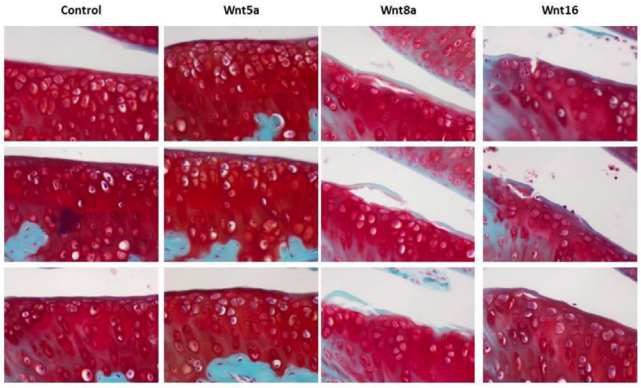
virus and 80% ($N = 5$) for Wnt16 overexpression, but only 20% ($n = 5$) for the control virus.

Conclusions: Members of the canonical Wnt signaling pathway produced in the synovium may play an important role in OA pathology by increasing the expression of MMPs in the synovium. In addition, synovium-specific overexpression of Wnt signaling members, as is found in experimental OA, induces cartilage damage in vivo. This underlines synovial Wnt/WISP1 expression to be a potential target for OA therapy.



Overexpression of Wnt8a and Wnt16, but not Wnt5a, results in increased cartilage damage. Genes of the Wnt signaling pathway were overexpressed *in vivo* with the use of adenoviral vectors. Seven days after overexpression, we found highly increased incidences of cartilage lesions for Wnt8a and Wnt16 overexpression as compared with overexpression of the control virus. Overexpression of Wnt5a did not result in increased cartilage damage.

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INFRAPATELLAR FAT PAD INDUCES AN INFLAMMATORY AND CATABOLIC PHENOTYPE ON AUTOLOGOUS FIBROBLAST-LIKE SYNOVIOCYTES FROM SEVERE KNEE OA PATIENTS

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Purpose: Infrapatellar fat pad (IFP) of the knee joint displays an inflammatory phenotype in osteoarthritis (OA). In addition to cartilage and bone tissues, OA pathophysiologic process involves synovial membrane, which is the seat of an heterogeneous inflammation. IFP location adjacent to the synovial membrane suggests that IFP could be involved in the induction of OA synovitis. We have investigated the response of fibroblast-like synoviocytes (FLS) to autologous IFP and subcutaneous adipose tissue (SCAT) from patients with severe knee OA.

Methods: IFP, SCAT and autologous synovial membrane closed to IFP were harvested during total knee replacement for severe OA from 28 patients. FLS from 14 patients were stimulated by autologous IFP- or SCAT-conditioned media and the gene expression and release of IL-6, IL-8, COX-2, mPGES, PGE2, MMP-1, MMP-3, and MMP-9 were evaluated. IL-6, IL-6R, IL-8, TNF-α, PGE2, IL-1β and IFN-γ secretion by IFP and SCAT were quantified by ELISA. FLS were treated with PGE2 receptor antagonists to evaluate the contribution of IFP-derived PGE2 in the inflammatory response of FLS to IFP.

Results: IFP conditioned media induced the expression and the release of IL-6, IL-8 and PGE2, the expression of COX-2 and the expression and/or secretion of MMP-1, MMP-3 and MMP-9 by FLS. The stimulation was always stronger when FLS were stimulated with IFP as compared to SCAT conditioned media. Significantly higher amount of IL-6, sIL-6R, IL-8, TNF-α and PGE2 was released from IFP to SCAT, especially PGE2 whose secretion was 70-fold higher by IFP ($p < 0.0001$). The rates of inflammatory mediators released by FLS were positively associated with PGE2 amounts produced by IFP. PGE2 receptor antagonists dose-dependently inhibited the release of IL-6, IL-8 and PGE2 by IFP-stimulated FLS.

Conclusion: Our results confirmed that IFP was a particular adipose tissue, with a higher inflammatory profile than SCAT from the same patient. We also brought out that IFP induced an inflammatory and catabolic phenotype on autologous FLS. Thus, in knee OA, IFP could contribute to the onset of inflammatory alterations within the synovial membrane especially through a high secretion of PGE2.

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CROSS-SECTIONAL AND LONGITUDINAL ASSOCIATIONS BETWEEN KNEE JOINT EFFUSION AND OSTEOARTHRITIC STRUCTURAL CHANGES IN OLDER ADULTS

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Purpose: Multiple joint pathological changes such as synovial effusion, cartilage and subchondral bone lesions are involved in osteoarthritis (OA). The causal relationship between joint effusion and other knee structural changes was not clear. This study aimed to determine the cross-sectional and longitudinal associations between knee joint effusion at different compartments and knee osteoarthritic changes in older adults.

Methods: A cohort of 976 randomly selected subjects from local community (mean 62 years, 50% female) was studied at baseline and 416 followed up 2.7 years later. Radiographic knee osteophyte and joint space narrowing (JSN) were assessed using the OARSI atlas. T2-weighted fat saturated magnetic resonance imaging (MRI) was utilized to assess knee effusion at 4 compartments: suprapatellar pouch, central portion, posterior femoral recess, and subpopliteal recess. Cartilage volume, cartilage defects, and bone marrow lesions (BMLs) were measured using MRI at baseline and 2.7 years later. Multivariable generalized linear models with Poisson regression analyses or linear regression were used to estimate prevalence ratios (PR) relative risks (RR) or regression coefficient (β).

Results: Cross-sectionally, knee effusion at suprapatellar pouch was associated with lateral tibial (β=-76.4, $p < 0.01$) and patellar (β=-119.04, $p < 0.01$) cartilage volume, cartilage defect presence at any compartment (PR: 1.18, $p < 0.01$), BML presence at any compartment (PR: 1.24, $p < 0.01$), any moderate to severe JSN (PR: 1.53, $p < 0.01$) and any osteophyte (PR: 1.53, $p < 0.001$). Effusion at central portion was associated with cartilage defect presence at any compartment (PR: 1.08, $p = 0.05$), BML presence at any compartment (PR: 1.19, $p < 0.01$) and lateral tibiofemoral osteophytes (PR: 1.69, $p = 0.01$). Effusion at posterior femoral recess was associated with patellar cartilage volume (β=-125.24, $p < 0.01$) and cartilage defect presence at any compartment (PR: 1.12, $p < 0.01$). Lastly, effusion at subpopliteal recess was associated with patellar cartilage volume (β=-79.35, $p = 0.01$), cartilage defect presence at any compartment (PR: 1.10, $p < 0.01$), BML presence at any compartment (PR: 1.13, $p = 0.01$), moderate to severe JSN (PR: 1.32, $p < 0.01$) and medial tibiofemoral osteophyte (PR: 1.31, $p = 0.03$).

Longitudinally, suprapatellar pouch effusion was associated with change in medial tibial cartilage volume (β=-0.82%, $p = 0.03$), increases in cartilage defects at patellar and medial and lateral tibiofemoral compartments (RR: 1.24-1.32, $p < 0.01$), and an increase in BMLs at lateral tibiofemoral compartment (RR: 1.24, $p = 0.04$). Effusion at posterior femoral recess was associated with increases in medial tibiofemoral (RR: 1.26, $p < 0.01$) and patellar cartilage defects (RR: 1.11, $p = 0.03$) and an increase in any BMLs (RR: 1.39, $p = 0.03$). Effusion at subpopliteal recess was associated with change in patellar cartilage volume (β=-0.70%, $p = 0.03$), increases in medial tibiofemoral (RR: 1.31, $p < 0.01$) and patellar (RR: 1.15, $p < 0.01$) cartilage defects. In contrast, effusion at central portion was not significantly associated with changes in cartilage volume, cartilage defects and BMLs.

All these analyses were performed after adjustment for after adjustment for age, gender, BMI, rheumatoid arthritis, and/or radiographic osteoarthritis (ROA).

Conclusions: Knee joint effusions are both cross-sectionally and longitudinally associated with knee osteoarthritic structural changes suggesting a potential causal relationship. While suprapatellar pouch effusion is most consistently associated with knee structural changes, central portion effusion is not associated with changes in knee structures over time.