Toward a major risk factor for atopic eczema: meta-analysis of filaggrin polymorphism data.

BACKGROUND: With an impressive series of replication studies, filaggrin (FLG) has become the gene with the most widely replicated association to atopic eczema (AE). However, studies published to date demonstrate differences concerning study design and strength of associations.

OBJECTIVES: We sought to provide a general and overall estimate of FLG effect sizes and to estimate allele and carrier frequencies.

METHODS: We searched Medline and Institute for Scientific Information Web of Knowledge databases for relevant studies and abstracts from professional societies that were published through June 30, 2007. Initially, we accounted for different study types and evaluated an overall estimate for case-control and family studies. In a second step, we combined those 2 study types and used a random-effects analysis approach to calculate overall odds ratios (ORs). Tests of asymmetry were applied to detect potential publication bias. RESULTS: Nine studies that met the inclusion criteria were included in the meta-analysis. For the combined genotype (R501X or 2282del4), we found an overall OR of 4.09 (95% CI, 2.64-6.33) from the case-control studies and a summary OR of 2.06 (95% CI, 1.76-2.42) from the family studies. CONCLUSION: The powerful effect of FLG variation on AE risk exceeds that of any other investigated candidate gene for AE thus far and makes FLG one of the strongest
genes known to date for complex diseases. CLINICAL IMPLICATIONS: These results underline the importance of a genetically determined epidermal barrier disruption in AE.