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Raise a Glass to Long Life

Chemical in red wine uncorks longevity in yeast and human cells

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Vintners and researchers who tout wine's health benefits now have another reason to toast the beverage: A molecule in red wine boosts survival of yeast and human cells, according to new research. The findings indicate that the compound activates the same life-stretching enzyme as austere diets do and offer a possible way to slow aging.

A menagerie of creatures live longer if they go hungry, and researchers have recently begun to unravel this phenomenon's molecular details. A protein called Sir2p extends life span, and this enzyme plays a crucial role in allowing calorie restriction to deliver its longevity-promoting effects, at least in yeast (see "Hungering for Simplicity" and Kaeberlein Perspective). Because Sir2p and related enzymes--the sirtuins--influence life span, molecular geneticist David Sinclair of Harvard Medical School in Boston and colleagues searched for molecules that stimulate the proteins and might promote longevity.

In test tube experiments, they sifted through a collection of compounds and determined which ones sped a human sirtuin's activity: lopping acetyl groups off a protein. The tests pinpointed 17 sirtuin activators, but the champion was resveratrol, an antioxidant found in red wine and many plants. Then the team measured how several of the molecules affected yeast survival, gauging longevity by the number of times a cell divides. Three compounds enhanced average life span, with resveratrol increasing it the most--by 70%. Cells lacking *SIR2* gained no benefit from resveratrol, bolstering the notion that the compound works by awakening Sir2p. The researchers also found that resveratrol shelters cultured human cells, increasing their tolerance for radiation. Additional experiments suggest that resveratrol cranks up a human sirtuin in the cells and that this enzyme boosts survival by hobbling p53, a protein that spurs cell suicide (see "Death and Aging, Together at Last"). "What we have are the first chemicals that activate these life-span-regulating pathways," says Sinclair, raising the possibility of manipulating aging "with a simple pill." Sinclair offers two hypotheses to explain why cells respond to resveratrol, which plants make during hard times. The effect might be coincidental: Resveratrol could happen to resemble a cellular molecule that rouses sirtuins. Alternatively, creatures might have evolved the ability to sense resveratrol, using it as an indicator of impending adversity, such as food scarcity.

The paper is important because it identifies small molecules that regulate sirtuins, allowing researchers to more easily manipulate the proteins and possibly test their therapeutic powers in people, says molecular biologist Brad Johnson of the University of Pennsylvania School of Medicine in Philadelphia. Biochemist John Denu of the University of Wisconsin, Madison, says that the study suggests tantalizing links between seemingly disparate factors, from yeast longevity proteins to plant stress molecules. However, he wants to see future work fortify these connections--including studies to establish that resveratrol's benefits stem from liaisons with sirtuins, not from its antioxidant prowess. Sinclair and colleagues are already measuring whether the compound prolongs the lives of nematodes and fruit flies; their preliminary findings suggest that it does. Drastic diets might extend our lives, but they wouldn't be fun. If resveratrol's effects are widespread, it might provide a more palatable way to live longer.

--Mitch Leslie *August 27, 2003*

References

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