African-American and European-Americans, and is located within an active enhancer region in neutrophils and modifies *TREML4* expression. *In vitro* patch methylation experiments confirmed the regulatory effects of *TREML4* methylation upon gene expression. Experiments to assess the functional effects of TREML4 overexpression in human neutrophils are underway in our laboratory. Interestingly, the DNA methylome was highly stable across disease activity levels and over time. Two sites cg26104306 (*SNX18*; FDR-adjusted P-value = 3.38 x 10^{-2}) and cg06708913 (FDR-adjusted P-value = 3.43 x 10^{-2}) were associated with changing disease activity levels in African-American patients. Demethylation of a CpG site located within *GALNT18* was associated with the development of active lupus nephritis.

Conclusion Lupus granulocytes demonstrate significant differences in DNA methylation patterns between African-American and European-American patients. DNA methylation profiles in lupus patients are influenced by ancestry-specific genetic variants and are highly stable over time independent of disease activity levels. Progressive demethylation in *SNX18* was observed with increasing disease activity in granulocytes from African-American lupus patients, and demethylation in *GALNT18* was associated with the development of lupus nephritis in our cohort during follow up.

1508 SINGLE-CELL EPIGENETIC PROFILING HIGHLIGHTS GENETIC IMPACT ON CHROMATIN ACCESSIBILITY IN SLE

[1,2,3]Sai Ma, [4]Richard C Pelikan, [4]Yao Fu, [4]Jennifer A Kelly, [4]David Murphy, [4]Graham B Wiley, [3]Vinay K Kartha, [5]Caleb Lareau, [2,3]Jason D Buenrostro, [4]Patrick M Gaffney*. *[1]Department of Biology, MIT, Cambridge, MA, USA; [2]Broad Institute of MIT and Harvard, Cambridge, MA, USA; [3]Department of Stem Cell and Regenerative Biology, Harvard University, Cambridge, MA, USA; [4]Genes and Human Disease Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, USA; [5]Department of Pathology, Stanford University, Stanford, CA, USA*

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Background Chromatin accessibility (CA) is a critical epigenetic feature identifying genomic loci that actively participate in gene-regulating functions, such as transcription and DNA repair. In turn, genetic polymorphisms within these loci can affect the magnitude of CA, i.e. a chromatin accessibility quantitative trait locus (caQTL). Changes in CA have been implicated in inflammatory disease, and previous genetic research has identified several risk haplotypes for systemic lupus erythematosus (SLE). However, it remains unclear how CA may interact with genetic risk factors in SLE pathogenesis. To better understand how CA in SLE may be driven by genetic variation, we performed single-cell assay for transposase accessible chromatin (sciATAC-seq) on peripheral blood mononuclear cells (PBMCs). SciATAC-seq is an efficient, scalable and sensitive assay that allows the epigenetic profiling of thousands of cells from an individual. By combining these profiles with genotypic data, we can search for caQTLs as evidence of genetic-epigenetic interaction specific to SLE.

Methods PBMCs were isolated from 45 SLE patients and 50 healthy controls. Each PBMC sample underwent both genotyping and sci-ATAC sequencing. DNA was then sequenced by Illumina Next-seq. Cell-specific ATAC reads were demultiplexed and quantified by custom software developed by the BROAD Institute (Cambridge, MA). Genotyping data was phased and imputed using the IMPUTE2 tool suite. Cell type-specific caQTL analysis was performed by RASQUAL.

Results An average of 980 cells were sequenced per sample, with a total of 745,697 CA sites measured. We identified a total of 153,716 caQTL relationships across 17 distinct immune cell types, involving 59,715 unique variants; 59% of which are also reported as expression QTLs in whole blood. The majority of caQTLs already implicated in autoimmune disease risk haplotypes occurred predominantly in B cells and plasmacytoid dendritic cells. CA profiles exhibit cell type-specific cluster orientation highly correlated with caQTL genotype. Genotypes at variant rs1131665, previously associated with an SLE risk haplotype in IRF7 and here as a caQTL, distinguished subpopulations of B cells and monocytes on the basis of global CA profiles. Increases of CA at the variant were present in SLE individuals compared to controls, suggesting caQTL variants contribute to a genome-wide epigenetic phenotype for SLE risk.

Conclusion Using advances in single-cell epigenetic profiling, we were able to identify thousands of genetic variants which influence epigenetic functions, in a cell type-specific way, through their association to CA. Understanding the molecular mechanisms for how caQTLs alter cell type-specific chromatin accessibility will provide new insights into the role of epigenetic regulation in SLE pathogenesis.

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1509 DIFFERENCES IN CHROMATIN ARCHITECTURE PRE- AND POST-INDUCTION THERAPY IN PEDIATRIC LUPUS PATIENTS

[1,2,3]Joyce S Hui-Yuen*, [4,5]Kaiyu Jiang, [3]Susan Malkiel, [3]Betty Diamond, [4,5]James N Jarvis. *[1]Division of Pediatric Rheumatology, Steven and Alexandra Cohen Children's Medical Center, Lake Success, NY, USA; [2]Department of Pediatrics, Hofstra-Northwell School of Medicine, Hempstead, NY, USA; [3]Center for Autoimmune, Musculoskeletal, and Hematologic Diseases Research, Feinstein Institute for Medical Research, Manhasset, NY, USA; [4]Department of Pediatrics, University at Buffalo, Buffalo, NY, USA; [5]Genetics, Genomics, and Bioinformatics Program, University at Buffalo, Buffalo, NY, USA*

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Background Systemic lupus erythematosus (SLE) may be triggered by gene-environment interactions. Data remain scarce on how epigenetic variance contributes to disease risk in pediatric SLE (pSLE). Our objectives were to identify differences in chromatin architecture in treatment-naïve pSLE compared to healthy children (HC) and pSLE patients after induction therapy.

Methods We used assays for transposase-accessible chromatin-sequencing (ATACseq) in 8 pSLE patients pre- and post-induction therapy and 5 HC to investigate whether regions of open chromatin unique to pSLE patients demonstrate enrichment for transcriptional regulators, using standard computational approaches and a false discovery rate of <0.05.

Results The mean age of onset was 13.75 (range 7-17) years in pSLE, and mean SLEDAI was 12.8 (range 6-24). We