

# New Hints Seen That Red Wine May Slow Aging

By [NICHOLAS WADE](#)

Red wine may be much more potent than was thought in extending human lifespan, researchers say in a new report that is likely to give impetus to the rapidly growing search for longevity drugs.

The study is based on dosing mice with resveratrol, an ingredient of some red wines. Some scientists are already taking resveratrol in capsule form, but others believe it is far too early to take the drug, especially using wine as its source, until there is better data on its safety and effectiveness.

The report is part of a new wave of interest in drugs that may enhance longevity. On Monday, Sirtris, a startup founded in 2004 to develop drugs with the same effects as resveratrol, completed its sale to GlaxoSmithKline for \$720 million.

Sirtris is seeking to develop drugs that activate protein agents known in people as sirtuins.

“The upside is so huge that if we are right, the company that dominates the sirtuin space could dominate the pharmaceutical industry and change medicine,” Dr. David Sinclair of the Harvard Medical School, a co-founder of the company, said Tuesday.

Serious scientists have long derided the idea of life-extending elixirs, but the door has now been opened to drugs that exploit an ancient biological survival mechanism, that of switching the body’s resources from fertility to tissue

maintenance. The improved tissue maintenance seems to extend life by cutting down on the degenerative diseases of aging.

The reflex can be prompted by a faminelike [diet](#), known as caloric restriction, which extends the life of laboratory rodents by up to 30 percent but is far too hard for most people to keep to and in any case has not been proven to work in humans.

Research started nearly 20 years ago by Dr. Leonard Guarente of the [Massachusetts Institute of Technology](#) showed recently that the famine-induced switch to tissue preservation might be triggered by activating the body's sirtuins. Dr. Sinclair, a former student of Dr. Guarente, then found in 2003 that sirtuins could be activated by some natural compounds, including resveratrol, previously known as just an ingredient of certain red wines.

Dr. Sinclair's finding led in several directions. He and others have tested resveratrol's effects in mice, mostly at doses far higher than the minuscule amounts in red wine. One of the more spectacular results was obtained last year by Dr. John Auwerx of the Institute of [Genetics](#) and Molecular and Cellular Biology in Illkirch, France. He showed that resveratrol could turn plain vanilla, couch-potato mice into champion athletes, making them run twice as far on a treadmill before collapsing.

The company Sirtris, meanwhile, has been testing resveratrol and other drugs that activate sirtuin. These drugs are small molecules, more stable than resveratrol, and can be given in

smaller doses. In April, Sirtris reported that its formulation of resveratrol, called SRT501, reduced glucose levels in diabetic patients.

The company plans to start clinical trials of its resveratrol mimic soon. Sirtris's value to GlaxoSmithKline is presumably that its sirtuin-activating drugs could be used to treat a spectrum of degenerative diseases, like **cancer** and **Alzheimer's**, if the underlying theory is correct.

Separately from Sirtris's investigations, a research team led by Tomas A. Prolla and Richard Weindruch, of the **University of Wisconsin**, reports in the journal PLoS One on Wednesday that resveratrol may be effective in mice and people in much lower doses than previously thought necessary. In earlier studies, like Dr. Auwerx's of mice on treadmills, the animals were fed such large amounts of resveratrol that to gain equivalent dosages people would have to drink more than 100 bottles of red wine a day.

The Wisconsin scientists used a dose on mice equivalent to just 35 bottles a day. But red wine contains many other resveratrol-like compounds that may also be beneficial.

Taking these into account, as well as mice's higher metabolic rate, a mere four, five-ounce glasses of wine "starts getting close" to the amount of resveratrol they found effective, Dr. Weindruch said.

Resveratrol can also be obtained in the form of capsules marketed by several companies. Those made by one company, Longevinex, include extracts of red wine and of a Chinese plant called giant knotweed. The Wisconsin

researchers conclude that resveratrol can mimic many of the effects of a caloric-restricted diet “at doses that can readily be achieved in humans.”

The effectiveness of the low doses was not tested directly, however, but with a DNA chip that measures changes in the activity of genes. The Wisconsin team first defined the pattern of gene activity established in mice on caloric restriction, and then showed that very low doses of resveratrol produced just the same pattern.

Dr. Auwerx, who used doses almost 100 times greater in his treadmill experiments, expressed reservations about the new result. “I would be really cautious, as we never saw significant effects with such low amounts,” he said Tuesday in an e-mail message.

Another researcher in the sirtuin field, Dr. Matthew Kaeberlein of the [University of Washington](#) in Seattle, said, “There’s no way of knowing from this data, or from the prior work, if something similar would happen in humans at either low or high doses.”

A critical link in establishing whether or not caloric restriction works the same wonders in people as it does in mice rests on the outcome of two monkey trials. Since rhesus monkeys live for up to 40 years, the trials have taken a long time to show results. Experts said that one of the two trials, being conducted by Dr. Weindruch, was at last showing clear evidence that calorically restricted monkeys were outliving the control animals.

But no such effect is apparent in the other trial, being

conducted at the [National Institutes of Health](#).

The Wisconsin report underlined another unresolved link in the theory, that of whether resveratrol actually works by activating sirtuins. The issue is clouded because resveratrol is a powerful drug that has many different effects in the cell. The Wisconsin researchers report that they saw no change in the mouse equivalent of sirtuin during caloric restriction, a finding that if true could undercut Sirtris's strategy of looking for drugs that activate sirtuin.

Dr. Guarente, a scientific adviser to Sirtris, said the Wisconsin team only measured the amount of sirtuin present in mouse tissues, and not the more important factor of whether it had been activated.

Dr. Sinclair said the definitive answer would emerge from experiments, now under way, with mice whose sirtuin genes had been knocked out. "The question of how resveratrol is working is an ongoing debate and it will take more studies to get the answer," he said.

Dr. Robert E. Hughes of the Buck Institute for Age Research said there could be no guarantee of success given that most new drug projects fail. But, he said, testing the therapeutic uses of drugs that mimic caloric restriction is a good idea, based on substantial evidence.