Loss-of-function mutations in the filaggrin gene and allergic contact sensitization to nickel.

Abstract:
Allergic contact dermatitis is one of the most frequent dermatological problems affecting 7% of the general population. Impaired skin barrier function facilitates the penetration of contact allergens and irritants into the epidermal layer and is regarded as an important cofactor promoting the process of allergic contact sensitization. Filaggrin is crucial for the maintenance of the skin barrier function. Loss-of-function mutations within the filaggrin (FLG) gene are associated with skin barrier diseases such as ichthyosis vulgaris and atopic eczema (AE). To assess the impact of FLG on allergic contact sensitization and plausible intermediate traits, the two prevalent FLG mutations R501X and 2282del4 were typed in 1,502 individuals of the KORA C population-based cohort with extensive dermatologic phenotyping. Associations of FLG mutations with AE could be replicated. Strong associations were seen with dry skin, palmar hyperlinearity, and keratosis pilaris. In addition, an association with contact sensitization to nickel and contact sensitization to nickel combined with intolerance to fashion jewelry, but not with other contact allergens, was observed. From these data, we conclude that a genetically determined FLG deficiency manifests as dry skin and features of ichthyosis vulgaris. In addition, FLG deficiency may also represent a risk factor for contact sensitization to allergens.