P129 ABSTRACT WITHDRAWN

P130 INCREASE IN GLOBAL DNA METHYLATION AT 3 MONTHS OF METHOTREXATE USE IS NOT ASSOCIATED TO RESPONSE IN EARLY RA PATIENTS

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Introduction Methotrexate (MTX) is a first-line therapy in early Rheumatoid Arthritis (eRA). However, up to 40% of treated patients do not adequately respond to MTX. MTX interferes with the folate cycle, where it indirectly inhibits the global DNA methylation donor S-adenosylmethionine (SAM). Thus, we hypothesised that global DNA methylation changes during MTX use are associated with treatment response.

Objectives To examine whether there is a change in global DNA methylation ($\Delta\%$ Meth) upon MTX use and if this change is associated to MTX response (Δ DAS28) in eRA patients.

Methods DNA was isolated from whole blood (n=120) and Peripheral Blood Mononuclear Cells (PBMCs, n=83) of eRA patients, before and 3 months after MTX use. Samples were collected from the Treatment in the Rotterdam Early Arthritis Cohort (tREACH), a multicenter, stratified single-blind clinical trial of eRA patients. Selected patients received triple (MTX +SSZ + HCQ) or monotherapy (MTX) combined with corticosteroids. 7 CpG sites within Long-Interspersed Nuclear Elements (LINE-1), a proxy for global DNA methylation, were quantified by Sequenom EpiTyper. Paired t-tests or Wilcoxon Signed Rank tests were conducted to assess a change in methylation. Δ DAS28 score over 3 months was used as a measure for response. Associations between Δ DAS28 and $\Delta\%$ Meth were corrected for baseline DAS28 in a linear regression model.

Results In leukocytes, $\%$ Meth did not significantly change over time. However, in PBMCs $\%$ Meth in CpG1 (Δ Meth=2.61%, p=0.008), CpG2 (Δ Meth=0.73%, p=0.039) and CpG11.12 (Δ Meth=0.56%, p=0.016) significantly increased over 3 months of MTX use after Bonferroni correction. $\Delta\%$ Meth in CpG8.9 was significantly associated to the Δ DAS28 (B=0.29, p=0.039), yet this was no longer significant after Bonferroni correction. $\Delta\%$ Meth was not significantly associated to Δ DAS28 in any of the other LINE1 CpG sites tested.

Conclusions PBMC global DNA methylation in LINE-1 CpG sites increased upon 3 months of MTX use. However, this change in methylation is not associated to MTX response. Further research is needed to investigate the role of global DNA methylation in these patients.

Disclosure of interest None declared

P131 STUDY OF URATE TRANSPORTERS IN PRIMARY GOUT AND HYPERURICEMIA

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Introduction The urate transporters are one of the main genetic determinants of serum uric acid concentrations. Primarily nonsynonymous polymorphisms in *ABCG2* and *SLC2A9* are clinically important for the development of primary gout and hyperuricemia. In this study we investigated the effects of allelic variants of urate transporters in a cohort with primary gout and/or hyperuricemia.

Methods The cohort was recruited in the Institute of Rheumatology, gout was diagnosed in 165 subjects (151 men/14 women) and hyperuricemia in 58 subjects (39 men/19 women). Coding regions of *ABCG2*, *SLC2A9*, *SLC22A11*, *SLC22A8*, *SLC17A3*, and *SLC17A1* genes were amplified and sequenced directly.

Results In *ABCG2* gene, we detected nine non-synonymous variants: p.V12M, p.Q141K, p.R147W, p.T153M, p.K360del, p.F373C, p.T434M, p.S476P and p.D620N. The minor allelic frequency of p.Q141K is 0.23, whereas for the European population it is 0.09. In addition, this variant is associated with early onset of the gout.¹ We identified novel intron variant c.689+1G>A which is associated with two abnormal splicing variants, leading to premature introduction of the stop codon.²

In *SLC2A9* gene, seven missense variants were identified: p.A17T, p.G25R, p.T275M, p.D281H, p.V282I, p.R294H, and p.P350L. In *SLC17A3* gene, the analysis revealed allelic variants p.A100T and p.G279R. Non-synonymous variants p.V202M and p.R343L were found in *SLC22A11*. Only one missense variant (p.T269I) was identified in *SLC17A1*. In *SLC22A8* gene, sequencing revealed three non-synonymous variants p.R149C, p.V448I and p.R513G.

Conclusions Genetic variants of *ABCG2*, common and rare, increased the risk of gout. The precise impact of *SLC22A11*, *SLC22A8*, *SLC17A3*, and *SLC17A1* in the context of hyperuricemia and gout in our cohort is unclear. Although knowledge of renal urate handling has been increased, current evidence is insufficient to fully understand the precise mechanism governing the bi-directional transport of urate.

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