Medical Xpress

Marshaling the body's own weapons against psoriasis

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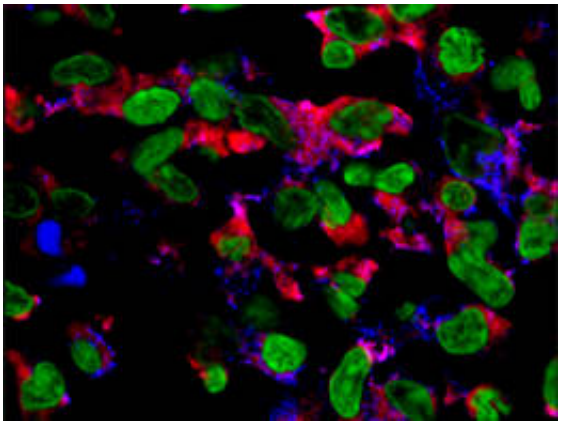

The picture shows cells in human psoriatic skin lesions of psoriasis patients before IL-4 therapy. The signaling molecule IL-23 was stained with a red dye, the cell nuclei with a green one. (Picture: E. Guenova, Y. Skabytska, W. Hoetzenecker, G. Weindl, K. Sauer, M. Tham, K.-W. Kim, J.-H. Park, J. H. Seo, D. Ignatova, A. Cozzio, M. P. Levesque, T. Volz, M. Köberle, S. Kaesler, P. Thomas, R. Mailhammer, K. Ghoreschi, K. Schäkel, B. Amarov, M. Eichner, M. Schaller, R. A. Clark, M. Röcken, und T. Biedermann, IL-4 abrogates TH17 cell-mediated inflammation by selective silencing of IL-23 in antigen-presenting cells, *PNAS*, Feb 2015, 112(7), 2163–2168, doi: 10.1073/pnas.1416922112.)

A three-character code brings relief to patients with psoriasis and sheds light on complex immunoregulation processes: IL-4, an abbreviation for the endogenous signaling molecule Interleukin 4. The substance's ability to inhibit inflammation is well known, but its mechanism of action was not fully understood. Scientists from the Technische Universität

München (TUM) and the University of Tübingen have now shown in an animal model and in a study on patients exactly how IL-4 helps against psoriasis at the molecular level and the important role it plays in our immune system.

Inflammation is a defense strategy of the body against invaders. Increased amounts of blood and fluid flow into the infected areas, and the release of signaling molecules summon immune cells to the site of infection to effectively neutralize the pathogens. However, poorly coordinated or misdirected immune reactions can trigger inflammation even in the absence of external agents, thus causing undue tissue damage. This is the case in psoriasis and other autoimmune diseases, such as multiple sclerosis and rheumatoid arthritis.

The body's own signaling molecule as a therapy candidate

"Together with colleagues from Tübingen, we were able to show in earlier studies that the signaling molecule IL-4 is a promising candidate for the treatment of psoriasis," explains Prof. Tilo Biedermann, who holds the chair for Dermatology and Allergology and is Director of the Clinic and Polyclinic for Dermatology and Allergology. "However, before IL-4 can be used as a standardized medication, we have to understand the exact mechanism of action - and we've now succeeded in doing just that."

The scientists followed a translational approach in their study - the laboratory findings were applied to patients without delay. They first used human and mouse cells to unravel the molecular effects of IL-4 on inflammation. To this effect, the scientists discovered that IL-4 inhibits specific immune cells in a natural way: it prevents the cells from synthesizing and releasing two signaling molecules, known as IL-23 and

IL-17.

"The discovery is very interesting in that IL-23 activates special T-cells in the body, thus triggering inflammation. Evidently IL-4 is able to effectively block this pathway," says Biedermann. In subsequent experiments with mice, the scientists also found that administration of IL-4 specifically inhibits inflammation of the skin via this mechanism.

IL-4 reduces psoriasis in patients

The scientists also checked the findings from the animal model in a patient study. Twenty-two patients with psoriasis received subcutaneous injections of IL-4 over a period of six weeks. Tilo Biedermann and his colleagues then examined samples from the patients' affected skin areas before and after the treatment.

The results confirmed the previous experiments: Before treatment with IL-4, the study participants had high levels of IL-23 and IL-17 in their inflamed and itchy skin. After successful treatment, the two substances were barely detectable. The result was that inflammation and psoriatic skin changes had disappeared.

"Our study results show that IL-4 very selectively and successfully suppresses inflammation. This therapeutic approach could therefore be very interesting for the treatment of other autoimmune diseases," explains Biedermann. "Moreover, we now have a better understanding of how IL-4 functions as an important 'checkpoint' in the immune system and will be able to better appreciate and exploit its significance in the future."

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