chromatin accessibility "peaks" were identified with MACS2. For each cell type, we identified the consensus set of epigenetically active peaks across all 14 subjects. We conducted enrichment tests of identified loci using the GREAT tool and performed differential accessibility analysis using the edgeR package in R. Transcription factor binding motif enrichment and overlaps with know SLE risk haplotypes were also determined.

Results Chromatin accessibility profiles among the three cell types shared common features as well as peaks specific to each cell-type profile. The peaks unique to each profile were enriched in genomic loci specific to their cellular function as well as their known immunologic molecular signatures in SLE. Quantitative analysis of differential chromatin accessibility loci which discriminate between individuals with SLE and healthy controls patients with high versus low disease activity. Motif analysis revealed that many consensus peaks occupy binding sites of cohesion complex subunits, suggesting that long-range chromatin interactions may mediate immune responses that drive SLE progression. In addition, 320 SLE risk SNPs were located within an open chromatin peak suggesting these as SNPs candidates for functional impact.

Conclusions Our analysis suggests that chromatin profiling may have power to differentiate patients from controls as well varying extremes of disease activity and can pinpoint putative functional SNPs. Additional insight will be gained from further refinement of immune cell compartments. Future studies will focus on long-range interactions driving differences in chromatin accessibility and integrating these data with transcriptome data. We expect this approach to exapnd our knowledge of how regulatory networks in specific cells and cell states drive SLE progression.

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GG-06 SINGLE CELL GENE EXPRESSION STUDIES IN LUPUS PATIENT MONOCYTES REVEAL NOVEL PATTERNS REFLECTING DISEASE ACTIVITY, INTERFERON, AND MEDICAL TREATMENT

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Background Our previous studies have shown that different cell types from the same sample demonstrate diverse gene expression, and important findings can be masked in mixed cell populations. In this study, we examine single cell gene expression in SLE patient monocytes and determine correlations with clinical features.

Materials and methods $CD14^{++}CD16^{-}$ classical monocytes (CLs) and $CD14^{dim}CD16^{+}$ non-classical monocytes (NCLs) from SLE patients were purified by magnetic separation. The Fluidigm single cell capture and Rt-PCR system was used to quantify expression of 87 monocyte-related genes.

Results Both CLs and NCLs demonstrated a wide range of expression of IFN-induced genes, and NCL monocytes had higher IFN scores than CL monocytes. Unsupervised hierarchical clustering of the entire data set demonstrated two unique clusters found only in SLE patients, one related to high disease activity and one related to prednisone use. Independent clusters in the SLE patients were related to disease activity (SLEDAI 10 or greater), interferon signature, and medication use, indicating that each of these factors exerted a different impact on monocyte gene expression that could be separately identified. A subset of anti-inflammatory gene set expressing NCLs was inversely correlated with anti-dsDNA titers (rho = −0.77, p = 0.0051) and positively correlated with C3 complement (rho = 0.68, p = 0.030) in the SLE patient group.

Conclusions Using single cell gene expression, we have identified a unique gene expression patterns that reflect the major clinical and immunologic characteristics of the SLE patients which are not evident in bulk cell data, supporting the critical importance of the single cell technique.

GG-07 SLE RISK HAPLOTYPES ARE ASSOCIATED WITH DEVELOPMENT OF SEROLOGIC AUTOIMMUNITY IN HEALTHY INDIVIDUALS

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Background Approximately 60 loci are associated with SLE in genotyping studies. These loci impact several pathways in the immune response. ANA are one of the earliest features of lupus, preceding the onset of clinical symptoms by many years. The genetic risk factors that underlie the development of serological autoimmunity are unknown. A genome-wide association study was undertaken to understand the genetics of ANA development

Materials and methods Serum and DNA were collected from 2,635 healthy individuals with no personal history of autoimmunity. Antinuclear antibodies were detected using an ELISA to human nuclear extract (INOVA). Sera from 724 individuals (ANA-, ANA+, and SLE) were assayed by protein microarray quantifying IgM and IgG responses to 96 human autoantigens. A nested cohort of 1,969 subjects consisting of all the ANA+ Caucasian individuals and age/gender matched ANA- controls were genotyped using the ImmunoChip SNP array.

Results In 2,635 healthy individuals, 16.2% had moderate and 8.0% had high levels of IgG antinuclear antibodies. High titer ANA was almost exclusively seen in female subjects (OR (CI): = 1.6 (1.1–2.1), p = 0.003). Age was not associated with the presence or titer of ANA. On the autoantigen microarray, ANA+ healthy individuals had a high prevalence of antibodies to non-nuclear and cytoplasmic antigens, while subjects with SLE predictably produced antibodies to a variety of nuclear antigens. A quantitative genetic association test with ANA identified genomic loci associated with high ANA phenotype. *HLA* was second strongest signal ($p = 6.2 \times 10^{-6}$). The frequencies of the SLE risk haplotypes at *STAT4*, *TNFAIP3*, *BLK*, *BANK1*, *NCF2*, *and NMNAT2* were also significantly ($p<0.05$) increased in the ANA high positive group compared to ANA negative healthy subjects. On the other hand, SLE risk haplotypes in *ITGAM*, *UBE2L3*, *IRF5-TNPO3* loci were only high in the SLE group, suggesting their main role in a transition to clinical disease.