Author's response to reviews

Title: Integrated Genome-wide Association, Coexpression Network, and Expression Single Nucleotide Polymorphism Analysis Identifies Novel Pathway in Allergic Rhinitis

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Re: "Integrated Genome-wide Association, Coexpression Network, and Expression Single Nucleotide Polymorphism Analysis Identifies Novel Pathways in Allergic Rhinitis"

Dear BMC Medical Genomics Editors,

Please find enclosed a copy of our manuscript, “Integrated Genome-wide Association, Coexpression Network, and Expression Single Nucleotide Polymorphism Analysis Identifies Novel Pathway in Allergic Rhinitis.” Our study should be of great interest to BMC Medical Genomics readers, as it demonstrates the utility of integrating genome-wide genotype and gene expression data to identify novel biologic context (mitochondrial pathways) for a highly prevalent disease: allergic rhinitis.

Allergic rhinitis, or hay fever, is a common disease whose genetic basis is incompletely explained. Here we report an integrated genomic analysis of allergic rhinitis. We performed genome wide association studies (GWAS) of allergic rhinitis in 5632 ethnically diverse North American subjects from the United States, Mexico, and Barbados. Many previous GWAS of varying diseases have sought context for their findings using gene expression data generated from subjects distinct from those genotyped. We pursued a more direct approach to identify relevant biologic context for our GWAS findings. We collected disease-relevant tissue (CD4+ lymphocytes) from subjects who had been genotyped and profiled their gene expression. We then integrated the GWAS and CD4+ lymphocyte gene expression data using expression single nucleotide (eSNP), coexpression network, and pathway approaches. We found consistent evidence for mitochondrial pathways as a novel pathway of interest and potential therapeutic target for allergic rhinitis. Our integrated method yielded an informed biological context for genetic variants associated with allergic rhinitis and may be applied to the study of other diseases to identify relevant biologic context for GWAS findings. Our approach may prove useful when studying complex traits and when studying populations of limited sample size.

This manuscript has been reviewed and approved by all listed authors. The authors have no conflicts of interest to disclose.

We respectfully suggest the following reviewers:
Joshua Akey, PhD (University of Washington, akeyj@u.washington.edu)
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We respectfully request that Klaus Bonnelykke (University of Copenhagen), Hans Bisgaard (University of Copenhagen), and David Strachan (St. George’s University of London) be excluded as potential reviewers of this manuscript due to competing research interests.
Thank you for considering our manuscript for publication in *BMC Medical Genomics*.

Sincerely yours,

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