-4 GBS, two from meningitis or septicaemia strains, and two control strains from non-invasive infection;
(2) identify potential virulence determinants through comparative genome analysis of GBS serotype III-4 strains with or without meningitis/septicaemia and other published GBS genomes;
(3) validate the prevalence of potential virulence factors; and
(4) demonstrate the mitogenicity of the virulence factors by using genetic mutants or fusion proteins constructed.

Methods: Whole genome sequencing on representative invasive GBS ST283 strains were performed and compared against strains from non-invasive sites. Comparative genomics were compared against 35 available whole genomes of GBS from public database. Potential virulence markers were identified. Isogenic mutants of phoB and mecA genes were constructed to demonstrate the mitogenicity with production of pro-inflammatory cytokines.

Results: Potential genes that were either truncated in the non-invasive strain or showed allele variation in these strains were identified. Deletion mutants of mecA gene and in particular of phoB gene, revealed significant mitogenic effects compared to wild type strain, and induced strong pro-inflammatory response in vitro.

Conclusions: Pangenome analysis of invasive and non-invasive GBS serotype III-4/ST283 strains unveiled a list of potential genes related to virulence. phoB plays an important role in the pathogenicity of GBS disease. Implications/Relevance The study provides insights to the pathogenicity of GBS disease. The resulting pangenome gene list enhances our understanding of GBS virulence and discovery of novel pathways to bacterial response to host, so as to improve preventative and therapeutic strategies against GBS invasive disease.

Project Number: 12110612

P139-0036

Identification of Innate Immune Defect Predisposing to Severe Influenza in a Chinese Population

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Introduction and Project Objectives: Influenza virus is a common cause of respiratory tract infection. However, only a small percentage of influenza patients develop severe disease. The emergence of 2009 pandemic influenza virus (A[H1N1]pdm09 virus) provided a unique opportunity for assessing genetic predispositions to severe influenza because many patients did not have pre-existing immunity against A(H1N1)pdm09 virus and did not have clinical risk factor for severe influenza. This study sought to identify innate immune defect predisposing to severe influenza in a Chinese population

Methods: In this case-control study, we compared Chinese patients in Hong Kong who had severe A(H1N1)pdm09 infection (required oxygen supplementation, admitted to the intensive care unit, or died), with those who had mild infection not satisfying the criteria for severe disease. Based on the results from a genome-wide association study involving 42 Chinese patients with severe A(H1N1)pdm09 infection and 42 with mild disease, 30 candidate single nucleotide polymorphisms related to the innate immune system were chosen for further genetic association study in a second cohort of patients with A(H1N1)pdm09 virus infection. Multivariate analysis was performed to control for confounding factors. In vitro studies were conducted to assess the role of the identified genes in influenza virus replication.

Results: For SFTPB gene which encodes surfactant protein B (SP-B), rs1130866 C allele was significantly associated with severe disease in the first cohort of patients (OR=3.37, P=0.0048). In the second cohort of patients, rs1130866 CC genotype was confirmed to be an independent risk factor for severe A(H1N1)pdm09 infection using multivariate analysis (OR=2.087, P=0.023). Compared to the general Han Chinese population, the CC genotype was overrepresented in patients with severe A(H1N1)pdm09 infection (OR=3.232, P=5.6 x 10^{-7}). Plaque reduction assay showed that the IC_{50} of SP-B were between 8-24 nM for A(H1N1) and A(H7N9). For PDE3A gene which encodes phosphodiesterase 3A, rs7314545 CT/TT and rs6487132 GG/GA were over-represented in patients with severe disease when compared to mild disease in the multivariate analysis (OR=3.45, P=0.006). In vitro study showed that viral titers of influenza A(H1N1) was higher in A549 cells with PDE3A knockdown than that without PDE3A knockdown.

Conclusions: SFTPB and PDE3A are independent host susceptibility genes for severe A(H1N1)pdm09 virus infection. In vitro experiments have confirmed that SFTPB and PDE3A are important host factors for affecting viral replication. Our findings have advanced the understanding of influenza virus pathogenesis and may be useful in identifying novel treatments for influenza virus infections.

Project Number: 13120842

P140-0176

Role of PACT in Host Antiviral Defence against Influenza A Virus

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Innate immune response is important in host antiviral defence against influenza A virus. To trigger innate antiviral response, influenza A virus RNA has to be recognized by cytoplasmic virus sensor RIG-I. We have recently identified a new double-stranded RNA binding partner of RIG-I in the activation of antiviral response. This partner named PACT is known to interact with influenza A virus NS1 protein and PA subunit of RNA polymerase. However, whether and how PACT might be involved in innate antiviral response to influenza A virus infection remain to be elucidated. In this study, we explored a new function of PACT in the suppression of influenza A virus replication, possibly through the binding with viral RNA and/or RNA-dependent association of polymerase subunits. Using the immortalized wild-type and PACT-knockout mouse embryonic fibroblast (MEF), we first revealed that PACT knockout in MEF strongly enhanced the expression of viral RNA during early and late influenza A virus infection. In addition, we found that interferon induction was severely dampened in PACT-knockout MEF during early influenza A virus infection. Several lines of evidence suggested that enhanced viral replication in PACT-knockout MEF was interferon-independent. Lastly, we found that overexpression of polymerases suppressed the PACT-mediated interferon production, but not RIG-I-induced interferon production in HEK293 cells. Our data suggested a new model that PACT might inhibit influenza A virus replication through the association of PACT with viral RNAs and polymerases, and overexpression of polymerase subunits inhibited the PACT-mediated interferon production.

Project Number: 12111312

P141-0167

Parents' Risk Perceptions and Protective Responses Regarding Varicella, Scarlet Fever and Hand, Foot and Mouth Disease in Hong Kong: A Multi-group Longitudinal Survey

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Background: Varicella, scarlet fever (SF) and hand, foot, and mouth disease (HFMD) mainly attack young children and cause considerable disease burden in Hong Kong. Varicella and HFMD usually cause institutional outbreaks and thereby considerable social impacts while SF cases are usually sporadic but have more severe clinical consequences. It remained unknown about how parents perceived the risk of these diseases and their associated protective behaviours.

Objectives: To compare parental risk perception and protective behaviours regarding these three diseases and test a model to disentangle the inter-relationships among information trust, risk perceptions and protective behaviours.

Methods: Three independent cohort studies were conducted for varicella, SF and HFMD, respectively. For each cohort, parents with at least one child aged≤12 years were recruited using random digital household telephone interview and invited to complete a baseline survey on information trust and risk perceptions of the disease in the respective peak season and re-contacted 1-2 months later for a follow-up survey on their protective behaviours. Descriptive analyses calculated and compared proportions of risk perceptions and protective behaviours while structural equation modelling (SEM) tested the inter-relationships among information trust, risk perceptions and protective behaviours

Results: A total of 605, 609 and 618 respondents completed the baseline survey on varicella, SF and HFMD, respectively, of whom 346 (57.2%), 394 (64.7%) and 452 (73.1%) completed their respective follow-up surveys. Of the respondents, 53.4%, 78.0% and 63.9% (X^2=103.53, df=4, p<0.001) perceived a “zero/very small/small” chance that their child would be infected while 67.8%, 85.4% and 76.4% (X^2=52.45, df=2, p<0.001) reported no worry about their child being

infected with varicella, HFMD and SF, respectively; 76.2%, 88.8% and 91.4% (X^2=72.85, df=4, p<0.001) believed that hand hygiene was "effective/highly effective" while 80.9%, 63.2% and 61.4% (X^2=69.91, df=4, p<0.001), respectively, believed that vaccination was "effective/highly effective", for preventing varicella, SF and HFMD, respectively. Across the three cohorts, the SEM consistently found that more trust in formal information (i.e., information from government-agency sources) was associated with greater belief in the effectiveness of hygiene in prevention while more trust in information from informal interpersonal communication was associated with both greater belief in hygiene effectiveness and disease worry; belief in hygiene effectiveness positively predicted subsequent adoption of hygiene measures.

Conclusion: Parents perceived overall low susceptibility of their child to all three pediatric infectious diseases. Public health interventions and risk communication should consider utilize the influence of informal information cues to motivate uptake of protective behaviours.

Project Number: 13120672

P142-0009

Development of Inhibitors against Signal Transducer and Activation of Transcription (STAT-3) Protein for the Treatment of Hepatitis C

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Hepatitis C is a liver disease caused by the hepatitis C virus (HCV) and is a highly infectious disease. Therefore, the identification of chemotherapeutics for HCV is of critical importance in arresting the spread of HCV amongst the general population and high risk groups.

We have utilized structure-based virtual screening to discover a natural product-like inhibitor of STAT3. Compound 1 was able to inhibit Signal Transducer and Activation of Transcription (STAT3) DNA-binding activity in a cell-free system and STAT3-driven luciferase expression in living cells, with potencies comparable to the well-known STAT3 inhibitor S3I-201. Additionally, compound 1 antagonized STAT3 dimerization and STAT3 tyrosine phosphorylation *in cellulo*. Computer-based hit-to-lead optimization was then carried out and a higher score modified compound 1a has been proposed.

We have discovered a novel cyclometallated rhodium(III) complex 12 that represents, to our knowledge, the first example of a substitutionally-inert, Group 9 organometallic compound utilised as a direct inhibitor of STAT3. Complex 12 targets the SH2 domain of STAT3, as revealed by a fluorescence polarisation assay, and was able to inhibit STAT3 DNA-binding activity *in vitro* and attenuate STAT3 phosphorylation, dimerization, and signaling activity *in cellulo*. Importantly, complex 12 was able to significantly reduce tumor size and weight in an *in vivo* mouse xenograft model. It is also noteworthy that the treated tumor tissues showed repressed STAT3 phosphorylation, VEGF expression and angiogenesis. We hypothesize that the anti-tumour effects of complex 12 in the mouse model is mediated, at least in part, by the inhibition of STAT3-directed gene expression by complex 12 *in vivo*, which could in turn be attributed to its ability to target the SH2 domain of STAT3 and inhibit STAT3 dimerization.

We anticipate that this cyclometallated rhodium(III) complex may serve as a useful scaffold for the further development of highly potent inhibitors of STAT3 dimerization as potential anti-neoplastic agents.

Project Number: 13121482

P143-0069

Identification of Hepatitis B X Protein Regions Responsible for the Regulation of HBV Transcription

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Introduction and Project Objectives: The hepatitis B X protein (HBx) is associated with the hepatitis B virus (HBV) covalently closed circular DNA (cccDNA) minichromosomal complex. It has been suggested that HBx regulates HBV replication by changing the acetylation status of cccDNA-bound histones. This study aimed to identify the specific HBx amino acid residue(s) responsible for this function.

Methods: We created a series of 30 HBx mutant expression plasmids, named MT1-30, with various alanine substitutions within the 154 amino acid (aa) HBx coding sequence by site-directed mutagenesis. These HBx mutant plasmids were co-transfected with an HBx-null full-length HBV DNA into HepG2-NTCP cells. Intracellular cccDNA, HBV RNA, encapsidated HBV DNA, and secretory hepatitis B surface antigen (HBsAg) were measured. Interaction between HBx and cccDNA and histone modifying enzymes were assessed using chromatin immunoprecipitation (ChIP), and the degree of interaction was expressed as % input.

Results: There was no significant difference in the expression levels of the wild-type and mutant HBx proteins. All HBx strains, including the wild-type and mutant strains, had comparable levels of cccDNA. However, significantly reduction in the levels of HBV RNA (59-77% reduction compared with wild-type) and intracellular HBV DNA (36-64% reduction; all p<0.05) were observed in 8 HBx mutants (MT2-4, 6, 11, 20-21 and 24). These mutants had mutations in HBx aa 55-64, 67-74, 94-96, 121-126, and 133-135, respectively. Six of these 8 mutants (MT3-4, 6, 20-21 and 24) also had a significant reduction of secretory HBsAg (71-81% reduction; all p<0.001). ChIP experiments showed that mutants MT2, 3, 20, and 21 (aa 55-64, 121-126) had a greatly reduced interaction with cccDNA (% input of mutants vs. wild-type: 0.02-0.64% vs. 3.08%; all p<0.05). Moreover, recruitment of histone acetyltransferases (CBP and P300) to cccDNA was reduced in mutant MT20, and recruitment of histone deacetylases (HDAC1 and Sirt1) to cccDNA was increased in mutant MT11 (aa 94-96; all p<0.05).

Conclusions: Several HBx coding regions (aa 55-64, 94-96, and 121-126) were demonstrated to play an important role in the regulation of HBV transcription via their reduced interaction with cccDNA. The recruitment of histone acetyltransferases and deacetylases to the cccDNA minichromosome were also affected by these important HBx mutations. Further studies on how HBx interacts with histone modifying enzymes will provide insights to the potential use of HBx as a therapeutic target against HBV.

Project Number: 13120782

P144-0081

Close Genetic Relatedness between Human and Swine Hepatitis E Viruses in Hong Kong

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Introduction and Project Objectives: Hepatitis E virus (HEV) is primarily transmitted through fecal-oral route in developing countries and is increasingly recognized as one common foodborne cause of human viral hepatitis in developed countries. In Hong Kong, the number

of locally-acquired HEV infections was steadily rising in the past decade. Here, we aim to evaluate the prevalence of HEV in high-risk food items and to delineate genetic relatedness between human and swine HEV strains.

Methods: From March 2014 to March 2016, we sampled from local groceries and wet markets five types of high-risk HEV food items: lamb, oyster, pig blood curd, pig intestine and pig liver. Twenty-two archived sera positive for HEV IgM from hospitalized acute hepatitis patients during the same period were retrieved. Total RNA from food samples and human sera were extracted and tested for HEV RNA by a broadly-reactive real time RT-qPCR assay. Nested PCR targeting ORF1 and ORF2/3 of HEV genome was performed for virus genotyping. PCR products were Sanger-sequenced. HEV sequences were analyzed for neighbor-joining phylogenetic inference by MEGA 7.

Results: A total of 244 lamb, 489 oyster, 244 pig blood curd, 245 pig intestine and 488 pig liver samples were collected and tested. HEV RNA was detected in 7 pig liver, 1 pig intestine and 1 oyster samples. The prevalence of HEV in pig liver, pig intestine and oyster samples was estimated to be 1.4% (95% confidence interval: 0.6%-2.9%), 0.4% (0.0%-2.3%) and 0.2% (0.0%-1.1%), respectively. Cycle threshold values of most positive samples were close to the lower limit of detection of the RT qPCR assay. Four HEV strains from pig liver samples and 14 HEV strains from human sera were successfully genotyped. All HEV strains belonged to genotype 4b except for 1 human and 1 swine strains that were grouped to genotype 4d.

Conclusion: Our findings showed a close genetic relatedness between human and swine HEV strains, supporting that consumption of high-risk food items such as pig liver might be the source of local human HEV infections.

Project Number: 13120172

P145-0161

Mutational Analysis of the Hepatitis B Core Protein DNA-binding Domain and its Role in HBV Transcription Regulation

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Introduction and Project Objectives: The hepatitis B virus (HBV) covalently closed circular DNA (cccDNA) is the template for HBV transcription. The hepatitis B core protein (HBc) has been suggested to interact with cccDNA and regulate HBV transcription. Thus interfering the binding of HBc to cccDNA can be a potential therapeutic approach. However, knowledge of HBc amino acid residue(s) which confer its binding ability to cccDNA is limited. This study aimed to identify the specific HBc region(s) responsible for HBV transcription regulation and its interaction with cccDNA.

Methods: Seventeen mutants with mutations at the four arginine-rich clusters (clusters I - IV) of the HBc carboxyl-terminal domain (CTD) were created by site-directed mutagenesis. These HBc mutant expression plasmids were co-transfected with an HBc-negative full-length HBV DNA in hepatoma cells. The effect of HBc mutations on the levels of HBV DNA, RNA, and hepatitis B surface antigen (HBsAg) were measured. The association of cccDNA with mutant HBc and histone acetyltransferases (HATs) was assessed by chromatin immunoprecipitation (ChIP).

Results: HBV RNA levels in the HBc mutants with mutations in clusters III and IV were significantly lower than that in wild-type HBc (all $P < 0.05$). HBc arginine clusters III and IV mutants also had a significantly lower levels of intracellular HBV DNA (<5% of wild-type; $P < 0.001$) and HBsAg (<10% of wild-type; $P < 0.0001$). Compared with wild-type HBc, HBc clusters III and IV mutants had a smaller degree of association with cccDNA ($P < 0.001$). The association between HATs with cccDNA were also low in these HBc mutants.

Conclusions: HBc CTD arginine residues, especially in cluster III and cluster IV, played an important role in the regulation of HBV transcription through its interaction with cccDNA. The findings in this study suggested that HBc CTD can be a potential therapeutic target against HBV. If therapeutic agents interfering the binding of HBc CTD to cccDNA are identified, they can be used together with existing antiviral agents to control HBV replication and further deplete or even eliminate HBV cccDNA.

Project Number: 12111282

P146-0106

Further Optimization of a Live Viral Vector for HIV-1 Vaccine Research

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Introduction and Project Objectives: Since the discovery of HIV-1 as the major causative agent of AIDS in 1983, the search for an effective vaccine has always been a top priority in the fight against the HIV/AIDS pandemic. To date, however, there is still no effective AIDS vaccine for clinical use. The AIDS vaccine Thai RV144 trial indicated the efficacy potential of a poxvirus-vectored vaccine, we aimed to further optimize the existing poxvirus vector MVTT that has a good safety record in Chinese people.

Methods: We test various strategies to improve HIV-1 gene expression, insertion and immunogenicity in the context of MVTT-based vaccine both *in vitro* and *in vivo*. We developed a Cre-loxP system to effectively construct the recombinant MVTT and subsequently evaluate the vaccine immunogenicity *in vivo*. The immunogenicity evaluation used ELISA, ELIspot, ICS and Tetramer assays.

Results: We successfully generated an optimized MVTT-based HIV-1 vaccine, namely $MVTT_{HKU\text{-}gpe/AE13}$, with excellent stability and transgene expression. We found that $MVTT_{HKU\text{-}gpe/AE13}$ induced robust HIV-1-specific T cell and antibody responses in combination with AD2-based vaccine.

Conclusions: We have established successfully a platform of technology useful to generate vaccinia-based vaccines. The heterologous MVTT/Ad2 regimen demonstrated encouraging immunogenicity profiles of inducing HIV-1-specific T cell and antibody responses.

Project Number: 13121272

P147-0136

Investigation of Staphylococcus aureus Extra-cellular Protein, Adenosine Synthase A, as a Vaccine Candidate

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Staphylococcus aureus (S. aureus) is a severe pathogen found in the community and in hospitals. Most notably, Methicillin-resistant S. aureus (MRSA) is resistant to almost all antibiotics, which is a growing public health concern. The emergence of drug-resistant strains has prompted

the search for alternative treatments such as immunotherapeutic approaches. Previous research showed that S. aureus exploit the immunomodulatory attributes of adenosine to escape host immunity. In this study, we investigated adenosine synthase A (AdsA), a S. aureus cell wall-anchored enzyme as possible targets for immunotherapy. Mice vaccinated with aluminum hydroxide-formulated recombinant AdsA (rAdsA) induced high-titer anti-AdsA antibodies, thereby providing consistent protection in three mouse infection models when challenged with two S. aureus strains. The importance of anti-AdsA antibody in protection was demonstrated by passive transfer experiments. Altogether, our data demonstrate that the AdsA is a promising target for vaccines and therapeutics development to alleviate severe S. aureus diseases.

Project Number: HK-09-01-20

P148-0137

Recombinant Salmonella Vaccine Platform for Clostridium Difficile

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Clostridium difficile-associated disease (CDAD) constitutes a great majority of hospital diarrhea cases in industrialized countries and is induced by two types of large toxin molecules: toxin A (TcdA) and toxin B (TcdB). Development of immunotherapeutic approaches, either active or passive, has seen a resurgence in recent years. Studies have described vaccine plasmids that express either TcdA and/or TcdB receptor binding domain (RBD). However, the effectiveness of one vector encoding both toxin RBDs against CDAD has not been evaluated. In the study, we constructed highly optimized plasmids to express the receptor binding domains of both TcdA and TcdB from a single vector. The DNA vaccine was evaluated in two animal models for its immunogenicity and protective effects. The DNA vaccine induced high levels of serum antibodies to toxin A and/or B and demonstrated neutralizing activity in both in vitro and in vivo systems. In a C. difficile hamster infection model, immunization with the DNA vaccine reduced infection severity and conferred significant protection against a lethal C. difficile strain. This study has demonstrated a single plasmid encoding the RBD domains of C. difficile TcdA and TcdB as a DNA vaccine that could provide protection from C. difficile disease.

Project Number: HK-09-01-21

P149-0142

A Prospective Randomized Trial to Compare the Safety and Immunogenicity of Intradermal and Intramuscular Influenza Vaccines in Patients with Inflammatory Bowel Disease in Hong Kong

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Introduction: Poor immunogenicity of the influenza A monovalent vaccine has been reported in patients with inflammatory bowel disease (IBD). The new intradermal (ID) influenza vaccine has been shown to be superior to intramuscular (IM) vaccine in elderly subjects. We compared the immune responses and safety of ID and IM trivalent (HIN1/H3N2/B) influenza vaccine (TIV) in IBD patients.

Methods: Adult patients with stable Crohn's disease (CD) or ulcerative colitis (UC) were randomly assigned to receive TIV given by IM or ID route. We measured the hemagglutination inhibition (HAI) and geometric mean titres (GMT) at baseline, day 21 and 6 month post vaccination.

Results: 127 IBD ((51.2% UC) patients were randomized to receive the ID (n = 63) and IM vaccine (n = 64). Immunogenicity at baseline and day 21 for all three vaccines' strains were comparable. There was no significant difference in the seroprotection rate, seroconversion rate or GMT-fold increase between the ID and IM groups. Fall in immunogenicity for H3N2 and B strains at 6 month was more significant for IM vaccine than ID vaccine. Local reactions of redness and swelling were more common in the ID group (redness: 61.9% vs. 4.7%; P<0.001, swelling: 61.9% vs. 6.3%; P<0.001) but there was no difference in systemic adverse events.

Conclusions: Both IM and ID TIV confer acceptable immune responses to IBD patients with no significant adverse effect. Immunogenicity for H3N2 and B strains was however lower in IM group at 6 month.

Project Number: 12111082

P150-0003

Use of Codon Usage Bias to Generate Influenza Virus of Vaccine Potential

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Introduction and Project Objectives: Proteins are encoded by messenger RNA (mRNA) in cells. A codon in a mRNA is a series of three nucleotides that encodes a specific amino acid residue in a protein or for the termination of translation (stop codons). We previously demonstrated that that humans and avian influenza viruses have different codon usage biases. These results further suggested that influenza virus might have change its codon usage bias after adapting in humans. These interesting observations also prompted us to hypothesize that, by using multiple silent mutations to make a human influenza viral genome having an avian virus-like codon usage bias, it might be possible to create a human virus that is specifically attenuated in mammalian cells.

Methods: Influenza A/Brisbane/59/2007 (H1N1) (BR59) was used as the prototype virus in this study. Using the codon bias differences between human and avian influenza viruses , silent mutations were introduced into the viral genome. These mutations were randomly introduced into the regions that are known to not be involved in viral RNP (vRNP) packaging and splicing. Sequence regions with out-of-frame ORFs (e.g., PB1 and PB1-F2 ORFs) were also excluded from mutagenesis. These mutations were specifically introduced into sites that are highly conserved at the amino acid sequence level (>99%) but not at the nucleotide sequence level. Both the wild-type and mutated viral RNA segments were then synthesized commercially. The wild-type and mutated viruses were generated by reverse genetics. The resultant viruses were characterized in vitro and in vivo assays.

Results: Silent mutations were introduced into 351 codon of the genome. The genome of the resultant BR59 mutant encoded wild-type BR59 viral proteins but the largest ORF of each segment had an avian influenza virus-like viral codon usage bias. The resultant mutant was significantly attenuated in mammalian cells and mice, yet it grew well in embryonated eggs. A single dose of intranasal vaccination induced potent innate, humoral and cellular immune responses, and the mutant could protect mice against homologous and heterologous viral challenges. The attenuated mutant could also be used as a vaccine master donor strain by replacing hemagglutinin and neuraminidase derived from other strains.

Conclusion: We demonstrated that codon usage alteration was a successful strategy to generate attenuated viruses of vaccine applications.

Project Number: 12110982

P151-0067

Understanding Vaccine Induced T cell Protection from Influenza Viruses

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A diverse array of Influenza viruses which circulate between different species, reassort and drift over time, requiring a broadly reactive immune response to enable protection against diverse influenza viruses. Current inactivated influenza vaccines mediate protection by stimulating antibodies towards the subtype specific HA-head with limited cross-reactivity. Therefore, it is essential to improve influenza vaccines by utilizing multiple arms of the immune system. Virus specific $CD4^+$ and $CD8^+$ T cells responses can directly kill virus infected cells and co-ordinate local innate immune responses. Importantly, T cells can react against different strains and subtypes of influenza due to sequence conservation of their targets resulting in broad reactivity. We have developed a novel vaccine using the immunogenic live vaccinia virus as a vaccine vector, containing multivalent influenza proteins derived from H5N1, plus IL-15 as an adjuvant. The vaccine protected mice against lethal challenge by increasing survival and significantly reducing virus loads against the most recent human H7N9, seasonal H3N2, pandemic-2009 H1N1 and highly pathogenic H7N7 influenza A viruses. An influenza-specific antibody responses was detectable after vaccination but were not neutralizing against heterologous viruses, nor able to mediate protection by passive transfer. Importantly, influenza specific $CD4^+$ and $CD8^+$ T cell responses are elicited by the vaccine, and recruited following viral challenge at the lung and periphery. Selective depletion experiments for T cell subsets revealed that memory T cell responses act in synergy, with higher viral loads in mice depleted of both $CD4^+$ and $CD8^+$ T cell responses. An important role of $CD4^+$ T cells was shown for heterosubtypic protection, especially in generating local lung NP specific antibody responses. This study has illustrated the potential use of multivalent-vaccinia virus as a universal influenza vaccine, and identified an essential role of $CD4^+$ T cells in providing universal protection against influenza established by a vaccinia-H5N1 vaccine.

Project Number: 13121142

P152-0132

A Systematic Review of the Design of Test-negative Studies for Vaccine Effectiveness

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Introduction and Project Objectives: Due to yearly changing of circulating strings of influenza type/subtypes, influenza vaccination are required to update to match with prevailing strings and vaccination effectiveness (VE) are required to be assessed annually. Recently there has been a drastic increase of published estimates of VE by a new convenient design termed the test-negative design (TND). TND is evaluated to be more accurate by reducing confounder of health seeking behavior. However, considerable variation in reporting VE estimation was found in TND studies, and some of the variation is likely due to different study design and statistical model used. One aim of this project is to identify methodological variations in published TND studies of influenza VE, and discuss the potential of the TND monitor influenza VE. The second objective is to compare VE estimates derived from inpatient and outpatient settings, restricting to the same country and influenza seasons.

Methods: The literatures were searched on Pubmed and Medline by a combination of key words. Studies on any type of influenza vaccination were considered. Articles that not use TND, or of reanalysis, interim estimated were excluded. We reviewed study design by retrieving variables including setting, country, influenza season, source population, case definition (positive and negative), exposure definition, outcome definition, study period, exclusion criteria and statistical model.

Results: 1944 published papers were found on Nov 8th 2013, 101 full-texts were examined and 29 were excluded. After further exclusion of interim study and reanalysis, 72 articles reporting VE estimates for 93 seasons were included. These studies reported for 22 countries in Europe, North America, Australia and Asia, from 2005 to 2014. The variables reported are varied enormously across studies. 72 studies used a total of 60 combinations of variables, with 1 to 11 variables in them. We found some inconsistent adjustments of confounders among studies, including age and high-risk status, and some over adjustments non-confounder covariates, including duration of symptoms. Besides, the numbers of cases in regression models were not reported by a large number of studies, which may all affect VE estimates. The studies were updated to July 2015 for VE comparison by setting, and we found no difference between inpatient and outpatient VE.

Conclusions: Further discussion on VE study reporting protocol including variables specification and data presenting are highly suggested. We found no evidence of difference in VE estimates between inpatient and outpatient settings by TND.

Project Number: HK-13-04-04

P153-0149

Epidemiology of Oral HPV Infection in the General Population in Hong Kong - Baseline Data before Implementation of HPV-based Screening and Vaccination Programmes

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Background: Oral infection of human papillomavirus (HPV) has been recognized as a risk factor for oropharyngeal cancer, but little is known about the prevalence and risk factors of oral HPV infection in Chinese populations. We aimed to evaluate the prevalence of oral HPV infection and its associated factors.

Method: A population-based, cross-sectional study was performed in Hong Kong between 2015 and 2016. From a primary care screening practice, subjects aged 18-64 were prospectively recruited via one media announcement covering all districts of Hong Kong. All participants completed a questionnaire on their socio-demographic details and behavioral habits, and subsequently provided oral gargle samples from oral cavity rinsing by normal saline for 20 seconds. HPV-DNA was extracted from the mouthwash solution, amplified by polymerase chain reaction and detected by Next-Gen sequencing assays. The main outcomes included the prevalence of oral infection with various HPV subtypes and their associated factors.

Results: Among 1,469 screening participants, the overall prevalence of any-type HPV, high-risk alpha-HPV, low-risk alpha-HPV and beta/gamma-HPV was 15.7% (95% CI, 13.9%-17.7%), 1.0% (95% CI, 0.51%- 1.54%), 1.8% (95% CI, 1.2%-2.5%) and 13.6% (95% CI, 11.9%-15.5%), respectively. There were 40 subjects who were infected by alpha-HPV: 15 belonged to high-risk, and the other 25 were low-

risk. HPV16 (n=5, 0.3%, 95% C.I. 0.1%-0.8%) was the most common high-risk type. Subjects who self-reported oral sex in the past 2 years had significantly higher odds of alpha-HPV (aOR=2.66, 95% CI: 1.40-5.04, p=0.003), high-risk (aOR=3.19, 95% CI: 1.07-9.47, p=0.017) and low-risk (aOR=2.53, 95% CI: 1.17-5.44, p=0.018) infection. Men were more likely to have high-risk HPV (aOR=6.14, 95% CI: 1.37-27.6, p=.018). Individuals who reported habits of tooth brushing more than 90% of the time were less likely to be infected by beta/gamma-HPV (aOR=0.64, 95% C.I. 0.47-0.89, p=0.007). Among all subjects with alpha-HPV infection, none were detected to have oropharyngeal cancer by endoscopic examination.

Conclusions: These findings reported low prevalence of oral infection with alpha-HPV among screening participants in a Chinese population, and identified significant factors associated with various subtypes of HPV infection. Further verification of the sensitivity of HPV-testing will help to identify the predictive ability of HPV-DNA based screening for oropharyngeal cancer.

Project Number: CU-15-C4

P154-0083

Development of Intranasal DNA Vaccine Delivery System using Non-Viral Vectors

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Introduction: The biggest obstacle of DNA vaccines is poor immunogenicity. One of the approaches to enhance the efficacy of DNA vaccine is to improve DNA delivery efficiency. Administration of naked DNA is usually inefficient with only a small fraction of DNA being taken up by the cells and subsequently expressed. This is because DNA is negatively charged, hydrophilic macromolecule; it is incapable to permeate across the biological membrane. A safe and efficient DNA delivery system can be employed to facilitate cellular uptake of DNA vaccines and hence induce high level of antigen expression and immune response.

Project Objectives: The overall aim of this project is to address the delivery problem of DNA vaccine, by developing a novel intranasal DNA vaccine formulation using non-viral vectors as DNA delivery agent.

Methods and Results: High DNA transfection efficiency is essential in the development of DNA vaccine, especially in professional antigen presenting cells (APCs) such as macrophages and dendritic cells. Initially, oligochitosans of different molecular weight were tested for the transfection efficiency on various mammalian cell lines. Although the polymer systems were effective in mediating DNA transfection in airway epithelial cells (Calu-3 cells), the transfection efficiency was poor in macrophages (RAW264.7 cells). Also, when they were used to deliver DNA encoding antigens, they failed to induce cytokines release in macrophages. Therefore, the alternative approach was adopted – a peptide-based vector, LAH4-L1 and its derivatives, were used as DNA carriers in the remaining of this study. The LAH4-L1 peptides were able to mediate DNA transfection in wide range of cells including airway epithelial cells, macrophages as well as dendritic cells (JAWSII cells). Furthermore, when these peptides were used to deliver DNA encoding antigen, they were able induce cytokines release, and promote dendritic cells maturation. However, when the peptide-based DNA delivery systems were administered to mice through the intranasal route, the level of expression was too low to be detected *in vivo*.

Conclusions: Oligochitosans were not successful in mediating effective DNA transfection in APCs. In contrast, LAH4-L1, and its NLS-modified analogues were effective in transfecting macrophages and dendritic cells *in vitro*. Unfortunately, when they were employed *in vivo* for intranasal delivery, their transfection efficiency was not satisfactory. A higher dose or repeated dose may be necessary. Further investigation is required to improve the design of the non-viral vector to make the delivery agent suitable as DNA vaccine carrier for intranasal use.

Project Number: 13121222

P155-0177

Immunogenicity of Twice-annual Vaccination against Seasonal Influenza for Two Hemispheres in Elderly in Hong Kong / Management of the Project on Immunogenicity of Twice-annual Vaccination against Seasonal Influenza for Two Hemispheres in Elderly in Hong Kong

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Introduction and Project Objectives: In the winter of 2014-15, emergence of a drifted non-matched influenza A(H3N2) strain led the Centre for Health Protection to administer the 2015 southern hemisphere (SH) seasonal influenza vaccine (SIV) for the older adults. An observational study was conducted to assess the immunogenicity of the SH SIV among older adults in Hong Kong and its effect on the immunogenicity of subsequent NH SIV in 2015-16.

Methods: In the summer of 2015 we enrolled older adults ≥75 years old who were receiving SH SIV, and collected pre- and post-vaccination sera (Group A1). We followed up these older adults through to the winter of 2015-16 when they received NH SIV and again collected pre- and post-vaccination sera (Group A2). For comparison we enrolled a separate group of older adults who received NH SIV in winter 2015-16 without prior receipt of the 2015 SH SIV (Group B2). We tested the sera against vaccine strains by haemagglutination-inhibition (HAI) assays. A subgroup of participants in each group had additional blood specimens collected pre- and post-vaccination for additional tests on cell-mediated immunity.

Results: We enrolled 978 people involving 470 vaccinations in Group A1, 419 vaccinations in Group A2 and 408 vaccinations in Group B2. In comparison with Group A1, Group A2 had significantly higher geometrical mean titre (GMT) ratios and proportions of seroconversion at Day 30 for A(H1N1) and B/Victoria but lower for A(H3N2) and B/Yamagata, and significantly higher proportions of seroprotection at Day 30 for influenza A (H1 and H3) but similar for both lineages of influenza B. In comparison with Group B2, significantly lower GMT ratios and proportions of seroconversion at Day 30 were observed across all four vaccine strains in Group A2. The proportions of seroprotection at Day 30 were higher in Group B2 than Group A2 for A(H3N2) and B/Yamagata but similar for A(H1N1) and B/Victoria. A significant reduction in responses of A(H3N2)-specific CD4 T cells with effector memory phenotype was seen after twice-annual vaccination but had only a modest association with low HAI GMT rises for the homologous virus.

Conclusions: There was blunting of immune responses in the twice-annual vaccination group compared to once-annual vaccination group, while protection was likely to have been improved during the summer for the twice-annual vaccination group that did receive SH vaccination. The relationship between twice-annual vaccination and reduced CD4 memory responses for impaired helper functions for antibody generation requires further exploration.

Project Number: CHP-PH-12 / HKS-15-E06

P156-0180

Impact of Increased Influenza and Pneumococcal Vaccine Coverage on the Burden of Influenza in the Elderly: A Comparison between Hong Kong and Brisbane

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Introduction and Project Objectives: Influenza and pneumococcal vaccine uptake has dramatically increased since 2003 in the older population of Hong Kong aged 65 years or over, but the impact of increased vaccination rates on influenza disease burden remains unknown. Here we conducted an ecological study to test the hypothesis that the relatively larger change in vaccination rate was associated with a greater reduction of influenza-associated disease burden in the Hong Kong older population than the stable vaccination rates in the older population of Brisbane, Australia.

Methods: Time series segmented regression models were applied to estimate weekly excess rates of cause-specific mortality or hospitalization to estimate annual excess rates associated with influenza in the elderly during the pre-SARS period of 2001-2002 when vaccine coverage was much lower (reference period), the post-SARS period of 2004-2008 and the post-H1N1 pandemic period of 2010-2012 when vaccine coverage was high in Hong Kong. The rate ratios (RRs) between these periods were subsequently calculated to quantify the relative change in influenza-associated disease burden in the older population of Hong Kong and Brisbane across these periods, respectively. The ratio of RRs between Hong Kong and Brisbane was used to the long-term change of influenza disease burden between these two regions.

Results: Compared to the pre-SARS period, influenza associated excess rates of mortality during the post-SARS period in Hong Kong decreased for CRD (RR=0.90, 95% CI 0.80,1.01), stroke (RR=0.74, 95% CI 0.50,1.09), and IHD (RR=0.45, 95% CI 0.34,0.58), while the corresponding RRs in Brisbane were 0.79 (95% CI 0.54,1.15), 0.33 (0.13,0.80), and 1.09 (0.62,1.90), respectively. But only IHD mortality shows a greater reduction in Hong Kong than in Brisbane (ratio of RRs=0.41, p=0.005). During the post-pandemic period, excess rates of all-causes mortality increased in Hong Kong, but to a lesser extent than in Brisbane (RR=1.41 versus 2.39, ratio of RRs=0.59, p<0.001).

Conclusions: This study provides some but limited evidence that markedly increased vaccination rates in the elderly of Hong Kong have reduced influenza disease burden. Our findings suggest that increased influenza and pneumococcal vaccination is effective at the population level, which strongly supports the policy of promoting annual influenza vaccination to the elderly.

Project Number: 13121282

P157-0183

Efficacy of Combined Influenza and 23-valent Polysaccharide Pneumococcal Vaccines in Healthy Smokers

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Background: Chronic smokers are at risk of premature death associated with underlying pulmonary or cardiovascular diseases. Dual influenza and pneumococcal vaccination has been shown to prevent death and hospitalization secondary to pulmonary or cardiovascular diseases in elderly persons. Its effect in chronic smokers remained unknown.

Methods: This is a prospective randomized open-labeled trial conducted from April 2010 to March 2013, comprising adult patients who were chronic smokers. Subjects were randomly assigned into 4 groups. Group 1 (study group) patients received both trivalent influenza vaccine (TIV) and the 23-valent polysaccharide pneumococcal vaccine (PPV). There were 3 control groups: Group 2 patients received the TIV only. Group 3 patients received the PPV only and Group 4 patients did not receive any vaccines. The TIV used was the Vaxigrip® (Sanofi Pasteur, France) and the PPV used was the Pneumovax®23 (Merck, USA). All enrolled patients were follow-up for at least 24 months post vaccination. Patient details, Charlson's comorbidity index, medications, subsequent hospitalization, diagnosis and mortality were recorded and analyzed.

Results: A total of 1006 subjects were enrolled and completed the study (Group PPV+TIV: 250; Group TIV: 254, Group PPV: 250 and Group None: 259). The baseline demographics and Charlson's comorbidity index were similar among subjects in the 4 groups. The median age was 48 years and 85.9% were male patients. Subjects who received the dual vaccination (Group PPV+TIV) had a significantly lower hospitalization rate (p<0.001), mean length of stay (P<0.001), and frequency of hospitalization (p<0.001) for cardiovascular or respiratory diseases than no vaccination (Group None) or single vaccination (Group TIV and Group PPV). There was no difference in mortality rate among the groups. Both vaccinations were well tolerated and no serious adverse events were reported.

Conclusion: Dual influenza and pneumococcal vaccinations protected chronic smokers against hospitalization secondary to pulmonary or cardiovascular causes. Annual influenza and a single pneumococcal vaccination should be promoted among chronic smokers.

Project Number: HK-09-01-17

P158-0163

Epidemiological Inference from Different Line Lists of Human Cases based on Publicly Available Data

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The influenza A(H7N9) virus emerged in China in 2013 and resulted in >130 laboratory-confirmed cases within three months. To effectively control the disease, evidence-based public health response is essential. This requires timely and high quality epidemiological and clinical data. There is a potential of using publicly available information from sources such as official health websites, news, or social media which is available to a wider community of experts. This study aimed to assess the use of publicly available line-lists to draw various types of epidemiological inferences in the first wave of H7N9 epidemic.

We obtained four line-lists of influenza A(H7N9) cases based on publicly available information from early April to end of May, 2013. These line-lists were created by Boston Children's Hospital (HealthMap), Virginia Polytechnic Institute and State University, FluTrackers, Bloomberg

News and School of Public Health, the University of Hong Kong. We analyzed demographical and epidemiological variables and compared with the analyses based on the official line-lists from the Chinese Center for Disease Control and Prevention.

We described several types of epidemiological inference for assessing severity and transmissibility of the influenza A(H7N9) epidemic in real-time. We compared estimated distributions of basic demographic and epidemiological variables, onset-to-admission, onset-to-discharge and onset-to-death durations, hospital fatality risk (HFR) and impact of live poultry market closure on human infections between the line-lists.

Similar age and sex distributions, epidemic curves, geographical spread, onset-to-hospitalization and onset-to-death distributions were estimated from all line-lists, at different times of the H7N9 epidemic. Live poultry market closure was consistently found to reduce H7N9 human cases in Shanghai, Nanjing and Hangzhou.

Compared to the official line-list, a shorter onset-to-discharge period was estimated based on the line-lists based on public information. While the outcomes of hospitalized patients were mostly available near the end of the epidemic, the estimated HFR from these line-lists did not converge to the final estimate.

Our results show that publicly available information is able to provide accurate information on demographic characteristics and case counts. However, information which requires follow-up, such as patient status, hospitalization or discharge, was less reliable. Inference on transmissibility or geographical spread is likely to be reliable but there information on disease severity was less reliable. Maintaining an open-access minimum dataset based on publicly available data, with key epidemiological variables in standardized format, definition and a time stamp could be beneficial to the control of emerging infectious diseases.

Project Number: HK-13-04-01

P159-0016

School-based Surveillance for Childhood Influenza in Hong Kong, 2014-15

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Introduction and Project Objectives: Influenza imposes substantial healthcare burden in terms of hospitalisation and mortality in children, which can be prevented by vaccination. Influenza vaccination coverage varies widely among childhood populations worldwide, which has significant impact on herd immunity and usefulness of influenza vaccine. However, there is limited real-life data on influenza vaccine effectiveness (VE) in children. This study aimed to investigate clinical spectrum of influenza infection and VE in preventing influenza in Hong Kong children.

Methods: This prospective cohort study recruited children aged 2-12 years from 15 kindergartens and primary schools. Parents completed a questionnaire on subjects' health status and history of influenza vaccination. Flocked nasopharyngeal swabs (NPSs) were collected at biweekly school visits during influenza seasons in 2014-15, and illness visits were arranged for children with influenza-like illness (ILI). Influenza A and B were detected and typed by polymerase chain reaction, and influenza immunity measured by haemagglutination inhibition (HAI).

Results: 623 children provided a total of 2,633 NPS samples. Two samples were obtained from 607 (97.4%) of subjects. Thirty-six (11.2%) subjects had influenza A or B in 2014 whereas all 19 (6.3%) subjects had influenza A in 2015. Seropositivity rates for A(H1N1)pdm09, A/H3N2, A/H3N2_Switzerland, B/Victoria-lineage and B/Yamagata-lineage were 92%, 91%, 68%, 49% and 85%, respectively. Ninety-nine subjects reported ILI and nine illness visits were arranged. Seasonal influenza vaccination was protective against ILI but not laboratory-confirmed influenza by surveillance. Influenza VE for ILI varied between 42.1 (10.5-63.1) % and 51.9 (24.5-70.1) % depending on the year of vaccination. Subgroup analyses showed higher VE for both ILI (70.9% vs 34.6%) and mild laboratory-confirmed influenza (44.0% vs -6.2%) in school-age children than preschoolers who were vaccinated within 12 months. HAI titres and seropositivity did not differ in subjects with and without ILI. Logistic regression confirmed protective effect of influenza vaccination against ILI. There was no reported transmission of influenza within subjects' classes and household.

Conclusions: Mildly symptomatic influenza is common in children during influenza seasons. Seasonal influenza vaccination is effective against ILI but not mild influenza identified by surveillance. HAI titres do not appear to indicate protective immunity for childhood influenza.

Funding: Health and Medical Research Fund (13120422)

Project Number: 13120422

P160-0018

Molecular Determinants of H9N2 Virus Haemagglutinin and Neuraminidase Affecting Virus Tropism for the Human and Swine Respiratory Tract

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Introduction and Project Objectives: Humans are susceptible to many strains of influenza viruses including H9N2 which at present is the most widespread and prevalent influenza virus in poultry found in Asia. The aim of this study was to determine the ability of H9 viruses isolated from humans and poultry to replicate in human lung and bronchus explants.

Methods: Eight strains of avian and human H9 influenza virus were used: A/Duck/Shantou/2030/2001(H9N1), A/Chicken/Hong Kong/NT449/2007(H9N2), A/Chicken/Hong Kong/YU341/2008(H9N2) and A/Chicken/Hong Kong/SSP117W/2009(H9N2); and A/Hong Kong/1073/99(H9N2), A/ Hong Kong /2108/2003(H9N2), A/Hong Kong/2269955/2008 (H9N2), and A/Hong Kong/464419/2009(H9N2), together with a rgD190E mutant. Two reverse genetics viruses with surface H9 and internal H1N1 genes were also used. Fresh human lung and bronchial explants were used as previously published.

Results: Productive replication in bronchus ex vivo cultures was observed with 2269955/08 and 464419/09 while lung ex vivo cultures supported the replication of all human and avian strains .The rgD190E mutant showed no difference in replication at the bronchial epithelium but appeared to show a greater degree of infection and replication in lung. Though H9 viruses infected the upper and lower respiratory tract, the majority of H9 viruses had a decreased ability to release virus from the bronchus compared to the lung. This may be attributed to a weak neuraminidase (NA) cleavage of carbon-6-linked sialic acid rather than carbon-3-linked sialic acid. The cleavage of Neu5Ac and Neu5Gc by NA in H9 virus was observed by the use of virus-like particles (VLPs), and recombinant H9N2 viruses with amino acids (38KQ) deleted in the stalk, and changing the amino acid at position 431 from Proline-to-Lysine. Using recombinant H9 viruses previously evaluated in the ferret, viruses which replicated well in the ferret did not replicate to the same extent in the human ex vivo cultures.

Conclusions: The human explant system should be considered as a model for H9 infection and may reduce the need for ferrets and mice in risk assessment models.

Project Number: 13120762

P161-0037

Impact and Severity Profiles of Respiratory Viruses in Children in Hong Kong

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Introduction and Project Objectives: Most respiratory virus infections lead to mild self-limiting illness, but on some occasions they may contribute to severe diseases such as viral pneumonia or secondary bacterial pneumonia. Whereas the burden of some respiratory viruses has been quantified before, particularly for influenza virus, much less research has been done on the severity profile of individual infections, i.e. for a person who becomes infected, what is the risk of seeking medical care, being hospitalized, requiring ICU admission, or death, have not been systematically investigated. In this project, we aimed to synthesize data from multiple sources to characterize the severity profile of infections with influenza A and B, RSV, parainfluenza, and adenovirus among Hong Kong children 0-15 years of age.

Methods: We used the data collected from a previous community-based study to estimate the proportion of symptomatic infections associated with each of the viruses of interest and to investigate the symptomatic profile for individual viral infections. A telephone questionnaire survey was conducted to examine the health-care seeking behaviours among patients with respiratory symptoms. A statistical model was applied to estimate the virus-attributable excess hospitalizations (including ICU admissions) and deaths that were used to derive the measurements of severity of infections, such as symptomatic hospitalization/ICU/fatality risk.

Results: Among Hong Kong children 0-15 years who presenting acute respiratory symptoms, around 70-90% of patients would choose to seek a medical consultation either through government-supported public clinics/hospitals or general practitioners/private hospitals without major differences between younger and older children. During the study period from 2009 through 2012, the annual excess hospitalization rate varied by virus while the excess burden of ICU admission and death was rare or low in both younger and older children. Therefore the risk of ICU admission and death was extremely low among sick children having symptomatic infections in Hong Kong.

Conclusions: Influenza viruses generally contributed to the highest disease burden in both young and old children among the viruses investigated in this study. Adenoviruses and parainfluenza viruses were more likely to cause severe outcomes in older children. RSV was associated with the highest risk of hospitalization among laboratory-confirmed symptomatic infections in children 0-5 years. The risk of virus-associated severe infections (measured by the risk of ICU admission and death) was extremely low among symptomatic sick children.

Project Number: 13120802

P162-0051

Risk Communication, Psychological and Behavioural Responses to Avain Influenza A (H7N9) In Hong Kong

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Introduction and Project Objectives: Avian influenza A(H7N9) virus has caused multiple epidemic waves of human infections leading to over 1000 laboratory-confirmed cases mainly in mainland China and 21 imported cases in Hong Kong since its first detection in early 2013. H7N9 cases dramatically decreased following the closure of live poultry markets in affected cities. Low pathogenesis of avian H7N9 virus infections made it difficult to reduce human exposure through early detection of virus in poultry. Relatively high severity of human H7N9 virus infection caused substantial anxiety and behavioural changes in the population. We conducted a study aiming to measure levels of exposure to live poultry, risk perception and behavioural responses towards H7N9, and attitudes towards specific control measures in Hong Kong population across the three epidemic waves in 2013-2015.

Methods: A series of cross-sectional population surveys were conducted in 2013-2015. Subjects who were Cantonese/Mandarin-speaking Hong Kong Chinese adults (≥18 y) were selected for interview through randomly dialed landline numbers generated by the computer. The questionnaire included demographics and items investigating live poultry exposure, H7N9-related risk perception, attitudes towards closure of live poultry markets and behavioural changes in response to the H7N9 epidemic.

Results: Response rates of the ten telephone surveys were ranging between 63.7%-94.2%. Across the population, the averaged annual visits to live poultry markets in Hong Kong and mainland China was 14.6 and 0.4 per person, respectively, and the number of visits generally decreasing with time while visits to live poultry markets were more frequent during winter seasons and holidays. Risk perception on H7N9 was generally low in the respondents. Respondents were more likely to support closure of markets in early surveys while decline in live poultry purchase and avoidance of visiting live poultry markets were more prominent during epidemic peaks (Figure 2). Younger age, lower educational attainment and visit to live poultry markets >1 time in the preceding year were independently associated with a less support for market closures.

Conclusions: Exposure to live poultry in Hong Kong general population changed in response to the H7N9 epidemics in mainland China. Female residents, those having a higher education attainment or a higher self-perceived risk of H7N9 infections were likely to avoid visiting poultry markets. A growing indifference to market closure policies among Hong Kong population might reflect a declining concern about infection with H7N9.

Project Number: RRG-12

P163-0179

Observational Study of Cough/Lower Respiratory Tract Infections (LRTI) in Hong Kong's Primary Care

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Acute cough is a common reason to prescribe antibiotics in primary care. This is a prospective multicentre observational study that included adults presenting with acute cough. This study aimed to explore help-seeking and antibiotic prescribing for acute cough in Chinese primary care population. Clinicians recorded patients' presenting symptoms, examination findings and medication prescription. Patients completed symptom diaries for up to 28 days by charting their symptom severity and recovery. Adjusted binary logistic regression models identified

factors independently associated with antibiotic prescription. Primary care clinicians (n = 19) recruited 455 patients. A total of 321 patients (70.5%) returned their completed symptom diaries. Concern about illness severity (41.6%) and obtaining a prescription for symptomatic medications (45.9%), rather than obtaining a prescription for antibiotics, were the main reasons for consulting. Antibiotics were prescribed for 6.8% (n = 31) of patients, of which amoxicillin was the most common antimicrobial prescribed (61.3%), as it was associated with clinicians' perception of benefit from antibiotic treatment (odds ratio (OR): 25.9, 95% confidence interval (CI): 6.7-101.1), patients' expectation for antibiotics (OR: 5.1, 95% CI:1.7-11.6), anticipation (OR: 5.1, 95% CI: 1.6-15.0) and request for antibiotics (OR 15.7, 95% CI: 5.0-49.4), as well as the severity of respiratory symptoms (cough, sputum, short of breath and wheeze OR: 2.7-3.7, all Po0.05). There was a significant difference in antibiotic prescription rates between private primary care clinicians and public primary care clinicians (17.4 vs 1.6%, P = 0.00).

Symptomatic medication was prescribed in 98.0% of patients. Mean recovery was 9 days for cough and 10 days for all symptoms,which was not significantly associated with antibiotic treatment. Although overall antibiotic-prescribing rates were low, there was a higher rate of antibiotic prescribing among private primary care clinicians. The is scope for further exploration of physician behaviour and for subsequent education and intervention.

Project Number: CU-10-01-04

P164-0052

Efficacy of Face Masks to Prevent Respiratory Virus Transmission

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Introduction and Project Objectives: Respiratory viruses are associated with considerable morbidity and mortality globally. They have been detected from infected patients while breathing, speaking and coughing, but there is little data on the efficacy of facemasks to filter respiratory viruses causing common acute respiratory illnesses (ARI) as a source control to prevent transmission. We aimed to examine exhaled breath virus generation rate of different respiratory viruses, and to determine the potential benefits of facemasks to prevent respiratory virus transmission.

Methods: We recruited patients ≥11 years old with ARI from an outpatient clinic in Hong Kong. Nose/throat swabs were obtained to determine the viral aetiology by the xTAG Respiratory Viral Panel. Exhaled breath was collected by a bioaerosol collecting device to measure the quantity of respiratory viruses in respiratory particles defined as either large droplets (≥5μm) or small aerosols (<5μm). Patients were randomly allocated to wear or not to wear a surgical mask for the first 30-minute collection, and then invited to provide a second collection of the alternate type. The probability of respiratory virus detection in exhaled breath was compared between patients with or without wearing facemasks.

Results: 1,746 patients were screened, 703 (40%) were eligible and 219 (31%) were recruited. With additional samples from an earlier study, in the analysis 303 exhaled breath samples were collected from 256 patients, including 151 samples collected without and 152 samples with wearing a surgical mask. 153/256 (60%) patients were identified with respiratory virus infection by the xTAG, and viral respiratory virus RNA was detected by RT-PCR in 20/152 (10%) exhaled breath samples - in aerosols 10/77 (13%) in control and 5/75 (7%) in mask group, and in droplets 5/77 (6%) in control and 0/75 (0%) in mask group, although there was no statistically significant reduction in the probability of virus detection in aerosols or droplets of exhaled breath for patients wearing a surgical mask.

Conclusions: The sample sizes of patients with each particular virus detected was relatively low, therefore we were not able to confirm for each virus the efficacy of surgical masks in reducing respiratory virus dissemination in exhaled breath. However, our study is the largest to date to examine respiratory viruses in exhaled breath, and makes an important contribution to our understanding of the infectiousness of different respiratory viruses in respiratory droplets and the efficacy of surgical facemasks in preventing respiratory virus transmission.

Project Number: 13120592

P165-0053

Anti-inflammatory and Antiviral Effects of Indirubin Derivatives in Influenza A (H5N1) Virus Infected Primary Human Peripheral Blood-derived Macrophages and Alveolar Epithelial Cells

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Introduction and Project Objectives: Human disease caused by highly pathogenic avian influenza A (HPAI) (H5N1) is associated with fulminant viral pneumonia and mortality rates in excess of 60%. Acute respiratory syndrome (ARDS) has been found to be the most severe form of acute lung injury caused by H5N1 virus infection while cytokine dysregulation and viral replication are thought to contribute to its pathogenesis. In this study, the antiviral and anti-inflammatory effects of two indirubin derivatives: indirubin-30-oxime (IM) and E804 on primary human peripherial blood-derived macrophages and type-I like pneumocytes (human alveolar epithelial cells) during influenza A (H5N1) virus infection were investigated.

Methods: Primary human macrophages and type-I like pneumocytes were pre-treated with IM or E804 for 1 hour and then infected with influenza A viruses, H5N1 and H1N1. Samples of culture supernatant were collected for virus titration or cytokine analysis. Total RNA was extracted from cells for analysis of cytokine gene expression by qRT-PCR .

Results: We found that both of the indirubin derivatives strongly suppress the pro-inflammatory cytokines including IP-10 (CXCL10), one of the key factors which contribute to the lung inflammation during H5N1 virus infection. In addition, we also demonstrated that the indirubin derivative delays the virus replication in the primary cell culture models.

Conclusion: Our results showed that indirubin derivatives have a potential to be used as an adjunct to antiviral therapy for the treatment of severe human H5N1 disease.

Project Number: 11100972

P166-0074

Symptom-specific Health-seeking Behavior among Persons With Common Infectious Diseases in Hong Kong and Implications in Disease Control and Surveillance

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Hong Kong has a high quality health care system with both public and private sectors providing services to the general population. From a patient's perspective, health-seeking behavior tends to be responsive to discomfort or symptoms rather than diagnosis or type of diseases which is unknown to them before medical consultation, hence symptom-specific behavior may more realistically reflect responses to risk communication during epidemic of emerging diseases and facilitate planning of health care resources.

This project described the general pattern of symptom-specific health-seeking behavior for common infectious diseases in Hong Kong. We also determined how specific symptoms will affect the contact pattern or preventive measure of a patient and identified the main factors associated with pattern of health-seeking behavior.

Longitudinal telephone surveys with respondents aged 16 years or above, recruited from randomly selected households, were conducted. We carried out 4 longitudinal surveys in different times (Mar and Jul 2014; Jan and May 2015) over a year to capture health-seeking behavior during periods with different disease pattern. Questions on symptoms and health-seeking behavior were asked for the last 30 days at the time of interviews. Analysis were carried to identified factors associated with choice of healthcare services and timing, accounting for within subjects correlation and right censoring.

We observed substantial variations in health-seeking behavior specific to different symptoms. Sick persons with fever were most likely to seek for healthcare service (91.2%), followed by diarrhoea and cough among the more commonly reported symptoms. Private general practitioner (GP) remains the most utilized mode of primary care service, followed by Chinese Medicine Practitioner and General Outpatient Clinic. Fever, cough, diarrhoea and vomiting are the leading common symptoms that prompt for seeking of healthcare service. Young patients (<16y) and female were also found to have much shorter delay (70% and 50% respectively) in healthcare seeking. Based on the health-seeking behavior, we were able to estimate that young age children have the highest burden of influenza-like illness.

Patients with respiratory or gastrointestinal diseases without fever or diarrhoea may take longer time to seek healthcare service and introduce delay in reflecting disease activity from sentinel surveillance system. They are also more likely to work while sick and could spread the diseases in workplace.

Project Number: 13121262

P167-0075

Optimizing Avian Influenza Surveillance Strategy in Live Poultry Market Setting

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Live poultry markets (LPMs) continue to operate in many Asian countries. Avian influenza viruses are often endemic in the poultry, and LPMs present the opportunity for human-poultry interactions and potential human infections with avian influenza viruses. During periods when human influenza viruses circulate, LPMs also present the opportunity for dual infections and viral reassortment either in poultry or humans. Surveillance at LPMs remains important as a multi-pronged approach to control avian influenza.

Our project optimized surveillance plan by utilizing paired fecal and drinking water samples, using avian influenza (H9N2) as example. We assessed surveillance strategy for monitoring endemic avian diseases and detecting introduction of newly emerging disease.

Surveillance data of H9N2 from paired fecal and drinking water samples in LPMs were analyzed during the period with 2 rest days per month. Transmission model was used to describe the detection probabilities and transmission dynamics within the LPMs. Simulations were carried out to assess different surveillance strategies under different underlying virus prevalence and market conditions.

From the dynamic transmission model, virus amplification can be observed both in the fecal and drinking water samples, though the latter required 1-2 days after the rest days to reach higher levels. The detection probability of a virus with a prevalence of 2% reached >60% in drinking water samples when testing 10 samples for 3 consecutive days, while the detection probability was <50% for fecal samples. H9N2 isolation rate reached its steady state in fecal water at around day 7 after the rest days, while the isolation rate in drinking water tended to increase over days.

Our project assessed the transmission dynamics and surveillance during the period with 2 rest days per month in LPMs. Fecal samples was found to be more stable for the purpose of monitoring avian influenza activity. For detection of novel virus, drinking water samples can be more sensitive if the efficiency of virus shedding to water is comparable to H9N2. Sampling at fixed date or time after market rest days or disinfection would enhance understanding of virus seasonality. Our results may not be directly extrapolated to other avian influenza viruses (e.g. H5N1 or H7N9) which may differ in their pattern of virus shedding via oral versus fecal routes. In view of the current LPM intervention where overnight holding of poultry is banned which limits contamination in drinking water, fecal samples would be more stable and sensitive for general surveillance purpose.

Project Number: 14130922

P168-0084

Molecular Diversity and Evolution of Bat Group C Betacoronaviruses: Implications on the Origin of the Novel Human Group C Betacoronavirus

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While the novel Middle East Respiratory Syndrome Coronavirus (MERS-CoV) is closely related to Tylonycteris bat CoV HKU4 (Ty-BatCoV HKU4) and Pipistrellus bat CoV HKU5 (Pi-BatCoV HKU5) in bats from Hong Kong, and other potential lineage C betacoronaviruses (betaCoVs) in bats from Africa, Europe, and America, its animal origin remains obscure.

To better understand the animal origin of this novel human lineage C betaCoV, we examined the molecular epidemiology, evolution and recombination potential of lineage C betaCoVs among different bat species in China. In a 10-year molecular surveillance study, betaCoVs were identified in alimentary samples from 267 (2.7%) of 9866 bats using RT-PCR for a 440-bp fragment of the RNA-dependent RNA polymerase (RdRp) gene. Phylogenetic analysis suggested the presence of five betaCoV species including the two known lineage C betaCoVs, Ty-BatCoV HKU4 (n=48) and Pi-BatCoV HKU5 (n=58); a potentially novel lineage C betaCoV, Hp-BatCoV HKU25 (n=2), identified in Chinese pipistrelle (Hypsugo pulveratus); SARSr-Rs- BatCoV HKU3 (n=105), a novel SARSr-Rf-BatCoV (n=2); and Ro-BatCoV HKU9 (n=52). Ty-BatCoV HKU4 and Pi-BatCoV HKU5 were found to be highly prevalent among lesser bamboo bat and Japanese pipistrelle in Hong Kong respectively, with detection rates ranging from 21 to 24%. MERS-CoV is more closely related to Pi-BatCoV HKU5 in RdRp (92.1% to 92.3% amino acid [aa] identity) but is more closely related to Ty-BatCoV HKU4 in S (66.8% to 67.4% aa identity) and N (71.9% to 72.3% aa identity). Molecular clock analysis showed that Ty-BatCoV HKU4 and

Pi-BatCoV HKU5 diverged from a common ancestor with MERS-CoV at least several centuries ago. The identification of another novel lineage C betaCoV, Hp-BatCoV HKU25, further supports Pipistrellus-related bats as important host for lineage C betaCoVs. This novel lineage C betaCoV, Hp-BatCoV HKU25 was identified in two Chinese pipistrelles captured in Guangdong Province, with genomes possessing 73.2-73.9% nucleotide identities to those of human/camel MERS-CoVs.

Genome analysis showed the two SARSr-Rf-BatCoVs from greater horseshoe bats (Rhinolophus ferrumequinum) possessed an ORF8 with exceptionally high aa identities (80.4-81.3%), compared to SARSr-BatCoVs from other horseshoe bats (23.2-37.3%), to that of human/civet SARSr-CoVs. Potential recombination events were identified around ORF8 between SARSr-Rf-BatCoVs and SARSr-Rs-BatCoVs, leading to the generation of civet SARSr-CoVs. Our findings showed SARS-CoV ORF8 is originated from SARSr-CoVs of greater horseshoe bats through recombination, which may be important for animal-to-human transmission of SARS-CoV during the epidemic.

Our findings offer new insights into the host diversity, evolution and emergence of betaCoVs including MERS-CoV and SARS-CoV.

Project Number: 13121102

P169-0089

The Application of Swine and Human Respiratory Organ Explant Cultures to Investigate Inter-species Transmission of Avian Influenza Viruses to Swine and Humans

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Introduction: Swine is the intermediate host in the emergence of pandemic influenza. The 2009 pandemic arose through reassortment of swine viruses of the Triple Reassortant (TR) and Eurasian avian (EA) virus lineages. EA influenza viruses (IAVs) arose through an inter-species transmission of avian viruses (av-IAVs) that established themselves in swine. TR viruses were derived through reassortment between swine, human and avian viruses. This highlights the importance of understanding the potential and mechanisms underlying the inter-species transmission of av-IAVs to swine.

Aim and objectives: We aim to establish the respiratory organ explant cultures of swine and identify the avian IAVs possess tropism for the swine respiratory tract. We investigated if a specific set of adaptive mutations is associated to the swine respiratory epithelium tropism. We defined whether these av-IAVs had increased capacity to infect and replicate in the human ex vivo respiratory tract cultures.

Study Design and Methods: Swine tracheal and alveolar epithelia were prepared from freshly scarified pigs. A total of 193 av-IAVs collected from 2003 to 2010 in the HK wild bird surveillance programme were used to inoculate the swine explant cultures. The five best replicating av-IAVs from each anatomical site were selected for serial passage. The tropism and replication kinetics of these selected wild-type viruses and the serially passaged virus were compared in each of the anatomical sites and in human respiratory cultures. The data collected from the wild type virus and serially passaged viruses was compared using two-tailed pair t-test.

Results and Conclusion: Among 188 av-IAVs, below 30% of them could replicate in swine respiratory explant cultures. Virus strains of H1, H4, H5, H6, H7, H8, H10, and H11 had both tracheal and lung tropism while H12 had lung tropism. Without prior adaptation, some H10 viruses can infect human bronchial explant culture and an H6 virus can infect human lung culture and this infers that a direct infection from an avian source is feasible.

The infectivity of these av-IAVs in the first screen were 12.7% in the swine trachea and 29.2% in the swine lung which implies the possibility of a sporadic infection. The low percentage of consistent replicating phenotypes (2.6% in trachea and 12.7% in lung) and the inability of the virus to be serial-passaged in swine respiratory epithelial explant cultures implies a species barrier for avian influenza viruses (av-IAV) to swine and the difficulties of establishing an av-IAV in the swine population.

Project Number: 12110992

P170-0092

Influenza B Viruses: Virus Tropism in Human and Swine Respiratory Organ Explant Cultures and Sero-epidemiology in Swine

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Introduction: Influenza B virus (IBV) is believed to be endemic in humans with sporadic isolation in non-human hosts. The retrospective sero-epidemiology analysis of seal sera identified a 2% IBV of antibodies prevalence. This proposal is to explore the role of swine in IBV epidemiology, by a better understanding of the tropism of IBV in swine respiratory tissues.

Objectives: 1) To evaluate IBV sero-epidemiology and tissue tropism of in swine and risk assess if IBV evolves and entrenched in the swine population. 2) To study the tissue tropism of IBV in human respiratory explant cultures.

Study Design and Methods: Pig sera (n = 4643 samples) collected between 2009-2012 were screened for IBV antibody specific to Victoria and Yamagata lineage using haemagglutinin inhibition assay. Swine and human respiratory organ cultures were used to assess the IBV replication kinetics and tissue tropism. The replication kinetics was evaluated by viral titration and the tropism was determined by immunohistochemistry.

Results: 1) 0.06% and 0.22% of pig sera contained IBV antibody against Yamagata, and Victoria lineage, respectively. 2) Four out of ten and seven out of twelve IBVs of Yamagata and Victoria lineage replicated in either swine tracheal or/and bronchial explant cultures while none of them were able to replicate productively in swine lung. 3) Fourteen IBVs replicated in the human bronchial explant cultures while three of these did not replicate in human lung culture.

Conclusion and Implication: IBV infection in pigs is possible but the serological data did not support a significant outbreak and circulation of IBV in the pig population. Spontaneous IBV infection can be found in experimental inoculation in pig's respiratory tissues, while IBVs have a higher replication competence in human organ cultures. This study implies that some of the IBVs strains are capable of infecting the trachea and bronchus of swine to a comparable level to IAVs, however, the invasion to lung might not be frequent. In case a good titer of IBV antibody has to be developed from an infection in lung rather than a spontaneous infection in the conducting airways, this might explain the low IBV sero-prevalence in our tests, as in other published data. The IBVs are readily infecting and replicating in human lungs. The severity of IBV infection in human should not be neglected when compared to

IAVs and research of IBV should not be overlooked.

Project Number: 13120772

P171-0099

Comparative Epidemiology of Influenza B Yamagata- and B Victoria-lineage Viruses In Households

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Introduction: Influenza B viruses split into 2 distinct lineages in the early 1980s, commonly named the Victoria and Yamagata lineages. There are few data on the comparative epidemiology of Victoria- and Yamagata-lineage viruses.

Methods: In 2007-2011, we enrolled 75 and 34 households containing index patients with acute respiratory illness who tested positive for Yamagata- and Victoria-lineage viruses, respectively, from outpatient clinics in Hong Kong, China. These index patients and their household contacts were followed up for 7-10 days. We examined overall risk of polymerase chain reaction-confirmed infection among household contacts and the risk of secondary infection within households using an individual-based hazard model that accounted for tertiary transmission and infections occurring outside the household.

Results: We found that for Victoria-lineage viruses, the risk of within-household infection among household contacts aged ≤15 years was significantly higher (risk ratio = 12.9, 95% credibility interval: 4.2, 43.6) than that for older household contacts, while for Yamagata-lineage viruses, the risk of within-household infection for household contacts did not differ by age. Influenza B Yamagata- and Victoria-lineage viruses have similar characteristics in terms of viral shedding and clinical illness.

Conclusions: In the household setting children had much higher susceptibility to Influenza B Victoria lineage virus than older people, while susceptibility did not vary significantly by age for Influenza B Yamagata lineage virus. This difference in age-specific pattern of infection risk could be due to the difference of age-specific pre-existing immunity against the two lineage viruses and an inherent difference in infectivity. Influenza B Yamagata and Victoria lineage viruses have similar pattern of viral shedding and clinical illness. The mechanisms underlying these epidemiologic differences deserve further investigation.

Project Number: HKS-15-E01

P172-0094

Quantity and Interspecies-transmissibility of Infectious Particles Released from Chickens Experimentally Infected with Avian H5N1, H9N2, or H7N9 Influenza Viruses that Cause Human Zoonotic Infections

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Introduction and Project Objectives: Zoonotic infections by avian influenza viruses occur at the human-poultry interface; however, the major modes mediating interspecies transmission are not fully understood. While the feasibility of contact and fomite transmission is supported by the detection of avian influenza viruses from infected poultry or contaminated surfaces at the human-poultry interface, the feasibility of droplet or airborne transmission mediated by influenza-laden particles in the air has not been investigated.

Methods: We applied both experimental and field studies to investigate the airborne transmission potential of avian influenza virus among poultry and between poultry and mammalian species.

Results: Experimental studies identified that direct contact with shared food and water source (co-housed condition) was the predominant mode mediating efficient chicken-to-chicken transmissions, despite of intrinsic differences in transmissibility of the viruses selected in this study. While airborne transmission among chickens is less efficient, chicken-to-ferret transmission via the airborne route was observed for all four avian influenza viruses of H7N9, H5N1, and H9N2 subtypes tested in this study, suggesting that ferrets may be more susceptible than chickens in acquiring infections via the airborne route. The field studies were performed monthly between July 2014 and October 2015 at live poultry markets in Guangzhou city and in Hong Kong. Viral genome and infectious avian influenza A viruses of H5N6, H7N9, and H9N2 subtypes were detected predominantly from particles larger than 1 μm in the air. The numbers of chickens sold on site as well as market rest day were associated with the quantity of virus-laden airborne particles detected in the air.

Conclusions: Our results support the feasibility of avian influenza virus-laden particles in mediating interspecies transmission at the human-poultry interface.

Project Number: RRG-01

P173-0098

A Community-based Longitudinal Seroepidemiological Study of Influenza Virus Infections in Hong Kong in 2013-14

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Introduction: Influenza viruses infect a considerable fraction of the population of Hong Kong each year, causing a substantial disease burden including hundreds of excess deaths and thousands of excess hospitalizations. Few studies have been done of the patterns in incidence of infections outside of pandemic periods in Hong Kong and elsewhere. We aim to estimate the age-specific attack rate of influenza A and B and evaluate risk factors of infections for influenza virus infection in a representative sample of the population based on longitudinal serology.

Methods: We extended follow-up of an existing cohort, collecting sera from 846 participants from December 2013 through March 2014, and 855 participants from October 2014 through January 2015. The primary outcome measure was laboratory-confirmed influenza infection assessed by four-fold or greater rise in consecutive sera.

Results: The age-standardized incidence among unvaccinated persons ranges from 3% to 7% for various influenza epidemics in 2013 and 2014. We also identified significant protective effect of baseline titers for influenza A(H1N1) epidemic, but not for influenza A(H3N2) and influenza B. Severity as measured by the average number of excess respiratory deaths per 100,000 infections differed across age groups and epidemics.

Conclusions: These are the first estimates of incidence of seasonal influenza virus infections in Hong Kong in the post-pandemic period. We have made the first comparison of the severity of seasonal and pandemic influenza virus infections on the basis of excess respiratory deaths per 100,000 infections. These data will be valuable inputs into

further analyses of the potential impact of alternative control strategies, and modeling studies of the dynamics of influenza epidemics in Hong Kong.

Project Number: 13120732

P174-0100

Mutagenesis Analysis to Identify Potential Mutations that Confer Resistance to Neuraminidase (NA) Inhibitors in N9 and N8 Glycoproteins Derived from H7N9 and H10N8 Influenza Viruses

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Introduction and Project Objectives: Avian influenza viruses enzootic among domestic poultry may cause spillover infections in humans leading to mild to severe clinical outcomes, including fatalities associated with acute lung respiratory distress. NA inhibitor is the mainstay therapeutic option for managing patients with avian influenza virus infections. Knowledge on the potential NA residues that may confer resistance to NA inhibitors is essential for monitoring the susceptibility of clinical specimens. Such information is available for N1 and N2 subtypes due to the clinical use of NA inhibitors against human seasonal H1N1 and H3N2 influenza, but there is limited information on other NA subtypes.

Methods: In response to human infections by H7N9 and H10N8 viruses, we applied both random mutagenesis and site-directed mutagenesis to investigate potential NA mutations in N8 and N9 proteins that may confer resistance to NA inhibitors.

Results: Random mutagenesis was applied to generate pools of recombinant H1N8 and H1N9 viruses containing random mutations in the NA head domain, which were passaged in vitro under increasing concentrations of oseltamivir and zanamivir. NA mutations including A266V in H1N8 virus and T87A, T247A in H1N9 virus were found enriched after serial passages; however, these mutations did not directly confer resistance to NA inhibitors when introduced into the respective recombinant H10N8 or H7N9 viruses.

Site-directed mutagenesis was applied to introduce NA mutations previously reported to confer resistance to NA inhibitors in N1 (E119V, Q136K, I222R, H274Y, N294S) and N2 subtypes (E119V, Q136K, I222R, A246T, R292K, N294S) into H10N8 or H7N9 recombinant viruses, respectively. These NA mutations showed comparable but not fully identical resistance profiles in the respective group 1 (N1 and N8) and group 2 (N2 and N9) NA proteins.

Conclusions: The NA mutations reported to confer resistance to NA inhibitors should be monitored clinically among H7N9 and H10N8 patients after receiving NA inhibitor treatment.

Project Number: RRG-15

P175-0102

Applying Glycan Array to Determine Neuraminidase Substrate Specificity of Pandemic H1N1 and Swine H1N1 Influenza Viruses

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Introduction and Project Objectives: The hemagglutinin (HA) and neuraminidase (NA) are surface glycoproteins of influenza viruses that recognize sialyl glycans with counteracting functions; the HA mediates attachment to the sialyl glycans while the NA hydrolyzes α-ketosidic linkage between sialic acid and the adjacent oligosaccharide. A functional balance between the HA sialoside binding activity and the NA sialidase activity is critical for influenza viral fitness.

Methods: To understand the mechanism for maintaining such a functional balance, we studied the HA binding profile and NA substrate specificity of A(H1N1)pdm09 and its precursor swine influenza viruses of H1N1 and H1N2 subtypes using a glycan array containing O-glycans, linear N-glycans of different LacNAc repeats, hybrid N-glycans, and bi-tri- or tetra-antennary complex N-glycans.

Results: Human and swine influenza viruses of H1 subtype shared a limited but comparable HA binding profile for α2,6-linked N-glycans. Using the same glycan array incubated with recombinant sNA proteins followed by binding of ECL and PNA lectins that recognize Gal(β1-4) GlcNAc and Gal(β1-3)GalNAc moieties of cleaved sialosides, we observed that the human and swine influenza NA proteins process a broad spectrum of O-glycans and N-glycans while differed in their activities for α2-3 and α2-6 sialosides. While all NA proteins prefer α2-3 glycans, human influenza NA proteins possess increased activity for α2-6-linked sialosides. Aluminium oxide-coated glass (ACG) slides containing selected sialosides conjugated with a polyfluorinated hydrocarbon (-C8F17) tail were produced for directly monitoring the cleavage of the terminal sialic acid but failed to produce clear detection signals under MALDI-TOF MS. Recombinant A(H1N1)pdm09 viruses with mismatched HA and NA proteins showed comparable replication efficiency in differentiated human airway epithelium cells, suggesting that influenza virus may tolerate the mis-matched HA-NA activities in vitro.

Conclusions: Overall, the results identified the differential and common glycans recognized by influenza HA and NA proteins. The human and swine influenza viruses showed comparable HA binding specificity but differed more significantly in their NA substrate specificity. However, the differences in NA substrate specificity did not significatly impair the replication efficiency of recombinant viruses that carry different NA genes in human airway epithelium cells. This could be due to the variable amount of NA proteins presented on the virion as epistatic NA mutations have been reported to increase NA surface expression. Further studies should be followed to understand the impact of HA and NA balance in vivo, especially the interaction between influenza NA proteins and host's mucin on the respiratory tract.

Project Number: 12111032

P176-0103

Epidemiological Assessment of MERS-CoV Outbreak in South Korea, May to June 2015

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Introduction: South Korea is experiencing the largest outbreak of Middle East respiratory syndrome coronavirus (MERS-CoV) infections outside the Arabian Peninsula. As of 19 June 2015, there have been 166 laboratory-confirmed cases, including 24 deaths, 30 recovered individuals discharged from hospital, and 112 still remaining in hospital [1]. The aim of our study was to conduct a preliminary epidemiological assessment of the MERS-CoV outbreak in South Korea in order to further describe and update key epidemiological determinants of MERS-CoV outbreaks.

Methods: We retrieved publicly available data from multiple sources, including the Korea Centers for Disease Control and Prevention (Korea

CDC), the Korean Ministry of Health and Welfare (MoH), the WHO and local Korean news reports to compile a line list of all confirmed cases reported by 19 June 2015. We fitted parametric distributions to the time intervals (i) from infection to onset (i.e. the incubation period) and (ii) from illness onset to case confirmation. We also fitted a nonparametric distribution on the incubation period. To estimate the case fatality risk (CFR) allowing for the uncertain clinical outcomes of those who remained in hospital on the date of analysis (19 June 2015), we used the methods proposed by Garske et al. which adjusts the fatality risk based on the time-to-death distribution.

Results: We found that a gamma distribution had the best fit to the incubation period distribution and was very similar to the nonparametric estimate. The fitted gamma distribution had a mean of 6.7 days (95% CrI: 6.1–7.3) and a 95th percentile of 12.1 days (95% CrI: 10.9–13.3). We found it unlikely that infectiousness precedes symptom onset. Based on currently available data, we predict an overall case fatality risk of 21.3% (95% credible interval: 14%–31%).

Conclusions: Our findings confirm that the epidemiology of MERS in South Korea is similar to that observed in the Middle East and in fact closely resembles that of the 2002–03 outbreak of SARS. The speed of this outbreak and the serious social and economic impact on South Korea emphasizes the importance of prompt identification of imported cases and maintenance of infection control standards for patients with acute respiratory infections.

Project Number: HKS-15-E05

P177-0105

Influenza Virus Epidemiology in Households of School-age Children, 2013-14

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Introduction: Influenza viruses are responsible for thousands of hospitalizations and deaths every year in Hong Kong. However, there are few studies on the patterns in incidence of influenza virus infections from year to year. We aim to evaluate the protection associated with influenza virus infections within and between multiple influenza seasons; to estimate the age specific annual attack rate of influenza virus infections, acute respiratory illnesses, and influenza-like illnesses; and to estimate secondary attack rate and serial intervals of influenza in households in Hong Kong.

Methods: We followed up an existing cohort of 484 households that had been recruited between August 2009 and February 2010 and followed up until September 2012. In the present study we extended follow up for 459 of those households through to September 2013, and then 428 of the households through to September 2014. Follow-up included serum collection at least once per year, and home visits to collect respiratory specimens from any ill individuals. The primary outcome measure was influenza virus infection in study participants and their household contacts indicated by a four-fold or greater increase in antibody titer between paired serum specimens, or by RT-PCR confirmation of influenza on a respiratory specimen. We analysed data from all five years of follow-up i.e. August 2009 through to September 2014.

Results: Over the five years of follow-up, between 23% and 39% of cohort members experienced laboratory-confirmed influenza virus infections each year, with 75% of children and experiencing at least one infection across the five-year period. We observed significantly higher proportion of laboratory-confirmed infections and clinical illnesses in children, compared with adults. We found statistically significant evidence of protection against H1N1pdm09 virus infection in year 2 and again in year 4 associated with prior H1N1pdm09 infection in year 1, consistent with homosubtypic immunity lasting multiple years. There was no evidence that heterosubtypic immunity spanned one or more years. On introduction of infection to a household, 6% to 18% of household contacts suffered secondary infections, with a serial interval of mean 2.5 days.

Conclusions: Influenza virus infections are extremely common in children and adults in Hong Kong. Our results highlight the burden of disease, and the importance of households in influenza transmission. These results increase our understanding of influenza epidemiology and provide a rich dataset for analysis of immunity across multiple years following natural infections.

Project Number: 13120602

P178-0109

Transmissibility and Pathogenicity Studies of the Recent H7N9 Human and Avian Isolates in a Ferret Model

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Introduction and Project Objectives: The H7N9 influenza virus that emerged in 2013 has become established in China and diverged into multiple regionally distinct lineages, raising global concerns about the new pandemic threats. It is essential to timely investigate changes in the transmissibility and pathogenicity of the viruses as they continue to segregate. Identification of amino acid substitutions associated with the increased virulence and transmissibility, or changes of the viral antigenicity, will provide insights into the molecular mechanisms of the virus behaviors.

Methods: Viruses isolated from our surveillance system were selected based on their phylogenetic differences and used for animal experiments. Ferrets, the most accepted animal model for human influenza research, were intranasally inoculated with the viruses or exposed to the infected ferrets via physical or airborne contacts. Deep sequencing was conducted on samples collected from the H7N9 infected ferrets to identify molecular changes that had occurred. Ferret antisera obtained were used for the antigenic analysis.

Results: Most of the H7N9 viruses were readily infectious and transmissible in the ferret model via direct physical contact. Compared to Wave 1 viruses, recent H7N9 isolates exhibited enhanced airborne transmissibility but similar level of pathogenicity in ferrets. Guangdong and Jiangxi viruses (Lineage B and C respectively) were more efficiently transmitted to all sentinel ferrets via airborne exposure than viruses from other lineages. Dual 627K and 701N mutations in the polymerase basic protein 2 (PB2) could readily occur during transmission of the virus among ferrets via direct physical contact. Although most of the H7N9 viruses have similar antigenicity, some strains from the C lineage have lower reactivity with ferret sera raised against the Wave 1 viruses.

Conclusions: The rapid expansion of the geographical distribution and genetic diversity of the H7N9 viruses poses a direct challenge to current disease control systems. The B lineage that caused the outbreaks in Guangdong and the C lineage that led to the wide spread of H7N9 during the third to fifth waves have showed better transmissibility than the other groups of viruses. Effective implementation of increased control measures especially in regions affected by these viruses, intensive surveillance in humans and other animals, and timely risk assessment of the novel lineages or variants are warranty and will lead to warnings to the public if indicators of a higher risk are identified.

Project Number: RRG-10

P179-0111

Active Influenza Surveillance in Poultry and Humans Focused on Guangdong and Zhejiang Provinces

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Introduction: The occurrence of human infections with a novel avian H7N9 influenza virus since 2013 in China demonstrated the continuing threat posed by zoonotic pathogens. Although the first outbreak wave that was centered on eastern China was seemingly averted, cases of human infections recurred in the cooler months of 2013 and the subsequent years, mostly identified in Zhejiang and Guangdong provinces. It was unclear how the H7N9 virus re-emerged and how it further developed, in turn potentially causing a long-term threat to public health.

Project Objectives: 1) Determining the prevalence of the H7N9 and related viruses in poultry in Guangdong and Zhejiang provinces during the second outbreak wave; 2) Early detection of interspecies transmission of H7N9 from poultry to humans by monitoring severe acute pneumonia in patients in Shenzhen; 3) Monitoring the further evolution of the H7N9 viruses occurring in poultry and humans and the likely implications for interspecies transmissibility.

Methods: Sampling at live poultry markets in Guangdong and Zhejiang and the isolation of influenza viruses from the samples were conducted following our established practices. With appropriate consent, patients with severe, acute, rapidly progressing pneumonia were screened for H7N9 viruses to enable early diagnosis and therapy. Full genome sequencing of all H7N9 and selected H9N2 isolates were undertaken. Evolutionary and molecular studies on the sequences of the H7N9 viruses were conducted to evaluate the changes in the viruses and to explore whether any novel reassortment events are occurring.

Results: H7N9 viruses have spread from eastern to southern China and become persistent in chickens, which led to the establishment of multiple regionally distinct lineages with different reassortant genotypes. Repeated introductions of viruses from Zhejiang to other provinces were documented, and the presence of H7N9 viruses at live poultry markets has fueled the recurrence of human infections.

Conclusions: The rapid expansion of the geographical distribution and genetic diversity of the H7N9 viruses poses a direct challenge to current disease control systems. These viruses have become enzootic in China and may spread beyond the region, following the pattern previously observed with H5N1 and H9N2 influenza viruses.

Project Number: RRG-14

P180-0120

Structure-based Drug Design of Anti-influenza Compounds Targeting Influenza Polymerase

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Influenza is a contagious respiratory illness causing annual epidemics and pandemics. Most recently, more than hundred human cases of avian influenza A H7N9 virus were confirmed in China. A highly pathogenic avian influenza A H5N8 virus has also been rapidly spreading. Furthermore, the trend of drug resistance developed in different strains of influenza viruses is worrying, thus it is of urgency to develop new drugs to combat this virus.

The ribonucleoprotein (RNP) of influenza virus was chosen as our target. RNP consists of four proteins, PA, PB1, PB2 and NP. The first three of them interact with one another to form the polymerase complex. Previous studies showed that disruption of the viral polymerase was effective for inhibiting influenza virus.

In the study, we employed in-silico screening to identify small molecules that could block the PAPB1 interaction and PB2-cap binding site. Compound databases were archived from ZINC (UCSF), NCI diversity database and commercial vendors (e.g. SPECS) and then virtually docked to the both targets. Virtual hits were purchased for biological evaluation.

For the PA-PB1 binding site, two hit compounds, compound 221 and its analog compound 312 were found to inhibit RNP activities of various influenza strains and attenuate viral growth at low micromolar level. Compound 312 also delayed the death of influenza virus PR8 infected mice. For PB2 cap binding domain, one compound (Compound 225) was discovered to show substantial anti-influenza property. It exhibited dose dependent inhibition of H1 RNP, reducing approximately 50% activity at 12.5 μM. Moreover, it inhibited influenza virus with an IC50 of 4.5 μM in plaque reduction assay.

In conclusion, we have identified three hit compounds that exhibit anti-influenza properties by in-silico structure-based drug design. The identification of hit compounds provides the basis for future optimization and lead development against influenza virus.

Project Number: 13120052

P181-0126

A Simplified 5-step Hand Hygiene Intervention Program to Increase Mild Intellectual Disability Schoolchildren's Handwashing Compliance and Reduce in School Absenteeism Rates

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Introduction: Schoolchildren with intellectual disabilities (ID) are more vulnerable to infectious diseases because their disabilities make it difficult for them to follow procedures involving multiple, complicated handwashing steps.

Project Objectives: The project aim was to develop and evaluate the effects and sustainability of a simplified 5-step hand hygiene intervention for students with mild ID when compared to those of the 7-step hand washing procedure as the usual practice in special schools. The hypotheses were that: (1) When compared with controls, the simplified hand washing intervention group would have a significant increase in fluorescent stain rating for both hands a) immediately post-intervention and b) 4 weeks post-intervention for sustainability testing; and (2) students in the intervention school would experienec a reduction in absenteeism.

Method: A quasi-experimental pilot study was developed using a pre-test (T0) and post-test (T1) design with a control grop and a sustainability component (T2). The hand hygiene intervention was a simplified 5-step hand washing program employing multimedia visualization teaching strategies, while the control group used the existing 7-step hand washing technqiue with usual teaching strategies in the special schools. Quality of hand hygiene using fluorescent stain rating test and sickness-related absenteeism rate were assessed as outcome measurements between the intervention and control groups using four methods: 1) a direct observation handwashing checklist; 2) a pre-test (T0) and post-test (T1) immediately following the 8-week intervention using a fluorescent stain

raing test; 3) a sustainability assessment 4-week after the intervention (T2); 4) a 12-month calculation of absenteeism rates.

Results: The intervention group experienced a significant increase in their hand washing scores for both right and left hands between the pre- and post-tests. The pre-test/post-test difference for the intervention group was significantly greater than that of the control group. There were no differences between the post-test and sustainability assessments in the intervention group. The intervention school had a significantly lower absenteeism rate (0.0167) than the control school in the same academic year (0.028, p=0.04).

Conclusions: The results indicate that students with mild ID who were trained to practice the simplified 5-step hand washing technique utilizing multimedia visualization teaching strategies experienced significant improvements in hand washing quality and reduced school absenteeism rates when compared with the control group. It is hoped that the findings will encourage the Hong Kong SAR's Centre for Health Protection to adopt this simplified 5-step hand washing program for standardized use in both special and ordinary schools.

Project Number: 13121452

P182-0128

Building a Theoretical Basis for the Hidden Geometry Underlying Global Transmission of Emerging Infectious Diseases

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Introduction and Project Objectives: Global spread of emerging infectious diseases (EIDs) including pandemic influenza, SARS, MERS-CoV, Ebola, and Zika virus have caused substantial health and economic burden. Over the past few decades, global metapopulation epidemic simulations built with worldwide air-transportation network (WAN) data have been the main tool for studying how EIDs spread from the origin to other parts of the world. However, it remains unclear how epidemic arrivals for different populations around the global depend on disease epidemiology and the structure of the WAN. Our objective is to develop a theory for explicitly characterizing how the epidemic arrival times (EATs) for different populations depend on the epidemiologic and WAN's network features.

Methods: We developed a novel probabilistic framework based on nonhomogeneous Poisson Process (NPP) to characterize global spread of EIDs. Specifically, our framework entails modelling the exportation of infections from the epidemic origin as NPPs and accounting for the effect of high outgoing air traffic (the 'hub-effect') and continuous seeding on local epidemic growth rate and mobility rate. To verify the accuracy of our framework, we developed a stochastic global metapopulation epidemic simulator comprising more than 2,300 populations and 54,000 flight connections.

Results: Comparing the simulated EAT with the analytically derived EAT, we showed that our analytical framework can provide very good estimates of EAT for all populations in the shortest-path-tree network of the WAN.

Conclusions: We reveal that the EATs in WAN-based global metapopulation models can be analytically measured with high accuracy from the epidemiologic and network parameters. In pursuit for analytical insights, we explicitly characterize how the dynamics of global spread of EIDs depend on the underlying epidemiologic and network properties.

Project Number: HKS-15-E03

P183-0129

A New Approach to Estimating Cumulative Incidence of Influenza Virus Infections from Serological Data

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Background: Cross-sectional seroprevalence data have been used to estimate the infection attack rates (IARs) of pandemic influenza A/H1N1 (pdmH1N1) in 2009. A different serological study design comprising serial serologic data from the same individuals can be explored using convenient blood samples from repeated blood donors in Hong Kong.

Methods: Serial blood samples from the same repeated blood donors were collected every week from the Hong Kong Red Cross Blood Transfusion Services (Red Cross) 15 months after their donation dates upon expiry. In total, 14,428 blood samples from 2,231 repeated donors were tested and a record of serial haemagglutination inhibition (HI) titers over time was obtained from each donor. Based on a binomial likelihood function with Bayesian inference, we estimated the monthly IARs of pdmH1N1 during 2010 to 2011 among the healthy population aged 20 to 60 in Hong Kong.

Results: The difference in seroprevalence at different cut-off HI titers (1:20, 1:40 and 1:80) were not obvious and thus it was difficult to estimate pdmH1N1 IARs solely from seroprevalence data. Using the proposed statistical method with the serial serologic data, we estimated the pdmH1N1 IARs during 2010 to 2011 were 22% (18-30%) among 20-29 year olds, 22% (18-28%) among 30-49 year olds and 23% (17-31%) among 50-59 year olds. There was an obvious pdmH1N1 infection wave during January to March 2011, which was consistent with the flu surveillance data from Centre for Health Protection.

Conclusions: We estimated the infection attack rates of pandemic influenza A/H1N1 during 2010 to 2011 were about 20% across all age groups among the population aged 20 to 60 in Hong Kong. Further analysis is needed to compare different serological study designs and explore a better way to interpret serologic data.

Project Number: HK-13-04-02

P184-0133

Population Psychological and Behavioural Responses to H7N9 in China

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Introduction and Project Objectives: The novel avian influenza A(H7N9) virus has caused the 2013 spring and 2013-2014 winter waves of human infections since its first emergence in China in March 2013. Few data are available on live poultry exposure and changes in risk perception and behavior following the influenza A(H7N9) epidemic in China. We therefore conducted the population-based surveys in urban and rural areas in mainland China aiming to examine human exposure to live poultry, and population psychological response and behavioral changes during the epidemic waves.

Methods: Cross-sectional population surveys were conducted in five large cities and four rural areas to represent diverse levels of socio-economic development and geographic location in China in 2013-2014. Subjects at age of ≥18 years were selected for a face-to-face interview

in the rural areas or interviews through randomly dialed landline numbers in the cities. The questionnaire included demographics and items investigating live poultry exposure, H7N9-related risk perception, attitudes towards closure of live poultry markets and behavioural changes in response to the H7N9 epidemic.

Results: We collected data from 2,504 urban residents in five cities and 1,227 rural residents. In general, the perceived risk of H7N9 was low among the respondents. Highest exposure to live poultry was reported in one of the cities surveyed where 47% of the respondents reported visiting a live poultry market at least once in the past year. The majority (77%) of the urban respondents reported changes in the habit of buying live poultry since H7N9 cases were first identified in March 2013. Only 30% of urban respondents would support permanent closure of live poultry markets to control the H7N9 epidemic. In rural areas, 48% of respondents reported raising backyard poultry.

Conclusions: Exposure to live commercial and private poultry was common in urban and rural residents in mainland China and remained a potential risk for human infection with novel avian influenza viruses.

Project Number: HK-13-07-02

P185-0134
Systematic Review of the Case Fatality Risk of Pandemic Influenza

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Introduction and Project Objectives: One of the immediate public health priorities during the 2009 pandemic was to establish the transmissibility and severity of the novel influenza A(H1N1) virus (denoted pH1N1 hereafter). Whereas transmissibility was estimated generally reliably from the early stages of the pandemic, there was greater difficulty in estimating severity. One measure of severity at the individual level is the risk of death among people who have the disease, and this conditional measure can be referred to as the case fatality risk (CFR). Our objective was to review published estimates of the CFR of pH1N1, identify challenges to real-time estimation of the CFR, and make recommendations for estimation of severity in the next pandemic.

Methods: Studies reporting estimates of the CFR of pH1N1 were retrieved from the PubMed electronic database on 20 April 2012. Eligible articles reported a CFR in the population for the first wave or the first year of the pandemic. Studies that only reported the CFR in population subgroups, such as pregnant women, or those with chronic diseases, were excluded. We defined the CFR as the number of influenza-associated deaths divided by the number of pH1N1 cases or infections in a population.

Results: We identified 46 articles reporting estimates of the CFR. The CFRs were measured using cumulative incidence of infection derived from serologic data, estimated cases, medically-attended cases or laboratory-confirmed infections as denominators. The earliest studies of the severity of pH1N1 provided high estimates of the CFR based on confirmed cases (CFRs of approximately 1,000 deaths per 100,000 cases). After the peak of the pandemic, the CFRs based on symptomatic cases were similar in those studies using estimated infections and estimated cases as denominators (CFRs of approximately 10 deaths per 100,000 cases). In age-stratified analysis, point estimates of the CFRs increased with age from approximately one death per 100,000 cases in older children to approximately 100 deaths per 100,000 cases in elderly.

Conclusions: The wide range in published estimates of the CFR led to challenges in identifying unbiased and comparable severity measure of the pandemic strain. While the choice of denominator could explain some of the variability, CFR estimates for the estimated case denominator still covered a very wide range. One clear limitation in estimating the CFR is the lack of consensus on the definition, computation and estimation of the CFR, highlighted by the variable denominators and the difference between directly and indirectly estimated numerators.

Project Number: HK-12-04-02

P186-0135
Systematic Review of the Fatality Risk among Hospitalised Cases of Influenza H1N1pdm09

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Introduction and Project Objectives: During the 2009 influenza pandemic, uncertainty surrounding the seriousness of human infections with the H1N1pdm09 virus hindered the calibration of the public health response. One measure of seriousness is the hospitalization fatality risk (HFR), defined as the probability of mortality among cases of H1N1pdm09 who required hospitalization for medical reasons. The objective of our study was to review published data on the HFR of H1N1pdm09.

Methods: We searched for relevant studies in PubMed, MEDLINE and EMBASE. Studies that reported population-based estimates of the HFR for H1N1pdm09 were included. We excluded studies that reported estimates of the HFR in population subgroups such as pregnant women or those at higher risk of severe outcome if infected (e.g. individuals with underlying chronic diseases).

Results: We included 187 estimates of the HFR from 184 published studies, reporting a total of 151,754 hospitalized cases and 7,010 deaths. In total, our analysis was based on reports from 49 countries or regions in every continent except Antarctica. We identified heterogeneity in published HFR estimates, with crude estimates of the risk of death ranging from 0% to 48% but in wealthy countries the estimate ranged from 1% to 4%. In children, the HFR of H1N1pdm09 and inter-pandemic influenza did not have substantial difference.

Conclusions: There was some variability in published estimates of the HFR, but much less variability than we found in our review of published estimates of the case fatality risk (Wong J et al., 2013 Epidemiol). Lower HFR in children could be due to reduced seriousness of infection, or a lower threshold for admitting children. Early in the next pandemic, estimation of the HFR may provide a reasonable picture of seriousness of infection and thereby inform risk assessment of the severity of the pandemic strain.

Project Number: HK-13-04-03

P187-0155
An Infection Control Study for Prevention of Exhaled Air Dispersion during Active Resuscitation and Application of Aerosol-generating Procedures

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Introduction & Project Objectives: As part of infection control

preparedness, we examined the exhaled air dispersion distances and directions in a negative pressure isolation room with 12 air changes/hr during a) non-invasive ventilation(NIV) via helmets and a total face mask, b) tracheal intubation and suction, and c) manual ventilation by different groups of healthcare workers on a Human-Patient-Simulator(HPS).

Methods: The HPS was positioned on the bed and programmed to mimic different severity of lung injury. Airflow was marked with intrapulmonary smoke for visualization. A leakage jet plume was revealed by a laser light-sheet and images captured by high definition video. Normalized exhaled air concentration in the plume was estimated from the light scattered by the smoke particles. Significant exposure was defined as where there was ≥20% of normalized smoke concentration.

Results: a) During application of NIV via a SeaLong helmet with the HPS lying at 45° and programmed in mild lung injury, exhaled air leaked through the neck-helmet interface with a radial distance of 150 to 230 mm when inspiratory airway pressure was increased from 12 to 20 cmH_2O, respectively, while keeping the expiratory pressure at 10 cmH_2O. During NIV via another helmet(StarMed) with air cushion around the neck, there was negligible air leakage. During NIV via a Respironics total facemask for mild lung injury, air leaked through the exhalation port to 618 and 812 mm when inspiratory pressure was increased from 10 to 18 cmH_2O, respectively, with the expiratory pressure fixed at 5 cmH_2O. b) Before intubation, exhaled air leaked through the mouth to 860(93) mm when the HPS was making normal coughing efforts but decreased to 460(127)mm after endotracheal intubation. Exhaled air distance was 259(45)mm during normal coughing when continuous endotracheal suction was performed. c) Intensivists/ anaesthetists demonstrated the best performance in preventing exhaled air leakage through the mask interface during manual ventilation. Addition of a viral-bacterial filter was more effective in eliminating the spread of exhaled smoke from the Ambu resuscitator than without.

Conclusions: Helmet with a good seal around the neck is needed to prevent nosocomial infection during NIV for patients with respiratory failure due to respiratory infections. Continuous sputum suction minimizes spread of aerosols when performing intubation, open suction or bronchoscopy for patients with respiratory infection. Apart from adding a viral-bacterial filter, experience and skills in ensuring good mask fit are important in preventing excessive air leakage through the mask interface during manual ventilation.

Project Number: 12110392

P188-0159
Identification of Virulence Molecules Secreted by Penicillium marneffei

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Introduction and Project Objectives: Penicillium marneffei is the most important thermal dimorphic fungus causing respiratory, skin and systemic mycosis in China and Southeast Asia. We previously demonstrated that Mp1p is an immunogenic surface and secretory mannoprotein of P. marneffei. Since Mp1p is a surface protein that can generate protective immunity, we hypothesized that Mp1p and/or its homologues are virulence factors of P. marneffei.

Methods: Mp1p homologs in P. marneffei genome were identified using TBLASTN searches with Mp1p as query. Phylogenetic relationships of Mp1p homologs were determined using maximum likelihood method with Mega 5. The pathogenicity of Mp1p homologs and its pathogenic role were examined using a mouse model. The intracellular survival of P. marneffei wild type (PM1), MP1 knockout mutant (ΔMP1), MP1 complemented mutant (ΔMP1(pAN8-1 MP1)) and MP1 knockdown mutant (shRNA MP1) in murine macrophages were measured.

Results: In the P. marneffei genome, in addition to Mp1p, 13 homologues were observed. All mice died 21 and 30 days after challenge with PM1 and ΔMP1(pAN8-1 MP1) respectively. None of the mice died 60 days after challenge with ΔMP1 ($P<0.0001$). Seventy percent of mice died 60 days after challenge with shRNA MP1 ($P<0.0001$), showing a dose-response effect. All mice died after challenge with MPLP1 to MPLP13 knockdown mutants, suggesting that only Mp1p played a significant role in virulence. The mean fungal loads of PM1 in the liver and lung of mice were significantly higher than those of shRNA MP1 and ΔMP1 and the mean fungal loads of PM1 in the kidney were significantly higher than those of ΔMP1. In the liver, the mean fungal loads of PM1 were >10-fold higher than those of shRNA MP1 and >100-fold higher than those of ΔMP1. Histopathological studies showed more abundant yeasts in the kidney, spleen, liver and lung with more marked hepatic necrosis in mice challenge with PM1 compared to ΔMP1. The mean fungal counts of Pichia pastoris GS115-MP1 in the liver ($P<0.001$) and spleen ($P<0.05$) of mice were significantly higher than those of GS115 at 24 h post-challenge, showing a gain-of-function. PM1 and ΔMP1(pAN8-1 MP1) survived significantly better than ΔMP1 at 48 h ($P<0.001$) post-infection, indicating that Mp1p mediates virulence by improving the survival of P. marneffei in macrophages, the primary defensive mechanism against the fungus.

Conclusions: Mp1p is a novel and key virulence factor of P. marneffei. Mp1p mediates virulence by improving survival of P. marneffei in macrophages.

Project Number: HK-09-01-12

P189-0165
Identification of Metabolome of Mycobacterium tuberculosis and Small Molecules for Rapid Diagnosis and Treatment of Tuberculosis

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Introduction and Project Objectives: Tuberculosis (TB) is an ancient but re-emerging disease caused by *Mycobacterium tuberculosis*. Despite its importance, current diagnostic methods are far from optimal. One of the potential solutions to improve the diagnosis is by the use of metabolomics techniques. The objectives of this project were to identify the potential diagnostics biomarkers for TB using metabolomics approach.

Methods: We compared the metabolome profiles of patient plasma and culture supernatant samples to identify specific biomarkers, using ultrahigh-performance liquid chromatography-electrospray ionization-quadruple time of flight-mass spectrometry (UHPLC-ESI-Q-TOF-MS) and multivariate and univariate analyses. For plasma samples, we compared the metabolome profiles of plasma samples of TB patients (n = 46), community-acquired pneumonia (CAP) patients (n = 30) and controls without active infection (n = 30). For culture supernatants, extracellular metabolomes of culture supernatants of M. tuberculosis strains (n = 9) and other Mycobacterium strains (four *M. avium* complex, one *M. bovis* Bacillus Calmette-Guérin (BCG), one *M. chelonae*, one *M. fortuitum* and two *M. kansasii*) were compared.

Results: Four significant metabolites were identified with higher levels in plasma samples of TB patients than those with CAP and controls. These four metabolites were 12R-hydrozy-5Z,8Z,10E,14Z-eicosatetraenoic acid [12(R)-HETE], ceramide (d18:1/16:0), cholesterol sulfate and 4α-formyl-4β-methyl-5α-cholesta-8-en-3β-ol, which may be involved in pathogenesis or host defence against TB. On the other hand, 24 metabolites were identified with significantly highers level in culture supernatant of *M. tuberculosis* than other *Mycobacterium* species. Among these 24 metabolites, 17 were unidentified by MS/MS against the existing database, suggesting that they may be potentially novel compounds. The other metabolites were identified as dexpanthenol, 1-tuberculosinyladenosine (1-TbAd), three previously undescribed derivatives of 1-TbAd, a tetrapeptide, Val-His-Glu-His, and a monoacylglycerophosphoglycerol, phosphatidylglycerol (PG) (16:0/0:0) respectively.

Conclusions: We have identified potentially important metabolites from plasma of TB patients and culture supernatants of *M. tuberculosis*. The findings may offer insights into the pathogenesis of *M. tuberculosis*. The metabolites identified from plasma of TB patients may represent potential biomarkers for diagnosis of TB.

Project Number: HK-09-01-10

P190-0168

Discovery and Validation of Antiviral Small-molecule Inhibitors for Influenza Virus Replication

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Influenza epidemics are responsible for significant morbidity, mortality and economic burden worldwide. Recurring emergence of new influenza virus strains that are resistant to currently approved antiviral medications has become a global health concern, especially in light of the new H1N1 influenza virus pandemic. Currently, almost all circulating strains of seasonal influenza A viruses are resistant to both classes of antiviral drugs including the adamantanes and neuraminidase inhibitors. New therapeutic approaches are critical to overcome the issue of recurring resistance. Through molecular docking on the crystal structures of different viral proteins, 159 compounds out of 230,000 compounds from the database were found to be effectively in suppressing the influenza virus replication. Five compounds showed influenza virus suppressive effects. We study a list of these compounds in vitro and then in vivo. The result showed that one of the compounds, compound 58, showed the strongest H1N1-suppressive effect. It is effective in reducing the viral titers of a wide range of influenza strains including the seasonal H1N1, H9N2/G1, H3N2 and the oseltamivir-resistant H1N1 virus. In vivo, compound 58 reduced the mortality rate of mice infected with influenza virus. The results will provide insights into applying computational biology and cell biology techniques to discover new drug candidates. Supplemented by virus-cell culture assays to confirm the antiviral effects in vitro, such techniques can be used expedite the discovery of new anti-influenza drugs. The information will have bearing in designing therapeutic strategies.

Project Number: 11101072

P191-0174

Neutrophil Mediated Host Responses during Influenza A Virus Infection, An In Vitro Study

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Introduction: Neutrophil (Nϕ) is the most abundant cell of the immune system in humans. In an acute influenza virus infection, Nϕs are already active in the early phase of inflammation-a time in which clinical biopsy or autopsy material is not readily available. However, the role of Nϕ in virus infection is not well understood. Here, we studied the role of Nϕ in host defense during influenza A virus infection, specifically assessing if it contributes to the differential pathogenesis in H5N1 disease.

Method: Nϕs were freshly isolated from healthy volunteers and subjected to influenza H1N1 and H5N1 virus infection. The susceptibility of Nϕ to influenza A virus infection was assessed by the viral matrix gene expression and viral titration assay. Innate immune response of Nϕ was evaluated by monitoring the gene and protein expression of the naïve Nϕ with and without influenza virus infection, using qPCR assay and ELISA.The induction of the de novo neutrophil extracellular trap (NET) was evaluated by scanning electron microscopy and SYTOX green staining.

Results: Our results demonstrated that naïve Nϕs were equally susceptible to H5N1 and H1N1 virus infection with similar viral gene transcription. Productive replication was observed in H5N1 infected Nϕs only. H5N1 induced higher cytokine and chemokine gene transcription and protein secretion than H1N1 infected Nϕs, including TNFα, IFNβ, CXCL10, MCP-1, MIP-1α and IL-8. This inferred a more intense inflammatory response posed by H5N1 than H1N1 virus. Strikingly, NET formation was only observed in H1N1 infected Nϕs at 6 hpi and it was not found in H5N1 infected cells.

Conclusions: Our data is the first to demonstrate that NET formation is abrogated in H5N1influenza virus infection and might contribute to the severity of H5N1 disease.

Project Number: 11101002

P192-0071

Modeling Host Susceptibility to Influenza H7N9 Virus in Inbred Mice: A Pilot Study

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Introduction and Project Objectives: Host susceptibility plays a significant role during H7N9 virus infection. It is noteworthy that studies in inbred mice have contributed substantially to our understanding of host susceptibility to influenza viruses.

Methods: We have used Next Generation Sequencing (NGS) technology to characterize mRNA and miRNA levels in C57BL/6J and DBA/2J mice before and after virus infection to elucidate the molecular mechanisms of host susceptibilities.

Results/ Conclusions: Host genes which may contribute to viral replication were identified, and the role of redox imbalance in controlling virus replication was further highlighted. In addition, a list of promising candidates responsible for host susceptibilities has been identified, and an integrated panel of miRNA regulation on these candidates was constructed. MiRNA-let-7b and miR-21a-5p were two miRNAs which may play an important role in regulating genes direct diverse host response to influenza infection.

Project Number: RRG-08

P193-0015

Association between Human Adenovirus-36 (Ad-36) Infection, Obesity, Glycemia and Other Obesity Related Cardiometabolic Risk Factors in Prospective Follow-up of Hong Kong Chinese School Children

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Increasing evidence suggest a link between obesity and viral infection. Adenovirus-36 (Ad-36) is the only human adenovirus known to be associated with obesity. We aimed to examine the associations of Ad-36 infection with cardiometabolic risk factors including obesity,glycemia and other obesity associated cardiometabolic risk factors in school children. Stored aliquots of Hong Kong Chinese school children from two territory-wide surveys conducted in 2003 and 2007-08 were examined for Ad-36 infection using serum neutralization test for Ad-36 antibodies. The school children were called back for repeated examinations of their anthropometric indices and cardiometabolic profile including fasting plasma glucose and lipid, as well as serum for their Ad-36 antibodies. A total of 983 school children (41.8% male) were called back for prospective study. Mean follow-up duration was 8.7 years (standard deviation, SD= 2.7 years). Mean age of the participants were 14.0 (SD 3.2) years and 22.7 (SD 4.9) years at baseline and follow-up respectively. The prevalence of Ad-36 infection at baseline was 1.5%, while the prevalence increased to 3.3% at follow-up (p=0.002). Using mixed-effects model, there was no significant association between Ad-36 infection status and obesity and obesity-associated conventional cardiometabolic risk factors including fasting plasma glucose after adjustment of age and sex. Likewise, there was no significant association between Ad-36 infection status and obesity and obesity associated cardiometabolic risk factors using one-way ANOVA analysis by comparing BMI with the status of Ad-36 infection. To conclude, the prevalence of Ad-36 infection in Hong Kong Chinese school children was low and there was no significant association between Ad-36 infection and obesity, glycemia and obesity associated cardiometabolic risk factors.

Project Number: 12110042

P194-0139

Prevalence and Risk Factors of Chlamydia Infection in Hong Kong: A Population-based Geospatial Household Survey

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Introduction and Project Objectives: Chlamydia causes infertility and increases risk of HIV infection, and population-based studies provide essential information for effective infection control and prevention. This study examined Chlamydia trachomatis prevalence and risk factors among a representative sample of 18-49-year-old residents in Hong Kong.

Methods: Census boundary map of 412 constituency areas was used as primary sampling units to construct the sampling frame and, residential buildings and units were randomly selected using geospatial modelling. A questionnaire on sexual practice and health was conducted, and polymerase chain reaction was used to test the urine for genital chlamydial infection. Invitation letters were sent to the selected households and a team of interviewers were sent to recruit one subject per household. Prevalence data was weighted according to the 2011 census and risk factors identified through logistic regression.

Results: Among 881 participants (response rate of 24.5%), the overall Chlamydia trachomatis prevalence was low at 1.4% (95%CI 0.8-2.5%) but sexually active young (18-26 years) women and men had relatively high prevalence 5.8% (95%CI 1.7-18.2%) and 4.8% (95%CI 1.2-17.6%) respectively in Hong Kong. A unique U-shape disease burden was observed with peaks in younger and older (40-49 years) women. Amongst the sexually active women, the risk factors of Chlamydia trachomatis infection were: younger age (aOR=25.4, 95% CI 2.81 - 230); living alone (aOR = 8.99, 95% CI 1.46 - 55.40); and, among all the sexually active participants, males (including the male partners of the female participants) who had travelled out of Hong Kong in the previous 12 months had higher risks of infection (aOR=5.35; 95% CI 1.25-22.8). A core-peripheral geographical distribution of Chlamydia trachomatis prevalence was also observed.

Conclusion: Young and older sexually active women in Hong Kong have high prevalence of chlamydia. Routine screening for sexually active women and young men should be considered. Further research on testing feasibility and linkage-to-care are urgently needed to control the infection.

Project Number: 13121242

P195-0166

Identification of Metabolome of Burkholderia pseudomallei and Small Molecules for Rapid Diagnosis of Melioidosis

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Introduction and Project Objectives: Melioidosis is a serious and potentially fatal disease caused by *Burkholderia pseudomallei*. To prevent relapse, a prolonged antibiotics regimen is required. Diagnosis of melioidosis is difficult especially for the cases with negative bacterial culture results. One of the potential solutions for designing more accurate diagnostic tests is by utilizing metabolomics techniques. The objectives of this project were to identify the potential diagnostic biomarkers for melioidosis using metabolomics approach.

Methods: To identify potential biomarkers for diagnosis of melioidosis, metabolome profiling of plasma and culture supernatant samples were performed and analyzed using ultrahigh-performance liquid chromatography-electrospray ionization-quadruple time of flight-mass spectrometry (UHPLC-ESI-Q-TOF-MS) and multivariate and univariate analyses. For plasma samples, metabolome profiles of samples from newly-diagnosed melioidosis patients (n = 22), other bacteremia patients (n = 24) and controls without active infection (n = 30) were compared. For culture supernatants, metabolome profiles of *B. pseudomallei* (n = 15), other *Burkholderia* closely related species, including *B. thailandensis* (n = 3), *B. cepacia complex* (n = 14), and other bacteria, *Pseudomonas aeruginosa* (n = 4) and *Escherichia coli* (n = 3), were compared.

Results: Twelve metabolites were identified with significantly higher levels in plasma samples from melioidosis patients than those with bacteremia or controls without active infection. These metabolites belonged to four lipid classes, acylcarnitine (6), lysophosphatidylethanolamine (LysoPE) (3), sphingomyelins (SM) (2)

and phosphatidylcholine (PC) (1). These lipids are involved in various lipid metabolic pathways which may be related to pathogenesis and host immune response against melioidosis. On the other hand, eight metabolites were identified with significantly higher levels in culture supernatants of *B. pseudomallei* than other bacterial species. Among these eight metabolites, five of them were unidentified by MS/MS against the existing databases, indicating that these compounds may be potentially novel. Of the other three metabolites, two were identified as tetrapeptides and one was identified as 4-methyl-5-thiazoleethanol, a degradation production of thiamine.

Conclusions: We have identified potentially important metabolites from plasma of melioidosis patients and culture supernatants of *B. pseudomallei.* The findings may offer insights into the pathogenesis and biological function in *B. pseudomallei*. Metabolites identified in plasma samples may be potential biomarkers for diagnosis of melioidosis.

Project Number: HK-09-01-11

P196-0175

Investigation of the Functional Significance of Phytase Activity in Human Fungal Pathogen Candida albicans

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Introduction and Project Objectives: *Candida albicans* is one of the most prevalent human fungal pathogens. In healthy individuals, *C. albicans* cohabits as a harmless commensal on the skin and mucosal surfaces of oral cavity, digestive tract and urogenital system. In cases of impaired immunity, *C. albicans* can become invasive and cause an infection (candidiasis). Mild superficial infection is not fatal, but disseminated candidiasis can be life-threatening. The ability of pathogens to colonize and proliferate in host tissues contributes to pathogenicity. Phosphorus is a building block of nucleic acids, ATP and is involved in phosphorylation and glycolysis. *Myo*-inositol plays key role in membrane formation, signal transduction and osmoregulation. More importantly, it is a precursor of cell surface glycosylphosphatidylinositol-anchored glycolipids, a *C. albicans* virulence trait through interactions with human macrophages. Phytate degradation by phytase liberates *myo*-inositol and inorganic phosphate, both are essential molecules for fungal growth and pathobiology. Our previous study demonstrated the presence of phytase activity in Candida fungi and suggested its potential involvement in host-pathogen interactions. The objectives of this study were: (1) To create *C. albicans* phytase null mutants and examine their phenotypic determinants; (2) To examine the effects of pH and transcription factors on phytase activity; and (3) To evaluate the importance of phytase activity in *C. albicans* fitness and virulence.

Methods: *C. albicans* phytase null mutants were created using a PCR-based gene targeting method. The phenotypic properties of the mutants were evaluated, including phytase activity, fungal growth, yeast-to-hyphal morphogenesis, adhesion to buccal epithelial cells (BECs), and virulence. The effect of pH on phytase activity was evaluated by incubating the fungal cells at different pH (from 4.0 to pH 8.5). The effect of transcription factors on phytase activity was investigated using quantitative PCR.

Results: *C. albicans* phytase null mutants have been created and verified. Biochemical analyses indicated that *PHO112* contributed to the *C. albicans* phytase activity. *C. albicans* pho112Δ/pho112Δ possessed decreased phytase activity, reduced ability to form hyphae in the presence of fetal calf serum at 37oC, and attenuated adhesion to BECs and virulence. pH and transcription factors had no effect on phytase activity.

Conclusions: The collective data of the present study suggest that *PHO112* is responsible for the *C. albicans* phytase activity, which is not affected by pH and transcription factors; and virulence.

Project Number: 11100992

P197-0160

Identification of Small Molecules for Rapid Diagnosis of Invasive Aspergillosis

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Introduction and Project Objectives: Aspergillus related infections have become emerging infectious diseases after the increasing use of immunosuppressive agents and high fatality associated with invasive aspergillosis. However, clinical diagnosis of Aspergillus infections remains difficult. Although molecular tests are also used for laboratory diagnosis, such tests cannot distinguish among environmental contamination, colonization and genuine invasive infection. In this study, we aimed at searching for potential biomarkers of invasive aspergillosis for the rapid diagnosis purpose.

Methods: All fungal strains were identified by phenotypic tests and molecular methods. Thirty strains of six pathogenic Aspergillus species (A. fumigatus, A. flavus, A. niger, A. terreus, A. nomius and A. tamarii) and 31 non-Aspergillus fungal strains were grown in defined culture medium. The fungal culture supernatants, patient samples with culture-documented or probable invasive aspergillosis and sera from mice experimentally infected by Aspergillus species were subjected to UHPLC-ESI-Q-TOF-MS and MS/MS analysis. Univariate analysis was used to identify the biomarkers specifically present in the Aspergillus culture supernatants. Accurate masses of the unique molecular features in Aspergillus group were selected for product ion scanning.

Results: Three of 11 strains reported as A. flavus were unambiguously identified as A. nomius (n=2) or A. tamarii (n=1) and the remaining eight strains were A. flavus by using DNA sequencing and metabolic fingerprinting. A. flavus, A. nomius and A. tamarii strains were separated into three clusters in metabolomic study. At least eight Aspergillus species-specific compounds were identified in Aspergillus culture, 23 metabolites were found to be expressed significantly higher in Aspergillus infected mice than non-Aspergillus infected mice, and 16 metabolites showed significant different in patients suffering from Aspergillosis than the control patients. One of the metabolite, Leu-Glu-Leu-Glu, observed in the six pathogenic Aspergillus species but not in other fungi, is a novel tetrapeptide that represents the first tetrapeptide found in Aspergillus species, named aspergitide. Two other closely related Aspergillus-specific compounds, hydroxy-(sulfooxy)benzoic acid and (sulfooxy)benzoic acid, specific to the Aspergillus species may possess anti-inflammatory properties, as 2-(sulfooxy)benzoic acid possesses a structure similar to those of aspirin [2-(acetoxy) benzoic acid] and salicylic acid (2-hydroxybenzoic acid), which are potent analgesics and anti-inflammatory agents used for decades for treatment of various inflammatory conditions through inhibition of cyclooxygenases (COXs).

Conclusions: Further studies to examine the potentials of these Aspergillus-specific compounds for laboratory diagnosis of aspergillosis are warranted and further experiments will reveal whether Leu-Glu-Leu-Glu, hydroxy-(sulfooxy)benzoic acid and (sulfooxy)benzoic acid are virulent factors of the pathogenic Aspergillus species.

Project Number: HK-09-01-13

P198-0181

Hospital Outbreak of Zygomycosis due to Contaminated Linen Items from Substandard Laundry

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Introduction: Healthcare laundry-related infection is rare, and pulmonary zygomycosis due to contaminated hospital linens has never been reported.

Methods: We reported an outbreak investigation of zygomycosis in Queen Mary hospital. Air samplers and environmental sample were collected for further analysis. The fungal isolates from clinical and environmental samples were identified by morphology, MALDI-TOF MS, and ITS1-5.8S-ITS2 rRNA gene cluster sequencing.

Results: From 2 June 2015 to 18 July 2015, 6 immunosuppressed patients developed pulmonary (n = 4) and/or cutaneous (n = 3) infection by a spore-forming mold, Rhizopus microsporus, through direct inhalation and skin contact of contaminated linen items supplied by a designated laundry. Seventy (27.8%) of 252 freshly laundered clothing and 15 (3.4%) of 443 nonclothing laundered linen items (pillow case, bed sheet, draw sheet) were contaminated by R. microsporus, which was significantly higher than those from other hospital laundries (0%, n = 451; P < .001) supplying linen to hospitals with no cases of zygomycosis reported during the same period. The fungal isolates from patients and linens were phylogenetically related. In sum, 61% of environmental samples and 100% of air samples at the designated laundry were also positive for zygomycetes, suggesting heavy environmental contamination.

Conclusions: Suboptimal conditions of washing, drying, and storage contributed to the massive linen contamination and the outbreak of zygomycosis.

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