**Investigating the chondroprotective potential of mesenchymal stem cells in arthritis**

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**Background:** Arthritis is a debilitating disease that reduces quality of life, affecting patients’ ability to carry out everyday tasks, their moods and emotions, social life and personal and social relationships. It is therefore important to find therapies to help combat the effects of this disease. Mesenchymal stem cells (MSCs) have anti-inflammatory and immunosuppressive properties and therefore have the potential to repair joint tissues that have been damaged in RA and OA. The aim of this study was to investigate the effect of injecting mesenchymal stem cells intra-articularly in mice. Previous work showed that introducing MSCs in the joints of mice with antigen-induced arthritis(AIA) resulted in less cartilage destruction. Murine mesenchymal stem cells (mMSCs) were isolated from bone marrow of mice and these mMSCs were injected into joints of mice with antigen –induced arthritis (AIA). This caused reduced joint diameter swelling compared to controls of phosphate buffered saline(PBS) injections in the other knee of the mouse. This study progresses from this work to investigate the mechanism of reduced cartilage destruction by MSCs in arthritis.

Proteoglycan loss is an indicator of early cartilage destruction. Aggrecan, the main proteoglycan in human cartilage, can be cleaved by both matrix metalloproteinases(MMPs) and a disintegrin and metalloproteinase with a thrombospondin type 1 motif(ADAMTS) at different sites. ADAMTS( or aggrecanase) cleaved aggrecan produces a NITEGE neoepitope and MMP-cleaved aggrecan produces a DIPEN neoepitope. Detection of these neoepitopes by antibodies can provide information about the major enzymes involved in aggrecan degradation in mouse cartilage and has therefore set a target for the development of new drugs designed to inhibit cartilage destruction in RA.

**Methods:** In this study, the both neoepitopes were detected by immunostaining in the cartilage of joints with AIA, using sections of joints from mice used in Kehoe’s study. The severity of cartilage damage was quantified by the presence of this stained neoepitopes after injection of MSCs, compared to control (no MSCs). Different timing of MSC administration was also tested (at day 3, 7, 14 and 28 after arthritis induction), to find which resulted in the least proteoglycan loss. This was quantified by counting the percentage of cartilage cells surrounded by NITEGE or DIPEN neoepitope-positive matrix.

**Results:** Results concluded that when normalized against the non-arthritic control, DIPEN staining scored more highly than NITEGE staining at day 3. With no MSC treatment, DIPEN staining scored more highly than NITEGE staining at all time points, but scored less than non-arthritic controls at days 14 and 28. Furthermore, on average DIPEN scored more highly than NITEGE for MSC-treated (+15.8%), no MSC (+13.1%) and controls (+7.4%).

**Conclusion:** These results suggest that MMP degradation may be more prominent than ADAMTS mediated degradation by day 3, although a larger sample size would be needed to test whether this difference is significant for later time points.