STEM CELLS

Progenitor cells found in osteoarthritic tissue

Regenerative cell biological therapy could provide an attractive treatment option for osteoarthritis (OA), so does diseased adult cartilage tissue contain cells with progenitor cell characteristics? Koelling *et al.* set out to address this issue, and report their positive findings in *Cell Stem Cell*.

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The researchers identified a migratory cell population with progenitor cell characteristics from tissue from humans with late-stage OA and further characterized these primary chondrogenic progenitor cells (CPCs) after immortalizing them (to avoid cell senescence). No single marker identified

the cells (similar to what is found in other progenitor cells), but they showed high levels of collagen type I and intermediate levels of SOX9 and RUNX2, and expressed the surface markers CD13, CD29, CD44, CD73, CD90 and CD105.

The CPCs were multipotent, and could be induced to undergo adipogenic, osteogenic and—most importantly—chondrogenic differentiation. Simply culturing the CPCs in a three-dimensional (3D) matrix in the absence of chondrogenic supplementation induced chondrogenic differentiation. The addition of transforming growth factor β 3 and bone-morphogenetic protein 6 to CPCs in 3D culture increased the extent of fiber formation and both the mRNA and protein levels of collagen type II compared with controls. Whereas SOX9 expression was unaffected by these chondrogenic mediators, the levels of RUNX2 transcripts decreased. As RUNX2 is a major osteogenic transcription factor, Koelling

et al. assessed the effects of its knockdown by RNA interference on the chondrogenic potential of CPCs. In 3D culture, RUNX2 knockdown resulted in an increase in the expression of chondrogenic markers, such as SOX9, aggrecan and collagen type II, and a decrease in their degrading enzymes.

Finally, CPCs were shown to migrate on diseased late-stage OA tissue *in vitro* and to populate this tissue *ex vivo*. As these cells are already present in diseased tissue, the investigators point out that they “...may be an ideal starting point for the exploration of osteoarthritis regenerative therapy options”, but correctly note that “Identifying the optimal conditions to manipulate CPCs such that they can exhibit sustained chondrogenic capacities will be crucial”.

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Original article Koelling, S. *et al.* Migratory chondrogenic progenitor cells from repair tissue during the later stages of human osteoarthritis. *Cell Stem Cell* 4, 324–335 (2009).