I40 LEUCOCYTE INFILTRATION DURING INFLAMMATION: WHY DOES IT GO WRONG IN RHEUMATOID ARTHRITIS?

Helen McGettrick
Rheumatology Research Group, University of Birmingham, Birmingham, UK

In RA, the inappropriate recruitment of leucocytes, in particular T cells, into the joint contributes to disease pathogenesis and joint destruction. My research focuses on identifying the endogenous regulatory pathways that control the inflammatory infiltrate during inflammation and how these go wrong in RA. Using primary human cells, we have shown that rheumatoid synovial fibroblasts activate neighbouring endothelium to inappropriately recruit neutrophils and lymphocytes. In contrast, synovial fibroblasts from healthy donors or patients with resolving arthritis have an immunosuppressive effect, limiting lymphocyte adhesion to inflamed endothelium. Interestingly, synovial fibroblasts from patients with early RA (<12 weeks symptom duration) have lost this immunosuppressive capacity, allowing endothelium to support elevated levels of lymphocyte adhesion. More recently, we have identified a novel endogenous peptide-mediated (PEPITEM) pathway that suppresses T cell migration during inflammation into a range of tissues. This pathway is dysfunctional in patients with RA but can be restored by the addition of exogenous recombinant PEPITEM, indicating its potential as a therapeutic agent in the treatment of RA. Collectively these studies highlight that patients with RA exhibit defects in more than one endogenous immunosuppressive pathway, leading to deregulation of the inflammatory infiltrate during the development and progression of RA. Re-establishing these endogenous regulatory cues to turn off the pathological recruitment of leucocytes to the joint represents a novel and potentially powerful approach to treating patients with early RA.

Disclosure statement: H.M has received research funding from the Pfizer I-CRP grant scheme.