aging mechanisms, diagnosis/prognosis of age-related disease and even novel treatment targets.

**Objectives:** To quantify relationships between circulating microRNA expression and biological aging and determine whether microRNAs may be a molecular clock.

**Methods:** This pilot work is a nested study within a prospective, longitudinal birth cohort from May/June 1947 (the Newcastle Thousand Families Study NTFS). Serum samples from 23 subjects taken at ages 50 and 62 years were extracted from the biobank. HTG EdgeSeq microRNA whole transcriptome assay was performed, measuring expression of 2083 human microRNA transcripts using an array followed by next generation sequencing. Global microRNA expression profiles were generated and analysed using this technology, profiling all known microRNAs from a small volume of serum (<15 μL). NIHRF funding has been secured for whole cohort analysis.

**Results:** Resulting data has shown very strong associations (up to p<10−17) for biological ageing, with 84 microRNAs meeting p-values<0.05 (see heat map). Analysing the whole cohort will independently validate and extend the findings, in order to identify an ageing signature; the molecular clock.

**Conclusions:** This study suggests very strong changes in microRNAs in individuals between 50 and 62, suggesting microRNA signature is a molecular clock. These observations need to be confirmed and extended to validate serum microRNAs as biomarkers for ageing, for early detection of age-related disease and as tools to monitor ageing trajectory.

**REFERENCES:**


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**Disclosure of Interest:** None declared

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for leukotriene A4 hydrolase, which converts LT(A4) to LT(B4); microsomal glutathione S-transferase, which converts LT(A4) to LT(C4); and gamma-glutamyltrans-
ferase (LT(C4) >LT(D4)). In contrast, Tr14, but not diclofenac strongly induced Nrf2 mRNA at 12–16 hours.

Conclusions: Tr14 and diclofenac had very different effects on the COX/LXO pathway after cutaneous wounding. Tr14 allowed normal autoinduction of COX2 mRNA by PGE2, but suppressed mRNA levels for the key enzymes in the leukotriene synthetic pathway. A likely explanation for these effects is that Tr14 strongly induced Nrf2 mRNA, which is known to co-repress the leukotriene enzymes via transcription factor Bach1.

Disclosure of Interest: None declared

THU0022

ANALYSIS OF 47 NON-MHC ANKYLOSING SERPONTILIS SUSCEPTIBILITY LOCI REVEALS SHARED ASSOCIATED VARIANTS ACROSS CAUCAUSANS AND CHINESE HAN

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Background: Genetic factors play a prominent role in AS pathogenesis. So far over 40 non-MHC Ankylosing Spondylitis (AS) susceptibility loci with genome-wide or suggestive significance have been initially reported in Caucasians, however, lack of association evidence of most loci was seen in Chinese Han and some results seemed controversial.

Objectives: Here, we present a systematic evaluation of 47 non-MHC AS susceptibility loci using GWAS datasets in Chinese Han.

Methods: Totally 1853 AS cases and 4048 newly matched controls in 4 cohorts were obtained, after imputation meta-analysis results of 93 589 variants within 47 reported loci were extracted. Best-guess genotype data were used for interaction analysis and weighted genetic risk score model construction which was then assessed by receiver operator characteristic analysis. Functional annotation was conducted using HaploReg, RegulomeDB and VarBase Database.

Results: We revealed 14 AS-associated variants with nominal evidence in Chinese Han, including rs10865331(p=2.96E-9), rs10050860 (p=1.84E-4) and rs80704683(p=2.81E-4) and found potential associated variants within 47 reported loci were extracted. Best-guess genotype data were used for interaction analysis and weighted genetic risk score model construction which was then assessed by receiver operator characteristic analysis. Functional annotation was conducted using HaploReg, RegulomeDB and VarBase Database.

Conclusions: Our results provided a detailed spectrum of non-MHC AS susceptibility loci in Chinese Han and highlighted 2 p15, ERAP1 and TBKBP1 may play a critical role in AS pathogenesis.

REFERENCES:

Disclosure of Interest: None declared

THURSDAY, 14 JUNE 2018:

Adaptive immunity (T cells and B cells) in rheumatic diseases

THU0023

COMPLEX IMMUNOPHENOTYPING STRATIFIES PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME, SYSTEMIC LUPUS ERYTHEMATOSUS AND SECONDARY SJÖGREN'S SYNDROME ASSOCIATED WITH SYSTEMIC LUPUS ERYTHEMATOSUS INTO DISTINCT CLINICALLY RELEVANT GROUPS WITH POTENTIAL THERAPEUTIC IMPLICATIONS

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Background: Similarities in the clinical and laboratory features of patients with primary Sjögren’s syndrome (pSS) and systemic lupus erythematosus (SLE) have led to attempts to treat pSS and SLE patients with similar biologic therapeutics. However, the results of many clinical trials are disappointing and no effective treatments are available for pSS and few for SLE patients with refractory disease.

Objectives: To identify novel patient endotypes using in depth immune phenotyping that facilitates the selection of biological therapies for patients regardless of diagnostic labels.

Methods: Peripheral blood was collected from patients with pSS (n=55), SLE (n=38), SS/SLE (n=15) and age/sex-matched healthy controls (n=34). In-depth phenotyping of peripheral B and T-cell subsets by flow-cytometry, followed by unsupervised cluster analysis were performed. ROC analysis identified immune signatures characteristic for every cluster (endotype).

Results: Patients with pSS, SLE and SS/SLE had both unique and shared defects in immune cell phenotype. Hierarchical clustering of CD19+ B-cells, CD4+ and CD8+ T-cells across the three disease groups identified five distinct endotypes spanning diagnostic boundaries. Three of the endotypes had distinct immune signatures, characterised by predominantly B-cell, T-cell memory or CD4+/CD8+ T-cell subset fingerprints respectively, while two clusters had no distinct immune profiles. Notably, clinical and disease features were not significantly different between clusters.