Researchers discover receptor chain involved in atopic dermatitis

February 19 2020

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Atopic dermatitis, a chronic inflammatory disorder, affects some 30 million Americans every year. It is the most common cause of eczema, a condition marked by unbearably itchy, flaky patches of skin.

A new Tel Aviv University study identifies the precise receptor chain involved in the development of atopic dermatitis. The researchers hope to develop an antibody based on this research to create a therapeutic drug.

Research for the study was led by Prof. Ariel Munitz of the Department of Clinical Microbiology and Immunology at TAU's Sackler School of Medicine and Prof. Itai Benhar of the School of Molecular Cell Biology and Biotechnology at TAU's George S. Wise Faculty of Life Sciences and their Ph.D. students Almog Bitton and Shmuel Avlas. It was published in *Science Immunology* on February 14.

"Atopic dermatitis is a serious, chronic condition that is usually detected in childhood. It's also associated with the development of such allergic diseases as asthma," Prof. Munitz explains. "We have now identified the chain of receptors involved in the pathology of this chronic condition that places such a burden on so many millions of people, not to mention health systems worldwide."

The clinical symptoms of atopic dermatitis are caused by two proteins, which are associated with multiple allergic diseases: interleukin 4 (IL-4) and interleukin 13 (IL-13). "The role of these proteins is so important that many pharmaceutical companies have targeted them for drug development for atopic dermatitis and for asthma," Prof. Munitz says. "In fact, recently the FDA has approved the use of an anti-IL-4 receptor antibody for the treatment of this condition."

While IL-4 and IL-13 mediate atopic dermatitis, the precise contribution of each of these proteins to the development of the disease was unknown. Both proteins use a complicated, often overlapping and complex set of receptors to mediate their activities.

In an attempt to better understand the pathology of atopic dermatitis and

to identify new drug targets for treatment of the condition, the TAU researchers set out to identify the precise contribution of IL-4 versus that of IL-13 in atopic dermatitis. To do so, they harnessed mouse models that lacked the specific receptor chain: IL-13 receptor α 1, as well as various preclinical mouse models of atopic dermatitis.

"We identified that the IL-13 receptor alpha chain plays a critical role in atopic dermatitis," Prof. Benhar says. "In fact, we show that IL-13Rα1 mice that lack the IL-13 receptor α 1 do not develop the disease at all.

"Finally, we showed that a newly generated antibody was capable of reducing atopic dermatitis in mice. To translate our findings into human atopic dermatitis, we generated a novel antibody targeting the human IL-13 receptor α 1 and demonstrated that this antibody may serve as a prototype to treat the disease as well as other allergic diseases such as asthma or eosinophilic esophagitis," Prof. Benhar concludes.

More information: Almog Bitton et al, A key role for IL-13 signaling via the type 2 IL-4 receptor in experimental atopic dermatitis, *Science Immunology* (2020). DOI: 10.1126/sciimmunol.aaw2938

Provided by Tel Aviv University