Forget the antioxidants? Researchers cast doubt on role of free radicals in aging

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For more than 40 years, the prevailing explanation of why we get old has been tied to what is called oxidative stress. This theory postulates that when molecules like free radicals, oxygen ions and peroxides build up in cells, they overwhelm the cells' ability to repair the damage they cause, and the cells age.

An industry of "alternative" antioxidant therapies -- such as Vitamin E or CoQ10 supplements in megadose format --has sprung up as the result of this theory. However, clinical trials have not shown that these treatments have statistically significant effects.

And now researchers at McGill University , in a study published in the February issue of the journal *PLoS Genetics*, are calling the entire oxidative stress theory into question. Their results show that some organisms actually live longer when their ability to clean themselves of this toxic molecule buildup is partially disabled. Collectively, these molecules are known as reactive oxygen species, or ROS for short.

Dr. Siegfried Hekimi of McGill's Department of Biology, said most of the evidence for the oxidative stress theory is circumstantial, meaning oxidative stress could just as easily be a result of aging as its cause.

"The problem with the theory is that it's been based purely on correlative data, on the weight of evidence," explained Hekimi, McGill's Strathcona Chair of Zoology and Robert Archibald & Catherine Louise Campbell Chair in Developmental Biology. "It is true that the more an organism

appears aged, whether in terms of disease, or appearance or anything you care to measure, the more it seems to be suffering from oxidative stress".

"This has really entrenched the theory," he continued, "because people think correlation is causation. But now this theory really is in the way of progress."

Hekimi and postdoctoral fellow Jeremy Van Raamsdonk studied mutant Caenorhabditis elegans worms. They progressively disabled five genes responsible for producing a group of proteins called superoxide dismutases (SODs), which detoxify one of the main ROS. Earlier studies seemed to show that decreased SOD production shortened an organism's lifespan, but Hekimi and Van Raamsdonk did not observe this. In fact, they found quite the opposite.

None of their mutant worms showed decreased lifespan compared to wild-type worms, even though oxidative stress was clearly raised. In fact, one variety actually displayed increased lifespan, the researchers said.

"The mutation that increases longevity affects the main SOD found in mitochondria inside the animals' cells," said Hekimi. "This is consistent with earlier findings that mitochondria are crucial to the aging process. It seems that reducing mitochondrial activity by damaging it with ROS will actually make worms live longer."

The researchers hasten to point out that they are not suggesting that oxidative stress is good for you.

"ROS undoubtedly cause damage to the body," Hekimi said. "However, they do not appear to be responsible for aging."

More information: dx.plos.org/10.1371/journal.pgen.1000361