

**Background and aims** To observe the effects of long term hydroxychloroquine treatment on blood lipid and left ventricular function of systemic lupus erythematosus(SLE) patients.

**Methods** 72 patients with SLE were randomly divided into two groups: Hydroxychloroquine treatment group(n=36)and non-hydroxychloroquine group(n=36). The level of blood lipid, left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), interventricular septum thickness(IVST), *left ventricular* posterior wall thickness (LVPWT), fractional shortening rate(FS), left ventricular ejection fraction(LVEF), E/A were measured before, 6 month, 12 month and 2 years after the treatment.

**Results** The long term applies of hydroxychloroquine can bring statistically different of TC, TG, LDL and HDL to SLE patients. LVEDD, LVWPT and E/A were statistically different ( $p<0.05$ ) before and after hydroxychloroquine were used.

**Conclusions** The long term applies of hydroxychloroquine can improve the lipidic metabolism and left ventricular function in SLE patients.

## Genetics, epigenetics, omics, biomarkers and personalised medicine in SLE and autoimmunity

262

### UTILITY OF SERUM FERRITIN AS A MARKER OF DISEASE ACTIVITY IN CHILDHOOD SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background and aims** To assess the usefulness of serum ferritin levels as a marker of disease activity and organ involvement in childhood systemic lupus erythematosus (cSLE) and to screen children with SLE for subclinical macrophage activation syndrome.

**Methods** Consecutive children who met the criteria of SLICC were enrolled. All patients interviewed and assessed for disease activity using SLE disease activity index (SLEDAI). Biochemical and serological tests including serum ferritin level and markers of disease activity and macrophage activation syndrome (MAS) including LDH, AST, triglyceride and CD25 were measured by standard laboratory procedure.

**Results** A total of 29 (24 female) SLE patients with a mean age of 10.9 ( $\pm 2.9$ ) years and mean of disease duration of 4 ( $\pm 2.4$ ) years were included. The most frequent manifestations were musculoskeletal in 25 patients followed by haematological in 15 then renal involvement in 13 patients. Twenty patients had active disease (SLEDAI  $>4$ ). Serum ferritin level was correlated significantly with SLEDAI ( $p<0.0001$ ) and markers of MAS (LDH, AST, triglyceride and CD25) and negative correlation with fibrinogen ( $p 0.02$ ). Interestingly, serum ferritin was weakly correlated with ESR but no correlation with CRP and proteinuria. Two patients confirmed to have MAS.

**Conclusions** Serum ferritin is a simple and probably a good marker of disease activity and screening for MAS in cSLE.

263

### UPDATE ON SLE-HLA ASSOCIATION: CONTRIBUTION OF ALLELE-SPECIFIC EXPRESSION IN ADDITION TO AMINO ACID CHANGES IN HLA ALLELES

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**Background and aims** A genetic contribution of the human leukocyte antigen (HLA) genes to SLE has been well documented (e.g., OR=1.65, Heritability explained by HLA=2%; *Nat Genet* 2016). To understand the association in HLA loci within the major histocompatibility complex (MHC) region in large cohorts genotyped for MHC SNPs, we developed an ethnicity-matched HLA reference panel (*PLoS One* 2014).

**Methods** Using the HLA imputation and various statistical approaches, we investigated HLA amino acid residues, HLA classical alleles and MHC SNPs simultaneously, and identified that the changes in amino acid positions 11, 13 and 26 of HLA-DRB1 explained the entire HLA association (*Nat Commun* 2014; *Nat Genet* 2016). Additionally, all the protein-coding HLA-DR beta genes (*HLA-DRB1*, *HLA-DRB3*, *HLA-DRB4* and *HLA-DRB5*) with similar functions were further investigated using imputation-based conditional regression and haplotype analyses. *HLA-DRB1* was solely associated with SLE and accounted for the associations of the other HLA-DR beta genes (*PLoS One* 2016). Finally, we measured allele-specific expression of *HLA-DRB1* in blood cells by RNA sequencing followed by an allele-specific read mapping method.

**Results** Strong allele-specific expression among *HLA-DRB1* classical alleles was observed, which caused relatively unequal expression of two heterozygous alleles in individuals. Disease association models, fitted by logistic regression including either the copy number or both the copy number and the relative expression of each allele as predictors, revealed that the SLE association was significantly better explained by adding the variables for the relative expression.

**Conclusions** These findings indicate that both the qualitative and quantitative effects of *HLA-DRB1* variants are driving SLE (Figure).

264

### PEARL: PATHWAY EXPLORATION AND ANALYSIS IN RENAL DISEASE IN THE ACCELERATING MEDICINE PARTNERSHIP (AMP) LUPUS NETWORK

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**Background and aims** Despite treatments, a substantial proportion of lupus nephritis (LN) patients progress to end stage renal disease and death. Detailed transcriptomic analyses of LN kidneys may identify new therapeutic targets. Our goal is to demonstrate the feasibility of single cell and low-input transcriptomic analyses of LN kidney and urine cells.

**Methods** Cells from urine and renal biopsies performed for clinical diagnosis from inform-consented patients (1 class III, 3 class IV+V, 1 class V) and 1 control (healthy part of tumour nephrectomy) were isolated, frozen, sorted and analysed by RNAseq.

**Results** Bulk flow sorted cell populations (CD45, epithelial) from kidney samples can separate LN from controls based on gene expression. IFN stimulated genes were differentially expressed in renal CD45 LN cells. Analysis of single cells sorted from 4 LN kidney biopsies revealed major differences in infiltrates composition, with 2 samples demonstrating a high percentage of B cells (average of 18% compared to no B cells in the other 2 samples) and CD4 T cells (18% vs 8%), and low percentage of CD8 T cells (9% vs 23%). A high transcriptomic lupus interferon signature was detected in urine CD45 cells. Distinct infiltrates and distinct expression profiles were detected across patients.

**Conclusions** The PEARL-Phase 0 project shows the feasibility of single cell isolation and transcriptomic analysis from LN kidney and urine. Analyses at a bigger scale in the two next phases of the project will accelerate discovery of new therapeutic targets and identification of biomarkers to guide therapeutic decisions in lupus nephritis and integrate the treatment effect.

265

#### THE EXPRESSION OF SIGLEC-10 IS ELEVATED ON B LYMPHOCYTES AND ASSOCIATED WITH DISEASE ACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background and aims** Siglec-10 (sialic acid-binding immunoglobulin-like lectins-10) is a member of Siglecs family and known to be expressed on B cells to regulate immune tolerance. This study aimed to investigate the expression of Siglec-10 on B cells of SLE and evaluate anti-inflammatory and immunosuppressive drugs impact on the expression of Siglec-10 on B cells *in vitro*.

**Methods** Peripheral blood mononuclear cells (PBMC) were obtained from patients with SLE (n=57) and healthy donors (n=30). Flow cytometry was performed to examine the expression of Siglec-10 on B cells. The potential association of these measures with the values of SLE disease activity index (SLEDAI) score was also analysed. *In vitro* cultivation of PBMC with Dexamethasone sodium phosphate and chloroquine phosphate, the expression of Siglec-10 on B cells were detected by flow cytometry after 16 hour.

**Results** The expression of Siglec-10 on B cells was significantly increased in SLE patients compared with normal controls ( $p < 0.001$ ). Moreover, it was positively correlated with SLE-DAI (OR=0.277,  $p < 0.05$ ) and elevated in non-treatment patient than patients after anti-rheumatic treatment ( $p < 0.05$ ). *In vitro* assay, Dexamethasone sodium phosphate and chloroquine phosphate could significantly decreased the expression of Siglec-10 on B cells respectively ( $p < 0.05$ ).

**Conclusions** The results from this study imply that Siglec-10 may play a potential role in progression and pathogenesis of SLE, which may represent a therapeutic target in SLE patients.

266

#### HUMAN AUTOANTIBODIES FROM CHILDREN WITH MOVEMENT AND PSYCHIATRIC DISORDERS TARGET THE EXTRACELLULAR N-TERMINUS OF DOPAMINE-2 RECEPTOR

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**Background and aims** We recently identified dopamine-2 receptor (D2R) autoantibodies in children with autoimmune movement and psychiatric disorders. This supported the hypothesis that a subgroup of patients may be autoimmune-mediated. However, the target epitope(s) remain unknown.

**Methods** Human D2R mutants modified in their extracellular domains were subcloned, and we analysed the region bound by 35 anti-D2R antibody-positive patient sera using quantitative flow cytometry on live transfected cells.

**Results** No anti-D2R antibody-positive patient sera bound to the three extracellular loops, but all patient sera (35/35) targeted the extracellular N-terminus. Overall, patient antibody binding was dependent on two main regions encompassing amino acids 20 to 29, and 23 to 37. Residues 20 to 29 contributed to the majority of binding (77%, 27/35), among which 26% (7/27) sera bound to amino acids R20, P21, and F22, 37% (10/27) patients were dependent on residues at positions 26 and 29, that are different between humans and mice, and 30% (8/27) sera required R20, P21, F22, N23, D26, and A29. Seven patient sera bound to the region 23 to 37 independently of D26 and A29, but most sera exhibited N-glycosylation-independent epitope recognition at N23. Interestingly, no evident segregation of binding pattern according to patient clinical phenotype was observed.

**Conclusions** We report a major biological role for D2R extracellular N-terminus as a regulator of receptor surface availability, and as a major epitope targeted and impaired in brain autoimmunity. This knowledge could help the design of novel specific immune therapies tailored to improve patient outcome.

267

#### NOVEL AUTOANTIBODIES AGAINST THE INTERFERON-RESPONSIVE MAJOR VAULT PROTEIN (MVP) IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background and aims** Autoantibody reactivity patterns are important disease and risk stratification marker in systemic lupus erythematosus (SLE). We have recently identified autoantibodies against the major vault protein (MVP) in SLE. Although the exact biological function of MVP is not well understood, MVP is an interesting autoantibody target, because it plays a pivotal role in virus-induced host response. MVP expression is induced by IFN $\gamma$  and induces upregulation of interferon (IFN) type I expression.

**Methods** Anti-MVP antibodies were discovered by high-content autoantibody profiling and validated in >700 SLE samples and autoimmune disease controls. To enable the development