the study with clinic visits on study days 0 (baseline), 3, 7, 14 and a follow-up telephonic visit on day 35.

Results A significant clinical and inflammatory cytokine response at Day 3 was seen in all dose groups and will be elaborated upon once the final datasets become available. There were no metabolic, physiological or hematological changes and all doses were well tolerated.

Conclusions On the basis of both the clinical response and the biomarkers, dapansutride™ is a safe and effective anti-inflammatory oral NLRP3 inhibitor in the treatment of acute gout with a broad therapeutic range and promise for further clinical development in this indication.

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Potential investigators conflicts of interest DS is founder and CEO of Olatec, CS is CMO of Olatec, RB is COO of Olatec, CD is CSO and SAB member of Olatec, LJ is SAB member of Olatec.

Disclosure of Interest None declared.

P161

THE RELATION BETWEEN THE INFLAMMATORY STATUS OF HUMAN END STAGE OA SYNOVIUM AND LEVELS OF LOW DENSITY LIPOPROTEIN

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Career situation of first and presenting author Student for a master or a PhD.

Introduction High systemic levels of low density lipoprotein (LDL) is a shared metabolic risk factor for osteoarthritis (OA) and atherosclerosis, which may point to common biochemical pathways. One of the key events in atherosclerosis is formation and uptake of oxidized LDL (oxLDL) as a consequence of macrophage-mediated inflammation. In mice, high LDL levels enhanced synovial activation during development of collagenase-induced OA, and injection of oxidized LDL in naïve macrophage depleted joints led to infiltration of myeloid progenitor cells. However, a role for (ox)LDL in human OA has not yet been shown.

Objectives In the present study, we investigated whether the inflammatory status of OA synovium is associated to systemic and local levels of (ox)LDL.

Methods Blood was collected from patients planned to undergo total knee replacement and LDL serum levels were determined (n=16). After surgery, synovial explants from the same patients (2–8 per patient) were collected and incubated at 37 °C for 24 hours in presence of LDL (50 µg ApoB/mL), oxLDL (50 µg ApoB/mL) or control medium. Levels of IL-1β, TNF-α, IL-10 and MCP-1 secreted in the conditioned medium were measured using Luminex, and S100A8/A9 using ELISA. Immunohistochemical staining of ApoB was performed to assess presence and uptake of (ox)LDL in the synovium. Hematoxylin and eosin-stained sections were used to score cell infiltration and synovial hyperplasia.

Results Around 50% of the patients in our cohort showed synovial activation exemplified by high secretion levels of IL-1β, TNF-α and IL-10. Cellular infiltration and synovial hyperplasia was observed in the majority of synovial tissue samples, their grades did however not correlate with cytokine secretion.

Secretion levels of IL-1β positively correlated with serum levels of LDL and total cholesterol and did not correlate with BMI, suggesting a link that runs via systemic metabolic processes rather than increased weight-mediated joint loading. Staining of LDL associated protein ApoB in the synovia showed distinct speck-like staining within macrophages and endothelial cells especially, suggesting oxLDL accumulation in these cells. Unexpectedly, presence of high concentrations of LDL or oxLDL during incubation of synovial explants did not significantly affect secretion of IL-1β, TNF-α, IL-10 and MCP-1.

Conclusions IL-1β secretion by end stage OA synovium is associated to systemic levels of LDL. Intervention with high concentrations of LDL or oxLDL for 24 hours after synovium extraction did however not alter cytokine secretion, suggesting that LDL and synovitis are linked through more long-term local interactions, or alternatively via systemic inflammatory factors.

Disclosure of Interest None declared.

P162

EXTRACELLULAR VESICLES FROM PATIENTS WITH ANKYLOSING SPONDYLITIS CONVEY PROTEINS RELATED TO IMMUNE RESPONSE: NEW SIGNALING PATHWAYS?

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Career situation of first and presenting author Young investigator.

Introduction Ankylosing spondylitis (AS) is a chronic inflammatory disease, whose pathogenesis is still unclear. Many studies show the proteins in extracellular vesicle (EVs) would change regularly in many diseases. However, none of study has focused on the proteins profiles of serum-derived EVs in AS patients.

Objectives The study aim to detect the proteins profiles of serum-derived EVs in AS patients by Label-free-LC-MS/MS technology.

Methods EVs were isolated by ExoQuick-TC™ kit. The protein contents were evaluated by Label-free-LC-MS/MS technology. Venn diagram, volcano plot, hierarchical cluster, Gene Ontologies (GO), Encyclopedia of Genes and Genomes (KEGG) pathway and Protein-Protein Interaction (PPI) network analysis were constructed. Enzyme-linked immunosorbent assay (ELISA) was used to confirm the expression of the differently-expressed proteins.

Results Label-free-LC-MS/MS results indicated a total of 677 proteins were detected, of which 65 were unique to AS group, 545 were identified in both AS and control group, and 67 were unique to control group. A heat map of the hierarchical clustering revealed a clearly distinct expression of proteins in AS group, compared with control group. With the cut off criteria of $|\log_2(\text{fold-change})| \geq 1$, $p \leq 0.01$ and unique peptides ≥ 2 , 31 up-regulated proteins and 42 down-regulated proteins were found in the AS group. Among them, Serum amyloid A-1 (SAA1) protein and Complement C4-B were highly expressed in AS group. PPI network analysis yielded a highly clustered network (clustering coefficient: 0.584), with prothrombin (F2) and c-reactive protein(CRP) as the central/hub proteins. GO analysis of the biological process indicated that the differentially expressed proteins were significantly enriched