the nine SNPs. Luciferase reporter assays were used to assess if the presence of any of the alleles influenced the enhancer activity of the constructs in the U2OS osteosarcoma cell line, which expresses both genes.

Results: There was a significant increase in PTHLH expression in OA females relative to NOF females (p = 0.02), however there was no evidence for any significant correlation between PTHLH expression and rs10492367 genotype in OA cartilage. Similarly, there was no correlation between KLHDC5 expression and rs10492367 genotype. In addition, although allelic imbalance was observed, it did not correlate with the OA association SNP genotype. In the U2OS cell line luciferase assays, the OA associated alleles of the intergenic SNPs rs11049206 and rs58649696 resulted in significantly reduced enhancer activity relative to the non-OA alleles (p = 0.0025 and p > 0.0001, respectively).

Conclusions: In OA cartilage, our data does not support an association of rs10492367 with OA by mediating its effect on PTHLH or KLHDC5 region. This may be due to the current analysis being limited to the aforementioned genes in end stage OA cartilage, as the OA associated region may be exerting its effects on other genes, in other tissue types or at different stages of development. However, luciferase reporter assays in an osteosarcoma cell line identified two intergenic SNPs in high LD with the associated SNP rs10492367 that independently resulted in reduced enhancer activity when the OA associated alleles were present. This current research therefore highlights the functional activity of the OA associated region marked by rs10492367.

424 ADIPOSE TISSUE ASSOCIATED GENES IN HAND OSTEOARTHRITIS IN FINNISH WOMEN

Purpose: Osteoarthritis (OA) is the most common joint disorder, the joints of the hand being the most frequent site affected. Available evidence suggests that genetic factors may play a major role in the etiology of OA. We chose to analyze in our hand OA material 21 single nucleotide polymorphisms (SNPs) from 10 adipose tissue associated genes (FTO, LEPR, ADIPOQ, RETN, NAMPT, SERPINA12, ITLN, RARRES2, and APLN) and their association with OA.

Methods: Bilateral hand radiographs of 542 occupationally active Finnish female dentists and teachers aged 45-63 years were examined and classified for the presence of OA by using reference images. The genotypes were determined by PCR-based methods. Data regarding joint pain and other risk factors were collected by a questionnaire. Associations between the SNPs and hand OA were studied by IBM SPSS statistical package Version 20 using principle component analysis based genetic weighted scores and logistic regression.

Results: Association of studied SNPs to hand OA phenotypes were found from LEPR, RARRES2, RETN and APLN genes. FTO and INTL1 SNPs had borderline significant associations to hand OA phenotypes. Principle component analysis resulted in 11 principle components weighted by their genetic scores. Component 4 including four ADIPOQ SNPs, component 6 including RARRES2 SNP, and component 8 including APLN SNP had association to hand OA phenotypes.

Conclusions: Our results suggest that ADIPOQ, LEPR, RARRES2, RETN and APLN genes may play role in hand OA etiology in Finnish women.

425 THE OSTEOARTHRITIS ASSOCIATION MARKED BY SNP rs6094710 MEDIATES ITS EFFECT BY REDUCING THE EXPRESSION OF NCOA3 IN JOINT TISSUES
M.D. Rushton, F.H. Gee, L.N. Reynard, J. Loughlin. Newcastle Univ., Newcastle upon Tyne, United Kingdom

Purpose: Recently it has been reported that the rare single nucleotide polymorphism (SNP) rs6094710 is associated with hip osteoarthritis (OA) in European populations. The SNP is a G/A transition, with the A-allele having a frequency of 4%. The A-allele is more common in OA cases versus controls and this association reached genome-wide significance, with a p-value of 7.9 • 10^{-9} and odds ratio of 1.28, rs6094710 is intergenic, maps to chromosome 20q12 and is located upstream of the gene NCOA3, which codes for nuclear receptor co-activator 3. This protein interacts with nuclear hormone receptors and has histone acetyltransferase activity. Prior to the genetic study there were no reports of this protein having a role in OA. rs6094710 is in perfect linkage disequilibrium with rs6094752, a missense polymorphism leading to an amino acid change at position 218 of the NCOA3 protein. Homozygosity of the rare (non-obesity-associated) that regulates appetite. Genome-wide association studies (GWAS) have identified several single nucleotide polymorphisms (SNPs) associated with obesity and MetS. One of the most investigated genes has been FTO (fat mass- and obesity-associated) that regulates appetite. Genome-wide association studies have identified that polymorphisms in the FTO gene are associated also with risk of OA.

Methods: We chose to analyze 58 SNPs from 45 genes and their association to knee OA in Finnish Health 2000 Survey material. The Health 2000 Survey was conducted in Finland between fall 2000 and spring 2001. It is a representative sample of the Finnish population (n = 3028). The subjects were aged between 30 and 99. Knee osteoarthritis was diagnosed in 6.1 % of men and 8.3 % of women. For the genetic analyses
Change in semi-quantitative feature at 24 months and prediction of case control status OR (95% CI) p

<table>
<thead>
<tr>
<th>Semi-quantitative feature</th>
<th>Case (JL and pain) (n = 194)</th>
<th>Super Control (n = 200)</th>
<th>Pain Case (n = 103)</th>
<th>JSL Case (n = 103)</th>
<th>Case (JL and pain) (n = 194)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in number of subregions affected by any BML</td>
<td>1.1 (1.0,1.4) 0.1572</td>
<td>Ref</td>
<td>1.0 (0.8,1.3) 0.8961</td>
<td>1.4 (1.1,1.8) 0.0059</td>
<td>1.3 (1.0,1.6) 0.0375</td>
</tr>
<tr>
<td>Max change in BML score across all subregions in knee</td>
<td>1.2 (1.0,1.4) 0.0122</td>
<td>Ref</td>
<td>0.9 (0.7,1.1) 0.3548</td>
<td>1.5 (1.2,1.9) 0.0013</td>
<td>1.3 (1.1,1.6) 0.0037</td>
</tr>
<tr>
<td>Change in number of medial tibio-femoral subregions affected by any BML</td>
<td>1.5 (1.1,1.8) 0.0023</td>
<td>Ref</td>
<td>0.9 (0.6,1.4) 0.7385</td>
<td>2.0 (1.4,2.8) 0.0002</td>
<td>1.8 (1.3,2.5) 0.0001</td>
</tr>
<tr>
<td>Max change in BML score in medial tibio-femoral subregion</td>
<td>1.5 (1.3,1.8) &lt;0.0001</td>
<td>Ref</td>
<td>1.0 (0.8,1.4) 0.7878</td>
<td>2.3 (1.8,2.9) &lt;0.0001</td>
<td>2.0 (1.6,2.5) &lt;0.0001</td>
</tr>
<tr>
<td>Change inter-condylar synovitis</td>
<td>2.2 (1.4,3.6) 0.0015</td>
<td>Ref</td>
<td>1.0 (0.5,2.2) 0.9106</td>
<td>1.7 (0.8,3.6) 0.1615</td>
<td>2.6 (1.4,4.7) 0.0018</td>
</tr>
<tr>
<td>Change in whole knee effusion</td>
<td>2.2 (1.6,2.8) &lt;0.0001</td>
<td>Ref</td>
<td>1.2 (0.8,1.8) 0.2946</td>
<td>1.5 (1.0,2.1) 0.0318</td>
<td>2.5 (1.8,3.5) &lt;0.0001</td>
</tr>
</tbody>
</table>

Imaging
427 PRELIMINARY ASSESSMENT OF PREDICTIVE VALIDITY OF SEMI-QUANTITATIVE MRI BIOMARKERS IN KNEE OA – THE FNIH OA BIOMARKERS CONSORTIUM

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Purpose: Identification of biomarkers associated with OA disease progression is of critical importance to advance the development of disease modifying therapies. The objective of this study is to investigate if change in semi-quantitative measures of joint morphology over 24 months is associated with clinically relevant progression in knee OA over a 48-month follow-up period.

Methods: The FNIH OA Biomarkers Consortium undertook a nested case-control study of progressive knee OA within the Osteoarthritis Initiative (OAI). The case group (n = 194) is defined by the combination of knee radiographic outcome (medial tibiofemoral joint space loss (mTF JSL) ≥0.7 mm) and symptom outcome (persistent worsening in WOMAC pain score, reaching a minimum clinically important threshold of 9 points (change from baseline) on a 0-100 normalised scale) each achieved for the first time at the 24, 36 or 48 month follow-up compared to baseline. Main inclusion criteria were a Kellgren Lawrence grade (KLG) 1, 2 or 3 at baseline from central reading and availability of knee radiograph and quantitative MRI (qMRI) measures in knee osteoarthritis (OA) – particularly those of large effect size. To maximise the sample size for analysis, controls were selected from the OAI as follows: those with a KLG of 0 at baseline from central reading and availability of knee radiograph and no evidence of any knee OA.

428 QUANTITATIVE MRI MEASURES OF BONE MARROW LesION VOLUME PREDICT TOTAL KNEE REPLACEMENT

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Purpose: Quantitative MRI (qMRI) measures in knee osteoarthritis (OA) capable of predicting key clinical endpoints such as total knee replacement (TKR) have promise as diagnostic biomarkers. Recently, it was reported that very large BML volume (measured semi-quantitatively) in the medial tibiofemoral joint predicted a TKR 1 year later. We now use a recently validated rapid qMRI software tool to examine whether BML volume and change in volume predicts TKR 1 and 2 years later. The purpose of this study was to examine the longitudinal relationship between BML volume and those who received a TKR, compared with control knees with the same radiographic grade that did not receive a TKR.

Materials and methods: A nested case-control study was conducted in the Osteoarthritis Initiative (OAI), a multicenter cohort of 4796 participants with or at risk for knee OA. Subjects who received TKR by the 48-month visit who also had MRI scans (3T sagittal intermediate-weighted turbo spin-echo fat-suppressed, 0.357 × 0.357 × 3.0 mm, TR 3200 ms, TE 30 ms, intermediate-weighted) available for the 12 and 24 month visit prior to the TKR were designated cases. Cases were matched 1:1 with subjects who did not receive TKR but were the same radiographic disease grade (K-L grade score), same gender and age of the case. Quantitative BML volumes in the tibia, femur and patella were