Researchers discover genetic basis for eczema, new avenue to therapies

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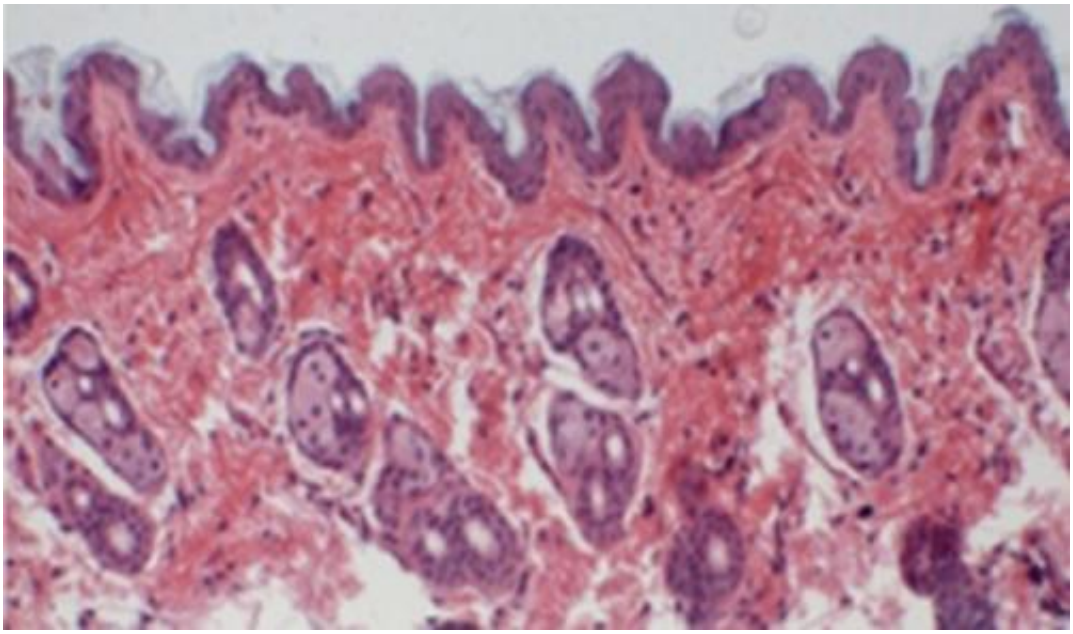


Normal skin from a mouse shows no sign of inflammation caused by eczema. Credit: Oregon State University

(Medical Xpress)—Researchers at Oregon State University today announced the discovery of an underlying genetic cause of atopic dermatitis, a type of eczema most common in infancy that also affects millions of adults around the world with dry, itchy and inflamed skin lesions.

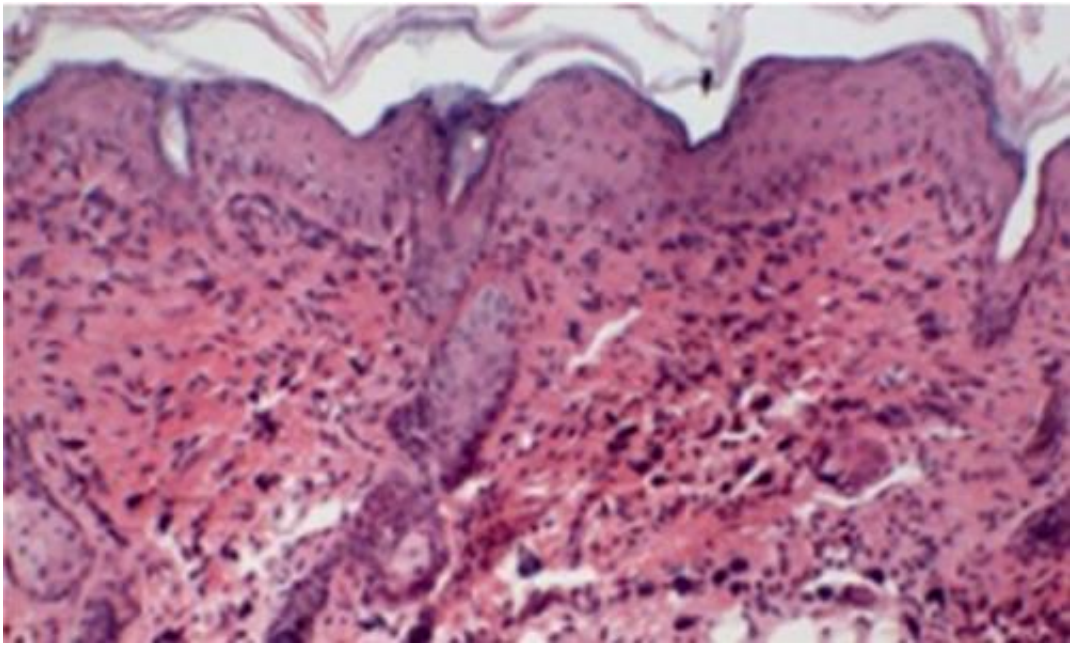
The findings were just published in PLoS ONE, a professional journal,

and may set the stage for new therapeutic approaches to this frustrating syndrome, which is difficult to treat and has no known cure. Eczema is also related to, and can sometimes cause asthma, a potentially deadly immune dysfunction.

Pharmaceutical scientists at OSU found in laboratory studies that eczema can be triggered by inadequate Ctip2, a protein and master regulator that affects other genetic functions. They have identified two ways in which improper function of Ctip2 can lead to eczema.

In a recent publication, they found that Ctip2 controls lipid biosynthesis in the skin, the fats that are needed to help keep skin healthy and hydrated. In the new study, they discovered that Ctip2 suppresses TSLP, a cytokine protein produced by skin cells that can trigger inflammation.

Levels of this inflammatory TSLP, which is ordinarily undetectable in human skin, were found to be 1,000 times higher in laboratory animals that had been genetically modified to have no Ctip2 production in their skin.



Skin on this mouse, which has no production of a gene called Ctip2, is heavily inflamed with eczema. Credit: Oregon State University

"In these studies, we've basically shown that inadequate Ctip2 is reducing the lipids in skin that it needs to stay healthy, protect itself and perform its function," said Arup Indra, an associate professor in the OSU College of Pharmacy. "At the same time this can allow unwanted formation of proteins that trigger inflammation. The skin's ability to resist inflammation is going down just as the amount of inflammation is going up, and the underlying reason is that Ctip2 is not doing its job."

"Either or both of these problems can lead to eczema," Indra said.

Atopic dermatitis is associated with a dysfunctional immune response, but researchers have never understood the underlying cause. Existing treatments use moisturizers to try to protect skin, and in difficult cases powerful steroid drugs can help, but they often have significant unwanted side effects, especially in long-term use.

"With a better understanding of just what is causing eczema on a genetic basis, we should be able to personalize treatments, determine exactly what each person needs, and develop new therapies," Indra said. "This might be with topical compounds that increase Ctip2 expression in skin cells, or customized treatments to restore an individual person's lipid profile. In the future, systemic epigenetic modification might even be possible."

The creation at OSU of the laboratory model to study this issue is also of considerable importance, Indra said. There's evidence it could be used to screen for drugs with potent anti-inflammatory activities.

Eczema is a persistent skin rash that can be fairly common in infants or youth, which some research indicates may be linked to food or pollen allergens. Most people outgrow it as they reach adulthood, but some suffer from the debilitating condition their entire life.

"Our skin is the largest organ in the human body and one of the most important," Indra said. "It's our first barrier of defense, is in a constant battle against external insults, is influenced by both genetics and the environment, and has to be finely tuned to do many jobs. In eczema, this process begins to break down."

Eczema allows significant loss of fluids through the skin, allows allergens to penetrate, and in severe cases can cause a systemic inflammatory response.

More information: Selective Ablation of Ctip2/Bcl11b in Epidermal Keratinocytes Triggers Atopic Dermatitis-Like Skin Inflammatory Responses in Adult Mice, www.plosone.org/article/info:doi%2F10.1371%2Fjournal.pone.0051262

Provided by Oregon State University