

Study finds how eczema develops

Like a fence or barricade intended to stop unwanted intruders, the skin serves as a barrier protecting the body from the hundreds of allergens, irritants, pollutants and microbes people come in contact with every day. In patients with eczema, or atopic dermatitis, the most common inflammatory human skin disease, the skin barrier is leaky, allowing intruders " pollen, mold, pet dander, dust mites and others " to be sensed by the skin and subsequently wreak havoc on the immune system.

While the upper-most layer of the skin " the stratum corneum " has been pinned as the culprit in previous research, a new study published today in the *Journal of Allergy and Clinical Immunology* found that a second skin barrier structure, consisting of cell-to-cell connections known as tight junctions, is also faulty in eczema patients and likely plays a role in the development of the disease. Tightening both leaky barriers may be an effective treatment strategy for eczema patients, who often have limited options to temper the disease.

Disruption of the Skin Barrier

"Over the past five years, disruption of the skin barrier has become a central hypothesis to explain the development of eczema," said Lisa Beck, M.D., lead study author and associate professor in the Department of Dermatology at the University of Rochester Medical Center. "Our findings challenge the belief that the top layer of the skin or stratum corneum is the sole barrier structure: It suggests that both the stratum corneum and tight junctions need to be defective to jumpstart the disease."

Currently, there are no treatments that target skin barrier dysfunction in eczema. To treat eczema, which causes dry, red, itchy skin, physicians typically prescribe anti-inflammatory drugs, like prednisone, and a variety of topical anti-inflammatory creams and ointments. But, modest benefit, negative side effects and cost concerns associated with these therapies leave patients and doctors eagerly awaiting new alternatives.

"We want to figure out what current eczema therapies do to both barrier structures and start thinking about new treatments to close the breaks that let irritants in and water out and subsequently drive the inflammation and dryness that is characteristic of the disease," noted Beck, who treats eczema patients in addition to conducting research on the condition.

Junctions of the Skin

To better understand the role of tight junctions in eczema, Beck and her team studied skin samples from eczema patients and healthy individuals. Using resistance and permeability tests, they discovered that tight junctions, which act like a gate controlling the passage of water and particles, were strong and tight in healthy skin samples, yet loose and porous in the skin of eczema patients.

On further investigation, they found that a particular tight junction protein, claudin-1, which determines the strength and permeability of tight junctions in skin, is significantly reduced in the skin of eczema patients, but not in healthy individuals or individuals with psoriasis, another common chronic skin disease. They demonstrated that reducing claudin-1 expression in skin cells from healthy donors made the tight junctions leaky and more permeable, a finding in line with results of other research groups.

"Since claudin-1 was only reduced in eczema patients, and not the other controls, it may prove to be a new susceptibility gene in this disease," said Anna De Benedetto, M.D., postdoctoral-fellow at the Medical Center and first author of the new study. "Our hypothesis is that reduced claudin-1 may enhance the reactivity to environmental antigens and lead to greater allergen sensitization and susceptibility in people with eczema."

New Treatment for Eczema?

If the team's hypothesis stands up in future research, increasing claudin-1 to combat eczema could be a new treatment approach worth exploring. The University of Rochester has applied for patent protection for increasing claudin-1 with drug compounds to treat eczema.

Barrier problems, and in particular tight junction defects, are recognized as a common feature in many other inflammatory diseases, such as inflammatory bowel disease and asthma, where the lining of the intestine and the airways is weakened, which is why Beck and her team decided to focus on the role of this barrier structure in eczema.

Eczema affects up to 17 percent of children and about six percent of adults in the United States " close to 15 million Americans. While there are varying severities of eczema, all have an itch that can make it difficult to focus on daily activities and to sleep. People with eczema are often counseled to minimize their exposure to allergens, but that is a difficult task given the hundreds of allergens people are exposed to each day.

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