**AB0145**

**EFFECTS OF IMMUNOSUPPRESSIVE MEDICATION ON TYPE I INTERFERON ACTIVATION: IN VITRO ANALYSIS SHOWS A DOWNREGULATING EFFECT ON IFN ACTIVATION OF HYDROXYCHLOROQUINE AND ASPIRIN**

M. J. Wahadat1,2, M. Lourens1, E. Huijser1, C. G. Van Helden-Meeuwsen1, S. Kamphuis2, M. Versnel1,1, Erasmus MC, Dept. Immunology, Rotterdam, Netherlands; 2Sophia Children's Hospital, Erasmus MC, Dept. Pediatric Rheumatology, Rotterdam, Netherlands

**Background:** Systemic Lupus Erythematosus (SLE) is prototypic Interferon (IFN) driven autoimmune disease characterized by an increased expression of type-I IFN stimulated genes, known as the IFN signature. The inhibitory effects of various drugs like Hydroxychloroquine and more recently Aspirin on IFN inducing pathways (1,2) led to the idea that some standard of care drugs might decrease the IFN score in patients. Data on the in vitro effect of immunosuppressive medication on IFN activation are limited. Testing immunosuppressive agents for their effect on IFN activation in vitro will give insight into the mechanisms of IFN activation in vivo and the effect of immunosuppressive medication on this activation.

**Objectives:** To study the effect of immunosuppressive medication on the type-I IFN signature in an in vitro model.

**Methods:** Freshly isolated human PBMCs were stimulated for 24 hours with or without CpG-A or Imiquimod (IQ) or transfected with the cGAS agonist G3-YSD to induce IFN upregulation through the TLR7/9- and DNA Sensing Receptor-pathway respectively. To assess the direct role of the medication on the downstream pathway of the IFNAR PBMCs were stimulated with IFN-a2b. Aspirin, diclofenac, HCQ, Mycophenolate Mofetil (MMF) and prednisone were added separately to these cultures followed by analysis of mRNA by qPCR as a readout for IFN type I activation. Cell viability in all culture conditions was above 85%.

**Results:** The type I IFN activation induced by CpG-A, IQ, G3-YSD and IFN-a2b was significantly reduced after addition of Aspirin, diclofenac showed a trend towards reduced levels in all conditions. HCQ was able to significantly reduce the TLR7 induced IFN activation by CpG-A and IQ while MMF and prednisone did not show an effect in any of the culture conditions.

**Conclusion:** The IFN activation induced by the stimulation of various IFN inducing pathways was significantly reduced by Aspirin and HCQ in an in vitro model. Combining both clinical and in vitro data from our longitudinal cohort of childhood-onset SLE patients will elucidate the effect of different immunosuppressive drugs on the type-I IFN signature in these patients.

**References:**

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2020-eular.5631

---

**AB0147**

**GENE EXPRESSION PROFILE OF PRIMARY SJÖGREN’S SYNDROME ASSOCIATED THROMBOCYTOPENIA IN B-LYMPHOCYTE USING HIGH-THROUGHPUT SEQUENCING**

S. Zhang1, J. Qu1, L. Wang1, M. Li1, X. Zeng1, M. J. Wahadat1,2, M. Lourens1, E. Huijser1, C. G. Van Helden-Meeuwsen1, S. Kamphuis2, M. Versnel1,1, Erasmus MC, Dept. Immunology, Rotterdam, Netherlands; 2Sophia Children’s Hospital, Erasmus MC, Dept. Pediatric Rheumatology, Rotterdam, Netherlands

**Background:** Primary Sjögren’s syndrome (pSS) is a classical systemic autoimmune disease. Thrombocytopenia is one of the hematological manifestations of pSS with great challenges in clinic.

**Objectives:** To identify the candidate genes and functionally enriched pathways in the immune gene expression and progression of primary Sjögren’s syndrome (pSS) associated thrombocytopenia.

**Methods:** High-throughput sequencing was performed on 3 patients with pSS, 3 patients with pSS associated thrombocytopenia and 3 healthy individuals. The differentially expressed genes (DEGs) were identified, and function enrichment analyses were performed. The protein-protein interaction network (PPI) was constructed, followed by calculation of topological characteristics and sub-module analysis in order to observe hub DEGs. The expression of some hub genes was verified by Real-Time PCR in 24 pSS patients.

**Results:** A total of 19 DEGs were identified. The enriched functions and pathways of the DEGs include Toll-like receptor signaling pathway, Salmo- nella infection, Viral protein interaction with cytokine and cytokine receptor, NF-kappa B signaling pathway and Human cytomegalovirus infection. Seven hub genes (TNF, IL1B, CXCL8, CCL3, CCL4, CCL3L1, CCL4L1) were identified and pathway enrichment analysis revealed that these genes were mainly enriched in toll-like receptor pathway. The relative expression of the CXCL8 mRNA was significantly lower in pSS-lymphocytes in patients with pSS associated thrombocytopenia than in the pSS without thrombocytopenia group. No differences were observed in the IL-1β or TNFa expression between these two groups.

**Conclusion:** PSS associated thrombocytopenia might be a subset characterized by a systemic inflammatory state. The identification of upregulated genes involved in thrombocytopenia of pSS provides insight in disease pathogenesis and opens avenues for the design of novel therapeutic strategies.

**References:**