Therefore, a very sensitive ELISA was established but again no differential binding to the two different binding sites could be observed using ETS-1 antibodies in competitive displacement experiments. ChIP assays using the ETS-1 antibodies also showed no divers binding to the two variants.
Conclusions: As all assays showed no differential binding of ETS-1 to the two variants, it can be excluded that ETS-1 is the responsible factor for the increased amount of N-cadherin in OASF. Now zinc finger transcription factors, especially ZNF35, and their potential effect on N-cadherin expression levels in OASF are analyzed. Furthermore, the function of high N-cadherin levels expressed by OASF in contrast to the protective effect of even higher N-cadherin levels in patients carrying the minor SNP variant has to be examined. In summary, these results show that the influence of N-cadherin on the aggressiveness of OASF is complex and requires further investigation.

401
IDENTIFICATION OF GENES INVOLVED IN THE INITIATION OF OSTEOARTHRITIS

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Objective: Osteoarthritis (OA) is the most prevalent form of arthritis and is characterized primarily by the degeneration of articular cartilage. Several gene expression studies have been performed to identify genes involve in the pathogenesis of OA. However, in order to obtain sufficient quantity and quality RNA for gene expression study, large regions of cartilage are often required. Cartilage is a very heterogeneous tissue, the cartilage used in prior studies may appear normal but they might consist of OA at different stages (different severity). The aim of this study is to select small areas from osteoarthritic cartilages which represent different severity to provide a more complete picture of the molecular alternations in OA pathogenesis as well as to identify genes involved in the initiation of OA.
Methods: Joint tissues were collected from the knee tibia plateau from primary OA and non-OA patients undergoing total knee arthroplasty. Severity of destruction was estimated based on histopathology assessment (OARSI grading system). Each tibia plateau was divided into three parts: outer lateral tibia (oLT) regions defined as undamaged stage (OARSI score: OA=5.23±1.95, n=67; Normal= 2±2, n=5), inner lateral tibia (iLT) regions defined as intermediate stage (OARSI score: OA=5.23±1.95, n=71; Normal= 4, n=5), and medial tibia (MT) regions defined as damage stage (OARSI score: OA=16.8±2.56, n=52; Normal= 4.8±1.09, n=5). Expression profiling analysis was performed using Agilent microarray (OA: n=17 at oLT, n=13 at iLT, n=12 at MT; and n= 4 from non-OA at the three regions) and real-time quantitative PCR using a second cohort of patients were performed for replication.
Results: Our results revealed that 958 transcripts were significantly up or down regulated at least 2-fold between these three stages. These genes were related to the cell matrix interaction, extracellular matrix remodeling, bone development, inflammation, cytokine, cell proliferation, WNT signaling.
Conclusion: This study revealed some novel genes which have not been reported in cartilage to play a role in the pathology of OA. These results identify molecular targets that can be further investigated in the search for therapy or as biomarker for OA.

402
GENETIC POLYMORPHISM IN GDF-5 GENE AS RISK FACTOR FOR DEVELOPMENT AND PROGRESSION OF OSTEOARTHRITIS KNEE

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Purpose: In a case-control study, investigate the association of SNP in GDF- 5 gene with osteoarthritis knee
Methods: In a case-control study, 300 cases with knee osteoarthritis and an equal number of age, gender matched healthy controls were included. Cases were diagnosed using the ACR Guidelines of knee osteoarthritis (KOA). Clinical symptoms were assessed with the knee specific WOMAC index and VAS for knee pain. The severity of disease was determined by radiological KL grades (Kellgren Lawren). The informed consent of the patients was obtained for the participation in this study. The study was approved by the Institutional Ethics Committee. The genomic DNA samples were isolated from blood and polymorphic study was done by polymerase chain reaction (PCR) with restriction fragments length polymorphism (RFLP). All statistical analysis was performed with the SPSS software package (version 16.0 for windows; SPSS Chicago, IL).
Results: The GDF-5 (BSiE1) genotypes were found to be present at significantly higher frequency in cases than in controls, resulting in about 1.62 fold increase of OA risk (P Value=0.040). OA knee was found to be significantly associated with BMI (P Value=0.00). A significant association was found with clinical score of knee OA - VAS with poor and good index (P value=0.010 and 0.026 respectively) and in WOMAC with poor index only (P value=0.0040). On stratifying all osteoarthritis subjects into 3 groups according to severity (KL grade 2 minimal, grade 3 moderate and grade 4 severe OA), no significant association was found.
Conclusions: GDF5, are now known to be consistently associated with the risk of knee OA, in different population. An association between the +104T/C GDF5 polymorphism with knee OA in Indian population further confirms a strong genetic influence of this SNP in KOA. This can serve as a potential biomarker and a risk factor for KOA. It may become a gateway for further research into epigenetic of this SNP, highlighting potential pathways for prevention and therapeutic intervention of knee osteoarthritis

Imaging & Joint Morphometry

403
JOINT SHAPE AS A PREDICTOR OF END-STAGE OSTEOARTHRITIS OF THE HIP: A 19 YEAR RETROSPECTIVE ANALYSIS OF THE CHINGFORD STUDY.

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Purpose: Abnormalities in the shape of the hip joint are thought to be important factors in the development of osteoarthritis (OA) of the hip. Quantifying these changes in shape may help us to understand their role in the progression of the disease. Active Shape Modelling (ASM) of the hip enables sensitive quantification of changes in hip morphology. In this study ASM was used to examine the relationship of hip shape and the risk of end-stage OA in a group of women who have undergone total hip arthroplasty (THA). The results were compared with a previous study by Nicholls *et al.* where morphological parameters of the hip were measured in the same subjects with Hip Morf 2.0 software.
Methods: 44 women (aged 45 - 65) were selected from 1003 participants in the Chingford Study. The subjects belonged to 2 groups: 22 who had undergone THA by year 20 of the study (THA group) and 22 randomly selected controls who were THA - free in both hips by year 20 (control group). Pelvic radiographs, taken at year 2 of the study, were examined. A 66 point ASM template was applied to one hip joint from each radiograph that included the proximal femur, osteophytes and part of the pelvis. The first 10 scores of shape variance, or mode scores, were calculated for each subject. T-tests and logistic regression were used to compare differences between the control and THA groups. Pearson correlation was used to compare the results of the ASM and Hip Morf outputs (SPSS v19).
Results: Mode 6 score was significantly higher in the THA group compared with the control group, (P=0.02), as seen in the figure. This was still significant after adjusting for age, height, weight and Kellgren Lawrence Grade, (P=0.04), odds ratio 3.3 (95% CI 1.1-10.2). A higher Mode 6 score was significantly correlated with several morphological parameters from the previous study (P<0.05) which were significantly associated with an increased risk of THA, including a higher alpha angle, a smaller joint space width (JSW), a wider femoral neck, an increased modified triangular index height and a lower femoral head - neck ratio. However it was not significantly correlated with the extrusion index or lateral centre edge angle, both of which were identified as key factors in the previous study.
Conclusions: The shape identified as high risk by ASM incorporated several individual morphological features identified by the Hip Morf software and is similar in appearance to the classical 'pistol-grip' shape