

Filaggrin Gene Mutations Mediate Severity of Alopecia Areata When Associated with Atopic Dermatitis

Marianna L. Blyumin¹, Shasa Hu¹ and Robert S. Kirsner¹

Journal of Investigative Dermatology (2007), **127**, 2494. doi:10.1038/sj.jid.5701137

Recently, several common loss-of-function mutations in the gene (FLG) coding for the epidermal protein filaggrin were found in several families with ichthyosis vulgaris (Smith *et al.*, 2006). Furthermore, the association between ichthyosis vulgaris and atopic dermatitis (AD) has led to additional studies demonstrating that these same mutations are important risk factors for AD (Stemmler *et al.*, 2007; Palmer *et al.*, 2006). FLG mutations are related to other manifestations of atopy, such as asthma, but only in the presence of AD. Given the association of alopecia areata (AA) with AD, Betz *et al.* (2007, this issue) studied the association between AA and two common loss-of-function *FLG* gene mutations, R501X and 2282del4, which lead to premature termination of the first filaggrin repeat. In their study of a European cohort of 449 patients with AA, they did not find an association between AA and *FLG* gene mutations. However, 34% of the cohort had concomitant AD. In this subset of 145 patients, 37 patients had AD and asthma and 27 had AD, asthma, and allergic rhinitis. Within this subset, the investigators found highly increased *FLG* mutations in patients with AD; mutations were reported to an even greater extent in patients with AD and other manifestations of atopy, such as asthma or allergic rhinitis. Interestingly, in further investigations of the severity of AA in this subset, patients with AD and other signs of atopy who had *FLG* mutations were more likely to have a more severe form of AA, such as alopecia totalis and alopecia universalis. Through the following questions we will delve into this paper in greater detail. For brief answers, please refer to <http://network.nature.com/group/jidclub>.



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QUESTIONS

1. What is the function of filaggrin protein in normal skin?
2. Mutations in filaggrin, associated with atopic dermatitis, have what implications in pathogenesis of atopic dermatitis and atopy?
3. What are the major findings of the present study?
4. What factors influence the subset analysis regarding atopic dermatitis and alopecia areata and the role of filaggrin mutations?
5. What are the clinical implications of the study?

¹Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, Florida, USA