

Trans-ethnic analysis in over 780,000 individuals yields new insights into the genetic etiology of allergic diseases

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Abstract

BACKGROUND: Increasing numbers of research have revealed an etiological association between peripheral blood markers and allergy. Nevertheless, whether these associations are causal and whether they vary among different allergic diseases and ethnicities remain unclear. **METHODS:** 32 peripheral biomarkers with consistent definition were collected from three nationwide biobanks (UK Biobank, FinnGen, and BioBank Japan). Summary-level data for asthma (n=774,328), dermatitis (n=880,733), and allergic rhinitis (n=893,300) were obtained from these biobanks. Mendelian randomization (MR) analyses and meta-analyses were applied to explore the generalizability and heterogeneity of causal effects among different allergic diseases and ethnicities. The clinical data (n=9,877) in China and US were collected to verify peripheral markers affecting allergy. **RESULTS:** The MR analyses provided consistent evidence for the causal effects of seven shared heritable factors (eosinophil, neutrophil, basophil, glomerular filtration rate, mean corpuscular hemoglobin concentration, platelet distribution width, and hematocrit) on broad allergic disease phenotype in both ethnic groups, three of which are new. These findings are further corroborated by our observational studies in China and US. Glucose showed a causal effect on allergy in Europeans while five factors, including c-reactive protein/CRP, LDL cholesterol/LDL-C, total cholesterol/TC, hemoglobin A1c/Hb1Ac, and glucose, are important for East Asians. Moreover, we observed trans-ethnic evidence for the causal effects of five factors (CRP, white blood cell/WBC, total protein, albumin, and hemoglobin concentration) on asthma, two factors (aspartate aminotransferase and WBC) on dermatitis, and LDL-C on allergic rhinitis, reflecting the etiological discrepancy among different allergic diseases. In East Asians, we also noticed the ethnic-specific causalities of triglyceride on asthma, alanine aminotransferase on dermatitis, and three factors (monocyte, albumin, and creatinine) on allergic rhinitis. **CONCLUSIONS:** Our results support the causal effects of 22 blood heritable factors on allergic diseases, providing novel insights into the comprehensive assessment of allergic risks and the design of universal and personalized interventions.

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