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Epigenome-wide association study of DNA methylation and adult asthma in the Agricultural Lung Health Study

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Distinct methylation signals are found in non-atopic and atopic asthma. Most are related to gene expression and are replicated in asthma-relevant tissues, confirming the value of blood DNA methylation for identifying novel genes linked in asthma pathogenesis. https://bit.ly/2VnbJg3

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ABSTRACT Epigenome-wide studies of methylation in children support a role for epigenetic mechanisms in asthma; however, studies in adults are rare and few have examined non-atopic asthma. We conducted the largest epigenome-wide association study (EWAS) of blood DNA methylation in adults in relation to non-atopic and atopic asthma.

We measured DNA methylation in blood using the Illumina MethylationEPIC array among 2286 participants in a case-control study of current adult asthma nested within a United States agricultural cohort. Atopy was defined by serum specific immunoglobulin E (IgE). Participants were categorised as atopy without asthma (n=185), non-atopic asthma (n=673), atopic asthma (n=271), or a reference group of neither atopy nor asthma (n=1157). Analyses were conducted using logistic regression.

No associations were observed with atopy without asthma. Numerous cytosine–phosphate–guanine (CpG) sites were differentially methylated in non-atopic asthma (eight at family-wise error rate (FWER) $p<9\times10^{-8}$, 524 at false discovery rate (FDR) less than 0.05) and implicated 382 novel genes. More CpG sites were identified in atopic asthma (181 at FWER, 1086 at FDR) and implicated 569 novel genes. 104 FDR CpG sites overlapped. 35% of CpG sites in non-atopic asthma and 91% in atopic asthma replicated in studies of whole blood, eosinophils, airway epithelium, or nasal epithelium. Implicated genes were enriched in pathways related to the nervous system or inflammation.

We identified numerous, distinct differentially methylated CpG sites in non-atopic and atopic asthma. Many CpG sites from blood replicated in asthma-relevant tissues. These circulating biomarkers reflect risk and sequelae of disease, as well as implicate novel genes associated with non-atopic and atopic asthma.