New risk variant for atopic dermatitis identified

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Scientists of the Max Delbrück Center for Molecular Medicine (MDC) Berlin-Buch and Charité - University Medical School, Berlin, Germany, in collaboration with researchers from the Klinikum rechts der Isar of Technical University Munich and Christian Albrecht University, Kiel, have identified a gene variant on chromosome 11 that is associated with an increased risk of atopic dermatitis. In a large genome-wide association study the researchers scanned the genomes of more than 9600 participants from Germany, Poland and the Czech Republic.

"Our findings cast new light on the pathogenesis of the disease," said Professor Young-Ae Lee (Charité / MDC). The pediatrician-researcher and her collaborators hope the study will lead to a new approach to targeted therapy for this chronic skin disorder.

More and more people suffer from atopic dermatitis, which is also known as atopic or infantile eczema. Atopic dermatitis is a chronic (long-lasting) inflammatory skin disease that typically affects the large flexures such as the bend of the elbows or the back of the knees. Patients suffer from recurrent flares of intense itching, dryness and redness of the skin, with weeping of clear fluid in the acute stage, and skin thickening (lichenification) in the chronic stage. Along with hay fever and asthma, atopic dermatitis is one of the most common allergic disorders. In the industrialized countries about 15 percent of young children are affected.

Atopic dermatitis is typically the first clinical manifestation of allergic

disease. In most cases atopic dermatitis appears within the first few years of life. For the majority of affected children this marks the beginning of an "allergic career", which in later years evolves into hay fever or asthma. Just what triggers the outbreak of atopic dermatitis is not yet fully understood. However, epidemiological studies indicate that the genetic contribution is substantial.

For that reason, of the total of 9600 study participants, the scientists decided to scrutinize the genomes of 3011 individuals more closely. These included children and adults with atopic dermatitis, healthy controls, as well as entire families in which at least two children have atopic dermatitis. The researchers scanned the entire genome, searching for genetic variants that are especially common in atopic dermatitis patients.

The study demonstrates that several genes are involved in the pathogenesis of atopic dermatitis. Most importantly, the researchers identified a variant on chromosome 11 that is particularly common in the patients with atopic dermatitis. This variant is located in a region containing the gene C11orf30 which encodes the protein EMSY. The scientists suspect that a mutation in this gene is associated with atopic dermatitis. However, the exact role of EMSY in atopic dermatitis still needs to be investigated.

Same variant also a risk factor for Crohn's disease

The same variant on chromosome 11 is also common in patients with Crohn's disease, a chronic inflammatory disease of the gastrointestinal tract. Scientists therefore suspect that this variant on chromosome 11 will unravel a novel common disease mechanism that can lead to chronic inflammation of various organs. The variant is very widespread: in Europe, 36 percent of the population are carriers. Now the MDC and Charité scientists want to decipher the exact function of EMSY in atopic

dermatitis.

Furthermore, the scientists show that other previously unknown variants in genes related to the outermost skin layer (epidermis) increase the risk for the disease. The researchers hope that their findings will contribute to improved treatment for atopic dermatitis sufferers. "To develop a targeted intervention," they explained, "we must first fully understand the underlying disease mechanism."

More information: A common variant on chromosome 11q13 is associated with atopic dermatitis, *Nature Genetics* doi: 10.1038/ng.347

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