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 coherence 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 expand our knowledge of how regulatory networks in specific cells and cell states drive SLE progression.

**Acknowledgements** This work was supported by the following grants from the National Institutes of Health: NIAID: U19AI082714; NIH: AR056360, AR063124; NIGMS: GM110766

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

1Priti Raj, 2Quan-Zhen Li, 1Igor Dzamarov, 3Nancy J Olsen, 3Kathy Skifs, 4Jennifer Kelly, 5Judith A James, 6Bernard Lauseries, 6Peter Gregersen, 7Karen Cerasale, 8David R Karp*, 9Edward K Wakeland, 10Department of Immunology, University of Texas Southwestern Medical Centre, Dallas, TX USA; 11Department of Medicine, Penn State Hershey Medical Centre, Hershey, PA USA; 12Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, OK USA; 13Pôle de pathologies rhumatismales, Institut de Recherche Expérimentale et Clinique, Université catholique de Louvain, Brussels, Belgium; 14Center for Genomics and Human Genetics, The Feinstein Institute for Medical Research, Manhasset, NY USA; 15Benaroya Research Institute, Seattle, WA USA; 16Department of Medicine, University of Texas Southwestern Medical Centre, Dallas, TX USA

10.1136/lupus-2016-000179.58

**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 (NOVA). 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+ Cau-isan 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 × 10^{-4}). The frequencies of the SLE risk haplotypes at STAT4, TNFAIP3, BLK, BANK1, NCF2, and MNAT2 were also significantly (<0.05) increased in the ANA high positive group compared to ANA negative healthy subjects. On the other hand, SLE risk haplotypes in TTAGM, UBE2L3, IRF3-TNPO3 loci were only high in the SLE group, suggesting their main role in a transition to clinical disease.