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Understanding the mechanism of activated protein C (APC) as a biological therapy in rheumatoid arthritis (RA)

A major project in the Sutton Laboratory is investigating the therapeutic effect of APC in RA. We have shown that APC can directly target RA features by i) normalising the body's immune response, ii) preventing blood vessel damage and iii) inhibiting synovial tissue invasion. Thus, unlike other biological treatments currently used for RA, which deplete specific inflammatory molecules or cells, APC has a broader action and is safe. These functions of APC are mainly mediated by its specific receptor endothelial protein C receptor (EPCR). Our most recent results show that APC can prevent arthritis in the collagen-induced arthritis model, a model of human RA. However, it cannot treat the disease once it is established. Similar results were seen in another model of RA, antigen-induced arthritis. Based on our recent publication (Xue et al, 2014, Rheum.), we now hypothesise that the high levels of tumour necrosis factor (TNF) in the disease block EPCR so that APC can no longer function - and that freeing up EPCR will allow APC to treat active disease. We aim to now conduct these experiments and provide proof-of-concept data for ultimate translation into human clinical trials.

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