Disclosure of Interest: H. Deckx Employee of: Galapagos NV, Belgium, S. Hatch Consultant for: Galapagos NV, Belgium, M. Robberechts Employee of: Galapagos NV, Belgium, S. Dupont Employee of: Galapagos SASU, France, J. Desrivot Employee of: has been employee of Galapagos SASU, France, H. Coleman Paid instructor for: Covance has been contracted by Galapagos NV to conduct the study, S. Larsson: None declared, A. Struglics: None declared, E. van der Aar Employee of: Galapagos NV, Belgium, A. Fiew Employee of: Galapagos NV, Belgium

DOI: 10.1136/annrheumdis-2018-eular.3101

FRI0540 IDENTIFICATION OF BIOMARKERS OF OA ASSOCIATED TO DEFECTIVE AUTOPHAGY

I. Lorenzo-Gomez¹, N. Oreiro², J.A. Pinto-Tasende², F.J. Blanco^{1,2}, B. Carames¹.

¹Rheumatology Division. Cartilage Biology Group, The Institute of Biomedical Research of A Coruña (INIBIC); ²Clinical Rheumatology Division, Complejo Hospitalario Universitario A Coruña (CHUAC), A Coruña, Spain

Background: In osteoarthritis (OA), defects in cellular homeostasis, and in particular in autophagy, are evident and precede joint damage. In this sense, we have shown that there is a defect in autophagy in OA human chondrocytes and cartilage, and pharmacological activation of autophagy protects against joint damage. These data suggest that joint damage could be due, at least in part, to a failure of autophagy, by inducing an abnormal accumulation of cellular products related to disease.

Objectives: These observations represent a unique opportunity to identify and validate potential biomarkers associated with autophagy defects that could facilitate the development of therapeutic strategies to prevent OA progression.

Methods: A comparative analysis of 86 autophagy genes was performed in blood from non-OA and knee OA patients. Non-OA patients (Age: 61,17±1,370 years; BMI: 25,76±0,69; Sex: Females; n=12) and Knee OA patients (Age: 65,75±1,528 years; BMI: 30,25±0,88; Sex: Females; n=12, OA grade III-IV) were profiled using a human autophagy PCR array (PrimePCR autophagy human panel, BioRad) and analysed using the PrimePCR analysis software, Biorad. In addition, we performed a quantitative proteomic analysis of defective autophagy by genetic deletion of Atg5 in human OA chondrocytes by using iTRAQ (isobaric tags for relative and absolute quantitation) labelling coupled with on-line 2D LC/MS/MS. Protein identification and quantification were performed using Protein Pilot Software 4.0. Each MS/MS spectrum was searched in the Uniprot/Swissprot database for *Homo sapiens*.

Results: 16 autophagy-related genes were significantly down-regulated in blood from knee OA patients compared to non-OA patients. No significant up-regulation was observed in blood from Knee OA patients, however a trend-toward up-regulation was detected in several genes involved in the mTOR signalling pathway. Importantly, 5 key autophagy-related genes, such as, ATG16L2, ATG12, ATG7, ATG4B and MAP1LC3B involved in initiating autophagy, phagophore extension and autophagosome formation were significant downregulated in knee OA patients compared to non-OA patients (p<0.05). Interestingly, HSP90AA1 and HSPA8, a chaperone-mediated autophagy genes involved in stress response and protein folding, were significant downregulated (p<0.001) in blood from knee OA patients. In addition, several regulators of autophagy and apoptosis, such as BNIP3, BCL-2 and BCL2L1 were a significantly downregulated in OA patients (p<0.01). Total proteome screening in human OA chondrocytes with defective autophagy, showed a significant reduction of Heat shock protein HSP90-alpha (HSP90A1) (p<0.05), suggesting that reduced autophagy is associated to OA pathology and could be a potential biomarker for OA progression and development.

Conclusions: This approach represents an unique opportunity to identify and validate early-stage biomarkers associated with defective autophagy that could facilitate the development of therapeutic strategies to prevent joint damage.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.5527

FRI0541 INCREASING A PERSON'S OWN PHYSICAL ACTIVITY AND STRENGTH CAN MINIMISE CARTILAGE VOLUME LOSS IN OLDER-ADULTS: A BETWEEN- AND WITHIN-PERSON ANALYSIS ON A POPULATION-BASED PROSPECTIVE COHORT

I.P. Munugoda¹, S. Balogun¹, K. Wills¹, F. Cicuttini², G. Jones¹, M.L. Callisaya¹, D. Aitken¹. ¹Menzies Institute for Medical Research, University of Tasmania, Hobart, Tasmania; ²Department of Epidemiology and Preventive Medicine, Monash University Medical School, Melbourne, Victoria, Australia

Background: The relationship between physical activity (PA) and osteoarthritis (OA) has been controversial, with some studies showing a detrimental effect and others showing either no effect or a beneficial effect. Traditionally, analysis has

focused on examining the effect PA and/or strength have on OA between individuals (between-person comparison). Yet, how the variability in PA and strength over time within the same individual (within-person comparison) is associated with OA is not well recognised. Statistical methods, such as multilevel models that properly capture the within-person processes can be used to tell us whether changes within an individual over time relate to changes in OA outcomes in that same individual.

Objectives: This study aimed to investigate the associations of between-person and within-person variability in PA and leg strength with knee cartilage volume loss over 10.7 years in older adults.

Methods: 479 community-dwelling older-adults (50% female, mean age 61±6 years, range 50–80 years) were studied at baseline, 2.7, 5.1, and 10.7 years. PA (measured objectively as steps/day) and leg strength (measured objectively in kg) were assessed at all four time-points. Knee cartilage volume was measured using MRI at baseline and 10.7 years. Linear mixed-effect regression models were used to estimate the association of between-person and within-person variability in PA and leg strength with cartilage volume loss over 10.7 years. Models were adjusted for age, sex, body mass index and history of knee injury or surgery.

Results: Mean cartilage volume loss over 10.7 years was 465±231 mm³. No between-person associations existed between PA and cartilage volume loss (Beta: 18.8 per 1000 steps/day, 95% CI –6.1, 43.7). However, within-person variability in PA was protectively associated with changes in cartilage volume, such that having higher PA compared to an individual's average level of PA minimised their cartilage volume loss over time (Beta: 32.8 per 1000 steps/day, 95% CI 20.8, 44.6). Between-person effects showed that participants with greater leg strength lost less cartilage volume over time (Beta: 5.4 per 1 kg, 95% CI 3.1, 7.8). Within-person variability in leg strength was also protectively associated with changes in cartilage volume, such that having higher leg strength compared to an individual's average strength minimised their cartilage volume loss over time (Beta: 3.3 per 1 kg, 95% CI 2.1, 4.5).

Conclusions: Our unique analysis method adds a new perspective to the PA and OA debate. The implication of these findings demonstrate that individuals can minimise cartilage volume loss by increasing their own PA and strength, which supports the clinical recommendations of promoting PA and strength to prevent and treat OA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3204

FRI0542 POTENTIAL NOCICEPTIVE PAIN RELIEF OF INTRA-ARTICULAR SALINE CONTROL IN CLINICAL TRIALS OF KNEE OSTEOARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMISED TRIALS

I. Simsek, T. Phalen, A. Bedenbaugh, J. Tambiah. Samumed, LLC, San Diego, USA

Background: Hyaluronic acid, corticosteroids and platelet-rich plasma (PRP) are widely used intra-articular (IA) therapies for the management of mild to moderate knee osteoarthritis (OA). Many trials evaluating the efficacy of IA-administered therapies commonly use IA saline injections as a placebo comparator arm. A previously published systematic review Altman et al, 2016 showed significant reductions in pain relief with IA saline in both the short- (3 months) and long-term (6–12 months).

Objectives: The aim of this updated systematic review and meta-analysis was to assess the clinical benefit and harm associated with use of IA saline in trials of IA therapies for patients with painful knee OA.

Methods: We searched MEDLINE and Embase databases for randomised controlled trials (RCTs) published up to and including October 12th, 2017. Two reviewers independently assessed the eligibility of potential reports and the risk of bias of included trials. We analysed short (≤3 months) and long-term (6–12 months) pain reduction from baseline of the saline arm of included trials using standardised mean differences (SMDs; estimated assuming a null-effect in a comparator group) that were weighted and pooled using a random-effects model. Pain scores were transformed to a 100-point scale when necessary. We summarised and presented treatment-related adverse events (AEs) descriptively.

Results: We included 46 RCTs, of which 44 provided sufficient data to be included in the meta-analysis for benefit. IA saline significantly improved short-term knee pain from baseline vs. a null effect for a comparator group across 36 studies involving 1908 patients (SMD –0.85, 95% CI –1.05 to –0.66; I²=87%). There was also significant reduction in long-term knee pain following IA injection with saline across 25 studies involving 1758 patients (SMD –0.78, 95% CI –1.02 to –0.55) with a substantial degree of heterogeneity (I²=90%). Thirty-three of the included trials reported on adverse events, none of which found any serious treatment-related AEs following IA injection with saline.

Conclusions: The pain relief observed with IA saline should prompt one to consider the added effectiveness of current IA treatments that use saline comparators in clinical studies, and challenges of classifying IA saline injection a "placebo."