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Photoacoustic Molecular Imaging of Osteoarthritic Pain

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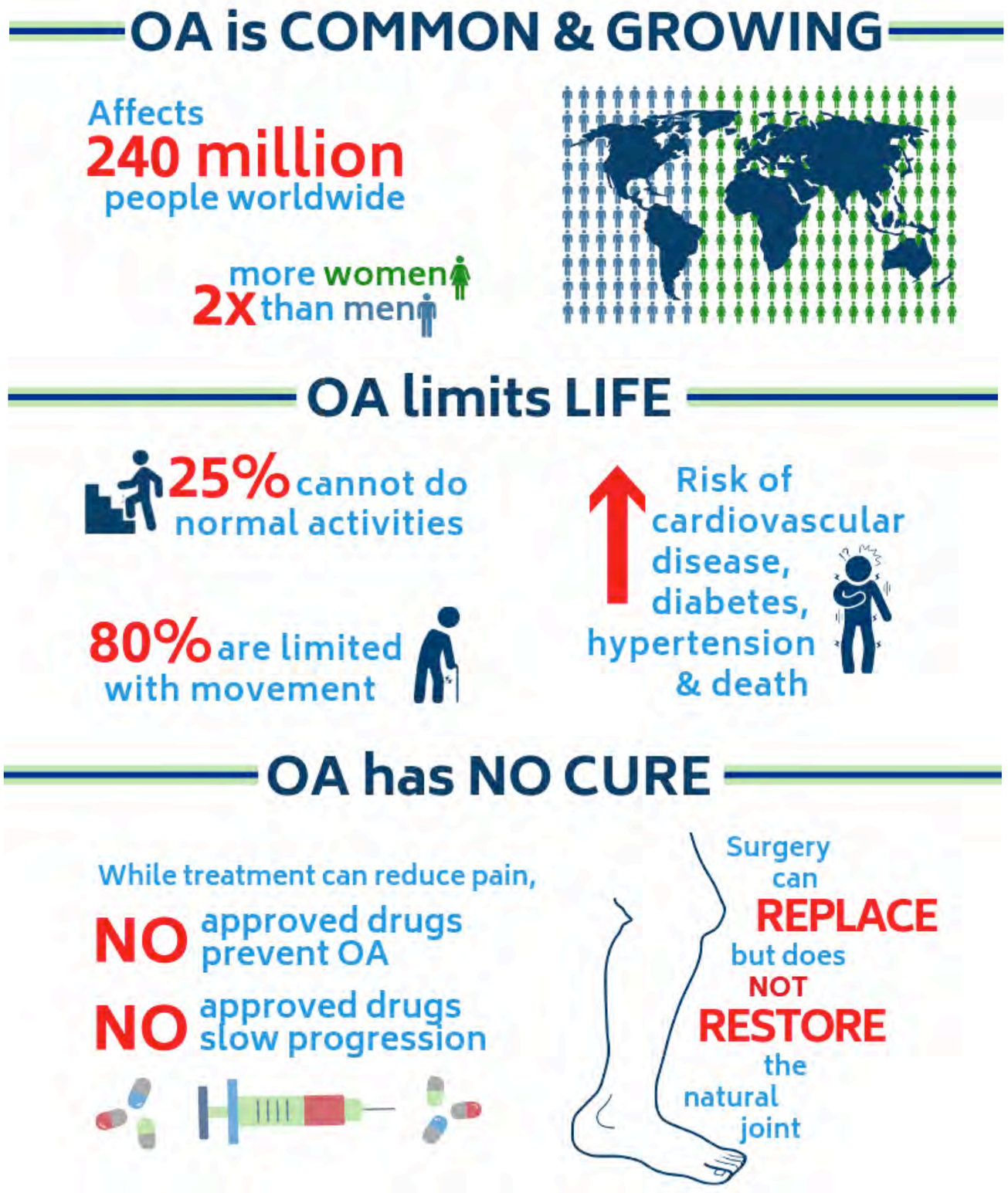
Osteoarthritis (OA) is a serious disease



Osteoarthritic knee

Wen CY, et al, Journal of Orthopaedic Translation (2014) 2, 16~25
Wen CY, et al., *Nat Rev Rheumatol*. 2014 Oct;10(10):577-8.

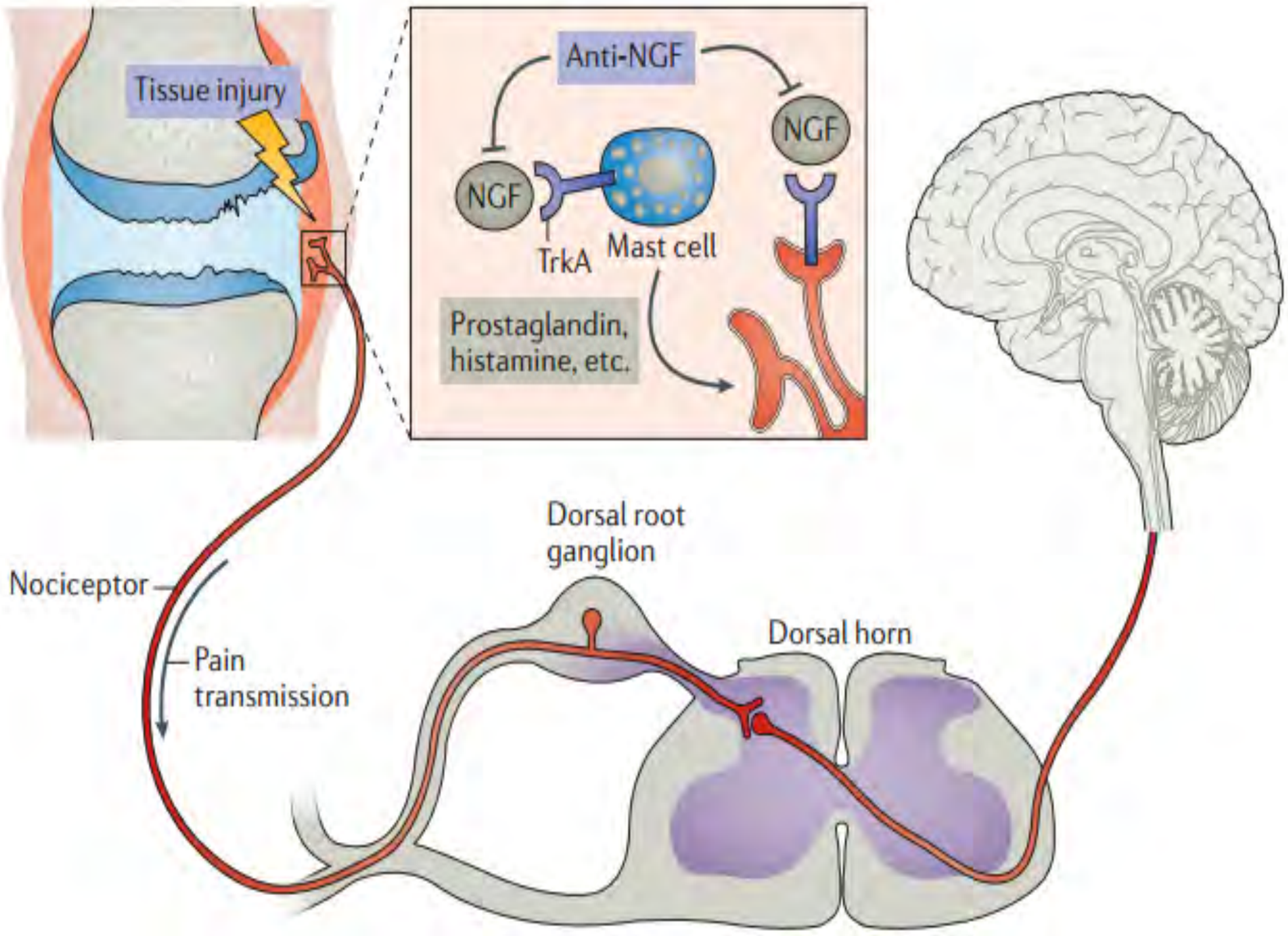
Direct Cost of OA: **0.28%** of GDP in 2000s with a prediction of **1-2.5%** of GDP by 2030s in Hong Kong

Type	Cost/person HKD	No.	Year total HKD
Prosthesis, first year	354,290	700	248 million
Prosthesis	150,330	2,800	421 million
Severe OA	46,820	36,000	1,685 million
Mild OA	14,990	80,000	1,199 million
All	—	120,000	3.5 billion

Woo J et al., Arthritis Rheum. 2003 Aug 15;49(4):526-34.

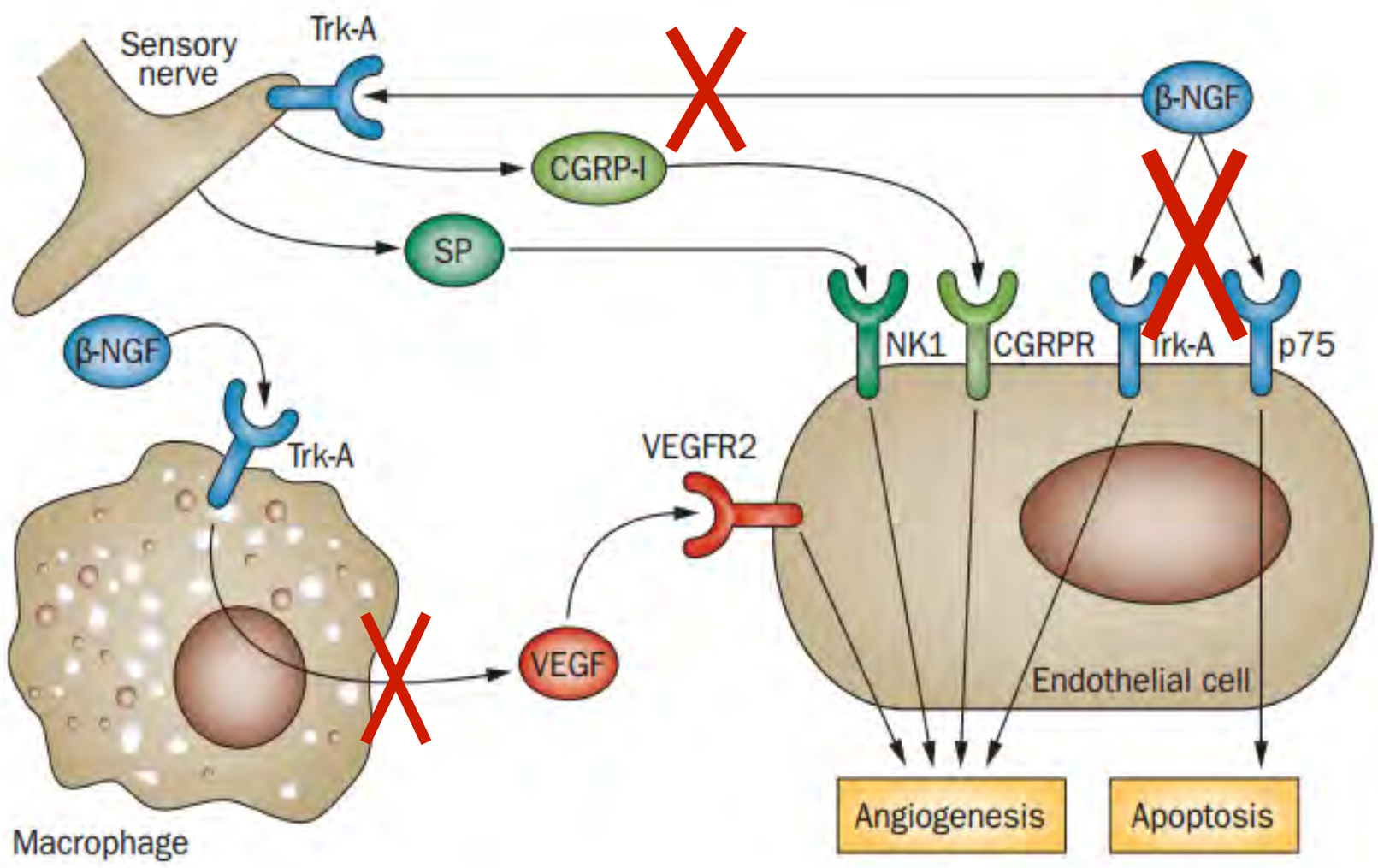
Nerve growth factor (NGF): an emerging target in OA pain mechanism and therapeutics

- NGF is a key mediator of acute and chronic pain



Lane, Nancy E., and Maripat Corr. Nature Reviews Rheumatology 13.2 (2017): 76.

- Anti-NGF therapy is a promising way for targeted OA pain relief



Mapp, Paul I., and David A. Walsh. Nature Reviews Rheumatology 8.7 (2012): 390.

HMRF Research Fellowship Training Program

Prof. Tonia Vincent

Arthritis Research UK | centre for osteoarthritis pathogenesis

Osteoarthritis

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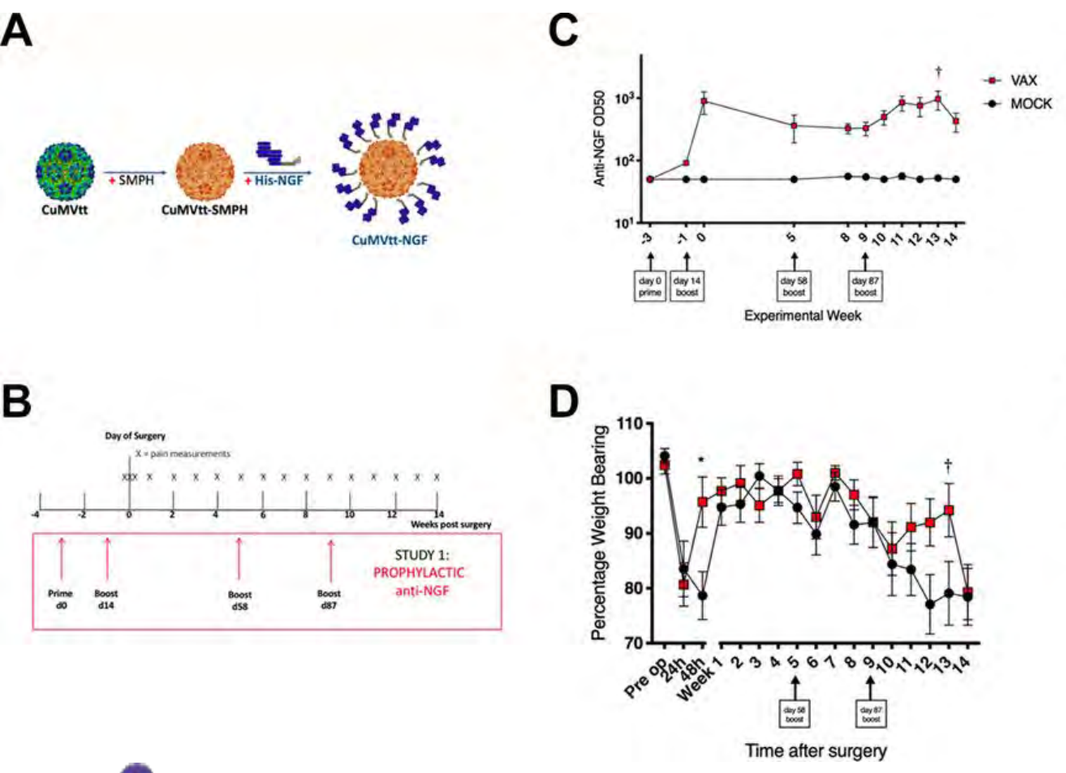
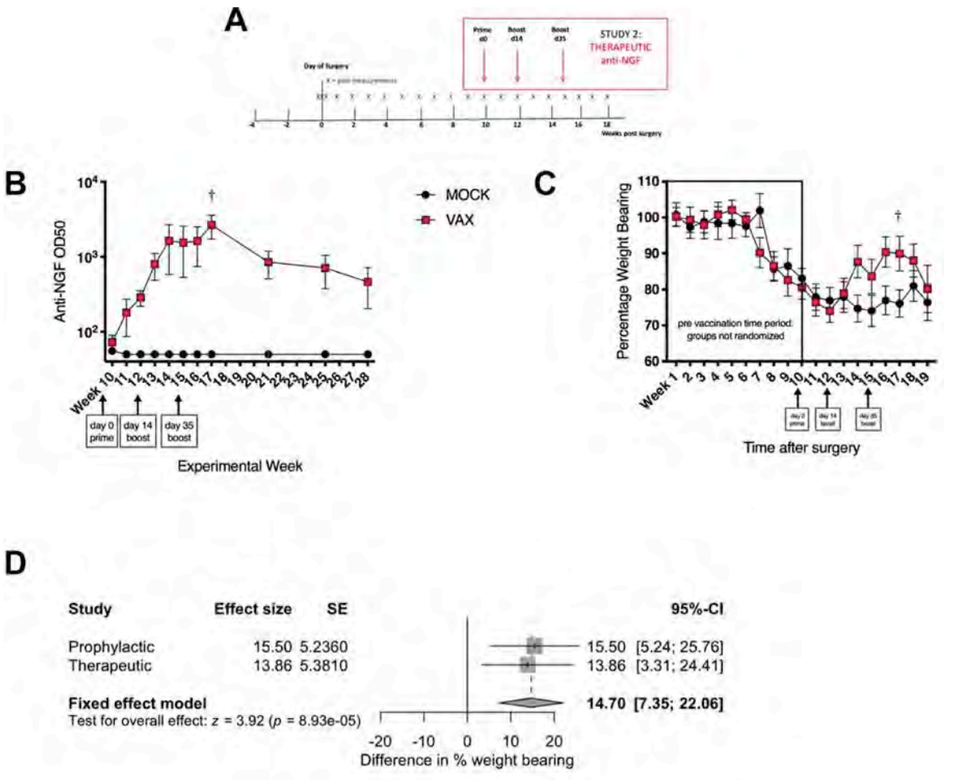
Active immunisation targeting nerve growth factor attenuates chronic pain behaviour in murine osteoarthritis

Isabell S von Loga,[1] Aadil El-Turabi,[2] Luke Jostins,[1] Jadwiga Miotla-Zarebska,[1] Jennifer Mackay-Alderson,[1] Andris Zeltins,[3] Ida Parisi,[1] Martin F Bachmann,[2,4] Tonia L Vincent[1]

Prophylactic NGF vaccination blocks murine OA pain



Therapeutic NGF vaccination reduces murine OA pain



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Isabell S von Loga et al. Ann Rheum Dis 2019;78:672-675

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Synthesis of Anti-NGF conjugated MoS_2-AuNR

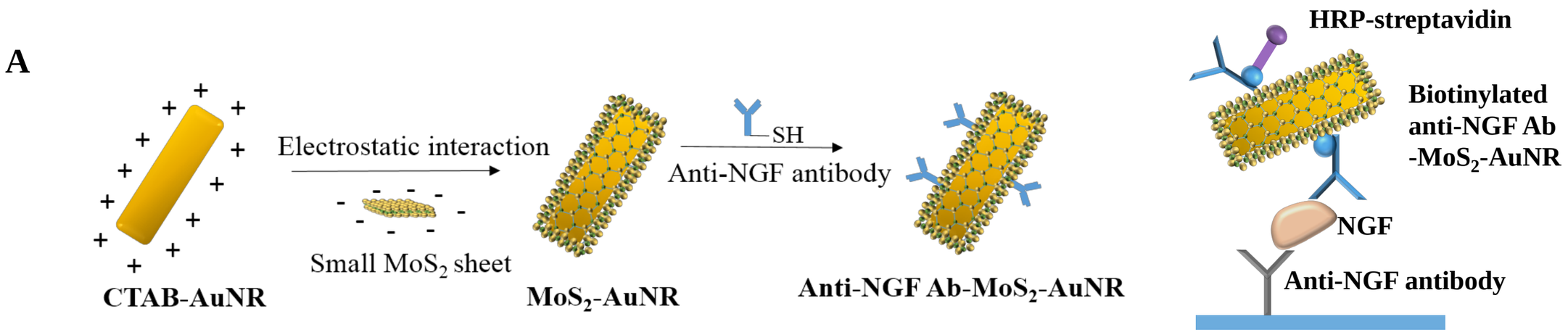


Fig. 1 **Preparation and characterization of MoS_2-AuNR**

(A) Schematic Diagram of anti-NGF Ab-MoS_2-AuNR for active targeting of inflamed tissue in OA joints

(B) Representative image of MoS_2-AuNR examined with transmission electron microscopy; scale bar 20um

(C) Zeta potential of anti-NGF Ab-MoS_2-AuNR

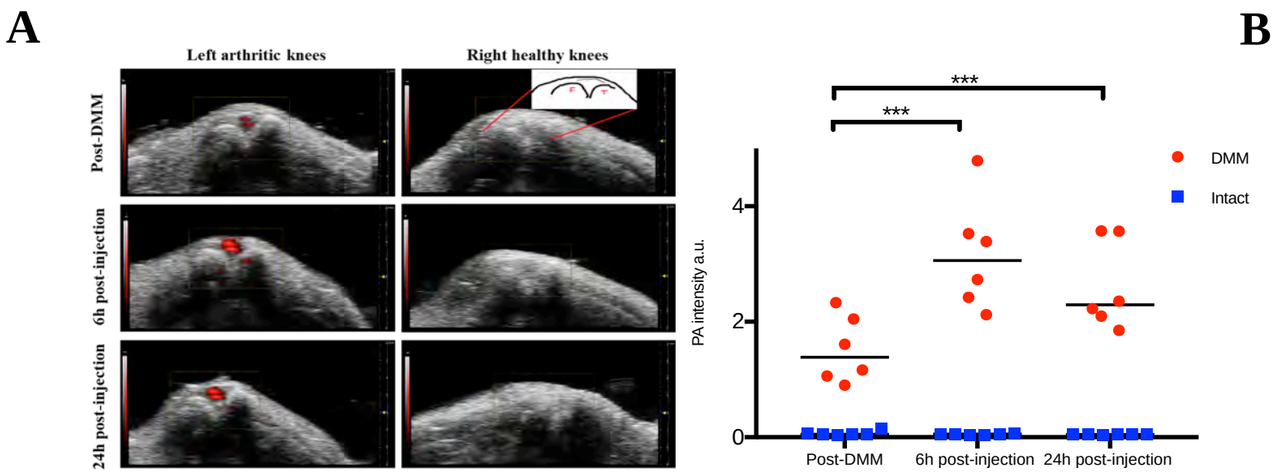
(D) Thermal image of MoS_2-AuNR with increasing concentration

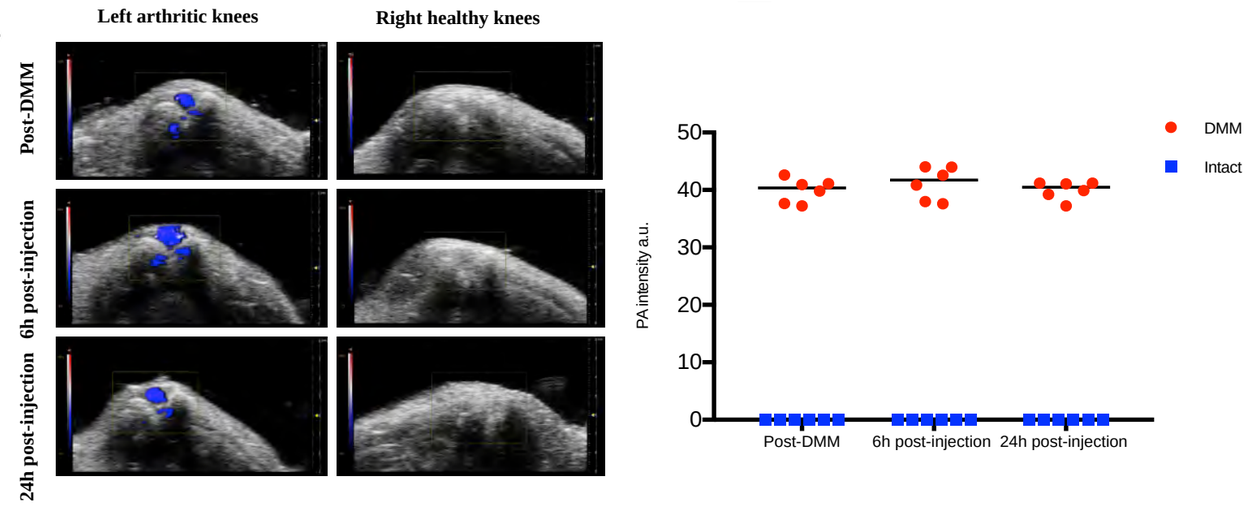
(E) In vitro PA imaging and quantitative curve of PA intensity of MoS_2-AuNR with different concentration

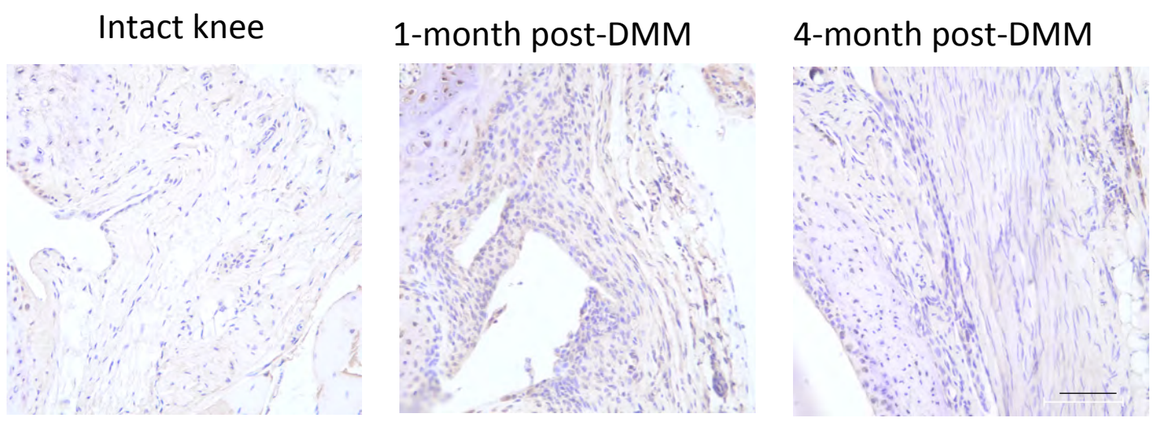
(F) Binding affinity of anti-NGF Ab-MoS_2-AuNR complex to NGF by ELISA

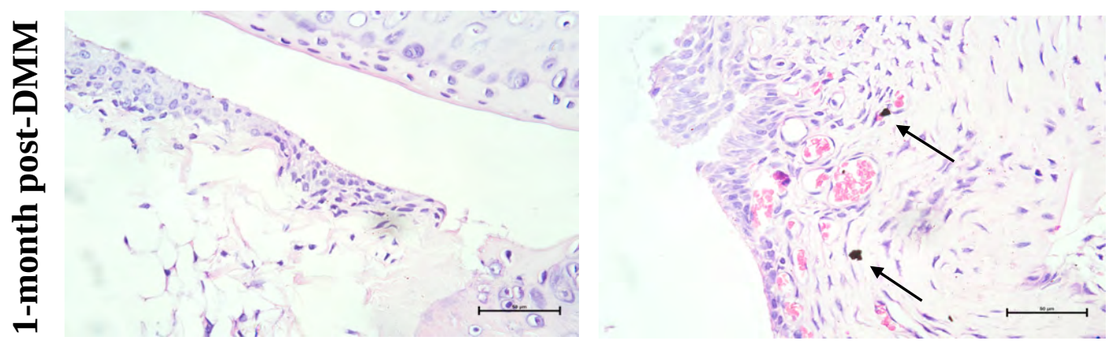
(G) In vivo PA imaging of PA intensity after subcutaneous injection of MoS_2-AuNR

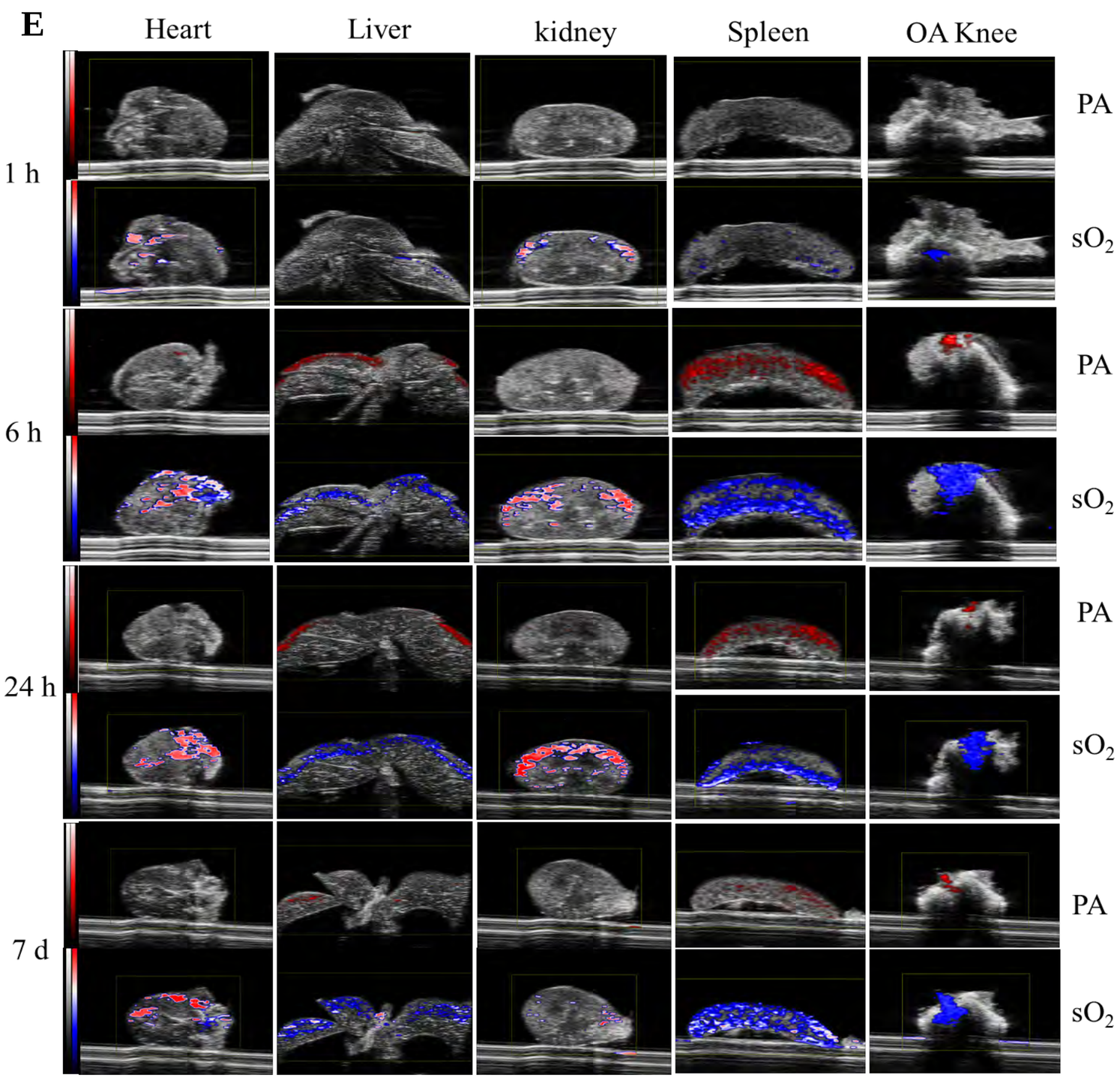
Targeting effect of anti-NGF Ab-MoS_2-AuNR

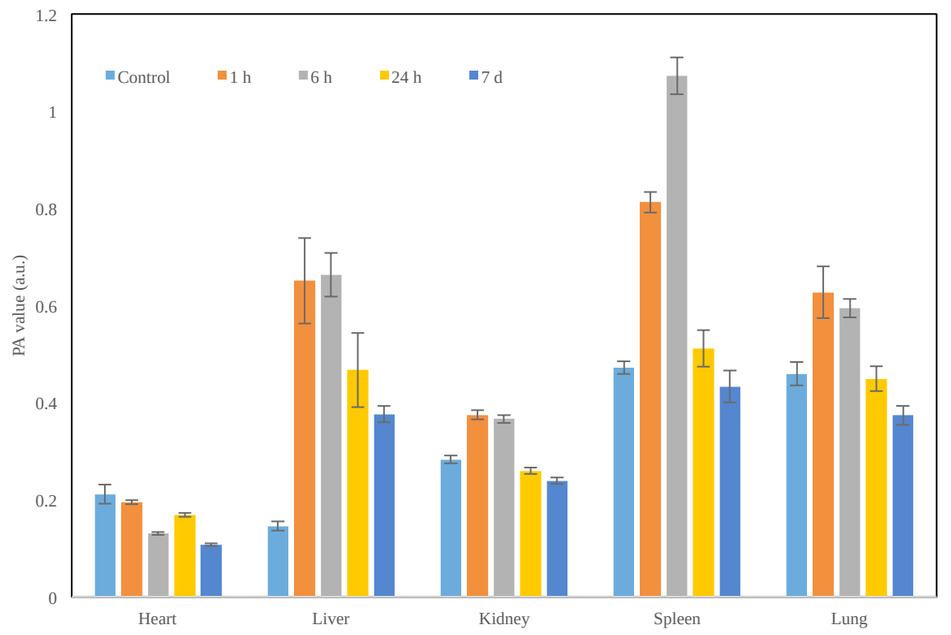


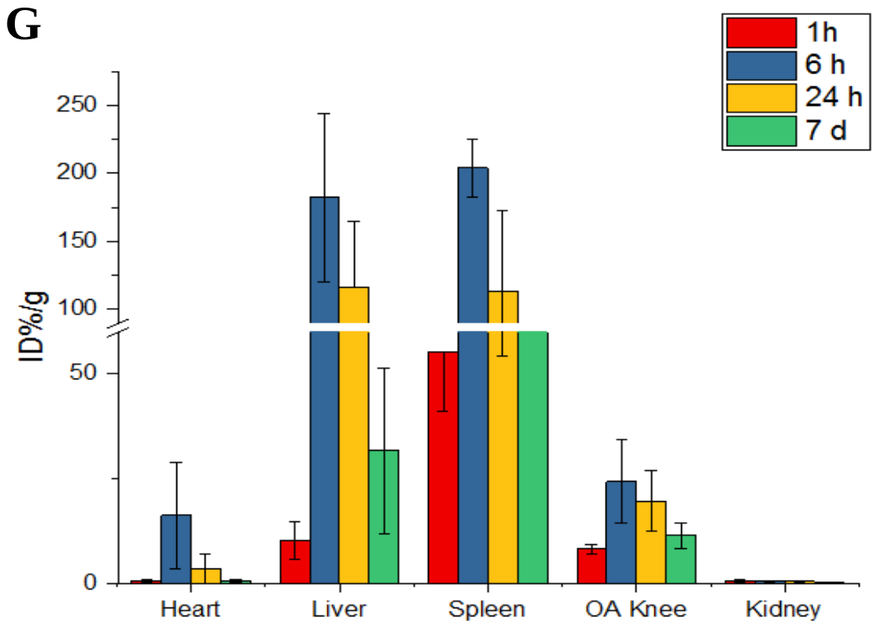












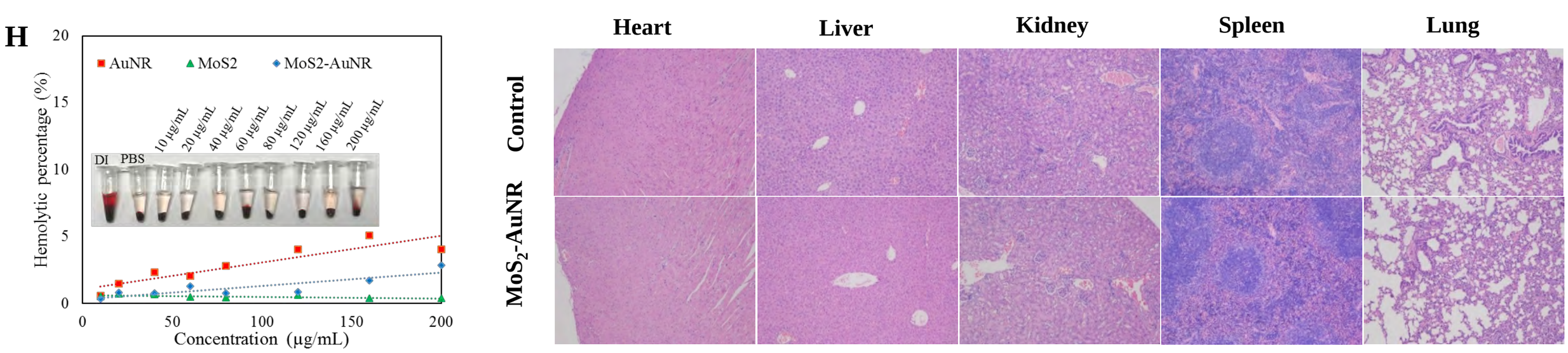


Fig. 2 **Targeting effect of of anti-NGF Ab-MoS_2-AuNR**

(A) *In vivo* Photoacoustic (PA) images showing accumulation of NGF-targeted nanoparticle at OA knees
(B) *In vivo* Photoacoustic (PA) images showing hemoglobin oxygen saturation (sO_2) at OA knees
(C) More blood vessels were found in OA knees than intact knees
(D) Accumulation of nanoparticles were found in OA knee than sham-operated knee
(E) Time-course PA images of major organs and knees
(F) Quantitative measurement of PA signal of major organs and knees
(G) ICP-MS analysis showing biodistribution of anti-NGF Ab-MoS_2-AuNR at different times after injection
(H) No haemolysis and toxicity effects

Anti-NGF conjugated MoS_2-AuNR for targeted OA pain imaging and therapeutics

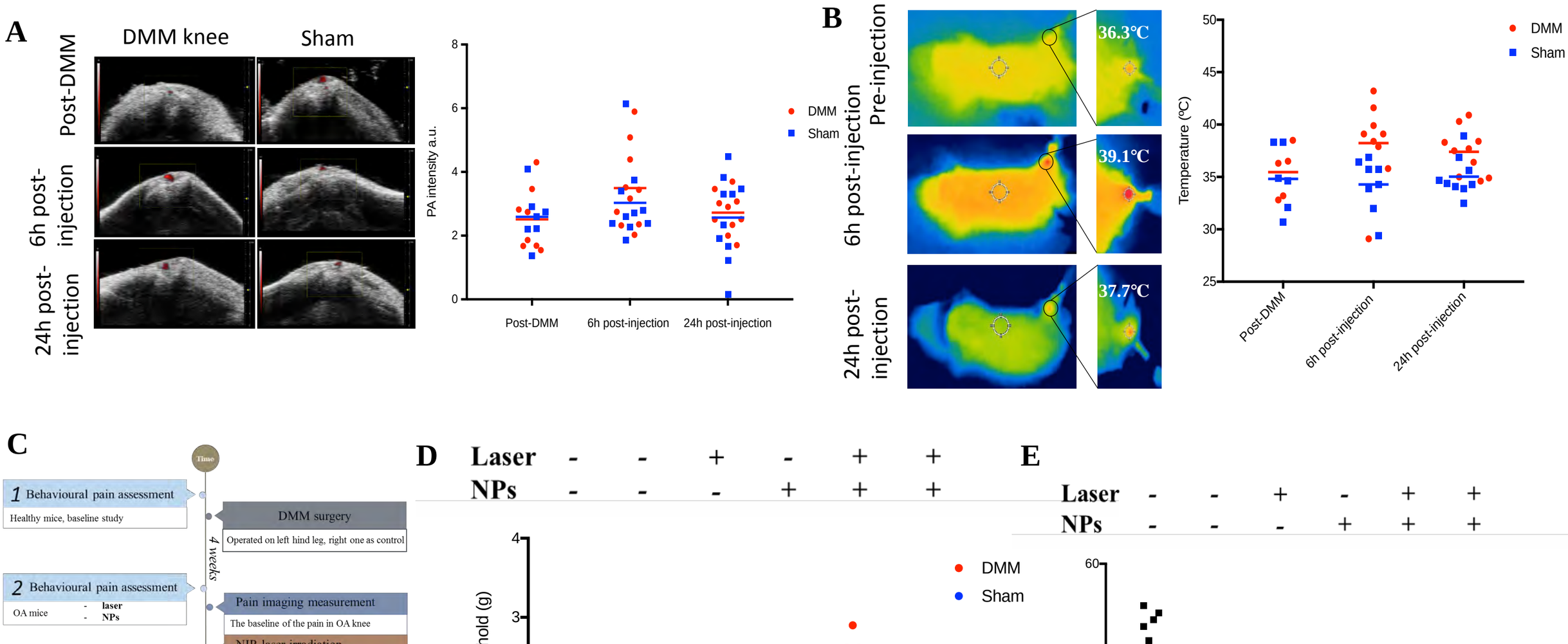


Fig.3 **Nanoprobe-guided pain imaging and OA treatment at later stage of disease (4-month post-DMM)**

(A) Photoacoustic images showing accumulation of NGF-targeted nanoparticle at OA knees
(B) Photothermal images of a mouse underwent DMM surgery before and after laser treatment
(C) Experimental protocol
(D) Withdrawal threshold in hind paw, measured by von Frey
(E) Latency to fall from rotarod
(F) Hematoxylin and eosin (H&E) staining of the articular cartilage (AC) from 22-week-old balb/c mice (magnification, x100)
(G) OARSI histopathology grading and staging scores were determined in sham (control), 4-month post–DMM surgery and surgery group with laser treatments of the animals
(H) NGF expression at synovium at 4-month post-DMM
(I) TrkA expression at synovium at 4-month post-DMM

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