profiling was carried out using Illumina chip array technology. After mapping genome-wide methylation quantitative trait loci (mQTLs) in *cis* (<1 Mb), we focused on known RA risk loci, integrating paired normalised gene expression measurements for transcripts within 500 kb of index CpGs. We also sought *trans* mQTLs, highlighting RA-specific effects.

Results CD4+ T lymphocyte *cis*-mQTLs co-localised with 30 independent (r2<0.8) RA-associated SNPs, whilst in B lymphocytes such mQTL effects were present at 31 RA SNPs. 80% of these variants functioned as *cis*-mQTLs in both cell types. CpG sites subject to *cis* effects at risk loci were depleted in regions associated with cell type-specific repressed chromatin marks, with enrichment at enhancer regions and those flanking transcription start sites, suggesting active roles in transcriptional regulation. Linear regression identified regulatory effects of these CpG sites on gene expression, and causal inference testing highlighted genes for which risk SNPs most likely modulate gene expression via CpG methylation. Such effects, robust to false discovery rate, were particularly prevalent in CD4+ T lymphocytes, for example implicating *ANKRD55*, *ORMDL3*, and *FCRL3* as causal genes in this cell type. Our analysis of mQTLs acting in *trans* identified inter-chromosomal SNP-CpG associations, also revealing instances of differential effect size in RA patients and controls.

Conclusions Here we highlight an important mechanism by which genetic variants may contribute to altered lymphocyte phenotype, and demonstrate the utility of DNA methylation profiling as a tool for the prioritization of candidate genes following GWAS studies in RA. The functional roles of highlighted genes in CD4+ T cells during RA pathogenesis await clarification.

Disclosure of Interest None declared.

P107 POLYMORPHISMS IN SLC2A9 AND SLC22A12 GENES ARE RELATED TO HYPERURICEMIA, GOUT AND ALSO TO HYPOURICEMIA

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

Introduction Serum uric acid concentration is significantly influenced by urate transporters, such as ABCG2 (encoded by *ABCG2* gene), GLUT9 (*SLC2A9* gene) and URAT1 (*SLC22A12* gene). The main function of ABCG2 is uric acid secretion, whereas GLU9 and URAT1 also ensure reabsorption. Pathogenic allelic variants in *SLC2A9* and *SLC22A12* are not only associated with hyperuricemia and gout, but they also lead to rare hereditary renal hypouricemia (type 1 – OMIM #220150 or type 2 – OMIM # 612076).

Objectives Previously, we analyzed *ABCG2* gene and detected non-synonymous variants that lead to hyperuricemia and early onset of the gout.[1] The aim of this study was to find a possible correlation between variants in *SLC2A9* and *SLC22A12* and hypouricemia, hyperuricemia and gout.[2]

Methods We recruited a cohort of 232 individuals with primary gout and hyperuricemia. We examined coding regions of *SLC2A9* (13 exons) and *SLC22A12* (10 exons) by Sanger sequencing. We also analyzed *SLC2A9* and *SLC22A12* in five patients with suspect hypouricemia.

Results In the cohort of 232 individuals, we detected five synonymous variants, 18 intron variants and seven missense variants in *SLC2A9*: A17T, G25R, T275M, D281H, V282I, R294H, and P350L. In *SLC22A12* gene, we found six synonymous variants and seven intron variants.

We detected several pathogenic variants in patients with suspect hypouricemia. Intronic variant c.1419+1G>A in *SLC2A9* most likely affects the splicing. In *SLC22A12*, we found rare pathogenic variants T467M and L415_G417del. These variants have according to our previous study high frequency in the Czech and Slovak Roma population.[3]

Conclusions The uric acid level is determined by a complex mechanism that is not yet fully understood. Disorders of urate transporters can not only lead to hyperuricemia, but in rare cases also to hypouricemia.

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P108/O28 FATTY ACID OXIDATION CAN DRIVE HUMAN MONOCYTE DERIVED CCL20 IN THE RA SYNOVIAL ENVIRONMENT

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Career situation of first and presenting author Post-doctoral fellow.

Introduction Metabolic pathways are considered to have a governing role in inflammatory cascades in myeloid cells. This is particularly evident in murine macrophages where glycolysis and fatty acid oxidation (FAO) have been implicated in inflammatory cascades and immune regulation respectively.[1] However, investigation of intracellular metabolism of human monocytes in the context of the hypoxic and inflammatory RA synovium is lacking.

Objectives To mimic the hypoxic RA environment *in vitro* and metabolically profile human monocytes. Determine if altered metabolic pathways have a functional impact on monocytes under disease-relevant conditions.

Methods Human monocytes were isolated from buffy coats and were exposed to hypoxia *in vitro*. Metabolic profiling of monocytes was carried out by LC-MS metabolomics. Inflammatory mediator release after LPS or RA-synovial fluid (RA-