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 bring statistically different of TC, TG, LDL and HDL to SLE patients. LVEDD, LVPWT and E/A were statistically different (p<0.05) before and after hydroxychloroquine were used.

Conclusions The long term uses 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 (± 2.9) years and mean of disease duration of 4 (± 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.

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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 SLEDAI (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 decrease 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.

Human autoantibodies from children with movement and psychiatric disorders target the extracellular N-terminus of dopamine-2 receptor


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.

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 pivot role in virus-induced host response. MVP expression is induced by IFNy 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