

Bile acids fire up fat burning

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Obesity arises from an imbalance between energy intake and energy expenditure. As a result, current treatments try to decrease calorie intake and/or increase energy expenditure.

The problem is maintaining long-term effects. Non-invasive treatments, like diets and drugs that reduce intestinal ingestion are widely unpopular among patients, while bariatric surgery seems to be the only reliable treatment for obese people, despite being both expensive and invasive.

But now a new study led by the lab Kristina Schoonjans at EPFL, suggests that a specific group of [bile acids](#) could directly burn away the lipids in our fat depots, effectively making it a new therapy against obesity.

Bile acids are important constituents of bile, a yellow-green fluid produced in the liver that is stored in the gallbladder and secreted into the intestines during a meal. Bile emulsifies dietary fat into tiny globules that can be broken down by digestive enzymes to be absorbed by the intestine.

The EPFL scientists discovered that bile acids can turn fat-storing [cells](#) into fat-burning ones. This process is called thermogenesis (literally, "heat production") and it helps maintain body temperature in cold environments.

There are three different types of fat cells: white fat cells, which store [energy](#); [brown fat cells](#), which expend energy; and the so-called "beige" fat cells, which are functionally related to brown cells while being located in typically white-fat depots.

Beige cells have recently attracted a lot of attention, especially because adults have very low numbers of active brown adipocytes that burn energy. But what can turn a white cell into a beige one - a process called "beiging" - and shift the balance from fat-storing to fat-burning?

The work of Schoonjans' team suggests that this process can be coordinated by secondary bile

acids, metabolites that are generated by our liver and gut bacteria.

The study shows that activating the bile acid receptor TGR5 with molecules that mimic the action of bile acids (so called "mimetics") induces a remodeling of white fat cells into beige fat cells. The bile acids accumulate in the blood and interact with the TGR5 receptor on white fat cells to change their metabolic function.

This is more than a mere change of color, as the researchers also found that these bile acids increase the number of mitochondria in the new fat cells. This indicates higher energy consumption in the new, beige fat cells.

The bile-acid mimetics also triggered lipolysis, the first step in fat degradation, allowing the [fat cells](#) to use fatty acids as their main fuel source.

The study provides a direct connection between bile acids and fat loss and envisions novel therapeutic intervention in obese people. "We showed that bile acids are much more than a soap for digestion," says Kristina Schoonjans. "When their concentration in the blood reaches a certain level, it can turn up the thermostat and increase fat burning for energy and heat production".

"What is exciting about our discovery is that low concentrations of TGR5-selective molecules are sufficient to promote the beiging of white fat-storing cells, thereby bypassing the need to increase the total bile [acid](#) pool," says Laura Velazquez, first-author of the paper.

"Moreover, this study highlights mitochondrial fission —or the splitting of mitochondria— as a pivotal mechanism by which bile acids turn white fat into beige fat," adds Alessia Perino, co-first author. "It will be interesting to explore if mitochondrial fission is a universal mechanism for beiging in response to other stimuli".

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et al, TGR5 signalling promotes mitochondrial fission and beige remodelling of white adipose tissue, *Nature Communications* (2018). DOI: [10.1038/s41467-017-02068-0](https://doi.org/10.1038/s41467-017-02068-0)

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