Researchers discover key to burning fat faster

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Enzymes involved in breaking down fat can now be manipulated to work three times harder by turning on a molecular switch recently observed by chemists at the University of Copenhagen. Being able to control this chemical on/off button could have massive implications for curing diseases related to obesity including diabetes, cardio vascular disease, stroke and even skin problems like acne. But the implications may be wider.

The results suggest that the switch may be a common characteristic of many more enzymes. Since enzymes are miniscule worker-molecules that control a vast variety of functions in cells, if the switches are standard, it may well be one of the most important discoveries in enzymology.

"If many enzymes turn out to be switched on in the same way as the ones we've studied, this opens a door to understanding- and maybe curing, a wide range of diseases", says professor Dimitrios Stamou.

Stamou heads a multidisciplinary team of scientists at the Nanoscience Center and Department of Chemistry at the University of Copenhagen who published their discovery in the prominent scientific journal Journal of the American Chemical Society.

Switch contradicts previous understanding

The discovery of the enzymatic ignition key contradicts previous ideas of how cells control the function of enzymes such as the fat eating lipase used in the current study.

Researchers used to think that these enzymes work continuously at varying levels of efficiency. But in fact they are quite lazy. Very much like construction workers they work at a fixed efficiency for a given amount of time (working hours), and then they rest. And that's good news for enzyme designers.

Tripping their newfound switch resulted in tripling the working hours of lipase enzymes, from 15 percent of the time to 45 percent by the Copenhagen team

Function follows form

In enzymes, function is decided by the shape of the molecule. So making them more efficient would have required a major reconstruction. In some cases so difficult that it is on the order of transforming a handsaw into a chainsaw, says the chemist, Assistant Professor Nikos Hatzakis, who was deeply involved in the scrutiny of the enzymes.

"Changing the fundamental shape of a tool is always difficult. Whether it's saw or an enzyme. But working longer hours with the same tool is infinitely easier. What we've achieved, is to make enzymes work longer hours", explains Hatzakis.

Scrutiny on the Nanoscale

Observing that enzymes even have an on-off switch may sound easy, but first the Bio Nano- team had to devise a way to study individual enzyme molecules. These are so small, that there are trillions in just a drop of water. So measuring the work of only one enzyme could be compared to looking down from the moon to detect each time a carpenter in a building in Copenhagen swings his hammer.

Light emitting fat

To perform their studies the researchers chose a fat degrading lipase enzyme model system in collaboration with Danish industrial enzyme producer Novozymes.

They used "fat" that would emit light each time the enzyme took a bite. This way they could monitor each and every catalytic cycle or single movement of work. To ensure realism the enzymes were placed on an artificial cell wall. An "in vivo like membrane system", says Stamou.

"Natural enzymes live in cells. Looking at them in a non native

environment, would tell us as much as looking at a carpenter working in outer space wearing a space suit would tell us about builders", explains Dimitrios Stamou and concludes:

"Now that we have understood how to switch enzymes on and off we could use this knowledge in the future both for curing diseases but also to design novel enzymes for industrial applications".

Provided by University of Copenhagen