PTGDR variants associated to Singaporean Chinese population

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ABSTRACT

Atopic asthma is a chronic disease which is caused by inflammation in the lungs. Human susceptibility is dependent on inherited genetic factors and environmental factors that they are exposed to. Being a complex disease, asthma phenotype is an accumulation of modest effect from multiple genes. PTGDR is acknowledged as one of many candidate gene in asthma pathophysiology, but studies finding association between variants in the gene promoter region and disease in Asian population yield no significant result. In this study, gene-gene and gene-environment interactions are considered while testing for significance to the disease. Results have yield significant association when PTGDR is compared to the disease while factoring in the effect of IFR1 (p=0.05), ADH5 (p=0.03) and alcohol consumption (0.02). This study provides the evidence that PTGDR can be significant as a candidate gene in Chinese population and a basis to perform functionality assay on the gene and other external factors.

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INTRODUCTION

Atopic asthma is a chronic disease related to an overreactive immune system. The prostaglandin D$_2$ receptor gene plays a significant role in the pathophysiology of immune response but yet no paper has reported significant association of single nucleotide polymorphism (SNP) of the gene to asthma in any Asian population. This study has found association between variants in the promoter region of the gene and the disease after considering the possible effect of gene-gene and gene-environment effect.

MATERIALS AND METHODS

The target population are the Chinese population in Singapore aged between 18 to 27 years. SNPs are identified through sequencing of 40 cases and controls drawn from the population and two SNPs are selected for further genotyping in 414 cases and 456 controls. Association tests are performed on the population stratified according to presence of other gene and environmental factor. Significance level is drawn at 5%.

RESULTS

A total of 25 SNPs are identified including three unreported SNPs. Two SNP, T-549C and T-197C is chosen for further genotyping. Similar to previously studied Asian population, no significant association between the two SNPs and disease are found in the study population.
Association is found to be significant only when T-549C is considered together with IFR1 and alcohol drinking.

**DISCUSSIONS**

This study has yielded similar results to studies based on other Asian populations and that there is no statistical association between the SNPs and the disease. However, this paper went forward to discuss possible reasons for the lack of association even though the two SNPs have been proven through functional assays that they have physiological role in regulating transcription efficacy of PTGDR via serving as binding site for transcription factors (Oguma et al. 2004). One of the reasons for low penetrance of the SNPs is failure on other investigators’ part to factor in gene-gene and gene-environment interactions, and is investigated by this paper. The other reason is it can be due to epigenetic modifications found in Asian population which inhibit binding of the transcription factors to DNA.

In conclusion, the result of this study can serve as a basis for future functional assays to be performed to elucidate the physiological relationship between the gene and other associated external factors.

**REFERENCES**