Skin as a living coloring book

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The pigment melanin, which is responsible for skin and hair color in mammals, is produced in specialized cells called melanocytes and then distributed to other cells. But not every cell in the complex layers of skin becomes pigmented. The question of how melanin is delivered to appropriate locations may have been answered by a study from researchers at the Massachusetts General Hospital (MGH) Cutaneous Biology Research Center (CBRC).

“Pigment recipient cells essentially tell melanocytes where to deposit melanin, and the pattern of those recipients determines pigment patterns,” says Janice Brissette, PhD, who led the study. “Recipient cells act like the outlines in a child’s coloring book; as recipient cells develop, they form a ‘picture’ that is initially colorless but is then ‘colored in’ by the melanocytes.” The report appears in the Sept. 7 issue of *Cell*.

In humans, melanin is deposited in both the skin and the hair; but in some other mammals such as mice, melanin is primarily deposited in the coat, leaving the skin beneath the coat unpigmented. Melanocytes deposit melanin via cellular extensions called dendrites that reach out to other cells in the epidermis (the outer layer of skin) or the hair follicles. But the mechanism determining whether melanin is delivered to a particular cell has been unknown.

The MGH-CBRC researchers theorized that a mouse gene known as Foxn1 might play a role. Lack of Foxn1 is responsible for so-called ‘nude mice,’ which have hair that is so brittle it breaks off, resulting in virtually total hairlessnes, and other defects of the skin. A similar

phenomenon exists in humans with inactivation of the corresponding gene.

When the researchers developed a strain of transgenic mice in which Foxn1 is misexpressed in cells that do not usually contain melanin, they found those normally colorless areas became pigmented. Examining the skin of the transgenic mice revealed that melanocytes were contacting and delivering melanin to the cells in which Foxn1 was abnormally activated. No pigment was observed in the corresponding tissues of normal mice. Examination of human skin samples showed that the human version of Foxn1 was also expressed in cells known to be pigment recipients.
Further experiments revealed that Foxn1 signals melanocytes through a protein called Fgf2, levels of which rise as Foxn1 espression increases.

“Foxn1 makes epithelial cells into pigment recipients, which attract melanocytes and stimulate pigment transfer, engineering their own pigmentation,” says Brissette, an associate professor of Dermatology at Harvard Medical School. She and her colleagues note that the Foxn1/Fgf2 pathway probably has additional functions in the skin and that it is probably not the only pathway responsible for the targeting of pigment.

“We know that Foxn1 and Fgf2 act in concert with other factors and function within a larger network of genes. Our next step will be to identify other genes that can confer the pigment recipient phenotype or control the targeting of pigment,” Brissette adds. Her research may eventually be relevant to disorders such as vitiligo – in which pigment disappears from patches of skin – age spots, the greying of hair and even the deadly melanocyte-based skin cancer melanoma.

Source: Massachusetts General Hospital