MedicalXpress

Surprising results casts new light on the free radical theory of aging

August 3 2015

When scientists in the Campisi lab at the Buck Institute bred mice that produced excess free radicals that damaged the mitochondria in their skin, they expected to see accelerated aging across the mouse lifespan - additional proof of the free radical theory of aging. Instead, they saw a surprising benefit in young animals: accelerated wound healing due to increased epidermal differentiation and re-epithelialization. The study published online on August 3rd in *Proceedings of the National Academy of Sciences*.

Senior scientist and Buck Institute professor Judith Campisi, PhD, said the finding sheds light on current apparent discrepancies regarding the role of free radicals as a driver of the aging process. Free radicals are especially reactive atoms or groups of atoms that have one or more unpaired electrons. They are produced in the body as a by-product of normal metabolism and can also be introduced from an outside source, such as tobacco smoke, or other toxins. Free radicals can damage cells, proteins and DNA by altering their chemical structure. Campisi said excessive amounts of free radicals are known to cause cellular damage that leads to aging, but in some mouse models and human studies lowering free radicals with antioxidants have not always conferred the expected benefits.

"This study shows that it's essential that we look across the entire lifespan when we examine mechanisms implicated in the aging process," Campisi said, adding that while increased free radical production showed benefit in younger animals, the mice paid a price over time.

Campisi said mitochondrial damage from excess free radicals caused some of the skin cells to go into senescence - they stopped dividing and started accumulating. Campisi said that over time the energy available to the epidermal stems cells was depleted - the stem cells simply became too scarce and the mice showed expected signs of aging, thin skin and poor wound healing. "In this case, we found unexpected pleotropic effects, mechanisms that benefit us when we're young, cause problems as we age."

Campisi said the mice used in this study more closely mimic the stress that occurs over time in human skin. "Mice are nocturnal and covered with fur; in their life, and in normal laboratory conditions, they don't experience the type of sun light-induced skin damage that occurs in humans. In this case we were able to breed mice that more closely respond in a manner similar to humans," she said.

In addition to the complications caused by senescence, lead scientist Michael Velarde, PhD, a postdoctoral fellow in the Campisi lab, said mitochondrial stress caused by the increase in free radicals also forced the skin cells in the younger animals to differentiate faster than normal, further depleting the pool of stem cells available to renew the skin over time. "This is not a simple process. It may be that nature used free radicals to optimize skin health, but because this process is not deleterious to the organism until later in life, past its reproductive age, there was no need to evolve ways to alter this mechanism," he said.

Campisi said there could be one practical implication of the study: taking large amounts of anti-oxidants might have deleterious effects, at least in the skin.

More information: *PNAS*
www.pnas.org/cgi/doi/10.1073/pnas.1505675112

Provided by Buck Institute for Research on Aging