# Discovery of hemoglobin in the epidermis sheds new light on our skin's protective properties

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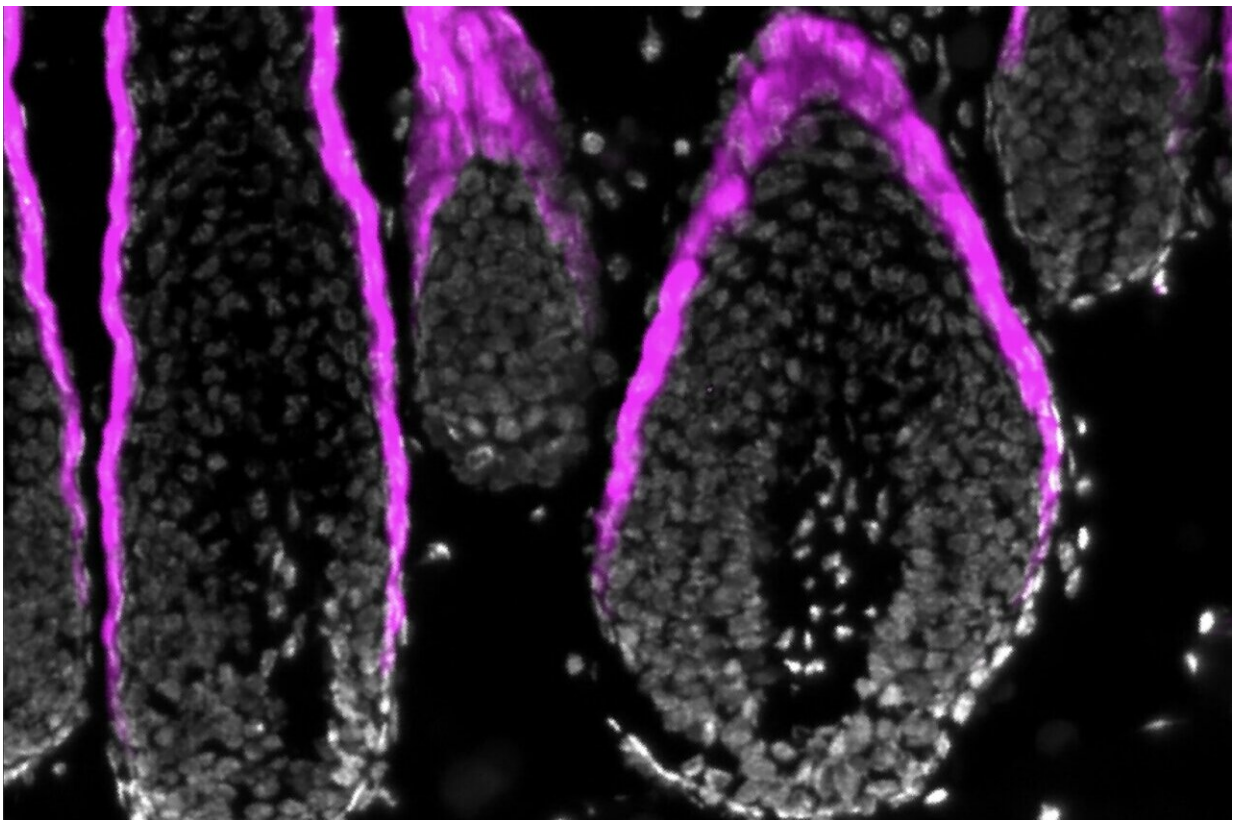

Hemoglobin α (magenta) in mouse hair follicles during the growth phase of hair cycles. Credit: Umi Tahara, Takeshi Matsui, Keitaro Fukuda, and Masayuki Amagai

Researchers have shown for the first time that hemoglobin, a protein found in red blood cells where it binds oxygen, is also present in the epidermis, our skin's outermost body tissue. The study, which appears in the *Journal of Investigative Dermatology*, provides important insights into the properties of our skin's protective external layer.

This research was driven by a curiosity about how the epidermis protects our delicate body from the environment and what unexpected molecules are expressed in the epidermis. Researchers discovered the hemoglobin α protein in keratinocytes of the epidermis and in hair follicles. This unexpected evidence adds a new facet to the understanding of the workings of our skin's defense mechanisms.

Lead investigator of the study Masayuki Amagai, MD, Ph.D., Department of Dermatology, Keio University School of Medicine, Tokyo, and Laboratory for Skin Homeostasis, RIKEN Center for Integrative Medical Sciences, Yokohama, explains, "The epidermis consists of keratinized stratified squamous epithelium, which is primarily composed of keratinocytes. Previous studies have identified the expression of various genes with protective functions in keratinocytes during their differentiation and formation of the outer skin barrier. However, other barrier-related genes escaped prior detection because of difficulties obtaining adequate amounts of isolated terminally differentiated keratinocytes for transcriptome analysis."

Hemoglobin binds gases such as oxygen, carbon dioxide, and nitric oxide , and it is an iron carrier via the heme complex. These properties make epidermal hemoglobin a prime candidate for antioxidant activity and potentially other roles in barrier function.

Professor Amagai continues, "We conducted a comparative transcriptome analysis of the whole and upper epidermis, both of which were enzymatically separated as cell sheets from human and mouse skin.

We discovered that the genes responsible for producing hemoglobin were highly active in the upper part of the epidermis. To confirm our findings, we used immunostaining to visualize the presence of hemoglobin α protein in keratinocytes of the upper epidermis.

"Our study showed that epidermal hemoglobin was upregulated by oxidative stress and inhibited the production of reactive oxygen species in human keratinocyte cell cultures. Our findings suggest that hemoglobin α protects keratinocytes from oxidative stress derived from external or internal sources such as UV irradiation and impaired mitochondrial function, respectively. Therefore, the expression of hemoglobin by keratinocytes represents an endogenous defense mechanism against skin aging and skin cancer," Professor Amagai concludes.

**More information:** Keratinocytes of the Upper Epidermis and Isthmus of Hair Follicles Express Hemoglobin mRNA and Protein, *Journal of Investigative Dermatology* (2023). DOI: 10.1016/j.jid.2023.08.008

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