osteoblast cultures produced using trabecular bone explants from the IT region of female hip OA cases was undertaken, in comparison with age and sex matched neck of femur fracture (NOF) cases; to elucidate the role of these genes during differentiation and mineralisation. The fracture cases were selected as epidemiological, clinical and molecular reports have shown an inverse
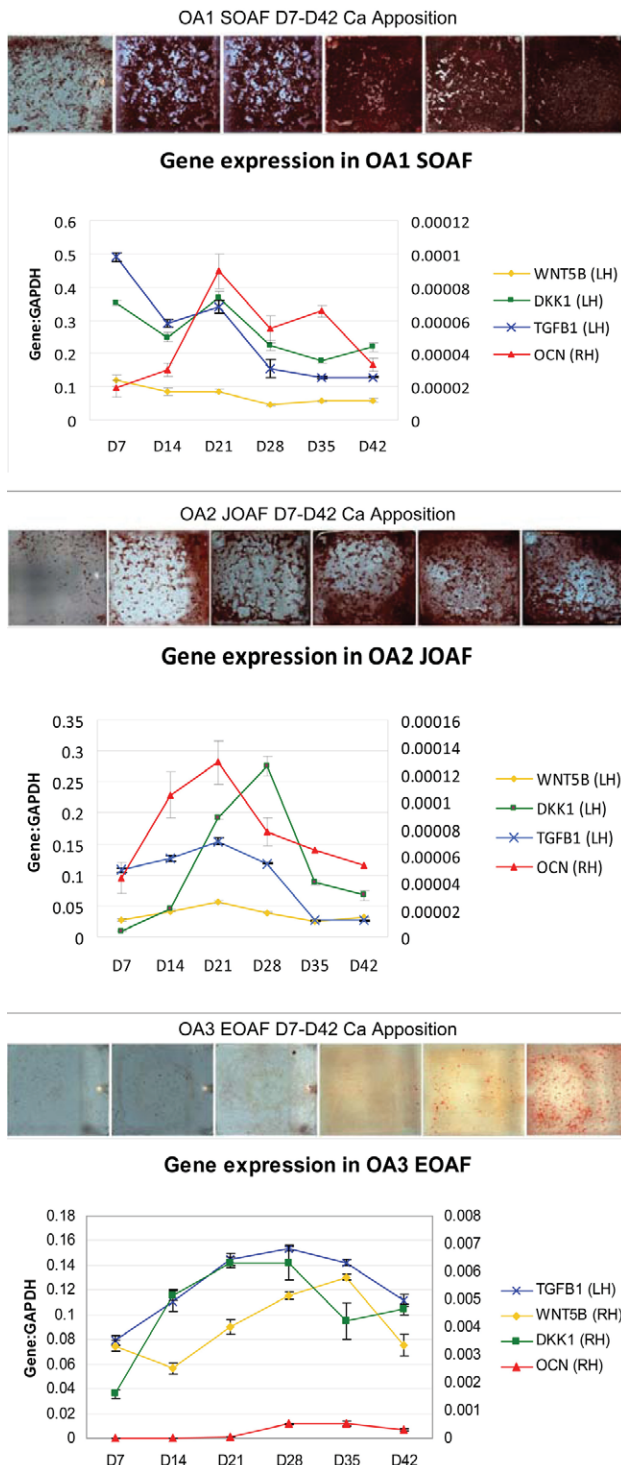

OA1 SOAF D7-D42 Ca Apposition

Gene expression in OA1 SOAF

OA2 JOAF D7-D42 Ca Apposition

Gene expression in OA2 JOAF

OA3 EOAF D7-D42 Ca Apposition

Gene expression in OA3 EOAF

Figure 1. Calcium apposition and gene expression profiles of four genes (WNT5B, DKK1, TGFB1 and OCN) across 42 days from three mineralising primary osteoblast cultures (P4), derived from the trabecular bone of three female OA donors. Data are presented as mean expression normalized to GAPDH, ± SEM of triplicate reactions, corresponding axis is specified at left side (LH) or right side (RH).

relationship between OA and NOFs, regarding incidence, bone density and gene expression. Three genes WNT5B, DKK1 and TGFβ1 were selected for further assessment. Selection was based on significant association with OA (t-score>|3.5|, p<0.05) as well as an elucidated role in osteoblast differentiation and mineralisation. The expression of these genes was compared to osteocalcin (OCN) a known marker of mature mineralising osteoblasts.

Methods: Primary osteoblast cultures were generated from six donors; three OA and three NOF cases. Cultures were passaged and then treated with osteogenic media across a 42 day timecourse. Gene expression profiles were quantified using real-time PCR; Student's t-test was used to validate significant differences. Mineralisation was assessed using Alizarin red stains to visualise and quantify calcium deposition, and energy dispersive X-ray scans to determine calcium:phosphorous (Ca:P) ratios.

Results: Examination of OA disease candidates in this *ex vivo* system has revealed peak expression of WNT5B across two OA donors at the same time point as OCN (Fig. 1). DKK1 expression appears to be highly variable occurring before, during and after peak OCN expression in OA (Fig. 1). TGFβ1 expression was suppressed following peak OCN expression in all three OA donors (Fig. 1). Significant variation in the comparative levels of calcium apposition and Ca:P ratios across the time course between OA and NOF cohorts was also observed (p<0.05).

Conclusions: The peak expression of WNT5B suggests a role in the onset of the mature phenotype and mineralisation in OA. The WNT pathway is known to be inhibited at the late stages of differentiation, WNT5B is also significantly up-regulated in OA (t-score=3.7, p<0.05) as such this canonical antagonist may be involved in the disease. TGFβ1 expression is associated with proliferation and as expected declines in expression during the late stages of differentiation concurrent with increased OCN expression, it is down-regulated in OA (t-score=-6.9, p<0.05) as such the levels of TGFβ1 expression may be aberrant. The variable OA Ca content and composition of mineral *ex vivo* may reflect the heterogeneity observed in OA pathology. Further studies will continue to elucidate the role of WNT and TGFβ signalling in osteoblast differentiation and its effects on mineralisation facilitating the identification of potential diagnostic and therapeutic targets against OA pathogenesis.

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TWO-YEAR INCIDENCE AND PREDICTORS OF FUTURE KNEE ARTHROPLASTY IN PERSONS WITH SYMPTOMATIC KNEE OSTEOARTHRITIS: PRELIMINARY ANALYSIS OF LONGITUDINAL DATA FROM THE OSTEOARTHRITIS INITIATIVE

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Purpose: There is little evidence to guide physicians when discussing future likelihood of knee arthroplasty with patients who have symptomatic knee osteoarthritis. Data from Osteoarthritis Initiative (OAI) was used to determine the incidence of and predictors for knee arthroplasty among patients with symptomatic knee osteoarthritis.

Methods: OAI data were collected on a sample of 778 persons aged 45 to 79 years with symptomatic knee osteoarthritis. An extensive set of measurements were obtained at baseline and persons were followed for 2 years to identify who underwent knee arthroplasty. Random forest analysis, an advanced Classification and Regression Tree approach was used to identify optimal variables that discriminate among those who did and those who did not undergo knee arthroplasty.

Results: The two year incidence of knee arthroplasty in the cohort

was 3.7% (95%CI, 2.6%, 5.3%). Because of the low number of knee arthroplasty procedures, the predictor analysis was preliminary in nature. The analysis identified several variables that could be used to assist in identifying patients at future risk for knee arthroplasty. Table 1 summarizes the ratings of importance from the Random Forest Analysis while Figure 1 illustrates variable importance graphically. The most powerful predictors of future knee arthroplasty were those that accounted for disease severity (OARSI Atlas grade of 3) and functional loss (SF-12 Physical Component Score and Mental Component Score, 400 meter walk time, and WOMAC Function score).

Values for the two importance indexes used in the Random Forest analysis

	Mean decrease in accuracy	Mean decrease in Node Impurity
Demographic		
V00AGE - Age (in years)	0.016	1.743
Highschoolorless - High school diploma or less (yes or no)	0.002	0.553
General Health		
V00CESD - CESD depression score (continuous measure)	0.003	1.319
BMIgr30 - BMI greater than 30 (yes or no)	0.002	0.511
Arthritis Health		
V00KGLRS - 0 to 10 global rating of effect of knee pain/arthritis	0.005	1.143
grade4klforprogressioncohort - Grade 4 modified Kellgren-Lawrence (yes or no)	0.06	2.215
Physical Examination		
Newcontractureprog - Knee flexion contracture (degrees)	0.013	1.850
Physical Performance or Disability		
V00400MTIM - Time for 400 meter walk test (sec)	0.014	1.981
V0 HSPSS - SF-12 Physical Component Summary score (continuous)	0.019	2.300

Conclusions: For persons at risk of knee arthroplasty, the two year incidence of knee arthroplasty is very low. Reasons for the low incidence cannot be determined from this study. These data could assist physicians in advising patients with knee osteoarthritis on future surgical care.

012

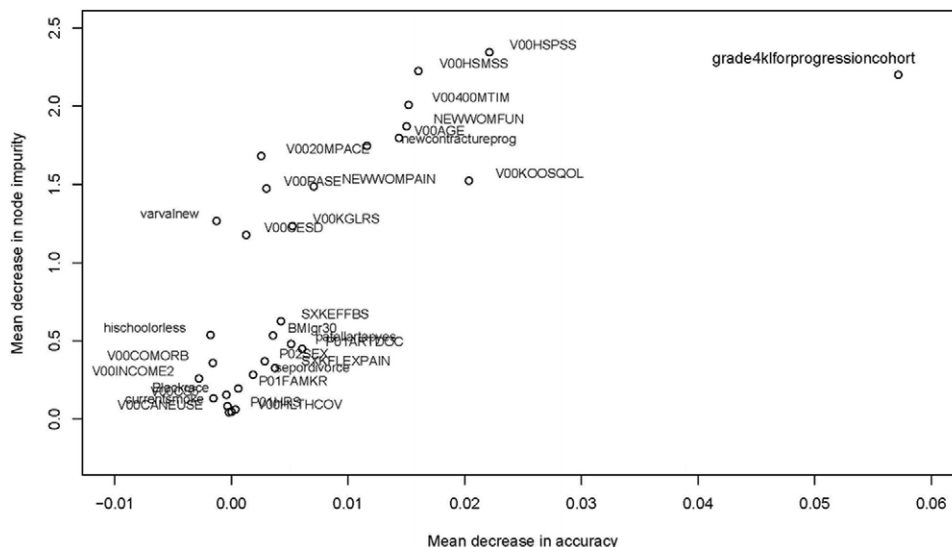### RISK FOR SYMPTOMATIC KNEE OSTEOARTHRITIS DOES NOT VARY BY KNEE EXTENSOR STRENGTH AND KNEE JOINT POSITION SENSE

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[1]Univ. of Iowa, Iowa City, IA; [2]Boston Univ., Boston, MA; [3]King's Coll. London, London, United Kingdom; [4]Univ. of California at San Francisco, San Francisco, CA; [5]Univ. of Alabama at Birmingham, Birmingham, AL

Purpose: Quadriceps weakness and impaired knee joint position sense (proprioception) have been linked cross-sectionally with knee OA. While neither of these factors has been independently associated with new onset disease, it is possible that one substitutes for the other and that only when both are impaired is the joint at risk. This study investigated whether sensoriomotor dysfunction - the combination of quadriceps weakness and impaired knee joint position sense - precedes development of symptomatic knee OA. **Methods:** The Multicenter Knee Osteoarthritis (MOST) Study is a longitudinal, observational study of adults age 50-79 years with knee OA or at high risk for knee OA. MOST subjects were excluded if they had symptomatic knee OA at baseline. Those with missing data or knee pain that interfered with strength testing were also excluded. Subjects underwent bilateral, weight bearing, fixed-flexion radiographs, right knee joint reposition tests, and isokinetic knee extensor strength assessments; completed the Physical Activity Scale for the Elderly (PASE) and WOMAC questionnaires; and had height, and weight measurements taken. Symptomatic knee OA was defined as the combination of knee OA (KL grade $\geq$2) and frequent knee pain or stiffness at follow-up. The relationship between combinations of the tertiles of sex-specific baseline peak KES and tertiles of JPS and development of incident symptomatic knee OA at 30-month follow-up was evaluated with logistic regression adjusted for age, BMI, knee injury, knee surgery, and PASE score. Secondary analyses defined joint position sense as (1) the subject-specific variance over the 10 trials and (2) the average joint position sense over the 10 trials, and also assessed the interaction of knee extensor strength and joint position sense in predicting the outcome using generalized linear models. **Results:** 1565 subjects (911 women and 654 men) met eligibility criteria and were included in this study. The mean$\pm$SD age was 62.1$\pm$8.0 years, BMI was 29.8$\pm$5.4kg/m^2, PASE score was 182.9$\pm$88.7, and WOMAC pain subscale was 2.2$\pm$2.8. There

Abstract 011 – Figure 1