Two novel genotypic markers affecting promoter activity of a CABP1 isoform in allergic rhinitis among chinese population

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ABSTRACT

Background: Allergic rhinitis (AR) affects 30% of the global population and causes heavy economic burden and low quality of life due to its sufferers. While genetic factors play an important role in the pathogenesis of AR, its underlying mechanisms are not fully understood. In this study, we aimed to functionally characterize the CABP1 gene in relation to AR. **Methods:** Genome wide association study was carried out on 2,146 cases (AR) and 2,039 control (non-AR) of Chinese individuals to identify potential single nucleotide polymorphisms (SNPs) associated with AR. Functional prediction was carried out using bioinformatics tools and promoter functional characterization was performed using dual-luciferase promoter reporter assay. **Results:** Logistic regression analyses revealed that the lead SNP (rs11065183) of a quantitative trait locus containing CABP1 gene had a suggestively significant association with AR [OR (95% CI) = 0.7891(0.7120–0.8745), p= 6.25E-06]. Two SNPs (rs12228187 and rs11065189), that were in high linkage disequilibrium (>80%) with rs11065183, were predicted to behave as transcription factor binding sites of a CABP1 isoform. Dual-luciferase promoter reporter assay revealed that CA haplotype (protective allele) of the two SNPs showed a significantly higher promoter expression level compared to TG haplotype (risk allele) at 24h and 48h post infection in the HEK293T cell line (1.42-fold, $p < 0.01$ for 24h; 1.50-fold, $p < 0.0001$ for 48h). **Conclusion:** Two SNPs (rs12228187 and rs11065189) were identified as novel genotypic markers in AR susceptibility among Chinese patients. CA haplotype of these SNPs was identified as the risk factor that demonstrated significantly decreased promoter activity of the CABP1 isoform. CABP1 functions to regulate the activity of a calcium channel subunit, Cav1.2, which is involved in antigen presentation. Further studies on the effect of the SNPs of CABP1 on antigen presentation would provide a better understanding in its role in AR pathogenesis.