Analysis of the high affinity IgE receptor genes reveals epistatic effects of FCER1A variants on eczema risk.

High levels of total and allergen-specific IgE levels are a key feature in allergic diseases. The high-affinity receptor for IgE, which is composed of one alpha (FCER1A), one beta (FCER1B), and two gamma (FCER1G) subunits, represents the central receptor of IgE-induced reactions. In a genome-wide association scan, we recently identified associations between functional FCER1A variants and total serum IgE levels. Previous studies had reported linkage and association of FCER1B variants with IgE and atopic traits. The FCER1G gene has not yet been investigated with regard to atopy. Filaggrin (FLG) is the strongest known risk gene for eczema, in particular the allergic subtype of eczema. We investigated the association of FCER1A, FCER1B, and FCER1G variants with IgE in a large population-based cohort (n = 4261) and tested for epistatic effects using the model-based multifactor dimensionality reduction (MB-MDR) method. In addition, we investigated a potential interaction between FLG and FCER1A variants in a large collection of eczema cases (n = 1018) and population controls. Three strongly correlated FCER1A polymorphisms were significantly associated with total and specific IgE levels as well as allergic sensitization. No associations...
were seen for FCER1B and FCER1G. After adjustment for FLG effects, a significant epistatic effect of the FCER1A variants rs10489854 and rs2511211 on eczema risk was detected. These results suggest that FCER1A variants by themselves and in combination influence IgE levels and act synergistically to influence eczema risk.