F2 - Photoacoustic Molecular Imaging of Osteoarthritic Pain – A Proof-of-concept Study

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(i) Training Programme

Kennedy Institute of Rheumatology (KIR), University of Oxford, is a world leading basic and translational inflammatory science center. KIR is known for the discovery of tumor necrosis factor (TNF)-alpha neutralizing antibody, which leads to a paradigm shift in the treatment of rheumatoid arthritis. Under the auspices of Health and Medical Research Fund Research Fellowship Scheme, Dr Wen received the training in KIR for OA pain behavioral analysis in rodents and established a research platform in Hong Kong. Prof Tonia Vincent, the director of OA pathogenesis research center funded by Arthritis Research UK, provided the training opportunity as the mentor of Dr Wen.

(ii) Research Project

Purpose: Osteoarthritis (OA) is a prevalent debilitating chronic painful condition. Nerve growth factor (NGF) levels are elevated in synovial fluid and associated with arthritic pain in OA patients. NGF is an emerging therapeutic target for OA pain. In this study, we aim to develop a novel theranostic approach targeting NGF using a functionalized gold nanorod for photoacoustic (PA) imaging and management of OA pain.

Methods: Destabilization of medial meniscus (DMM) surgery was performed to induce post-traumatic OA in one knee of the balb/c mouse with the sham operation on the contralateral knee as the control. Gold nanorod conjugated with NGF antibody (NGF-Ab-AuNR) was synthesized and injected via the tail vein at 1-month and 4-month post-surgery. Photoacoustic (PA) imaging was taken to delineate the distribution of the nanoparticles in vivo. DMM knees were then exposed to near infrared (NIR) therapy for 10 minutes under photothermal camera. Von Frey and rotarod tests were performed to assess the locomotive ability and balance of the animals respectively. Knee joints were harvested 24 hours after gold nanorod injection and processed for the histological and immunohistochemical analysis.

Results: PA imaging revealed the accumulation of NGF-Ab-AuNR in the inflamed synovial tissue of DMM knee compared to the contralateral one. ICP-MS biodistibution analysis confirmed the nanoparticles accumulated in the injured knee joint as well as the spleen and liver. Both PA and ICP-MS data showed the accumulation of nanoparticles reached its peak after 6 hours of injection and started to decrease afterwards and cleared out of body at 7 days post injection. All animals showed hindered locomotive ability represented by a lower withdrawal threshold in von Frey test and shorter time on rod in rotarod test after DMM surgery. The locomotive deficits caused by DMM surgery could be rescued by NIR treatment at the early stage of OA but not at later stage of disease. Histological examination identified the nanoparticles leaked from the newly formed blood vessels in the inflamed synovial tissues, and co-localized with TRAPV1-positive peripheral nerve endings around vasculature.

Conclusions: Integration of the cutting-edge nanotechnology and PA imaging modality provides a novel OA pain imaging and management approach. The safety of god nanoparticles as well as NGF neutralizing antibody (Pfizer) has been proved in humans, which will shorten the translation of our research findings into clinical practice.

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