

**Results** Tregs from SLE patients showed a significantly reduced number, elevated apoptosis rates and impaired suppressive capacity compared with NCs. The increased Tregs apoptosis was negatively correlated with the total number of Tregs and positively correlated with disease activities. Microarray profiles of Tregs from SLE subjects reveal a cellular response that could make the cells sensitive to apoptosis, partially due to the stress responses, DNA-damaging and cytokine stimulation.

**Conclusions** This global picture of pathway-specific expression signatures is a step further dissecting Treg cells defects in the pathogenesis of SLE, and may shed light on the newly therapeutic strategies towards the aberrant Tregs apoptosis and reconstruction of SLE immune homeostasis.

## 52 THE PATHOGENIC RELEVANCE OF T FOLLICULAR HELPER CELLS-PLASMA BLASTS AXIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

S Nakayama\*, S Kubo, M Yoshikawa, Y Miyazaki, K Sakata, K Nakano, S Iwata, I Miyagawa, K Saito, Y Tanaka. *University of Occupational and Environmental Health, First Department of Internal Medicine, Kitakyushu, Japan*

10.1136/lupus-2017-000215.52

**Background and aims** The aim of this study was to assess the peripheral immune cell phenotypes in a correlation with clinical findings in patients with systemic lupus erythematosus (SLE).

**Methods** Peripheral blood mononuclear cells were obtained from 143 SLE patients and 26 healthy donors (HD). Circulating B, T and dendritic cells were defined based on flow cytometric analysis for human immune system termed “the Human Immunology Project” proposed by the National Institutes of Health (NIH) and the Federation of Clinical Immunology Societies (FOCIS).

**Results** The proportions of CD3<sup>+</sup>CD4<sup>+</sup>CXCR5<sup>+</sup>ICOS<sup>+</sup> T follicular helper (Tfh) cells, but not CD3<sup>+</sup>CD4<sup>+</sup>CXCR3<sup>+</sup>CCR6<sup>-</sup> Th1 and CD3<sup>+</sup>CD4<sup>+</sup>CXCR3<sup>-</sup>CCR6<sup>+</sup> Th17 cells, were higher in SLE than the HD. The proportions of CD19<sup>+</sup>CD20<sup>+</sup>IgD<sup>+</sup>CD27<sup>+</sup> central memory B cells and CD19<sup>+</sup>CD20<sup>+</sup>IgD<sup>-</sup>CD27<sup>-</sup> effector B cells were higher in SLE. The largest difference relative to the HD was observed in the proportion of CD19<sup>+</sup>CD20<sup>-</sup>CD27<sup>+</sup>CD38<sup>+</sup> plasmablasts, which was higher in SLE and correlated with BILAG index. The proportion of Tfh cells correlated with serum IgG level, and the proportion of activated Tfh cells correlated with serum anti-Sm antibody level. Among helper T cell subsets (Th1, Th17, Treg and Tfh), Tfh cells only showed positive correlation with the proportion of plasmablast ( $r=0.24$ ,  $p=0.02$ ).

**Conclusions** Peripheral immuno-phenotyping confirmed the importance of Tfh-plasmablasts axis in patients with SLE, *i.e.* activation of Tfh cells correlated with autoantibody production while plasmablast did with disease activity of SLE. Our findings supported the relevance of Tfh-plasmablasts axis as a potential therapeutic target for SLE.

## 53 REPOSITORY CORTICOTROPIN INJECTION EXERTS DIRECT ACUTE EFFECTS ON HUMAN B CELL GENE EXPRESSION DISTINCT FROM THE ACTIONS OF GLUCOCORTICOIDS

<sup>1</sup>N Olsen\*, <sup>1</sup>A Benko, <sup>1</sup>C McAloose, <sup>2</sup>T Sunyer, <sup>2</sup>P Becker, <sup>1</sup>W Kovacs. <sup>1</sup>*Penn State Hershey, Medicine, Hershey, USA*; <sup>2</sup>*Mallinckrodt Pharmaceuticals, Clinical Translational Research, Hazelwood Missouri, USA*

10.1136/lupus-2017-000215.53

**Background and aims** Repository corticotropin injection (RCI; H.P. Acthar Gel) is a porcine pituitary-derived ACTH preparation approved by the FDA for therapy in selected cases of SLE. Previous studies have shown that RCI directly inhibits human B cell function *in vitro*.

**Methods** We used RNA-Seq to identify elements of the transcriptome that are acutely modulated by RCI in human B cells activated *in vitro* by IL4 and CD40 ligand. We compared RCI effects to those of a synthetic glucocorticoid (dexamethasone; Dex) under the same conditions.

**Results** 115 unique gene transcripts were significantly and reproducibly upregulated by RCI after 24 hours in culture. Pathways analysis revealed that upregulated genes were over-represented in “immune system response” (2.8-fold;  $p=0.026$ ) and “response to stress” (4.16-fold;  $p=0.0069$ ). 74 gene transcripts were down-regulated by RCI, and these were over-represented in two pathways: “immune system response” (2.91-fold;  $p=0.035$ ) and “cellular process” (1.73-fold;  $p=0.0036$ ). In Dex-treated cells, 65 gene transcripts were upregulated and 23 gene transcripts were down-regulated. There was no overlap between the set of genes upregulated by RCI and Dex. Two genes (PARM1 and RANKL) were downregulated by both RCI and Dex. Pathways analysis of Dex-treated samples did not reveal significant overrepresentation of regulated genes in any specific ontologic pathway.

**Conclusions** These data suggest that RCI exerts direct effects on human B cells to acutely modulate gene expression. These effects are distinct from those of glucocorticoids, supporting potential differences in mechanism of action of these two agents for treatment of autoimmune diseases.

## 54 RO52 AUTOANTIBODIES ARISE FROM SELF-REACTIVE PROGENITORS IN A MOTHER OF A CHILD WITH NEONATAL LUPUS

<sup>1</sup>J Reed\*, <sup>2</sup>M Gorny, <sup>2</sup>L Li, <sup>3</sup>T Cardozo, <sup>4</sup>J Buyon, <sup>4</sup>R Clancy. <sup>1</sup>*Garvan Institute of Medical Research, Immunology, Darlinghurst, Australia*; <sup>2</sup>*New York University School of Medicine, Pathology, New York, USA*; <sup>3</sup>*New York University School of Medicine, Pharmacology, New York, USA*; <sup>4</sup>*New York University School of Medicine, Medicine, New York, USA*

10.1136/lupus-2017-000215.54

**Background and aims** Autoantibodies targeting Ro52 occur in systemic lupus erythematosus, Sjogren’s syndrome and idiopathic inflammatory myopathies. Yet the most compelling evidence for their pathogenesis is the development of cardiac conduction abnormalities, a manifestation of neonatal lupus, in