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Focus on Filaggrin Accumulates: New Swedish Data

Dr Elisabeth Ekelund and colleagues publish their research in 406 Swedish families, comprising 1514 individuals, 921 of whom have eczema, and confirm a strong association between eczema and loss-of-function gene variants R501X and 2282del4 in the filaggrin gene. This gene encodes the profilaggrin protein, a major component of the keratohyalin granules in the upper layers of the epidermis. Thus, eczema associated with a fault in the epidermis could be regarded as "an epidermal disease". If the mutations are homozygous they lead to ichthyosis vulgaris, a disorder that can occur without associated eczema.

Dr Ekelund et al. observe associations with severity of eczema and atopic eczema and allergic asthma and allergic rhinoconjunctivitis (in the context of eczema). This is surprising, as in a study of different chromosomal regions and their association with atopic eczema, asthma and psoriasis, Bowcock & Cookson observed greater overlap between atopic eczema and psoriasis than between atopic eczema and asthma (1).

Do all patients with atopic eczema have loss-of-function gene variants? Many do, but not all. According to a recent review, 6.7–56% of the patients within the different studies have the variants (see Table I in (2)). This means that one can have atopic eczema without the presence of loss-of-function gene variants in the filaggrin gene.

How is it that an epidermal "abnormality" leading to decreased epidermal skin barrier function is associated with immunological changes giving rise to an increased risk of having allergic asthma and allergic rhinoconjunctivitis, which again are strongly associated with IgE increase? The influence could lie in the establishment of the peripheral T-lymphocyte immune system, probably via the cross-talk taking place in the thymus between thymic epithelium and the pre-T cells. Various cytokines (TARC, cTACKL, TLSP, and others) are probably involved, but this is more difficult to study. And it is likely that many more genes are involved; it has been observed recently that changes in ORMDL3 expression are associated with risk of childhood asthma (3).

Atopic dermatitis is an early-life event, which in most cases develops early in childhood and subsequently disappears. Dr Ekelund et al. have studied adults with continued disease expression, thus perhaps introducing a bias. Their confirmatory observations of loss-of-function gene variants in the filaggrin gene and highly significant associations of these variants with the development of atopic eczema provide new clues to understanding this interesting and very common disease. However, the significant increase in incidence of eczema and atopic eczema in countries with a so-called "western lifestyle" is not yet understood.

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