Proceedings of German Society for Stem Cell Research - 2010 (PGSSCR)
(5th Annual Meeting)
Factors regulating stem cell behaviour – O2

Migratory progenitor cells in osteoarthritis and rheumatoid arthritis are driven by inflammatory mediators and sex hormones

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Published on 23 Oct 2010

The regeneration of diseased hyaline cartilage continues to be a great challenge, mainly because degeneration—caused either by major injury or by age-related processes—can overextend the tissue’s self-renewal capacity. Adult osteoarthritic cartilage and cartilage from rheumatoid arthritis were obtained from the knee joints of patients (ages: 65 - 75 years) suffering from late-stage osteoarthritis (OA) or rheumatoid arthritis (RA) after total knee replacement. Light microscopy, ultrastructural investigations, cell isolation, cloning and immortalization, as well as multipotent differentiation experiments were performed. Furthermore, quantitative real-time RT-PCR, Western blotting, SILAC proteomics as well as RNA interference were applied. We have recently shown, that repair tissue from late stages of osteoarthritis in humans harbors a unique progenitor cell population, termed chondrogenic progenitor cells (CPCs). These exhibit stem cell characteristics such as clonogenicity, multipotency, and migratory activity. CPCs are governed by the osteogenic transcription factor runx-2 and the chondrogenic transcription factor sox-9. They show gender differences and exhibit estrogen and progesterone receptors. Treatment, especially with estrogen, at least in vitro, can enhance their chondrogenic potential. We have now isolated a similar CPC population from RA cartilage tissue, RA-CPC are regulated via IL-17 and novel TCR receptors. Our results offer new insights into the biology of progenitor cells in the context of diseased cartilage tissue and are relevant in the development of novel therapeutics for osteoarthritis and rheumatoid arthritis. DFG IMMUNOBONE Bl 1122/1-1 Koelling S, Kruegel J, Irmer M, Path J, Sadowski B, Miró X, Miosge N (2009) Migratory chondrogeniprogenitor cells from repair tissue during the late stages of human osteoarthritis Cell Stem Cell 4:324-335. Koelling S, Miosge N (2010) Sex differences of chondrogenic progenitor cells in late stages of osteoarthritis. Arthritis and Rheumatism 64:1077-1087. Koelling S, Miosge N (2009) Stem cell therapy for cartilage regeneration in osteoarthritis. Expert Opinion on Biological Therapy 9:1-7.