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Published by admin on Mon, 08/19/2013 - 12:58pm

Title
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Publication Type
Journal Article

Year of Publication
2012

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Journal
Vaccine

Volume
30

Issue
32

Pagination
4778-84

Date Published
2012 Jul 6

ISSN
1873-2518

Keywords
Adult, Anthrax Vaccines, Antibodies, Bacterial, Antibody Formation, European Continental Ancestry Group, Female, Genes, MHC Class II, Genetics, Population, Genome-Wide Association Study, Genotyping Techniques, Haplotypes, Humans, Immunoglobulin G, Male, Middle Aged, Models, Genetic, Polymorphism, Single Nucleotide, Promoter Regions, Genetic, RNA-Binding Proteins, Suppressor of Cytokine Signaling Proteins

Abstract
Several lines of evidence have supported a host genetic contribution to vaccine response, but genome-wide assessments for specific determinants have been sparse. Here we describe a genome-wide association study (GWAS) of protective antigen-specific antibody (AbPA) responses among 726 European-Americans who received Anthrax Vaccine Adsorbed (AVA) as part of a clinical trial. After quality control, 736,996 SNPs were tested for association with the AbPA response to 3 or 4 AVA vaccinations given over a 6-month period. No SNP achieved the threshold of genome-wide significance (p=5 × 10(-8)), but suggestive associations (p<1 × 10(-5)) were observed for SNPs in or near the class II region of the major histocompatibility complex (MHC), in the promoter region of SPSB1, and adjacent to MEX3C. Multivariable regression modeling suggested that much of the association signal within the MHC corresponded to previously identified HLA DR-DQ haplotypes involving component HLA-DRB1 alleles of *15:01, *01:01, or *01:02. We estimated the proportion of additive genetic variance explained by common SNP variation for the AbPA response after the 6 month vaccination. This analysis indicated a significant, albeit imprecisely estimated,
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Published on UAB School of Public Health (http://www.soph.uab.edu)

contribution of variation tagged by common polymorphisms (p=0.032). Future studies will be required to replicate these findings in European Americans and to further elucidate the host genetic factors underlying variable immune response to AVA.

DOI 10.1016/j.vaccine.2012.05.032
Alternate Journal Vaccine
PubMed ID 22658931
PubMed Central ID PMC3387748
Grant List
272201000023C-0-0-1 / / PHS HHS / United States
HHSN272201000023C / AI / NIAID NIH HHS / United States
N01 AI040068 / AI / NIAID NIH HHS / United States
N01-AI40068 / AI / NIAID NIH HHS / United States