Fat cells outlive skinny ones

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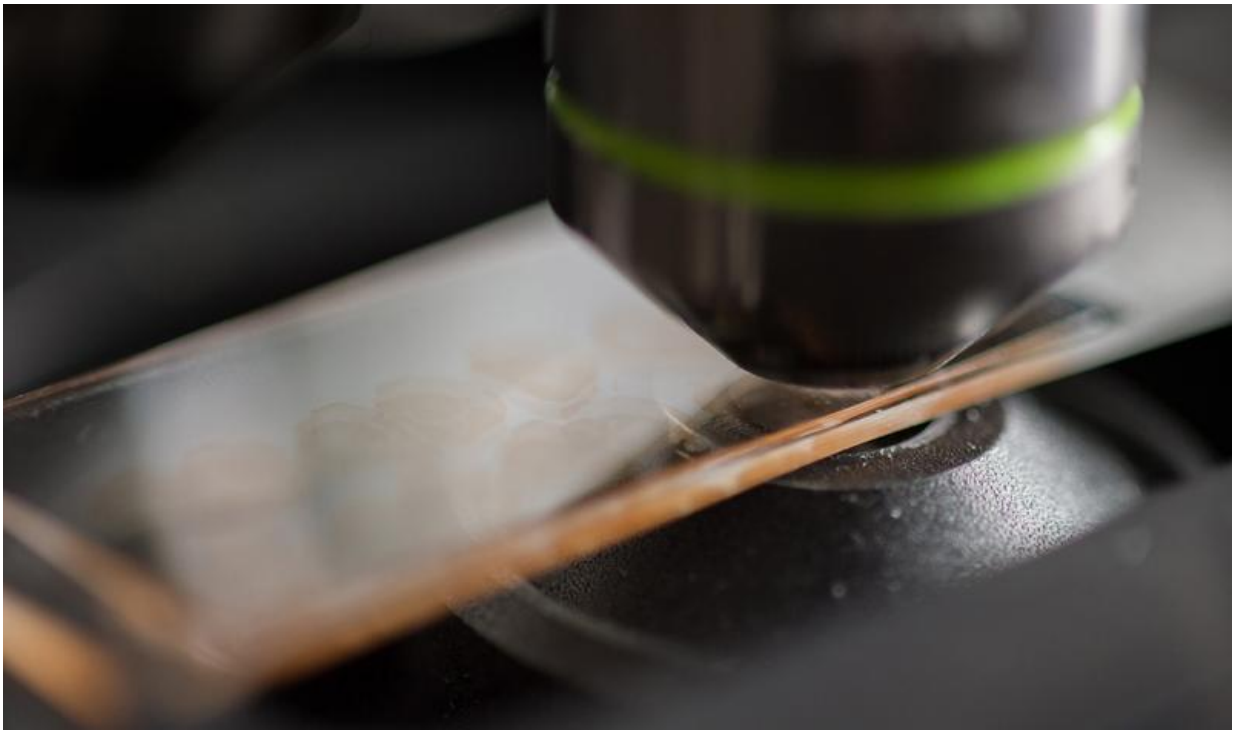

Credit: Courtesy of MSU

Cells with higher fat content outlive lean cells, says a new study from Michigan State University.

This study has implications for larger organisms, such as humans, as the results support the phenomenon known as the "obesity paradox." This concept shows that overweight people have the lowest all-cause mortality rates while fit people, oddly enough, have mortality rates comparable to

those categorized as slightly obese.

"The obesity paradox baffles scientists across numerous disciplines," said Min-Hao Kuo, MSU biochemist and molecular biologist who published the study in the current issue of *PLoS Genetics*. "But when it comes to yeast, which is an excellent model for the studies of human aging, increasing the cellular content of triacylglycerol, or fat, extends the lifespan."

Kuo's team was the first to show a positive correlation between Triacylglycerol, or TAG, content and lifespan. The connection provides support for the obesity paradox theory, he added.

TAG is a fat found in all eukaryotes that include animals, plants and fungi. The lipid's ability to store excessive energy, provide insulation and accumulate in response to many stressors is well known. What's perplexing, though, is how TAG influences lifespan.

"Our team used genetic approaches to manipulate the cellular capacity of triacylglycerol reproduction and degradation," Kuo said. "Via sophisticated analyses, we demonstrated that it preserves life through a mechanism that is largely independent of other lifespan regulation pathways common in yeast as well as humans."

The first thing Kuo's team did was delete TAG lipases, enzymes that break down the lipid into smaller molecules for different uses including energy extraction. Unable to utilize TAG, these yeast accumulated fat inside the cells. In addition, Kuo and his colleagues boosted the production of the fat by increasing the enzyme for TAG synthesis.

In both cases, blocking TAG breakdown and forcing its production, yeast cells are fatter and have longer lifespan. In contrast, yeast cells depleted of the ability to synthesize TAG are lean but die early.

Overexpressing a TAG lipase in an otherwise normal strain forces TAG breakdown. These cells also suffer from a shorter lifespan.

Interestingly, those fat and long-living yeast cells do not seem to suffer from obvious growth defects. They mate and produce progeny well. They also have normal resistance to different environmental stresses. On the other hand, other common methods of extending lifespan, such as caloric restriction and deletion of genes key to nutrient sensing, frequently cause cells to grow slowly or be less tolerant of environmental stresses.

While the team suspects that the pro-longevity function exists in humans, they've yet to prove that triacylglycerol could drive the intriguing phenomenon in humans.

"Our paper likely will stimulate a new wave of research that has broad and deep impacts, including potential advances in human medicine," Kuo said.

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