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ferences were found in the percentages of the immune cell populations studied between these tissues, luminex analyses of fat-conditioned media revealed significantly higher concentrations of IL-6, TNFα, adipsin and adiponectin from IFP than Sc adipose tissue. Similar differences were found in adipocyte-conditioned media from these two adipose tissues. Moreover, a positive correlation between TNFα release from fat-conditioned medium and body mass index was found in IFP ($r = 0.338$, $p = 0.046$).
Conclusions: We show profound differences in inflammatory factors secreted from IFP compared to Sc adipose tissue. Moreover, our data indicate an influence of BMI on the inflammatory mediators released by IPF. In summary, these data suggest that IFP is qualitatively different from Sc adipose tissue and IFP-derived soluble mediators could contribute to pathophysiological processes in the OA knee joint.

014

A COMPOSITE SCORE OF MULTI-JOINT RADIOGRAPHIC OSTEOARTHRITIS: THE JOHNSTON COUNTY OSTEOARTHRITIS PROJECT

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Purpose: To determine whether a psychometrically derived composite score could be developed to capture the whole-body burden of radiographic OA (rOA) in multiple joint sites (hands, tibiofemoral joint (TFJ), patellofemoral joint (PFJ), hips, and lumbosacral spine).
Methods: Factor analysis was used to determine the number of distinct variables into which information from individual body sites could be meaningfully classified, using data from a cross-sectional sample of the Johnston County OA Project, including individuals participating in the 2nd follow-up (n=1079) and in the 1st cohort enrichment (n=1012), with available multi-joint radiographic data (67% women, 34% African Americans, mean age 65±11 years). Radiographs of the hands (bilateral posteroanterior [PA] views, 30 total joints), TFJ (PA fixed-flexion views), and hips (supine anteroposterior pelvis) were read for Kellgren-Lawrence grade (KL 0-4) at each joint. Radiographs of the lumbosacral spine (lateral view) were read for osteophytes (OST) and disc space narrowing (DN), and the PFJs (sunrise views) were read for OST(0-3), using the Burnett atlas. A single expert reader with previously shown high reliability read all radiographs (intra-rater κ=0.89).
Based on the eigenvalues (measure of the information contained in a factor), 3 factors were retained and oblique rotation performed to allow correlation between factors. Radiographic variables with loadings <0.4 were dropped from the final model (hip KL, lumbosacral OST/DN, 1st metacarpophalangeal (MCP) joints and carpometacarpal joints). The sum scores and reliability (reliability=α, the proportion of variance in a score attributable to the "true" score) of the 3 factors were determined. These factors were subjected to higher order factor analysis to determine loadings and weighting. Finally, a sum score of all 3 factors was determined.
Results: Factor analysis of the retained radiographic variables produced 3 strong factors. Factor 1 consisted of the bilateral 1st interphalangeal joints, distal interphalangeal (DIP) joints 2-5, and proximal interphalangeal (PIP) joints 2-5 (18 joints), with α=0.96. Factor 2 included MCP joints, bilateral 2-5 (8 joints), with α=0.81. Factor 3 included bilateral TFJs and PFJs (4 joints), with α=0.87. Higher order factor analysis showed similar loadings of all 3 factors on one higher order factor, indicating that the 3 factors could be incorporated into one score using their unweighted averages. However, the eigenvalue for this higher order factor was <1, so the individual factors contain more information than the single composite score, which also had a lower α (0.59).
Conclusions: The 3 factors obtained in this analysis suggest that the variables contained in each factor share an underlying cause. OA in the DIP and PIP joints share a similar cause, while the MCP joints appear to be distinct. OA in the TFJ and PFJ also appear to share a similar cause. These 3 factors were more reliable individually than as an overall sum score, indicating that they provide more information separately. Using such factors to reflect multi-joint rOA in statistical models can reduce the number of variables needed (i.e. from 30 scores to 3 factors) and increase precision. The weak loading of some radiographic variables could reflect a problem with standard measurement (hip KL, spine OST/DN), or a true difference in underlying cause for OA at these joints.

015

ACCELERATION OF OSTEOARTHRITIS PROGRESSION BY INDUCED EXPRESSION OF DISCOIDIN DOMAIN RECEPTOR 2 IN MATURE ARTICULAR CARTILAGE OF MOUSE KNEE JOINTS

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Purpose: Discoidin domain receptor 2 (DDR2) is a cell membrane tyrosine kinase receptor for native type II collagen. Results from this and other laboratories indicate that activation of DDR2 by the interaction of the receptor with native type II collagen induces matrix metalloproteinase 13 (MMP-13) and increases expression of the receptor itself in chondrocytes. Data from our studies also demonstrates that increased expression of MMP-13 is associated with elevated expression of DDR2 in human osteoarthritic (OA) cartilages and in knee and temporomandibular joints in mouse models of OA. Moreover, the reduction of Ddr2 expression attenuated the OA progression in the joints of the mouse models of OA. It is of interest to note that the pericellular matrix, which separates chondrocytes from the interterritorial matrix of mature articular cartilage, contains no type II collagen. We hypothesize, therefore, that at the very early stage of OA progression, depletion of proteoglycans in the extracellular matrix, and particularly the degradation of the pericellular matrix, exposes chondrocytes to type II collagen. As a consequence, DDR2 is activated to induce MMP-13 in chondrocytes.
Methods: We used the tetracycline-inducible expression system (Tet-off) to overexpress DDR2 in mature articular cartilage of mouse knee joints under the control of the mouse cartilage oligomeric matrix protein gene promoter. Pregnant mice were treated with doxycycline and females with litters were continuously treated with doxycycline until weaning (4-week-old). Transgenic mice and their wild-type littermates were maintained with regular water and food and sacrificed at the ages of 8, 12 and 16 weeks, at which time the knee joints were collected. Serial paraffin sections of the knee joints were prepared (n=8/group/stage). Transgenic mice and wild-type littermates at 12 weeks of age were also subjected to microsurgery to cause destabilization of the media meniscus (DMM). Serial paraffin sections of the knee joints were prepared from mice at 2, 4, 8 and 12 weeks following the surgery (n=8/group/time point). Immunohistostaining was performed with polyclonal antibodies against DDR2 and Tet-Repressor protein (TetR). DDR2 mRNA was measured by real-time PCR. Joint morphology was examined by Safranin O/Fast green staining and evaluated by a modified Mankin scoring system.
Results: Increased expression of DDR2 was detected in mature articular cartilages of knee joints from transgenic mice. The level of DDR2 mRNA was increased about 2.5-fold in transgenic mice, compared to the wild-type littermates. No OA pathologic change was observed in transgenic mice overexpressing DDR2 at any post-natal stage. However, upon challenge with DMM surgery, we found that the OA pathologic progression was accelerated in the knee joints of the DDR2-overexpressing transgenic mice.
Conclusions: These results are consistent with our hypothesis that the pericellular matrix is a critical structure to prevent type II collagen from binding DDR2. In the case of our transgenic mice, although there was more DDR2, the receptors were separated from the type II collagen fibrils by the pericellular matrix in normal conditions. Thus, DDR2 was not activated and MMP-13 expression and activity were not induced in chondrocytes in the transgenic mouse knee joints. In contrast, the up-regulated expression of DDR2 accelerates OA progression caused by the DMM surgery. We conclude that DDR2 can accelerate OA progression, but cannot initiate articular cartilage degeneration, in the absence of biochemical or biomechanical disruption of the pericellular matrix.

016

MICE OVER-EXPRESSING SALMON CALCITONIN HAVE STRONGLY ATTENUATED BONE AND CARTILAGE CHANGES AFTER DESTABILIZATION OF THE MEDIAL MENISCUS

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Purpose: The pathogenesis of osteoarthritis (OA) involves both bone and