Abstracts

autoimmunity for several years prior to the onset of clinical disease. Measuring anti-nuclear antibodies (ANA) is a common test for humoral autoimmunity. It is sensitive (95%+) for SLE, but not specific as up to 25% of healthy controls (HC) will have a measurable ANA. While very few of the ANA+HC will develop SLE, they represent a group at higher risk of the disease. Understanding the risks for ANA positivity provides essential knowledge about the development of SLE.

Methods Serum and DNA were collected from 2903 healthy individuals with no personal history of autoimmunity. Anti-nuclear antibodies were detected using Inova QuantaLite ELISA. Sera from subset (n=724) individuals (ANA+HC, ANA+HC, and SLE) were assayed by protein microarray quantifying IgM and IgG responses to 89 previously known human autoantigens. A nested cohort consisting of all the ANA +Caucasian individuals and age/gender matched ANA−controls were genotyped using the ImmunoChip1. SNP array.

Results In HC, 16% had moderate and 10% had high levels of IgG ANA. Autoantigen microarray data showed that ANA+HC 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 as well. A quantitative genetic association test with ANA identified the locus c11orf30 or EMSY, associated with high ANA phenotype in the healthy population (see figure 1). This locus codes for a negative transcriptional regulator. A haplotype comprised of many potentially regulatory polymorphisms at EMSY contributed to strong risk for ANA in healthy individuals ([p=3.83E-04, OR=2.60]). eQTL data suggests that the ANA-associated EMSY haplotype leads to reduced expression of EMSY protein in human macrophages and EBV cell lines. Autoantibody profiles of serum samples from healthy individuals with the EMSY risk genotype exhibited high titers of anti-IgG and IgA antibodies targeted to multiple autoantigens as well as food and environmental allergens.

Conclusions EMSY, a locus previously linked with atopy, psoriasis and inflammatory bowel disease was associated with ANA in healthy individuals. The EMSY protein is a BRCA2-associated transcriptional repressor. Individuals with risk haplotypes in EMSY make a wide variety of disease-associated antibodies, suggesting an early common pathway for autoimmune and allergic conditions.

**GG-08 IMMUNE REPERTOIRE AND GENETIC RISK ALLELES IN HEALTHY PEDIATRIC POPULATIONS WITH AUTOIMMUNE INDICATORS**

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Background The antibody specificities of an infant progressively form in response to infections, environmental exposures, and vaccinations. While many adults develop antibodies to self-antigens, it remains unknown if these are present in infants and toddlers.

**GG-09 A ROLE FOR EBNA2 IN MECHANISMS THAT ARE RESPONSIBLE FOR LUPUS AND OTHER AUTOIMMUNE DISEASES**

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Background Explaining the genetics of many diseases is challenging because most associations localize to incompletely understood regulatory regions.