Researchers identify cellular basis for how anti-aging costmetics work

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A team of investigators from UC Davis and Peking University have discovered a mechanism that may explain how alpha hydroxyl acids (AHAs) -- the key ingredient in cosmetic chemical peels and wrinkle-reducing creams -- work to enhance skin appearance. An understanding of the underlying process may lead to better cosmetic formulations as well as have medical applications.

The findings were published in the Journal of Biological Chemistry in an article entitled "Intracellular proton-mediated activation of TRPV3 channels accounts for exfoliation effect of alpha hydroxyl acids on keratinocytes."

AHAs are a group of weak acids typically derived from natural sources such as sugar cane, sour milk, apples and citrus that are well known in the cosmetics industry for their ability to enhance the appearance and texture of skin. Before this research, little was known about how AHAs actually caused skin to flake off and expose fresh, underlying skin.

The cellular pathway the research team studied focuses on an ion channel -- known as transient receptor potential vanilloid 3 (TRPV3) -- located in the cell membrane of keratinocytes, the predominant cell type in the outer layer of skin. The channel is known from other studies to play an important role in normal skin physiology and temperature sensitivity.

In a series of experiments that involved recording electrical currents

across cultured cells exposed to AHAs, the investigators developed a model that describes how glycolic acid (the smallest and most biologically available AHA) enters into keratinocytes and generates free protons, creating acidic conditions within the cell. The low pH strongly activates the TRPV3 ion channel, opening it and allowing calcium ions to flow into the cell. Because more protons also enter through the open TRPV3 channel, the process feeds on itself. The resulting calcium ion overload in the cell leads to its death and skin exfoliation.

"Our experiments are the first to show that the TRPV3 ion channel is likely to be the target of the most effective skin enhancer in the cosmetics industry," said Jie Zheng, professor of physiology and membrane biology at UC Davis and one of the principal investigators of the study. "Although AHAs have been used for years, no one until now understood their likely mechanism of action."

Besides being found in skin cells, TRPV3 also is found in cells in many areas of the nervous system and is sensitive to temperature as well as acidity. The authors speculate that the channel may have a variety of important physiological functions, including pain control.

Lead author Xu Cao, who conducted the study with UC Davis scientists as a visiting student from Peking University Health Science Center, focuses on TRPV3 channel research. With a team of researchers in China, he recently contributed to the discovery that a mutation in TRPV3 leads to Olmsted syndrome, a rare congenital disorder characterized by severe itching and horny skin development over the palms of the hands and soles of the feet. While in the UC Davis Department of Physiology and Membrane Biology, Cao discovered that AHAs also utilize the TRPV3 channel.

"Calcium channels are becoming increasingly recognized as having vital functions in skin physiology," said Cao. "TRPV3 has the potential to

become an important target not only for the cosmetics industry but for analgesia and treating skin disease."

The other study author and co-principal investigator is KeWei Wang of Peking University School of Pharmaceutical Sciences, where the research was conducted.

Provided by UC Davis