

regulation of oxidative metabolism and potential roles in development of systemic lupus erythematosus (SLE).

**Methods** CD4 +T lymphocytes isolated from 97 SLE patients, 30 RA patients, 10 AS patients and 20 healthy donors were used in our *in vitro* experiments. Total RNA of CD4 +T lymphocytes isolated from 4 SLE patients and 3 healthy donors were used to perform small RNA sequencing. Total RNA of CD4 +T lymphocytes transfected with synthetic tRF-3009 or negative control (a random sequence, single strand) were used to perform next generation sequencing. CD4 +T lymphocytes isolated from healthy donors were transfected with tRF-3009/negative control or tRF-3009 siRNA/si-NC *in vitro*, with/without IFN-alpha treatment, to analyze OCRROS and ATP concentration. Real-time qRT-PCR was performed to analyze expression of tRF-3009 and related gene expressions.

**Results** We have identified a series of tRFs expressed abnormally in SLE CD4 +T lymphocytes. Interestingly, almost all up regulated tRFs were from 3end of mature tRNA while down regulated ones were from 3end of tRNA precursors. We have found that expression of tRF-3009 was correlated with lupus nephritis (LN) and urine protein (PRO). The expression of tRF-3009 could be induced by IFN-alpha treatment *in vitro*. Knockdown of tRF-3009 by siRNA could rescue the metabolism change of CD4 +T lymphocytes induced by IFN-alpha. Transfection of tRF-3009 alone could up regulate oxidative phosphorylation of CD4 +T lymphocytes *in vitro*.

**Conclusions** This study identified a series of abnormally expressed tRFs existed in CD4 +T lymphocytes isolated from SLE patients. One of these small RNAs, tRF-3009 also enriched in kidney and correlated with occurrence of lupus nephritis. tRF-3009 anticipated in metabolism regulation, may play important roles in SLE pathogenesis.

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### PREDICTORS OF HYDROXYCHLOROQUINE TREATMENT ADHERENCE AMONG PEOPLE WITH LUPUS

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**Background** Treatment adherence is associated with better disease control, improved morbidity and mortality and increased quality of life.<sup>1</sup> Studies examining treatment adherence predictors have varied in examined characteristics and results. This study analyzes demographic and socioeconomic factors, perceptions, and experiences influencing hydroxychloroquine (HCQ) treatment adherence among people with lupus. HCQ has long been used to treat lupus, and has been shown to reduce damage accrual and has protective effects on diseases such as diabetes and hyperlipidemia as well as overall survival in people with lupus.<sup>2</sup>

**Methods** Cross-sectional study data was obtained through the 2015–2016 Lupus Needs Survey, an online national needs assessment among 3022 adults self-reporting a lupus diagnosis. Univariate analyses were conducted using chi-square and simple logistic regressions among 21 variables, which were subsequently dichotomized. Variables with rates of missing values >15% of total sample were removed in further analysis.

**Abstract 232 Table 1** Results of Binary Logistic Model of Predictors of HCQ Treatment Adherence

	Odds Ratio	95% Confidence Interval	p-value
Black	0.35	0.18–0.67	0.002*
Other (mixed, American Indian/Alaskan Native, Pacific Islander, or Middle Eastern)	0.35	0.14–0.85	0.021*
Moderate severity of lupus at diagnosis	0.57	0.31–1.03	0.061
HCQ improves/helps treat my symptoms	2.49	1.25–4.92	0.009*
Positive impression of HCQ	2.14	1.08–4.24	0.029*
Rheumatologist as primary doctor treating lupus	2.0	1.01–3.95	0.046*

\*Significant p-value<0.05.

Next, 13 variables with a p-value<0.20 were entered into a binary logistic model using backwards stepwise selection.

**Results** 2028 individuals reported currently taking HCQ with 1581 (78.0%) individuals reporting taking the medication exactly as prescribed all of the time, 385 (19.0%) reporting some of the time, and 62 (3.1%) reporting sometimes or never taking HCQ as prescribed. People with lupus were twice as likely to adhere to HCQ if they reported having a rheumatologist as the primary doctor treating their lupus (p=0.046, OR=2.00) and more than twice as likely if they reported having a positive impression of HCQ (p=0.029, OR=2.14) or experienced improvement in treating their symptoms using HCQ (p=0.009, OR=2.49). Notably, African Americans and those indicating race as Other (mixed, American Indian/Alaskan Native, Pacific Islander or Middle Eastern) were 65% less likely to adhere to HCQ treatment (p=0.002, OR=0.35; p=0.021, OR=0.35, respectively).

**Conclusions** The study confirms the importance of experiential factors such as medication impression and patient-reported symptom improvement in HCQ treatment adherence. Additionally, results highlight the potential significance of having a specialist as the primary lupus doctor. This may be due to rheumatologists higher awareness of the value of HCQ for lupus patients compared to other providers. Further exploration is needed on cultural factors negatively influencing treatment adherence among certain racial groups, particularly African Americans and Other racial groups (mixed, American Indian/Alaskan Native, Pacific Islander or Middle Eastern). Treatment adherence is particularly important in lupus given the complex nature of the disease and fluctuation of disease activity, which may be exacerbated by poor adherence.

**Funding Source(s):** UCB Pharma funded study data collection.

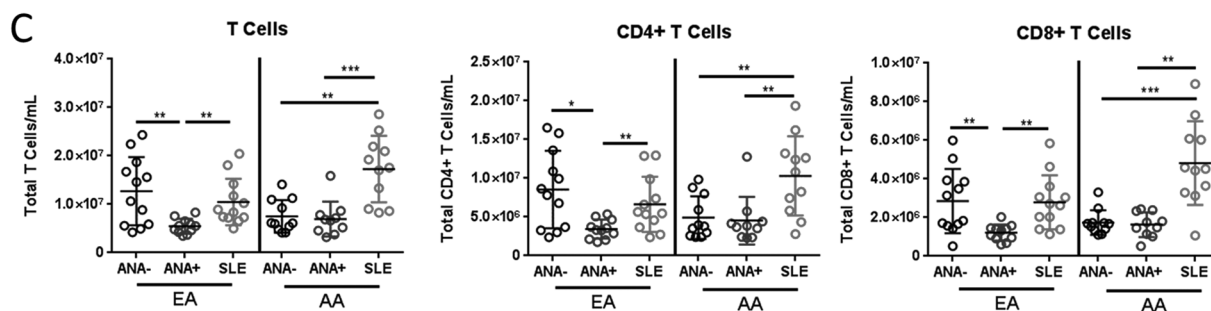
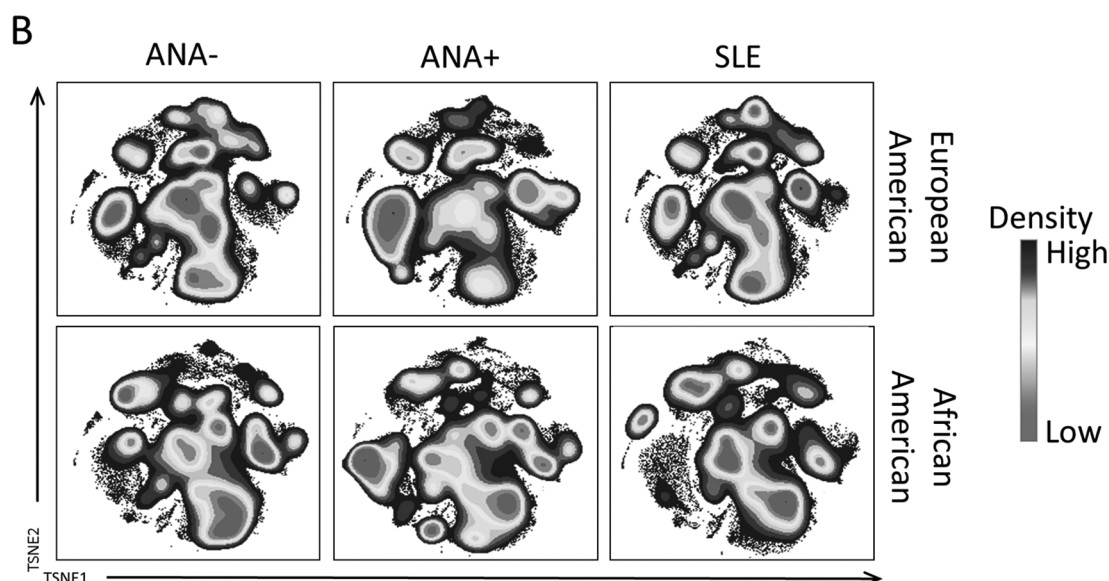
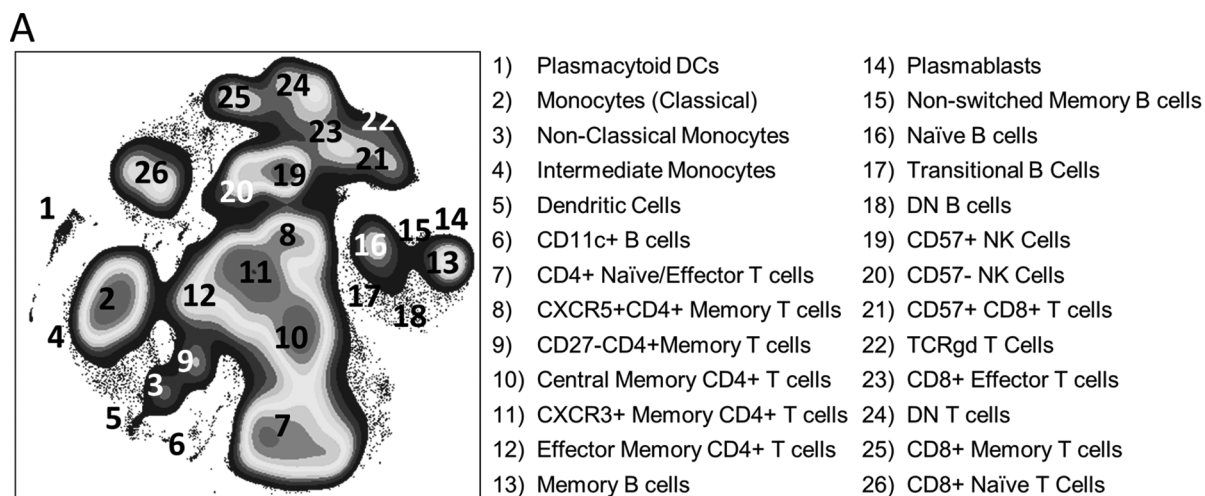
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### AUTOANTIBODY-POSITIVE HEALTHY INDIVIDUALS CONSTRAIN T CELL PATHWAYS TO REGULATE AUTOIMMUNE DISEASE

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**Background** Anti-nuclear antibody (ANA) positivity is a principal feature of individuals with an autoimmune disease, yet up to one in five healthy individuals are ANA-positive (ANA+)



**Abstract 233 Figure 1** Calculated cell numbers indicate elevated T cells in SLE patients and suppressed T cells in EA ANA+ healthy individuals. 20 cell surface marker expression is shown using dimensionality reduced t-SNE plots from PBMC data (110,00 cells) derived from 72 samples. (A) A density map is shown depicting the density of cells and are numbered according to phenotypic subset. (B) Density maps depicting European and African American ANA-, ANA+ and SLE patient PBMC t-SNE plots created using all 33 surface markers are plotted. All plots were derived from cumulative data from 12 individuals per group. (C) Cells numbers were calculated from cell subsets using frequencies and total cell counts. Cell numbers for T cells, CD4+ T cells, and CD8+ T cells are shown. \*p<0.05, \*\*p<0.01, \*\*\*p<0.001

and will never develop overt disease. Understanding differences in immune cell physiology between ANA+healthy individuals and individuals with clinical SLE remains a critical goal in the understanding of SLE pathogenesis across ethnicities.

**Methods** Blood specimens and information on disease activity were collected from European (EA) and African American (AA) individuals classified and matched in groups as ANA-healthy controls (n=24), ANA +healthy (n=24) or SLE patients (n=24). Single-cell analysis of cell surface markers was completed by mass cytometry on PBMCs and cellular heterogeneity was visualized using tSNE (figure 1A–B) and manual gating. Further, phospho-specific flow cytometry was used to measure basal levels of pERK, pPLCg2 and p38 and expression following CD3/CD28 (TCR) and anti-IgG and IgM (BCR) stimulation. Whole genome RNA-sequencing was performed on flow cytometry sorted T cells, B cells and monocytes from 35 matched ANA-, ANA +and SLE patients followed by weighted correlation network analysis (WGCNA) and pathway enrichment analyses.

**Results** Both European and African American SLE patients were distinguished from healthy individuals by T cell proliferation (p=0.002) (figure 1C), plasmacytoid dendritic cell activation (p=0.021) and elevated stem cell factor (p=0.0003). EA ANA+healthy individuals exhibited greater immune regulation with reduced T cell numbers (p=0.002) (figure 1C), decreased activation of dendritic cells (p=0.039) and transitional B cells (0.033), and elevated expression of the inhibitory receptor CD85j (p=0.042) on specific immune cell subsets compared to ANA- healthy subjects. Further, a module associated with hematopoiesis, T cell activation and intrinsic apoptosis signaling pathways is expressed at a higher level in T cells of EA ANA+individuals. In contrast, AA ANA+healthy individuals had elevated plasma levels of IL-6 (p=0.018) and reduced inhibitory receptor expression (p=0.0089) compared to ANA-healthy controls. Gene expression modules associated with viral responses and type I IFN pathway activation were identified in AA SLE patient B cells, while similar expression modules were only found in the monocytes of European American SLE patients.

**Conclusions** These results highlight the importance of stem cell factor and T cell expansion in SLE pathogenesis, and suggest that mechanisms of SLE pathogenesis differ by ethnicity. ANA +European Americans may have more effective regulatory mechanisms in place to prevent transition to classified autoimmune disease.

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#### CLINICIANS WITH LUPUS LOSING SKILLS AND DIVERSITY FROM HEALTH SERVICES RESULTS FROM AN ON-LINE SURVEY

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**Background** It is well-documented that people with systemic lupus erythematosus (SLE) have high levels of workplace disability and unemployment. We present the data from a sub-group of participants in an on-line survey designed to

understand the barriers and facilitators to employment in people with lupus as a first step towards solutions. Three hundred and ninety-three detailed questionnaires were returned, demonstrating that the overarching barriers to continuing employment were fluctuation, invisibility and fatigue, facilitators were flexibility in working pattern, part-time working understanding management and colleagues. Participants suffered from high levels of anxiety and distress about their loss of income and likely future inability to work. Those claiming benefits felt guilt, shame and humiliation.

**Methods** The on-line survey was conducted in UK adults with SLE, through the LUPUS UK website, and was designed to find out about the difficulties and successes that people with SLE have in maintaining employment. The data from participants working in a clinical profession or employed by the National Health Service (NHS) in a clinical-related activity were identified from the cohort. Their data is currently being analysed to see if those working in NHS organisations have consistently good experiences of workplace support and better chances of retention.

**Results** Fifty-five of the sample of 393 (14%) worked or had worked in the NHS in a clinical or clinically-related role. Roles include doctors, managers clinical coders, midwives, podiatrists, pharmacists, operating department assistants. The largest group were nurses including two in senior roles and untrained nursing assistants. Most of the sample had reduced hours or stopped working completely directly as a result of lupus, support was variable with some attributing workplace flexibility to NHS employment but others experiencing harassment. A recently introduced method of calculating sick leave militates against people with fluctuating conditions.

**Conclusions** SLE presents specific difficulties for maintaining employment fatigue, fluctuation and invisibility not addressed by current anti-discrimination legislation or currently-available reasonable adjustments. As Europe's largest employer with a core mission of treating illness the NHS could set an example of how to overcome barriers to employment in people with fluctuating conditions, like lupus. There is clear evidence of loss of skills from the organisation and emerging evidence from this study suggest variable support and levels of knowledge from managers and colleagues. Personal pain from loss of role and income were high in participants. Further data will be available.

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#### IKZF1 AND IKZF3 INHIBITION IMPAIRS B CELL DIFFERENTIATION AND MODULATES GENE EXPRESSION IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background** Polymorphisms in IKZF1 (Ikaros) and IKZF3 (Aiolos), which are transcription factors essential for B cell activation, maturation and differentiation, have been associated with Systemic Lupus Erythematosus (SLE). However the functional role of IKZF1 and IKZF3 in the context of failed B