Cellular channel may open doors to skin conditions, hair growth

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Skin and hair follicles are constantly renewed in the body, maintained by specialized stem cells. New research from Children's Hospital Boston identifies a small cellular channel that regulates skin and hair growth and that could be targeted with small-molecule drugs, potentially treating variety of skin conditions, as well as thinning hair or unwanted hair growth. Findings appear in the April 16 issue of *Cell*.

Several known factors regulate the growth and specialization of cells in the epidermis. Two key players are transforming growth factor alpha (TGF-alpha) and the receptor for epidermal growth factor (EGFR). Without them, mice have wavy hair; when they are over-active, mice are hairless and develop skin cancer. However, these growth factors don't make ideal targets for a drug treatment since they are found throughout the body, and any drug targeting them would have substantial side effects.

The new study, led by David Clapham, MD, PhD, of Children's Hospital Boston, and Haoxing Xu, PhD, of the University of Michigan, finds that another protein found mainly in skin, TRPV3, "supercharges" the TGF-alpha/EGFR pathway. When TRPV3 was knocked out, the mice had a thinner outer skin layer with a dry, scaly texture, and appeared to be a less intact, more permeable barrier. By comparison, the normal mice formed a thick, robust outer skin barrier, with more tightly linked, toughened cells (a process known as cornification).

The mice lacking TRPV3 also developed a wavy coat and curly

whiskers. Clapham believes the waviness resulted from abnormal functioning of the epidermal cells at the base of the hair follicle, normally rich in TRPV3, causing the follicles to point in different directions and preventing them from smoothly extruding hair.

TRVP3 is an ion channel, a small pore that opens to admit calcium ions into the cell. Experiments showed that it is activated by EGFR, causing an influx of calcium that triggers many signaling pathways inside the cell, including one that stimulates release of TGF-alpha. This, in turn, increases EGFR signaling, providing a positive feedback loop that "supercharges" the system. When TRPV3 was knocked out, TGF-alpha/EGFR signaling was impaired.

Clapham speculates that drugs that stimulate TRPV3 activity may offer a new approach to treating multiple skin conditions, such as burns, bed sores, eczema, psoriasis, itch, fungal infections and oral mucositis (a sloughing off of skin in the mouth due to cancer chemotherapy). It might also be possible to develop cosmetic treatments that make the skin more firm, pliable and youthful. "If you activate TRPV3, you might get thicker skin," he says.

On the flip side, reducing TRPV3 activity could curb uncontrolled cell growth in skin cancer. "Some skin cancers may be potentiated by TRPV3," says Clapham.

A more speculative possibility is that TRPV3 could be targeted to create hair growth or hair removal agents, he adds.

Unlike growth factors, which act in many tissues and can have significant side effects, TRPV3 is found mainly in skin keratinocytes, although it is also found in the brain. Because TRPV3 has also been found to play a role in pain sensation, pharmaceutical companies have already been developing small molecule drugs targeting it.

More information: Cheng X et al. TRP Channel regulates EGFR signaling in hair morphogenesis and skin barrier formation. Cell 2010 Apr 16; doi:10.1016/j.cell.2010.03.013

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