EXPERIMENTAL RHEUMATOLOGY

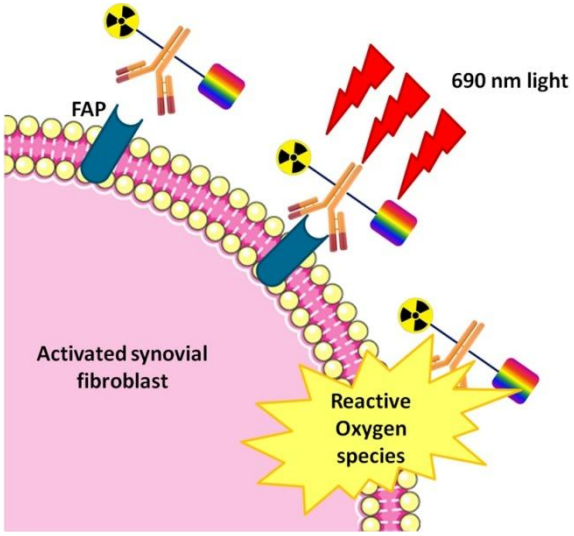
Photodynamic therapy to treat rheumatoid arthritis

Clinical Relevance

Rheumatoid Arthritis (RA) is a systemic autoimmune disease that affects up to 1% of the population worldwide. The RA pathology is characterized by chronic inflammation of the joints, leading to progressive physical disability and pain. Although the development and use of various biologicals targeting specific pathways has improved prognosis for some RA patients, approximately 30% of patients still fail to respond adequately. Therefore, the search for new therapeutic targets in RA treatment needs to continue.

Background

RA is currently treated through systemic oppression of the immune response, which is associated with systemic side-effects. A more localized, targeted therapy would be preferred to limit off-site effects. To this end targeted photodynamic therapy (PDT) is being explored as a way to selectively deplete one cell type in the affected joints.



In RA the normally quiescent synovial fibroblasts becomes activated. These activated synovial fibroblasts contribute to the disease process by producing a host of cytokines and chemokines as well as proteases, one of which is fibroblast activation protein or FAP. Depleting FAP-expressing fibroblasts could potentially disrupt the pro-inflammatory cycle that takes place in an RA joint.

Goals

We have previously demonstrated that targeting FAP using photodynamic therapy can selectively induce cell death in fibroblasts that express this marker. Depleting one cell type may invariably have effects on the surrounding cells and tissue. These effects may be beneficial in resolving the inflammation, but may also be deleterious. Therefore we wish to investigate the effects of depleting fibroblasts on other, neighbouring cells. Within this project co-cultures of activated fibroblasts and other joint resident cells will be made. The off target effects of PDT on FAP-positive fibroblasts will be investigated to characterize the consequences of this approach for other/surrounding cell types.

We Offer

The department of Experimental Rheumatology is an internationally renowned laboratory with high output in the arthritis field. Under the supervision of a PhD student and a postdoctoral fellow you will participate in a very interesting research project on a ‘hot topic’ in the RA field, while using various techniques like western blot, qPCR, luminex, FACS analysis and PDT. In addition, you will use various cell types derived from RA patient material and differentiate these to answer the research question. During this internship you will have your own specific research topic within this PDT project, and have the opportunity to learn from and contribute to our ongoing arthritis and immunology research.

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