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GLADSTONE INSTITUTE OF CARDIOVASCULAR DISEASE NEWS

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GLADSTONE SCIENTISTS REVEAL THAT FAT SYNTHESIZING ENZYME IS ALSO KEY TO HEALTHY SKIN AND HAIR

DGAT1 Regulates Retinoic Acid

SAN FRANCISCO, CA – February 5, 2009 – Scientists at the Gladstone Institutes of Cardiovascular Disease (GICD) have found that an enzyme associated with the synthesis of fat in the body is also an element in healthy skin and hair.

The enzyme is acyl CoA:diacylglycerol acyltransferase 1 or DGAT1. Mice that lack DGAT1 have many interesting characteristics. For example, they are lean, resistant to diet-induced obesity, are more sensitive to insulin and leptin, and have abnormalities in mammary gland development and skin.

When Gladstone researchers in the laboratory of Robert V. Farese, Jr. used genetic engineering to delete the enzyme in mice, they found that lack of DGAT1 caused levels of retinoic acid (RA) to be greatly increased in skin and resulted in the loss of hair. Their findings were reported in *The Journal of Biological Chemistry*.

“For some time, we have been studying the enzymes that make triglycerides,” said Robert V. Farese, Jr., senior investigator and senior author on the study. “We found that one of these enzymes is a major regulator of retinoic acid actions in the skin.”

RA, which comes from vitamin A (retinol) has been used to treat skin disorders, such as acne and psoriasis, and certain cancers, but it is fairly toxic and must be carefully controlled.

In mice without DGAT1, the skin was very sensitive to retinol. The loss of DGAT1 also caused alopecia, or hair loss. Both of these effects could be prevented by depriving the mice of a source of retinol in their diet. It turns out that DGAT1 can convert retinol to a relatively inert storage form. Without DGAT1, this ability is lost, and any excess retinol in the skin can be converted to RA.

“Our results show that DGAT1 is an important component for controlling retinoic acid levels in the skin of mice,” said Michelle Shih, the lead author on the study. “These findings may have implications for the treatment of human skin or hair disorders.”

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About the Gladstone Institutes

The J. David Gladstone Institutes, an independent, non-profit biomedical research organization, affiliated with the University of California, San Francisco (UCSF), is dedicated to the health and welfare of humankind through research into the causes and prevention of some of the world’s most devastating diseases. Gladstone is comprised of the Gladstone Institute of Cardiovascular Disease, the Gladstone Institute of Virology and Immunology and the Gladstone Institute of Neurological Disease. More information can be found at www.gladstone.ucsf.edu.

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