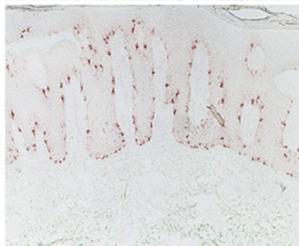
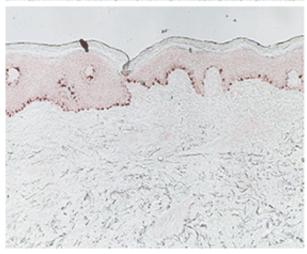


Psoriasis researchers identify molecular changes responsible for skin discoloration

7 February 2014, by Leslie Church







Leaving a mark. Melanocytes, which give skin its color, are present in healthy skin (top), but increase during a

psoriasis flare-up (middle). When the flare-up subsides, the cells are pushed toward the surface, causing dark marks to appear (bottom). Researchers have discovered that two immune system molecules play a role in these pigmentation changes.

(Medical Xpress)—Itchy, painful rashes—such as those that occur with psoriasis—are uncomfortable, but at least they fade when the flare-up subsides. Mostly. Evidence often remains in the form of dark, discolored areas of skin, serving as a reminder of the disease. A new study supported by the Milstein Medical Research Program at The Rockefeller University, however, has uncovered the molecular roots of skin discoloration that is often associated with psoriasis, suggesting the possibility of new treatments for pigmentation changes seen not only in psoriasis, but also in other conditions such as eczema and acne.

In psoriasis, the culprit is a class of immune system molecules known as cytokines. Cytokines play a key role in a signaling process that brings immune cells out to fight off an infection. But two cytokines—interleukin-17 (IL-17) and tumor necrosis factor (TNF)—are overexpressed in psoriasis, leading the immune system to attack a person's own skin cells. It's well-known that these two molecules play an important role in causing the painful rashes that are characteristic of the disease, but Claire Q. Wang, a research associate in James Krueger's Laboratory of Investigative Dermatology, wanted to see if IL-17 and TNF might also have something to do with the dark spots that psoriasis leaves behind.

"One of the treatments for psoriasis is light therapy," says Wang. "Patients will receive artificial UVA and UVB light as a way to reduce inflammation, and although the light doesn't cause sunburn, it was still commonly assumed that this was causing the pigmentation changes. Our



research showed that this was not the case."

The scientists found that the IL-17 and TNF cytokines were disrupting the pigment production of "In addition, the results of this study provide new patients' melanocytes—the cells that produce melanin, the pigment that gives skin its color. The researchers treated normal human melanocytes with IL-17 and TNF, and found that the two cytokines worked together to suppress melanin production. The researchers also looked at the gene expression of skin cells from people with psoriasis and found decreased expression of the genes involved in pigmentation signaling, correlated with increased amounts of IL-17 and TNF.

The two cytokines were also found to promote the formation of melanocyte clusters and stimulate the production of growth-promoting cytokines. Psoriasis lesions that contained high levels of IL-17 and TNF also had more melanocytes than healthy skin.

"This was very surprising," says Wang. "Melanocytes are believed to only replicate in the initial growth stage of melanocyte tumors, including melanomas. Here, in psoriasis, their numbers were doubled, sometimes tripled, but this was noncancerous skin. This shows us that these cells are not as dormant in healthy individuals as scientists believe."

This finding, together with the inhibition of pigment function in melanocytes, paints a picture of what's happening in the skin when a psoriasis flare-up fades.

"During a flare-up, there can be parts of skin with hypopigmentation—white spots," says Wang. "Then after it subsides, the spots turn dark. We think the increase in IL-17 and TNF induces this build-up of melanocytes, but prevents them from expressing the melanin until the inflammation settles down. Then the build-up is released, and the skin shows hyperpigmentation—dark spots."

"Knowing that immune cytokines can change pigment production in melanocytes, while also knowing that chronic inflammation has the potential to increase the number of melanocytes, has clear implications for the design of future therapies to

address a set of common skin disorders," says Dr. Krueger, director of Milstein Research Program and D. Martin Carter Professor in Clinical Investigation. mechanisms for how abnormal pigmentation associated with some melanocytic nevi and melanomas might arise as a result of immune responses to the growths."

Dr. Wang plans to continue studying the effects of TNF and IL-17 on melanocytes, and would like to expand the research to 3D skin models—fabricated samples of tissue in vitro that behave like human skin—that would give a better visual of how the melanin production process is being disrupted by these two cytokines during skin inflammation or wound healing.

More information: "IL-17 and TNF Synergistically Modulate Cytokine Expression while Suppressing Melanogenesis: Potential Relevance to Psoriasis." Claire Q F Wang, Yemsratch T Akalu, Mayte Suarez-Farinas, Juana Gonzalez, Hiroshi Mitsui, Michelle A Lowes, Seth J Orlow, Prashiela Manga and James G Krueger. Journal of Investigative Dermatology (2013) 133, 2741–2752; DOI: 10.1038/jid.2013.237; published online 27 June 2013

Provided by Rockefeller University



APA citation: Psoriasis researchers identify molecular changes responsible for skin discoloration (2014, February 7) retrieved 8 June 2022 from https://medicalxpress.com/news/2014-02-psoriasis-molecular-responsible-skin-discoloration.html

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