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UF scientists reveal how dietary restriction cleans cells

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Reduce, recycle and rebuild is as important to the most basic component of the human body, the cell, as it is to the environment. And a University of Florida study shows just how much the body benefits when it "goes green," at least if you're a rat: Cutting calories helps rodents live longer by boosting cells' ability to recycle damaged parts so they can maintain efficient energy production.

"Caloric restriction is a way to extend life in animals. If you give them less food, the stress of this healthy habit actually makes them live longer," said Christiaan Leeuwenburgh, Ph.D., chief of the division of biology of aging in UF's Institute on Aging. Understanding how the process works at the cellular level in rodents could help scientists develop drugs that mimic the process in humans, Leeuwenburgh added.

How does it work? During the aging process, free radicals . - highly reactive byproducts of our cells' respiration - wreak havoc on our cellular machinery. Mitochondria, the tiny power plants that keep a cell functioning, are especially vulnerable to this type of damage. The effects can be disastrous - if malfunctioning mitochondria aren't removed, they begin to spew out suicidal proteins that prompt the entire cell to die. Cell death, on a whole-body scale, is what aging is all about.

Fortunately, younger cells are adept at reducing, recycling and rebuilding. In this process, damaged mitochondria are quickly swallowed up and degraded. The broken down pieces are then recycled and used to build new mitochondria. However, older cells are less adept at this process, so damaged mitochondria tend to accumulate and contribute to aging.

"Cell survival is dependent upon the ability of the cell to reduce and recycle by a mechanism called autophagy," said William Dunn Jr., Ph.D., a professor of anatomy and cell biology in UF's College of Medicine and senior author of the study, which was published online this month in the journal Rejuvenation Research. "When a cell is under stress, autophagy is turned on to clean up the cell by removing damaged cellular components, while recycling building blocks necessary to rebuild the cell. It's there to protect the cell. But in aged cells, they're basically not able to adjust to stress as well."

UF scientists studied 22 young and old rats, comparing those allowed to eat freely with those fed a low-calorie, nutritious diet. The stress of a low-calorie diet was enough to boost cellular cleaning in the hearts of older rats by 120 percent over levels seen in rats that were allowed to eat what they wanted. The diet had little or no effect on younger rats.

"Autophagy is a housekeeping mechanism that keeps cells free of damaged and thereby detrimental mitochondria and other toxic materials while recycling their building blocks - nutrients needed by the cell," said Stephanie Wohlgemuth, Ph.D., a lecturer in UF's department of aging and geriatrics and the study's lead author. "So if that process is maintained with age - or even increased - that can only be beneficial."

Stephanie Wohlgemuth, Ph.D., a lecturer in UF's department of aging and geriatrics (Photo by Ann Griswold)

To determine how dietary restriction boosted cells' ability to reduce the toxic trash, the scientists studied how the amount of certain proteins changed with the rats' age and diet. They found that some proteins responsible for degrading the damaged parts of the cell by autophagy were more abundant in older, calorie-restricted rats.

Boosting autophagy is especially important in the heart, a vital organ packed with mitochondria, Wohlgemuth said. Swift disposal of damaged cellular components is essential to maintaining an abundance of healthy heart cells as we age.

"Cardiac cells have lost the capability to divide readily to replace dying cells. So the maintenance of the cells' survival mechanisms is crucial for the heart," said Wohlgemuth.

Now that some of these proteins have been identified, UF researchers say the next step is to figure out how the proteins can be activated without inflicting dietary stress.

"What if we bypass the caloric restriction and find a way of increasing autophagy?" asked Dunn. "That is, instead of starving yourself you can find another way of enhancing autophagy that will allow the enhanced removal of various damaged organelles that accumulate in aged cells."

Ulf Brunk, M.D., Ph.D., a professor emeritus of experimental pathology at LinkÃ¶ping University in Sweden, said the study builds on past research showing that removal of toxic mitochondria may extend life in a variety of mammals.

"The paper is a further step in the direction of showing that the stimulation of autophagy may be beneficial," Brunk said.

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