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Natural anti-oxidant deserts aging body: Cell's reserve fighting force shrinks with age

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When the body fights oxidative damage, it calls up a reservist enzyme that protects cells – but only if those cells are relatively young, a study has found.

Biologists at USC discovered major declines in the availability of an enzyme, known as the Lon protease, as human cells grow older.

The finding may help explain why humans lose energy with age and could point medicine toward new diets or pharmaceuticals to slow the aging process.

The researchers showed that when oxidative agents attack the power centers of young cells, the cells respond by calling up reinforcements of the enzyme, which breaks up and removes damaged proteins.

As the cells age, they lose the ability to mobilize large numbers of Lon, the researchers reported in *The Journals of Gerontology*.

Senior author Kelvin J. A. Davies, a professor at the USC Leonard Davis School of Gerontology, used a war analogy to explain that no "standing army" of Lon protease can endure an attack by invading oxidants without calling up reserves.

"Once the war has started, what's your capacity to keep producing ... to protect your vital resources and keep the fight going?" he asked.

Since aging is the longest war, the USC study suggests a more important role for the reservist enzyme than previously known.

Lon protects the mitochondria – tiny organisms in the cell that convert oxygen into energy. The conversion is never perfect: Some oxygen leaks and combines with other elements to create damaging oxidants.

Oxidation is the process behind rust and food spoilage. In the body, oxidation can damage or destroy almost any tissue. Lon removes oxidized proteins from the mitochondria and also plays a vital role in helping to make new mitochondria.

"We know that mitochondrial function declines with age, which is a major limitation to cells. One of the components of that decline is the loss of Lon. The ability of Lon to be induced by [oxidative] stress is a very important component of overall stress resistance," Davies said.

Davies and his team worked with a line of human lung cells. They exposed the cells to hydrogen peroxide, a powerful oxidant that is a byproduct of energy production and that also can result from metabolism of some drugs, toxins, pesticides and herbicides.

To fight the oxidant, young cells doubled the size of their Lon army within five hours and maintained it for a day. In some experiments, young cells increased their Lon army as much as seven-fold.

Middle-aged cells took a full day to double their Lon army, during which time the cells were exposed to harmful levels of oxidized proteins.

Older cells started with a standing Lon army only half as large and showed no statistically significant increase in Lon levels over 24 hours.

The Davies group, which discovered Lon in 2002, previously had shown

that Lon's standing army gets smaller with age and that the anti-oxidant power of Lon depends more on its reserves than on enzymes present when stress first hits the body.

The latest study completes the picture of Lon's sluggish response as senescent cells – a technical term for cells that mimic several key features of the aging process – try to cope with stress.

"In the senescent cells, the Lon levels are drastically low to begin with, and they don't increase" in response to stress, Davies said.

Scientists have known for decades that mitochondria become less efficient with age, contributing to the body's loss of energy.

"It may well be that our ability to induce Lon synthesis and our loss of adaptability to stress may be an even more significant factor in the aging process," Davies said.

Davies and others are investigating potential treatments to boost the function of Lon. Costly enzyme supplements are useless, Davies noted, since the digestive system breaks down the enzyme to amino acids before it can reach its target.

"It's a lot cheaper to buy a piece of meat and get the same amino acids," he said.

Provided by University of Southern California