Immunomodulatory effects of equine chondroprogenitor cells in an animal model of osteoarthritis

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Osteoarthritis (OA) is a painful and debilitating joint disease with no permanent cure. Cartilage breakdown is a key feature of OA which results in pain, joint swelling and lameness. It is estimated that 60% of lameness in horses is OA-related which translates to millions of horses being affected by this disease.

Cartilage is a complex tissue to repair and even after decades of research, the efforts to completely and permanently repair cartilage have been unsuccessful. Stem cells have recently become popular as a strategy to repair cartilage in patients with OA, most commonly using cells collected from bone marrow or fat (Mesenchymal Stromal Cells (MSCs)). Although they have some advantages in healing injured cartilage, the effects are short-lived, and the repair tissue deteriorates over time. Recent research also shows that MSCs primarily act as a 'signalling cell', producing anti-inflammatory factors to help in healing and lessen pain rather than directly causing repair of the damaged cartilage.

We have found a stem cell population (Articular ChondroProgenitors (ACPs)) in normal joint cartilage that has several advantages which make it superior to MSCs as a stem cell for cartilage repair. Unlike bone marrow MSCs, they have the ability to divide and expand in culture long-term without loss of their cartilage-forming ability. In published studies and our work using horse chondroprogenitor cells, ACPs show the ability to suppress inflammation under cell culture conditions at similar levels as MSCs. But there are no studies to date that have explored if ACPs have anti-inflammatory and immunosuppressive properties in a whole living organism. This is an important piece of information that will add to the clinical utility of ACPs for the treatment of OA.

In this study, our goal is to test if injecting horse ACPs into the joints of mice with OA will result in improvement of disease symptoms and increased healing in comparison with MSCs. In addition, we aim to compare the bioactive factors secreted by ACPs and MSCs, and whether the differences in these factors can explain the differences we see in the animals receiving the different treatments. This is the first attempt to understand the immunosuppressive abilities of ACPs in an animal model. With the significant advantages that ACPs offer, an understanding of their immunosuppressive properties could increase their utility as a promising cell source for the treatment of OA. If ACPs prove to have strong immunomodulatory capacities, this will validate and increase their potential use as a cell-based product or their secreted molecules as a cell-free product for cartilage therapy.