

Macrophage targeted positron emission tomography (PET) for the imaging of inflammatory arthritis; an in vivo and in vitro investigation of translocator protein (TSPO) tracer uptake

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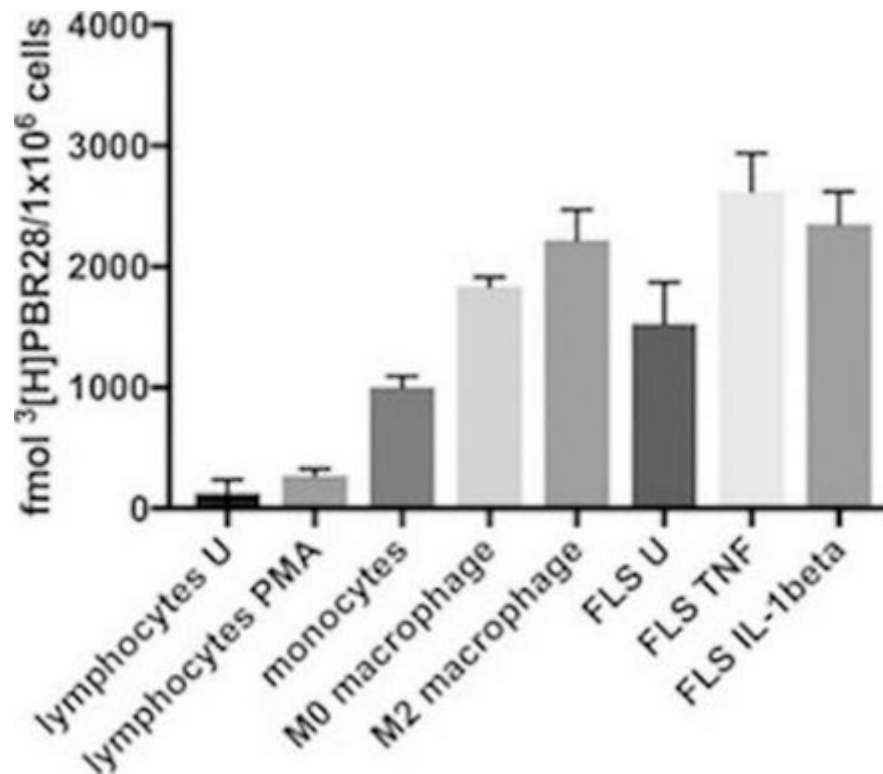
Abstract

Background TSPO targeted PET tracers are increasingly recognised as cellular imaging markers of macrophage infiltration, due to the high expression of TSPO on activated macrophages. Previous work demonstrated the ability of [¹¹C]PK11195 TSPO PET to detect subclinical inflammation in RA, and predict flare in both those with established RA and ACPA positive arthralgia. However, high background uptake of [¹¹C]PK11195 in bone, and inability of [¹¹C]PK11195 to detect lesions in AS has driven the investigation of newer TSPO tracers for the detection of inflammatory arthritis.

Objectives Here, we present data confirming the ability of the TSPO tracer [¹¹C]PBR28 to detect and quantify synovitis in both RA and PsA, and in vitro work that assesses more fully what TSPO tracer accumulation in inflamed synovium actually reflects at a cellular level, especially considering TSPO is ubiquitously expressed.

Methods 10 patients (5 with RA, 5 with PsA) with evidence of inflammation in one or both knees (as confirmed by clinical examination and US) and 4 healthy volunteers underwent PET/CT both knees using the TSPO tracer [¹¹C]PBR28. Arthritis patients underwent synovial biopsy of one knee within 7 days of scan. Healthy synovium was obtained from patients undergoing knee arthroscopy for ligamentous injury. Synovial tissue was stained for CD68, CD163 and TSPO. For in vitro work, human monocytes, lymphocytes and synovial FLS from RA patients were harvested, and macrophages differentiated from monocytes. RNA was extracted for PCR. Other cells underwent density centrifugation to extract the cytoplasmic cell fraction, and a radioligand binding assay with [³H]PBR28 was undertaken, to assess tracer binding to TSPO in each cell type

Results Tracer uptake correlated significantly with severity of inflammation on clinical examination and ultrasound, as did synovial sublining staining for CD68, TSPO and CD163 (see [table 1](#)). There was negligible staining for all stains in healthy control synovium. qPCR demonstrated highest TSPO mRNA in stimulated FLS (fold change 62.75±10.03) and M2 macrophages (60.69±2.38), with lymphocytes having the least TSPO expression. PBR28 saturation binding confirmed these findings at protein level (see graph 1).



Conclusions Our data demonstrates that the TSPO tracer PBR28 is capable of detecting and quantifying synovitis in RA and PsA. PBR28 tracer uptake correlates with macrophage marker staining, but not with fibroblast marker staining in our patient cohort. mRNA and protein data demonstrate, however, that there is a similar expression of TSPO in activated macrophages and activated FLS, hence TSPO tracer accumulation is as likely to represent FLS activation as it is macrophage activation.

References

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Disclosure of Interest None declared