Filaggrin to treat dermatological disorders

Icthyosis vulgaris is a skin barrier disease that is the result of filaggrin (FLG) insufficiency. In some cases, the loss of filaggrin expression may result in atopic dermatitis, a common skin disease characterized by itchy, scaly and often inflamed skin. There are currently no therapies that treat the underlying cause of these dermatological disorders. In healthy patients, the FLG protein is expressed in the cytoplasm of epithelial cells and plays an essential role in the proper keratinization and squamation of epithelial cells, formation of the epidermal barrier, and skin hydration. A lack of filaggrin protein, due to mutations in the flg gene, is often associated with these dermatological disorders.

We have developed a therapeutic approach, which is the first to target the underlying etiology, employing a recombinant filaggrin, derived from a single flg repeat combined with flanking sequences for processing, and a cell importation signal. Studies conducted by Dr. Stout and his colleagues have demonstrated:

- Robust cell internalization of rFLG-RMR to cytoplasm
- Topical application to human skin models results in cell uptake at pathologically relevant layers
- rFLG-RMR is internally processed to function monomeric size
- Topical application of rFLG-RMR restores the cornified envelope in filaggrin-deficient mice (see image below)
- Topical application of rFLG-RMR to filaggrin-deficient mice reverses abnormal flaky phenotype and improves barrier function

**Applications**

- Skin cream containing rFLG-RMR for topical application to treat dry skin disorders such as ichthyosis vulgaris, atopic dermatitis
- Possibility to screen for patients with flg mutations

**Development stage**

- Pre-clinical studies ongoing
- In vivo tests on human and mouse keratinocyte cell lines
- Proof of concept on a mouse model using rFLG-RMR formulated in a dermal cream.

Pending patents: US13/511,267; AU2010321784; AU2014203006; CA2,781,537; EP10832312.2


*Available for licensing or partnering*

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