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### **Gender differences in the differentiation and chondrogenic potential of progenitor cells in human osteoarthritis**

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#### **Introduction:**

Osteoarthritis (OA) is such a widespread complication of age that it is expected to become the fourth leading cause of disability by the year 2020. The prevalence and the incidence rates are significantly higher in women. The healthy, homogeneous population of chondrocytes in articular cartilage changes in the pathogenesis of OA to a heterogeneous mixture of OA chondrocytes, newly emerging elongated chondrocytes and progenitor cells, mainly found adjacent to the OA defect.

#### **Materials and Methods:**

With the help of fluorescence associated flow cytometry (FACS), micro-array and real time RT-PCR we characterized the different cell types from different patients to evaluate their chondrogenic and differentiation potential according to the gender.

#### **Results:**

In vivo, elongated chondrocytes from women and men exhibit a more fibroblast-like expression pattern than the OA chondrocytes. Micro-array analysis (Affymetrix Human Genome U133A 2.0) of healthy cartilage tissue and of the cell populations of OA tissues revealed gender specific differences: e.g., SOX-9, collagen type II and COMP turned out to be regulated; whereas fibronectin, integrin alpha 5 and collagen type I expression was unregulated between women and men. FACS analyses demonstrated progenitor cells from late stages of human OA positive for "so called" stem cell markers. Tested for their differentiation potential in vitro, the OA chondrocytes were not able to differentiate even after dedifferentiation on plastic. In contrast, approximately 20% of the elongated chondrocyte population and 75% of the progenitor cell population can be differentiated into chondrocytes, osteocytes and adipocytes.

**Discussion:**

We present evidence that the elongated chondrocytes from late stages of OA originate from the progenitor cell population. These progenitor cells have a strong chondrogenic potential which can be enhanced by suppressing their osteogenic differentiation. Their differentiation potential and their matrix production capacity differ between women and men, which is in line with the differences in the prevalence and the incidence rates of OA. The regulatory influences leading to these differences need further investigations to allow a better understanding of the pathogenesis of OA and hopefully to reveal new aspects for therapeutic interventions. The results support our opinion that the progenitor cells seem to be a promising starting point for new concepts of a cell biological treatment of OA.

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