K2 - Genomic Study on Molecular Pathways of Cancer Development and its Relevance to Cancer Precision Medicine

Prof LEUNG Suet-yi, *MBBS, MD, FHKAM (Pathology), FHKCPath, FRCPath (UK), FRCPA*
Associate Dean (Research), Y W Kan Professor in Natural Sciences,
Chair of Gastrointestinal Cancer Genetics and Genomics,
Hereditary Gastrointestinal Cancer Genetic Diagnosis Laboratory,
Department of Pathology, Li Ka Shing Faculty of Medicine,
The University of Hong Kong,
Queen Mary Hospital, Hong Kong

Professor Suet-yi Leung is the Associate Dean (Research), Li Ka Shing Faculty of Medicine at The University of Hong Kong. She is also the YW Kan Endowed Professor in Natural Sciences and Chair in Gastrointestinal Cancer Genetics and Genomics in the Department of Pathology. Her research interests are focused on the molecular genetics, epigenetics and genomics of gastric and colorectal cancers, and their applications in molecular classification and genetic diagnosis to facilitate cancer prevention and treatment. Using genomic technologies, including next generation sequencing, her group has identified many novel gastric cancer driver genes, including ARID1A, RHOA and RNF43, and defined the genomic and epigenomic landscapes of various molecular subtypes of gastric cancer. Her team also established and systematically characterized a large repertoire of organoids from patient gastric normal and cancer tissues, encompassing comprehensive molecular subtypes, thus provides a valuable resource for understanding both cancer biology and anti-cancer drugs that may facilitate the development of precision cancer therapy. Her team has first described the heritable germline methylation of the MSH2 gene promoter as a cause of Lynch Syndrome, and subsequently identified EPCAM deletion as the cause of MSH2 methylation, the latter has become a standard genetic diagnosis test for Lynch Syndrome. Her team also uncovered the critical role of BRAF and RNF43 in the serrated neoplasia pathway, provided critical molecular data to support the pathogenic role of RNF43 germline mutation in Serrated Polyposis Syndrome families. The long term goal of her laboratory is to identify novel genes that are important for the causation of gastric and colorectal cancer, and to explore the use of some of these genes as markers for early detection, prognostication or drug targets.

Genomic studies of cancer have revealed the molecular diversity and organ-specific differences in pathways of cancer development with therapeutic implications. Using gastrointestinal cancers as model, gastric and colorectal cancers shared some common oncogenic pathways yet with marked divergent differential incidence of oncogenic pathway alterations. Some of these molecular alterations are emerging as biomarkers for prognostication, guiding patient treatment as well as prediction of genetic predisposition for focused preventive screening. Emerging technologies including next generation sequencing can facilitate the discovery of novel genes or pathways that contribute to development of inherited or sporadic gastrointestinal cancers. Coupled with development of new generation organoid cancer cell models, it enables direct culture of patients' cancer cells for drug sensitivity testing, and correlation with genomic changes to identify genomic determinant of drug response. Overall, coupling genomics and organoid-based drug screening, linking back to patient pathology and therapeutic response will empower the development of precision cancer therapy.