

FLG gene

filaggrin

Normal Function

The *FLG* gene provides instructions for making a large protein called profilaggrin, which is found in cells that make up the outermost layer of skin (the epidermis). Profilaggrin is cut (cleaved) to produce multiple copies of the filaggrin protein, which is important for the structure of the epidermis. The profilaggrin molecule can contain 10, 11, or 12 copies of the filaggrin protein, depending on the genetics of the individual. Further processing of the filaggrin protein produces other molecules that play a role in hydration of the skin.

The epidermis acts as a barrier to help minimize water loss and protect the body from foreign substances, including toxins, bacteria, and substances that can cause allergic reactions (allergens), such as pollen and dust mites. Filaggrin plays an important role in the skin's barrier function. It brings together structural proteins in the outermost skin cells to form tight bundles, flattening and strengthening the cells to create a strong barrier. In addition, processing of filaggrin proteins leads to production of molecules that are part of the skin's "natural moisturizing factor," which helps maintain hydration of the skin. These molecules also maintain the correct acidity (pH) of the skin, which is another important aspect of the barrier.

Health Conditions Related to Genetic Changes

Alopecia areata

MedlinePlus Genetics provides information about Alopecia areata

Atopic dermatitis

Mutations in the *FLG* gene are strongly associated with a skin disorder called atopic dermatitis (also known as atopic eczema). This condition is characterized by dry, itchy skin and red rashes. Twenty to 30 percent of people with atopic dermatitis have an *FLG* gene mutation compared with 8 to 10 percent of the general population without atopic dermatitis.

Having a mutation in this gene only increases the risk of developing atopic dermatitis. Not everyone with an *FLG* gene mutation will develop the disorder. Other genes and

environmental factors contribute to atopic dermatitis. Individuals with a mutation in both copies of the *FLG* gene are at greater risk of developing atopic dermatitis than those with a mutation in only one copy of the gene. The condition is typically more severe in people with two mutated copies.

In addition to *FLG* gene mutations, the number of filaggrin proteins produced from each profilaggrin molecule is associated with development of atopic dermatitis; individuals with genetic instructions for producing 10 copies are at greater risk of developing the disorder than those with instructions for producing 11 or 12 copies.

Approximately 40 mutations in the *FLG* gene have been identified in people with atopic dermatitis. These mutations lead to production of an abnormally short profilaggrin molecule that cannot be cleaved to produce filaggrin proteins. The resulting shortage of filaggrin can impair the barrier function of the skin. Further, a lack of filaggrin leads to a shortage of natural moisturizing factor, which allows excess water to be lost through the skin and causes dry skin in affected individuals.

Research suggests that the impairment of the skin's barrier function caused by a shortage of filaggrin contributes to development of allergic disorders. Atopic dermatitis is not initially caused by an allergic reaction, although sometimes substances that can cause allergic reactions (allergens) are thought to contribute to flare-ups of the rashes. In addition, people with atopic dermatitis have an increased likelihood of developing other allergic disorders, including asthma, hay fever, and food allergies. (The tendency to develop allergic disorders is known as atopy.)

Other disorders

More than 40 *FLG* gene mutations have been found to cause a relatively common skin disorder called ichthyosis vulgaris, which is characterized by dry, scaly skin, particularly during the winter when humidity in the air is low. Affected individuals can also have unusually prominent creases on the palms of their hands and soles of their feet (palmar and plantar hyperlinearity) and an increased risk of allergic disorders, including atopic dermatitis (described above).

Typically, individuals with a mutation in one copy of the *FLG* gene are mildly affected; they may have symptoms only seasonally, or they may never have obvious skin problems. Individuals with two mutated copies of the gene have more severe symptoms that may be present year-round.

Some of the mutations associated with atopic dermatitis are also found in people with ichthyosis vulgaris. As in atopic dermatitis, the mutations lead to production of an abnormally short profilaggrin molecule that cannot be cleaved to produce filaggrin proteins. A lack of filaggrin and the molecules produced from its processing lead to the dry, scaly skin characteristic of ichthyosis vulgaris. Impairment of the skin's barrier function likely contributes to the development of allergic diseases in some people with ichthyosis vulgaris.

Individuals with *FLG* gene mutations have an increased risk of developing asthma, but only if they also have atopic dermatitis. *FLG* gene mutations also increase the risk of

hay fever, food allergies, and skin sensitivity to nickel, regardless of whether the person has atopic dermatitis. Additional factors, such as living with a cat and smoking tobacco products, may increase the risk of atopic dermatitis and asthma, respectively, in people with ichthyosis vulgaris.

Other Names for This Gene

- ATOD2
- epidermal filaggrin

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of FLG ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=2312\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=2312[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28FLG%5BTI%5D%29+OR+%28filaggrin%5BTI%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D%29%29%29>)

Catalog of Genes and Diseases from OMIM

- FILAGGRIN; FLG (<https://omim.org/entry/135940>)
- ICHTHYOSIS VULGARIS (<https://omim.org/entry/146700>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/2312>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=FLG\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=FLG[gene]))

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Genomic Location

The *FLG* gene is found on chromosome 1 (<https://medlineplus.gov/genetics/chromosome/1/>).

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