When our protective armor shows weakness

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New knowledge points to the fact that a genetically induced lack of filaggrin, a key protein of the skin barrier, plays a decisive role in the origin of allergies. In a large study on more than 3000 school-children scientists of the Helmholtz Zentrum München and the Technische Universität München found that about 8% of the German population carry variations of the filaggrin gene, which raise the risk to develop atopic dermatitis more than threefold. In addition, these genetic variations predispose to hay fever and asthma in those with atopic dermatitis.

Allergic diseases have increased considerably in the past decades in most industrial countries. A combination of genetic and environmentally related factors is said to be the cause. In recent years, several genes were examined for a role in allergic diseases, and one of them actually turned out to be a key player. This gene encodes filaggrin, an essential protein in the horny layer of the skin. If this protein is reduced or lacking due to a genetic defect, the natural cornification is impeded and the natural barrier function of the skin is limited.

In 2006 filaggrin mutations could be identified as cause of the so-called fish scale disease or ichthyosis vulgaris, and as risk factors for the development of atopic dermatitis, a genetic breakthrough made by the Irish research team around Irwin McLean and Alan Irvine.

In an international collaboration, Dr. Stephan Weidinger from the Technische Universität München and Dr. Thomas Illig from the Helmholtz Zentrum München now investigated 3,000 school children,

representing the population as a whole. The study was carried out together with Dr. Michael Kabesch of the Children's Hospital of the Kudwig-Maximilians-University Munich. The Munich scientists found that almost 8% of the children in Germany suffer from a genetically determined deficiency of filaggrin protein in the skin. These children have a more than threefold increased risk to develop atopic dermatitis.

"In general, our results show that mutations in the filaggrin gene are extremely strong risk factors for atopic dermatitis and beyond that for hay fever. In the case of pre-existing eczema they may also cause asthma," explained Weidinger The asthma results were especially surprising, because filaggrin is not present in the respiratory tract, but appears to be of importance in the skin only."A weakened skin barrier function might enable allergens to penetrate more easily and thereby promote the development of allergies."

In addition, in another recent study on 1600 adults from the KORA cohort (Co-operative Health Research in the Augsburg Region), which represents the German population as a whole, Weidinger and Illig found out that a deficiency of filaggrin protein due to genetic variants also increases the risk for allergic contact eczema, especially of allergic reactions to nickel, which is often found in costume jewelry.

The current results show that the skin plays a crucial role in the development of different allergic diseases. "We are now interested in finding out the precise consequences of filaggrin mutations," declared Illig. "The next thing to do is to examine the metabolic pathway of this important protein. In addition, we want to clarify which molecular mechanisms play a role at the genetic level, but also concerning the protein itself. Then, the final aim, of course, is to find a therapy for patients with atopic diseases," added Illig. "If a lack of filaggrin is such an important factor in allergic diseases, it would be almost conceivable to increase production of this protein or to replace its function in other

ways".

Source: Helmholtz Zentrum München