Filaggrin and atopic dermatitis

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Abstract

Atopic dermatitis (AD) is a chronic pruritic skin disease, resulting from complex interplay between genetic and environmental factors. From candidate gene studies, Filaggrin (FLG) gene had been identified as a major gene for AD. However instead of focusing on exon 3 as in recent literatures, this study attempts to identify Single Nucleotide Polymorphisms (SNPs) from the other regions of the gene including 2kbp upstream and 1kbp downstream (possible regulatory regions) which are associated with AD. 40 random subjects were sequenced to generate linkage disequilibrium blocks for further genotyping work. A total of 23 SNPs and 2 deletions were identified with several SNPs showing strong LD.

Introduction

FLG gene has been identified as a major gene in AD through candidate studies as summarised by Morar et al. Smith at al. was the first to demonstrate that 2 premature stop codon causing mutation at exon 3 of the FLG gene causes a complete absence of FLG protein in the ichthyosis vulgaris patients after which subsequent studies replicated the results in other European population. However, similar candidate gene studies using Asian population (Chen et al. and Nomura et al.) failed to yield the same results. Furthermore, recent literature focused only on exon 3 of the FLG gene. This study aims to comprehensively search for all possible variations that are present within other portions of the gene including possible regulatory regions in the promoter (2kbp upstream), and downstream regions (1kbp) as well as the gene itself. Linkage Disequilibrium (LD) patterns will be determined to identify representative SNPs which will subsequently be used in a case-control association study to evaluate genetic association with atopic dermatitis, and to detect potential gene-gene and gene-environment interactions affecting the aetiology of the disease.

Materials and Methods

Buccal cells were collected using a mouthwash and the individual was asked to complete a questionnaire and to undergo a skin prick test for common allergens; dust mite Dermatophagoides pteronyssinus, dust mite Blomia tropicalis, fungus Curvularia lunata and oil palm pollen Elaeis guineensis. Genomic DNA was extracted from the buccal cells and amplified for further usage. PCR followed by sequencing was done on 40 randomly chosen cases and controls. Linkage disequilibrium blocks were generated using Haploview.

Results and Discussions

Results showed 23 novel SNPs and 2 deletion mutation identified. Genotyping of more samples will be carried out to validate the correlation between the SNP and AD. Proteomics identification of level of FLG protein in cases and controls will show the direct link between genetics and the expression of the FLG protein.
References


