Abstracts

**Abstract Withdrawn**

**P044**

**TRANSGLUTAMINASE-2 IN OSTEOARTHRITIS: MMP-13 PRODUCTION THROUGH ENHANCED FOXO3A NUCLEAR TRANSLLOCATION**

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**Disclosure of interest** None declared

**P045**

**ABSTRACT WITHDRAWN**

**P046**

**ABSTRACT WITHDRAWN**

**P047**

**ANTI-COLLAGEN TYPE II ANTIBODIES ARE ASSOCIATED WITH EARLY INFLAMMATION IN MALAYSIAN RHEUMATOID ARTHRITIS PATIENTS WITH THREE DIFFERENT ETHNICITIES**

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**REFERENCES**


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**Introduction**

Transglutaminase 2 (TG2) also known as tissue transglutamase, is a calcium-dependent enzyme that has a variety of intracellular and extracellular substrates. It has been well known that TG2 increases in osteoarthritis (OA) tissue and can be used as a biomarker of OA. Objectives To elucidate the molecular mechanism of TG2 during the cartilage degradation in OA. Methods The surgical destabilisation of the medial meniscus (DMM) model is used to induce OA in 10-week-old male C57BL/6j mice. Primary chondrocytes were obtained from E15.5 long bones, and ZDON, a cell-permeable, peptide-based, irreversible inhibitor of TG2, was used to inhibit the function of TG2 and calcium ionophore to stimulate TG2. Results TG2 expression was increased in articular cartilage and growth plate in surgical OA model. When treated with various growth factors, only TGFβ1 increased TG2 expression of primary chondrocyte in a dose-dependent manner. Intra-articular injection of specific TG2 inhibitor, ZDON, ameliorated the severity and MMP-13 expression in surgically-induced OA. ZDON attenuated MMP-3 and MMP-13 expression in TGFβ-induced calcium ionophore-treated chondrocytes in a Runx2-independent manner. TG2 activation by calcium ionophore induced phosphorylation of FoxO3a and ZDON decreased total FoxO3a as well as nuclear FoxO3a level. FoxO3a and TG2 were co-localised in primary chondrocytes and immunoprecipitation analysis revealed a direct interaction of FoxO3a and TG2, suggesting enhanced nuclear translocation of FoxO3a by TG2.

Conclusions Our data provide an evidence of TG2 as an enhancer of FoxO3a-nuclear translocation which was responsible for the TG2-dependent MMP-13 expression.

**Disclosure of interest** None declared

**Objectives**

We have previously shown that Caucasian rheumatoid arthritis (RA) patients with anti-collagen type II antibodies (anti-CII) have an acute onset phenotype with elevated levels of C-reactive protein (CRP) and erythrocyte sedimentation rate, as well as higher disease activity score and number of swollen joints [Manivel et al. Ann Rheum Dis 2017 September;76(9):1529–1536]. Our aim was to replicate this in a multi-ethnic Malaysian RA cohort. Methods Anti-CII, anti-CCP2, IgM RF and IgG RF were measured in 1,105 Malaysian early RA patients and 1,565 healthy controls of Malay, Chinese or Indian ethnicity in the Malaysian Epidemiological Investigation of RA (MyEIRA) case control study, and related to baseline CRP and to HLA-DRB1* alleles. Results 106/1,105 (9.6%) of the RA patients had elevated anti-CII. Anti-CII levels were higher in RA patients than in controls (p<0.0001), generally higher in Malay than in Indian or Chinese subjects, and also higher in Malaysian than in Swedish healthy controls. All measured autoantibodies associated with elevated baseline CRP. The occurrence of anti-CII did not associate with the occurrence of anti-CCP2, IgG RF and IgM RF, and when patients with only one antibody were compared to antibody negative patients, only anti-CII associated with elevated CRP (p=0.0310). HLA-DRB1*12:01 positive patients has higher levels of anti-CII (p=0.01) whereas Malaysian Malay patients with HLADRB1*12:02 had lower anti-CII levels (p<0.002) as compared to individuals lacking the corresponding genotype. Conclusions Elevated anti-CII levels at the time of RA onset associate with an early inflammatory RA phenotype not only in Caucasian, but also in an Asian RA population. This supports our hypothesis that the association between early elevations of anti-CII and the acute onset RA phenotype is a finding of global validity.