Lab 'failure' leads to potential treatment for obesity

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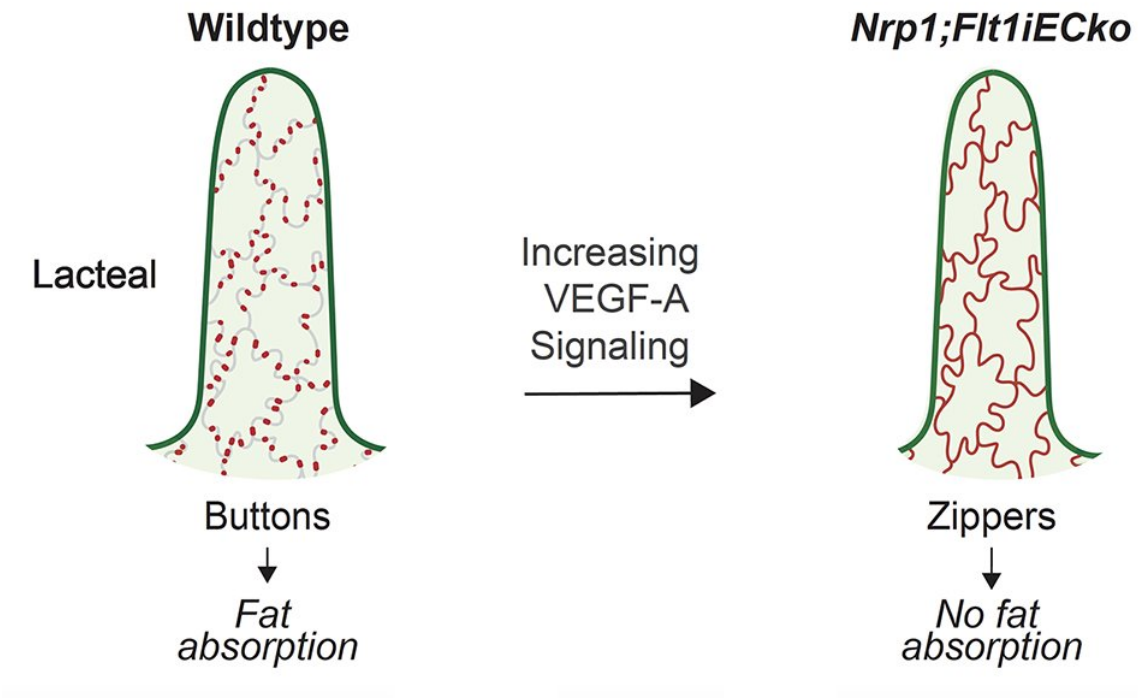

Manipulating two genes enabled scientists to replace “buttons” on surface of lymphatic vessels to “zippers” which turn away fat molecules. Credit: Yale University

Yale scientists set out to create a morbidly obese mouse. They failed miserably. What they found was much more interesting.

"We created a mouse that eats fat but doesn't get fat," said Anne Eichmann, Ensign Professor of Medicine (Cardiology) and Professor of Cellular And Molecular Physiology.

The "failure" led Eichmann's team headed by Associate Research Scientist Feng Zhang to discover that the absence of two molecules helped "zip up" specialized vessels in lymphatic tissue and prevent the uptake of fat particles called chylomicrons, they report Aug. 10 in the journal *Science*. Instead of incorporating lipids as fat, mice lacking the two genes excreted lipids and gained little weight despite being fed a high-fat diet.

Lipids are taken up in lymphatic tissue in the gut through portals in vessels called lacteals. In most cases, the entrance of lipids to the vessels are controlled through easily penetrated button-like structures. However, in mice lacking vascular endothelial growth factor 1 and neuropilin1 vessels become "zippered" and lipids are excreted rather than taken up by vessels. Zippering can be also induced in normal mice by inhibiting the Rho kinase ROCK.

Eichmann noted that an inhibitor of ROCK is already used in a drug to treat glaucoma and could be tested for its effects on lipid uptake and weight gain as well.

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More information: Lacteal junction zippering protects against diet-induced obesity. *Science*. DOI: 10.1126/science.aap9331

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