Association of a Single Nucleotide Polymorphism of PAR-2 (F2RL1) Gene with Asthma

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Abstract

Proteinase-Activated Receptor-2 (PAR-2) is a G protein coupled receptor, expressed in the human body, involved in inflammation and controlled by the F2RL1 gene. Previous study showed that PAR-2 SNPs were associated with allergic reactions in Korean children and BMI in African Americans.

The purpose was to determine if PAR-2 (F2RL1) single nucleotide polymorphisms may be preferentially present in patients with severe asthma, and if the levels of PAR-2 expression on intermediate monocytes is associated with the presence of these polymorphisms. We also wanted to see the effects of PAR-2 SNPs on Th2 inflammation.

We recruited 21 severe and 34 mild/moderate asthmatics from the University of Alberta Hospital and collected basic demographics. We extracted genomic DNA and selected two mutations, rs1529505 and rs631645 for genotyping. PAR-2 polymorphisms were analyzed according to the severity of the asthma, PAR-2 mRNA in the blood, protein expression in monocytes, and Th2 inflammation.

Subjects with the T allele of PAR-2 rs1529505 polymorphisms had significantly higher number of eosinophils compared to the C in dominant (CC vs CT+TT) and allele models (C vs T) (p=0.009 and p=0.007) and showed a higher trend of intermediate monocytes expressing PAR-2 (p=0.238). Subjects having the T allele of PAR-2 rs1529505 polymorphisms had significantly lower PAR-2 mRNA expression compared to subjects having C allele in dominant model (p=0.012). However, there was no significant genetic differences between severe and mild/moderate asthmatics. Subjects with the T allele of PAR-2 rs1529505 polymorphism were associated with higher levels of CD4+ T

lymphocytes in whole blood (p=0.063), mRNA expression of Th2 cell markers (p= 0.054) and higher levels of serum IL-13 (p= 0.014) compared to C allele.

These results suggest that PAR-2 rs1529505 polymorphism is associated with PAR-2 expression, eosinophils and Th2 inflammation.