ABSTRACT INTRODUCTION:

Osteoarthritis (OA) is a disease of articular joints that affects millions of people. The disease leads to total destruction of the articular cartilage, sclerosis of underlying bone, osteophyte formation etc., all leading to loss of movement and pain. It is still largely unknown what causes OA. However, it is thought that developmental processes important in embryonic development are recapitulated in osteoarthritic cartilage. Several members of the wnt and frizzled (Fzd) families are involved in embryonic development of cartilage and bone. The aim of this study is to perform a longitudinal expression analysis of Wnt/Fzd-related genes during developmental processes for OA and to verify the expression of selected genes in human tissue obtained from knee replacement surgery.

RESULTS SECTION:

Several genes from the wnt and Fzd families, as well as genes that are involved in wnt-signaling, were detected and/or regulated in the OA models. Wnt-induced secreted protein-1 (WISP-1) was strongly upregulated compared to control (left) knee joints (Figure 1). In the synovium, expression of WISP1 at day 7, 21 and 42 was increased 39-fold, 160-fold and 9-fold respectively. Experiments using STR/ort mice reinforced these results, since WISP1 (cartilage and synovium) and Wnt16 (synovium) were also upregulated in STR/ort tissue compared to CBA tissue. The increased cartilage expression of WISP1 in experimental OA was validated in human OA cartilage. In concordance with the experimental OA, WISP1 expression in human knee joint cartilage was significantly upregulated (2.65 fold, p<0.03) compared to naïve, left knee joints. The increased synovial expression of WISP1 can inhibit the matrix producing effects on matrix production by chondrocytes in OA cartilage, since it indicates that the increased expression of WISP1 may have inhibiting effects on matrix production by chondrocytes in OA cartilage. Another novel finding is the enhanced expression of WISP1 in synovial tissue, since WISP1 (cartilage and synovium) and Wnt16 (synovium) were also upregulated in STR/ort tissue compared to CBA tissue. These results show that during experimental OA, Wnt-related processes are regulated as was indicated by the markedly increased synovial expression of wnt2b and wnt16, a gene that has been implicated in the dedifferentiation of chondrocytes. Another novel finding is the enhanced expression of WISP1 in synovium and cartilage. This does not only signify that wnt-signaling pathways are activated, but it also indicates that the increased expression of WISP1 may have inhibiting effects on matrix production by chondrocytes in OA cartilage, since it has been described that WISP1 can inhibit the matrix producing chondrocyte phenotype.

DISCUSSION:

These results show that during experimental OA, Wnt-related processes are regulated as was indicated by the markedly increased synovial expression of wnt2b and wnt16, a gene that has been implicated in the dedifferentiation of chondrocytes. Another novel finding is the enhanced expression of WISP1 in synovium and cartilage. This does not only signify that wnt-signaling pathways are activated, but it also indicates that the increased expression of WISP1 may have inhibiting effects on matrix production by chondrocytes in OA cartilage, since it has been described that WISP1 can inhibit the matrix producing chondrocyte phenotype.

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