

binds FcγRs, as well as some nuclear proteins, including snRNPs. Pentameric (native) CRP has previously been suggested to inhibit production of IFNs in peripheral mononuclear cells (PBMCs) in response to ICs formed by autoantibodies against snRNP, an effect which was further investigated herein.

Methods PBMCs or magnetically (MACS) purified pDCs were retrieved from whole blood of healthy volunteers. Type I IFN gene transcription and production was stimulated by addition of snRNP containing ICs ± pentameric CRP (pCRP) or monomeric CRP (mCRP) in different sequential order. IC formation was achieved through simultaneous addition of snRNP and bulk IgG, retrieved from an SLE patient with high levels of snRNP autoantibodies, directly to the cells. Type I IFNs and inflammatory cytokines were investigated using quantitative PCR, ELISA and cytometric bead array, and cells responsible for production of the IFNs were characterized using flow cytometry. For statistics a two-tailed t-test was performed.

Results pCRP had an inhibitory effect on the IFN gene expression in PBMCs after incubation with ICs, $p=0.044$ for IFN α 4 and $p=0.047$ for IFN β at the 4h time-point compared to IC only. pCRP also showed a dose-dependent inhibitory effect on the type I IFN production in the cells. The monomeric form of CRP showed modest or no effect on IFN levels, $p=0.82$ for IFN α 4 and $p=0.58$ for IFN β at the 4h time-point compared to IC only. A pre-incubation of the cells with pCRP increased the inhibitory effects compared to simultaneous addition of pCRP and ICs, suggesting that initial binding to the cells is a critical step for inhibition. Flow cytometry suggested that pDCs are the main producer of the type I IFNs. In addition, pCRP seems to have a more general inhibitory effect on type I IFNs, as seen in the reduction of IFN production in response to the TLR-9 ligand CpG.

Conclusions pCRP has a distinct inhibitory effect on type I IFNs, which is largely not seen for the dissociated form of CRP (mCRP). The more general inhibitory effects shown by pCRP highlights its immune regulatory function in pathologies characterized by high production of type I IFNs. The identity of the initial receptors responsible for pCRP mediated effects, as well as of the involved signaling pathways, will be further investigated.

P107

INTERFERON-INDUCED METABOLIC PERTURBATIONS SHAPE THE INFLAMMATORY STATUS OF HUMAN MONOCYTES: IMPLICATIONS FOR INNOVATIVE THERAPEUTIC ENGINEERING IN SLE AUTOIMMUNITY

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Immune cells have unique metabolic requirements to support the energetic and biosynthetic burden during their activation. Delineation of the metabolic tuning of immune cells could lead to novel strategies in treating metabolically-

demanding processes including autoimmune diseases. Among innate effectors, monocytes have a distinct role in systemic lupus erythematosus (SLE) pathogenesis. We have previously described robust type-I interferon (IFN α) signaling in patients with SLE. IFN α -stimulated monocytes from healthy individuals (IFN-Mo) develop mitochondrial hyperpolarization and increased oxidative stress resembling SLE monocytes (SLE-Mo).

Here we sought to delineate the metabolic repercussion of IFN α -mediated signaling that could explain metabolic shifts pertaining to autoimmunity. To this end, we combined transcriptomic data with metabolic flux analysis (Seahorse technology) and Gas Chromatography (GC-MS) in healthy monocytes, IFN-Mo and SLE-Mo. Our preliminary results indicate an increased, glucose-dose dependent glycolytic flux in IFN α -treated healthy monocytes recapitulating the SLE-Mo phenotype. Blockade of hexokinase 2 (HK-2)-dependent glycolysis with the use of 2-DG inhibitor attenuated proinflammatory cytokine secretion and the expression of surface markers characteristic of activated monocytes, supporting the deregulated metabolic profile in SLE autoimmunity.

Combination of these data with targeted metabolomics (LC-MS) analyses and the application of pathway-specific inhibitors are implemented *in vitro* to reverse the inflammatory state of SLE monocytes. Together, our data are expected to yield unique insights into the role of immunometabolism in SLE and the potential use of metabolites as novel therapeutic targets in autoimmunity.

P108

OXIDATIVE STRESS IN NK CELL AND ITS CORRELATION WITH EXPRESSION OF KILLER IMMUNOGLOBULIN RECEPTORS IN SLE PATIENTS

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Background Oxidative stress i.e. accumulation of reactive oxidative species has been found to be implicated pathogenesis of many autoimmune diseases including systemic lupus erythematosus. Although our body has natural process of scavenging reactive oxidative species but whenever balance inclines towards accumulation, oxidative stress begins to build in. These accumulated ions lead to damage at cellular level and at molecular levels also. In our NK cell specific study we evaluated oxidative stress and expression level of killer immunoglobulin receptors. Killer cell immunoglobulin like receptors binds to mhc class 1 receptors. They work in antagonistic manner they are either activating for NK cell activity or inhibiting. So the balance between two categories is critical for self tolerance. We have evaluated expression level of kir2dl4 which binds to HLA-G ligand and activating in nature and KIR3DL1 on other hand interacts with HLA-Bw4 and prevent NK cell killing of healthy cells.

Methods *Lupus Patient and healthy subjects* Lupus patients are enrolled from outpatient department (OPD) of rheumatology clinic, PGIMER, Chandigarh.

Flowcytometric analysis PBMC isolated were incubated with antibodies conjugated to APC, PE, PerCP/cy5.5 for surface staining of antigens cd56, kir2dl4 and kir3dl1. DCFDA dye based analysis was done for estimation cellular ROS levels.