

## Towards a better treatment of eczema

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*A study reports that damage to skin cells triggers a rapid response intended to quickly eliminate damaged cells and prevent inflammation. This discovery paves the way for better treatment of chronic inflammatory conditions, such as those responsible for eczema.*

The skin is the largest organ in the human body, covering an area of about 1.7 m<sup>2</sup> and accounting for about 15% of body weight.

The three main layers of the skin, the epidermis, the dermis and the hypodermis play extremely important roles, especially by acting as a barrier that protects the body from the many microorganisms or physical aggressors that can threaten the integrity of the body.

### INFLAMMASOMES: INTRACELLULAR SMOKE DETECTORS

In addition to this role as a physical defensive barrier, the skin also contains sophisticated biochemical systems that play very active roles in protecting against attacks.

One of the best examples is what are called inflammasomes, clumps of proteins located inside cells that are specialized in the recognition and neutralization of different aggressors (virus, bacteria, cell damage) that can threaten the integrity of the body.

Activation of the inflammasome triggers a cascade of events highly complex intended to eliminate the threat and/or the cells that have been damaged by this attack.

A bit like our smoke detectors that allow us to respond quickly to the threat of a fire before it spreads, inflammasomes can therefore be considered as early detectors of the presence of a situation that is likely to be dangerous for the cell.

### FAILED MITOCHONDRIA

According to a recent study, skin cells contain a new type of inflammasome that specializes in detecting damage that specifically affects a constituent cells, the mitochondria. (1)

Let's remember that these mitochondria are the compartment of the cell specialized in the production of the energy (in the form of ATP) required to maintain cell function and that damage affecting these structures have disastrous consequences for the normal cell function.

The researchers observed that a protein (called NLRP10) was able to detect defective mitochondria and in response triggered the activation of an inflammasome intended to eliminate the cells containing these defective mitochondria.

This rather drastic response makes it possible to quickly eliminate the deficient cells and thus avoid the development of a chronic inflammation that could spread to other areas of the skin.



### INFLAMMATORY MUTATIONS

Eczema (atopic dermatitis) is arguably the most common chronic inflammatory skin disease, affecting up to 20% of children and 3% of adults. This disease causes sometimes intense itching that can disrupt sleep and significantly reduce the quality of life.

Interestingly, the cell-specific inflammasome defective mitochondria identified in the study mentioned above early on could play an important role in the development of eczema: researchers have observed that mutations in the NLRP10 gene are associated with a higher risk of eczema.

Expression of these mutants in skin cells prevented the elimination of damaged cells, generating at the same time a chronic skin inflammation.

The development of therapeutic agents specifically targeting this NLRP10 protein could therefore prove to be a very interesting new strategy for the treatment of inflammatory skin diseases.

- (1) Próchnicki T et al. Mitochondrial damage activates the NLRP10 inflammasome. *Nat Immunol.* 2023; 24:595-603.