

Agent in red wine found to keep hearts young

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How, scientists wonder, do the French get away with a clean bill of heart health despite a diet loaded with saturated fats?

The answer to the so-called "French paradox" may be found in red wine. More specifically, it may reside in small doses of resveratrol, a natural constituent of grapes, pomegranates, red wine and other foods, according to a new study by an international team of researchers.

Writing this week (June 3) in the online, open-access journal *Public Library of Science One*, the researchers report that low doses of resveratrol in the diet of middle-aged mice has a widespread influence on the genetic levers of aging and may confer special protection on the heart.

Specifically, the researchers found that low doses of resveratrol mimic the effects of what is known as caloric restriction - diets with 20-30 percent fewer calories than a typical diet - that in numerous studies has been shown to extend lifespan and blunt the effects of aging.

"This brings down the dose of resveratrol toward the consumption reality mode," says senior author Richard Weindruch, a University of Wisconsin-Madison professor of medicine and a researcher at the William S. Middleton Memorial Veterans Hospital. "At the same time, it plugs into the biology of caloric restriction."

Previous research has shown that resveratrol in high doses extends lifespan in invertebrates and prevents early mortality in mice given a

high-fat diet. The new study, conducted by researchers from academia and industry, extends those findings, showing that resveratrol in low doses and beginning in middle age can elicit many of the same benefits as a reduced-calorie diet.

"Resveratrol is active in much lower doses than previously thought and mimics a significant fraction of the profile of caloric restriction at the gene expression level," says Tomas Prolla, a UW-Madison professor of genetics and a senior author of the new report.

The group explored the influence of the agent on heart, muscle and brain by looking for changes in gene expression in those tissues. As animals age, gene expression in the different tissues of the body changes as genes are switched on and off.

In the new study - which compared the genetic crosstalk of animals on a restricted diet with those fed small doses of resveratrol - the similarities were remarkable, explains lead author Jamie Barger of Madison-based LifeGen Technologies. In the heart, for example, there are at least 1,029 genes whose functions change with age, and the organ's function is known to diminish with age. In animals on a restricted diet, 90 percent of those heart genes experienced altered gene expression profiles, while low doses of resveratrol thwarted age-related change in 92 percent. The new findings, say the study's authors, were associated with prevention of the decline in heart function associated with aging.

In short, a glass of wine or food or supplements that contain even small doses of resveratrol are likely to represent "a robust intervention in the retardation of cardiac aging," the authors note.

That finding may also explain the remarkable heart health of people who live in some regions of France where diets are soaked in saturated fats but the incidence of heart disease, a major cause of mortality in the

United States, is low. In France, meals are traditionally complemented with a glass of red wine.

The new resveratrol study is also important because it suggests that caloric restriction, which has been widely studied in animals from spiders to humans, and resveratrol may govern the same master genetic pathways related to aging.

"There must be a few master biochemical pathways activated in response to caloric restriction, which in turn activate many other pathways," explains Prolla. "And resveratrol seems to activate some of these master pathways as well."

The new findings, according to Weindruch and Prolla, provide strong evidence that resveratrol can improve quality of life through its influence on the different parameters of aging such as cardiac function. However, whether the agent can extend lifespan in ways similar to caloric restriction will require further study, according to the new report's authors.

Source: University of Wisconsin-Madison

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