

Insights on genetic risk factors of allergic rhinitis

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ABSTRACT

Allergic rhinitis (AR) is common chronic condition, which results from a complex interaction between genetic and environmental factors. Previous studies done on twin siblings showed that there was a higher concordance of the rate of allergic symptoms identified in monozygotic twins, compared to dizygotic twins that demonstrated genetic inheritance of this disease. Studies to identify the genetic risk factors of AR have been performed using three study designs; genome wide association studies (GWAS), candidate gene association studies (CGAS) and family linkage studies. In this review, data from 5 GWAS and 2 meta-GWAS encompassing 137,908 AR cases and 878,758 controls, 121 CGAS and 15 meta-CGAS encompassing 47,853 AR cases and 61,602 controls and 2 family linkage studies encompassing 188 AR individuals from 48 families were evaluated. A total of 56 loci and 89 nearest genes were identified from GWAS/meta-GWAS studies, 80 loci and 112 nearest genes from CGAS/meta-CGAS studies and 2 loci and 5 nearest genes from family linkage studies. Among the nearest genes identified, the majority of candidates (79.1% were common to multiple atopic conditions) while the remaining were specific to AR. The susceptible genes identified showed involvement in the known AR pathogenic pathway, as well as other pathways such as the cell cycle, metabolism, neuronal function, immune regulation, smell function and lung function. I next investigated if ethnic differences influenced the genetic susceptibility to AR. From the genetic variants identified, 18 were replicated across different ethnic groups, while 20 variants from 7 nearest genes were unique between different ethnic populations. The presence of unique variants adds to the complexity in the understanding of AR pathogenesis. The genetic variants identified were next evaluated in terms of its involvement in biological pathways. It was identified that the susceptibility genes of AR were mainly involved in the immune systems pathways. These findings echo the findings from studies done in individuals with other atopic diseases such as asthma and atopic dermatitis. Finally, I evaluated the effects of the gene variants on phenotypic markers involved in AR. A total of 25 nearest genes were associated to IgE levels, 8 genes to eosinophil activity and 4 genes to nasal function. The effects of genes on the phenotype also appears to have ethnic-based variations. This review highlights the need for more genetic susceptibility studies to be done within the Asian population, in order to gain a clearer understanding on the pathological mechanisms of AR.