Conclusions Autoantibody profiling using 86 antigens provides an opportunity for identifying subgroups of patients with distinct marker profiles for designing clinical trials and evaluating clinical response in defined patient subgroups.

Methods Peripheral blood mononuclear cells were obtained from 80 active SLE patients (with one or more BILAG category A, or two or more BILAG category B). Circulating B, T and dendritic cells were defined based on flow cytometric analysis for human immune system termed "the Human Immunology Project". Based on these results, the immunophenotype was visualised by principal component analysis and SLE patients classified into subgroups by cluster analysis. Results Principal component analysis indicated that the immunophenotype of active SLE patients was consistent with T and B cell axes. Among these correlations, Th17 and Treg cells were statistically close, and showed positive correlation (p<0.001). Furthermore, Th0 and Th1 cells were also statistically close, and showed positive correlation (p=0.04). The same pattern was also noted between Th0 and plasmablasts (p=0.02). Cluster analysis showed that SLE patients were divided into three subgroups (with high proportions of plasmablasts in all groups); patients did not show any characteristic features other than increased plasmablasts (T cell-dominant group), patients with high percentage of Th0 cells (Th0-dominant group), and patients with high proportions of activated Treg and memory Treg and low proportion of naïve Treg (Treg-dominant group).

Conclusions Our study indicates that SLE patients can be divided into three subgroups based on T cell heterogeneity. This heterogeneity should be taken into consideration not only in basic research but also in patient selection in clinical trials for development of new drugs.

Background and aims Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease. Twin studies indicate a strong genetic contribution to lupus, yet often the pathogenic variant remains unknown. A better understanding of the individual genetic causes of SLE will enable personalised therapies. Using next generation sequencing technologies (WES/WGS) it is now possible to identify rare/novel gene variants that cause disease.

Methods We have used WES/WGS to identify rare genetic variants with strong effects that contribute to SLE and complex autoimmunity. The effect of variants on protein function were evaluated using in vitro biochemical and over-expression assays. Immunophenotyping of patient PBMCs and the use of bespoke mouse models engineered by CRISPR/Cas9 to harbour patient-specific variants were used to dissect disease mechanisms.

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targeting type-I interferons. Using our validated bioinformatics pipeline and methodology, we have now identified two other cohorts of patients with genetic variants that impair thymic tolerance and T1-IFN signalling, respectively. Biochemical assays confirmed the variants impair protein function. Furthermore, flow cytometry identified immunophenotypes in the patients’ PBMCs that may explain disease pathogenesis. The mechanisms by which they drive SLE pathogenesis are being evaluated in patient-specific mouse models.

**Conclusions** By understanding the precise genetic mechanisms that contribute to SLE pathogenesis, our data is able to stratify patients and, through a personalised approach, identify tailored therapeutic options.

**Background and aims** Risk for progression of CKD in humans is associated with an interstitial molecular signature containing 68 genes. Of these, a decrease in renal expression of EGF with a concomitant increase in urinary EGF improves the ability to predict CKD expression.

**Methods** To determine whether these 68 genes can be used in pre-clinical studies to model disease and therapeutic responses, we analysed microarray data of kidneys from three mouse lupus strains at various disease stages and after remission induction. Renal macrophage gene expression was assessed using RNASeq.

**Results** 61/64 genes have mouse gene IDs and are represented on the mouse microarray chip. Of these 49 were regulated in the same direction as in humans in at least one mouse strain with 28 common to all three strains. 9/61 genes, including EGF and TIMP1 only became abnormally regulated during established disease or during complete proteinuric relapse, confirming their association with CKD progression. Renal C1qa is a CKD marker produced mainly by renal macrophages but has a similarly high expression level in isolated pre-nephritis and nephritic renal macrophages. It can therefore be used as a biomarker of increased macrophage infiltration, a known poor prognostic feature in human lupus nephritis.

**Conclusions** Mice with lupus nephritis have a similar pattern of CKD-related gene expression to humans and these genes can be used to track therapeutic responses. Downregulation of EGF and upregulation of TIMP1 indicate progressive disease and C1qa can be used as a marker of macrophage infiltration. The fibrosis signature is best modelled in NZW/BXSB mice.

**Background and aims** RNA profiling was performed on 1760 SLE patients from two, large Phase III clinical trials, ILLUMINATE-1 and -2. SLE was compared to both healthy controls and other autoimmune diseases, including rheumatoid arthritis, psoriasis and psoriatic arthritis. The goals of this study were to characterise gene expression networks in SLE using these large cohorts, and to compare gene expression phenotypes in SLE to healthy controls and other autoimmune diseases.

**Methods** Blood was collected at baseline and RNA was interrogated on all samples using Affymetrix HTA 2.0 microarrays and on select SLE samples using NanoString nCounter™. Complete demographics, serum IgG anti-dsDNA antibodies, and complement were measured in SLE. Analyses of gene expression and gene pathways were performed.

**Results** Baseline elevation of interferon responsive genes (IRG) was detected in SLE and associated with younger age, elevated anti-dsDNA antibodies, elevated SLEDAI and decreased levels of C3. Significant differences in SLEDAI organ domain involvement between IRG-positive and IRG-negative groups were observed. Elevated expression of IRG, genes involved with B cell and plasma cell biology, and with cell cycling and signalling were detected in SLE. A bimodal expression pattern of IRG was unique to SLE. Substantial heterogeneity of expression of IRG and complex relationships in interferon (IFN) gene networks were observed.

**Conclusions** There was substantial heterogeneity of gene expression in IFN gene networks when examining individual IFN genes and complex relationships were observed among IFN gene networks. Low IFI27 was identified as a novel subtype of IFN signature in SLE.