Gene X Environment Interactions in Systemic Lupus Erythematosus: Polymorphisms in ITGAM and Smoke Exposure among African Americans

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***Abstract*— Systemic Lupus Erythematosus (SLE) is an autoimmune disease that disproportionately affects young African American females. Studies have shown associations between SLE risk and single nucleotide polymorphisms (SNPs) in the ITGAM gene, and associations between SLE risk and smoking. We investigated the potential for a gene x environment interaction between ITGAM polymorphisms and smoke exposure in SLE by conducting a case control study in a population-based registry of Gullah African Americans. We genotyped two SNPs in ITGAM, rs1143679 and rs7190807, using polymerase chain reaction (PCR) tests and analyzed findings with attention to passive childhood smoke exposure. Despite compelling prior results, we found no statistically significant associations between SLE and either SNP, or between the SNPs, secondhand smoke, and SLE, but were limited by sample size.**

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease characterized by immune complex-mediated tissue inflammation and injury. While a genetic component of SLE etiology has been established, a relatively low concordance for identical twins suggests that environmental factors are also involved [1]. The ITGAM gene, which has been associated with SLE, codes an integrin chain that modulates certain immune cells. In autoimmune diseases, ITGAM is suspected to interact with an environmental trigger to stimulate an immune response on a self-antigen. Specifically, the single nucleotide polymorphism (SNP) in the ITGAM gene, rs1143679, prevents the coded integrin from phagocytizing apoptotic cells [2]. This SNP, along with rs7190807, a SNP related to rs1143679, were the focus of our study.

Prior studies conducted at the Medical University of South Carolina examined genes and chemicals with suspected associations with SLE among Gullah African Americans. Those studies found ITGAM risk alleles for SLE [3] and increased SLE risk with passive childhood tobacco smoke exposure [4].

To examine the potential for a gene x environment interaction between passive childhood smoke exposure and the two aforementioned SNPs, we randomly selected 23 SLE female patients and 22 unrelated female controls from a population-based registry of Gullah African Americans. The patients and controls selected were not included in the prior Gullah studies [4]. Information on secondhand smoke exposure was collected at an in-person visit. Genomic DNA was used to genotype the two SNPs using polymerase chain reaction (PCR) tests. The presence of the minor allele in a heterozygous or homozygous minor genotype indicates the polymorphism. Two controls were excluded from analyses for SNP rs1143679 because of unclear genotype determinations.

Nine patients (39.13%) and eight controls (36.37%) self-reported passive, secondhand smoke exposure during childhood. There is no significant difference in smoking history between the cases and controls. For both SNPs, there were no statistically significant differences in genotypes between the cases and controls (Fig. 1). No association was found between having the minor allele present and having SLE for rs1143679 or rs7190807 (p=.672 and p=.531 respectively). There were also no associations found between having the minor allele present and having passive childhood smoke exposure with having SLE for the two SNPs (p=1.00, p=1.00).

Despite compelling findings from the prior larger study, we found no statistically significant associations between passive childhood smoke exposure and SNPs in ITGAM. However, due to a limited sample size, we did not have adequate statistical power to conclude that no interaction exists. We did note, however, that significant numbers of both patients and controls had exposure to secondhand smoke. The high prevalence of secondhand smoke exposure and known adverse health outcomes is of public health concern, whether or not SLE ultimately is proven to be one of those health outcomes.

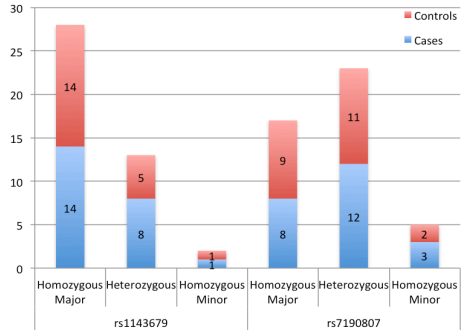

Figure 1. Comparison of genotype determinations between cases and controls for SNPs rs1143679 and rs7190807.

ACKNOWLEDGMENT

The authors thank Carol Feghali-Bostwick, Ph.D. for all her guidance, Catherine Svetcharnik for her assistance in the lab, and Paula Ramos Ph.D. and Beth Wolf Ph.D. for their assistance and valuable input.

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