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Relief from red, itchy skin: Unraveling the secrets of vitamin D

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Vitamin D helps to reduce the inflammation associated with psoriasis, a common skin condition that causes red, itchy patches on the skin, shows a new study.

The findings help explain the success of Vitamin D therapies for psoriasis and related conditions like dry skin or eczema. Both topical vitamin D treatment and UVB rays (which activate vitamin D), are currently used to treat the chronic, autoimmune skin disease.

Typically, psoriasis occurs when the immune system sends out false danger signals that activate protein complexes called inflammasomes and ramp up the body's inflammatory response to damage, leading to flares of psoriatic plaques on the skin. Now Jürgen Schauber and colleagues show that free-floating or cytosolic DNA is involved in psoriasis inflammation. The researchers also highlight how vitamin D is able to counteract this response.

The researchers took skin biopsies from psoriasis patients and compared the diseased skin cells with the skin cells from healthy volunteers. By extracting RNA from the skin samples and examining gene expression levels, Schauber and colleagues found that a gene encoding a receptor called AIM2 was highly activated in the skin of psoriasis patients. AIM2 works with other proteins to assemble the inflammasome.

The inflammasome then activates Interleukin-1 beta, one of the main drivers of inflammation. Yet this chain of events can be shut down by

the binding of an antimicrobial peptide called cathelicidin to DNA. It turns out that vitamin D controls cathelicidin production in human skin, and can increase the binding of cathelicidin to DNA. By ramping up the binding of cathelicidin to DNA, Vitamin D helps to prevent DNA from activating the AIM2 receptor and the inflammasome that triggers inflammation. The authors suggest that cathelicidin and its relationship to vitamin D may be more specific target for therapy.

More information: "Cytosolic DNA Triggers Inflammasome Activation in Keratinocytes in Psoriatic Lesions," by Y. Dombrowski et al., *Science Translational Medicine* (2011) DOI: 10.1126/scitranslmed.3002001

ABSTRACT

The proinflammatory cytokine interleukin-1β (IL-1β) plays a central role in the pathogenesis and the course of inflammatory skin diseases, including psoriasis. Posttranscriptional activation of IL-1β is mediated by inflammasomes; however, the mechanisms triggering IL-1β processing remain unknown. Recently, cytosolic DNA has been identified as a danger signal that activates inflammasomes containing the DNA sensor AIM2. In this study, we detected abundant cytosolic DNA and increased AIM2 expression in keratinocytes in psoriatic lesions but not in healthy skin. In cultured keratinocytes, interferon-γ induced AIM2, and cytosolic DNA triggered the release of IL-1β via the AIM2 inflammasome. Moreover, the antimicrobial cathelicidin peptide LL-37, which can interact with DNA in psoriatic skin, neutralized cytosolic DNA in keratinocytes and blocked AIM2 inflammasome activation. Together, these data suggest that cytosolic DNA is an important disease-associated molecular pattern that can trigger AIM2 inflammasome and IL-1β activation in psoriasis. Furthermore, cathelicidin LL-37 interfered with DNA-sensing inflammasomes, which thereby suggests an anti-inflammatory function for this peptide. Thus, our data reveal a link between the AIM2 inflammasome, cathelicidin LL-37, and

autoinflammation in psoriasis, providing new potential targets for the treatment of this chronic skin disease.

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