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DOI: [10.1159/000163083](https://doi.org/10.1159/000163083)**Filaggrin Mutation c.3321delA in a Korean Patient with Ichthyosis Vulgaris and Atopic Dermatitis**

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Key Words

Filaggrin mutation • Ichthyosis vulgaris • Atopic dermatitis

Filaggrin plays a major role in the production of the epidermal barrier function. It is initially produced as profilaggrin in the granular layer and is then processed to filaggrin at the junction of the granular layer and corneal layer of the epidermis. Filaggrin functions to aggregate keratin filaments so that effective corneocytes are produced. Filaggrin is then degraded into individual amino acids, becoming the natural moisturizing factor of the stratum corneum. Filaggrin deficiency has obvious adverse effects on stratum corneum function.

Atopic dermatitis (AD) and ichthyosis vulgaris (IV) are relatively common heritable skin diseases. Recent studies showed that both diseases are closely related to loss-of-function mutations in

the filaggrin gene (*FLG*). The homozygous or compound heterozygous loss-of-function mutations p.R501X and c.2282del4 in *FLG* have been identified in moderate or severe IV patients from Ireland, Scotland and the USA [1]. These variants are carried by approximately 9% of European people and were also revealed to be important predisposing factors for AD [2]. Meanwhile, c.3321delA and p.S2554X mutations in *FLG* were identified as prevalent in Japanese IV and AD patients [3]. However, in that study the frequency of *FLG* mutations in the Japanese AD cohort was much lower than that seen in Europeans (5.6 and 48%, respectively) [3]. Recently, the same research group has reported additional nonsense *FLG* mutations (p.S2889X and p.S3296X) in Japan and extended the statistical significance of *FLG* null mutations in Japanese cases to >20% [4]. These findings imply that *FLG* mutations are predisposing factors for IV and AD, and show the presence of population-specific recurrent *FLG* mutations.

In this regard, we analyzed *FLG* mutations in a 35-year-old Korean man who presented with a history of IV and AD since childhood. His sister and 2 daughters were affected by AD and xerosis. Marked adherent fine scales were clearly visible on his trunk. He also showed hyperlinear palms (fig. 1a, b). Histology revealed no keratohyalin granules in the granular layer (fig. 2). We performed direct sequencing of the *FLG* gene in this patient, as well as screening for the previously reported mutations. Analysis revealed that he was a heterozygous carrier of the *FLG* mutation c.3321delA (fig. 3). This mutation has already been reported by Nomura et al. [3] in Japanese cases.

Fig. 1. Clinical features of the patient with IV and AD, showing marked adherent fine scales on the trunk (a) and hyperlinear palms (b).

Fig. 2. No keratohyalin granules are seen in the upper granular layer. HE. $\times 400$.

From this finding, we can assume that at least some proportion of AD and/or IV patients of Korean origin are affected by *FLG* null mutations, and that population-specific recurrent mutations are closely related to Japanese cases. Further extensive case-control studies are required to reveal the contributing effects of *FLG* mutations in both diseases in the Korean population. Also, further *FLG* mutation analysis in different populations will uncover the full spectrum of mutations and assess their contributions to both diseases globally.

Fig. 3. Detection of *FLG* mutation c.3321delA. A heterozygous deletion mutation in filaggrin repeat 2 in exon 3, 3321delA, was identified in the patient.

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