Researchers identify signals during embryonic development that control the fate of skin cells to be sweaty or hairy

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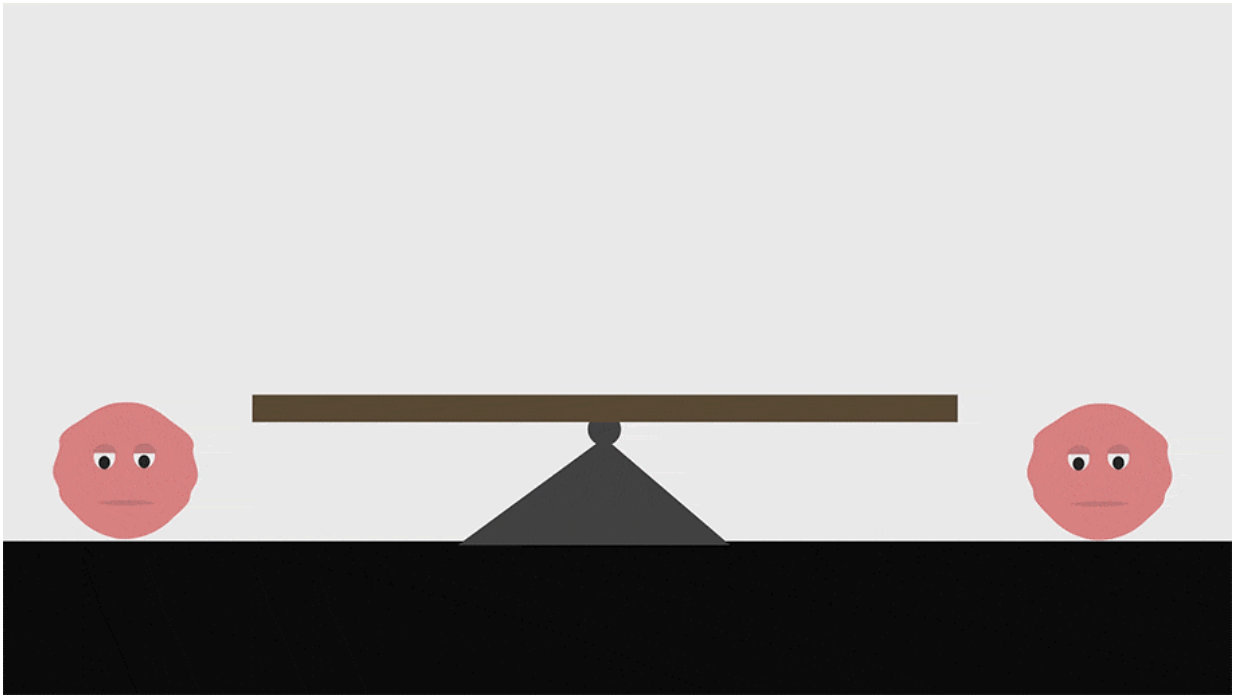

The fate of progenitor skin cells – to ultimately become either hair follicles or sweat glands – is governed by competing signals. Credit: Carla Schaffer/AAAS

(Medical Xpress)—A team of researchers with the Rockefeller University has identified the signals and timing that are involved during embryonic development controlling whether skin cells grow to be sweaty

or hairy. In their paper published in the journal *Science*, the team describes how they used the unique attributes of mice to learn more about the process of skin cell development. Yung Chih Lai and Cheng-Ming Chuong with China Medical University Hospital offer a Perspective piece on the work done by the team in the same journal issue, and offer suggestions on how the work may be used in future skin therapy development efforts.

As the researchers note, humans are one of the few mammals that are able to prevent overheating by sweating—an ability, they note, that allowed our ancestors to hunt by chasing down prey. Prior research has shown that skin cells can develop in ways that promote the development of sweat glands or hair follicles, but the means by which that differentiation arises has not been well understood. In this new effort, the researchers looked at skin cells in both mice and humans to gain a better understanding.

Mice are unique because they have skin cells on their backs that only allow for the development of hair follicles and skin cells on their feet that only allow for the development of sweat glands. This allowed the researchers an opportunity to learn more about such development by comparing the two. They found that stem cells that led to skin development in mice had differences in RNA expression of proteins that were involved in controlling which type of cell structure would develop—one type, called mesenchymal-derived bone morphogenetic proteins, were, for example, more plentiful in cells found in the feet—one in particular, Bmp5, was found to play a particularly important role. When it was blocked, the number of sweat glands that developed in mice feet was greatly reduced. The team also found other mechanisms involved, such as WNT and FGF proteins, which, when switched in mice, resulted in cells developing swapped end results, e.g. hair follicles instead of sweat glands.

The team compared these results with human skin cell samples and found that BMP and FGF proteins were expressed at higher levels during week 17 of fetal development than during week 15, which prior research has shown is a period when skin cell progression moves from hair to sweat-bud formation.

More information: C. P. Lu et al. Spatiotemporal antagonism in mesenchymal-epithelial signaling in sweat versus hair fate decision, *Science* (2016). DOI: 10.1126/science.aah6102

Abstract
The gain of eccrine sweat glands in hairy body skin has empowered humans to run marathons and tolerate temperature extremes. Epithelial-mesenchymal cross-talk is integral to the diverse patterning of skin appendages, but the molecular events underlying their specification remain largely unknown. Using genome-wide analyses and functional studies, we show that sweat glands are specified by mesenchymal-derived bone morphogenetic proteins (BMPs) and fibroblast growth factors that signal to epithelial buds and suppress epithelial-derived sonic hedgehog (SHH) production. Conversely, hair follicles are specified when mesenchymal BMP signaling is blocked, permitting SHH production. Fate determination is confined to a critical developmental window and is regionally specified in mice. In contrast, a shift from hair to gland fates is achieved in humans when a spike in BMP silences SHH during the final embryonic wave(s) of bud morphogenesis.