



Biochemist Brenner sees promise in a finding from his lab for mitigating some diseases associated with aging.

New vitamin extends the life span of yeast

If you Google “longevity,” you’ll find oodles of empty promises about antiaging pills and potions. And that concerns DMS’s Charles Brenner, Ph.D. The reason is that his lab has discovered a vitamin with the ability to increase longevity in yeast cells. And although he believes the finding could one day lead to pharmaceutical or nutritional treatments for age-associated diseases in humans, he’s dismayed that it’s been cast in the popular press as a veritable fountain of youth.

NR: Previous work by Brenner, a professor of genetics and of biochemistry, showed that this vitamin—NR (short for nicotinamide riboside), a natural product found in milk—is a building block for a small molecule that is required for many cellular functions. This molecule—NAD⁺ (short for nicotinamide adenine dinucleotide)—has long been known to be essential for the synthesis of ATP, the major energy source within cells.

Interest in NAD⁺ has been rekindled in recent years by experiments that show it to be essential for other cellular pathways, including those involved in controlling longevity and protecting nerves from damage.

The most effective way known to extend the life span of model organisms, such as yeast or mice, is by calorie restriction. Cutting calories in yeast cells promotes longevity by activating an enzyme called Sir2. Yeast Sir2, and related mammalian enzymes called sirtuins, require NAD⁺ for function. In animal systems—from worms and flies to mice and people—there is increasing evidence that activating sirtuins may contribute to more graceful aging. In addition, these enzymes appear to mediate some of the beneficial effects of calorie restriction.

Cell: The scientific challenge has been to identify something—ideally a small, water-soluble, nontoxic molecule—that offers the same benefits as cutting calorie intake. Brenner’s team, which includes graduate students Peter Belenky and Katrina Bogan, discovered that NR is capable of activating Sir2 and thus increasing the life span of yeast. The finding was published in the journal *Cell* and was also highlighted in *Cell*, *Nature*, and *ACS Chemical Biology*.

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Although the discovery was made in yeast, the relevant cellular pathways are very similar to those in humans. Of course human aging is much more complex. But Brenner believes that the findings in yeast will be applicable to humans.

Forget about just taking a daily NR pill and living longer, however. There was much speculation to that effect in the popular press, especially in health-related blogs, after Brenner announced the finding. He was even likened to the Spanish explorer Juan Ponce de León, who sought a supposed fountain of youth in Florida 500 years ago.

Brenner balks at the comparison, however. “Although some people are excited by the idea that they could live longer,” he says, “we are actually focused on mechanisms of disease in which increased NAD⁺ biosynthesis could be protective.” He doesn’t consider aging to be a disease, but he does think NR could be used to prevent or treat diseases associated with aging—such as neurodegeneration and some cardiovascular conditions.

Damage: And as a researcher associated with Dartmouth’s Norris Cotton Cancer Center, Brenner is especially interested in how the vitamin might help protect patients against the side effects of chemotherapy. “One of the NR pathways that prolongs yeast life span has an application in preventing chemotherapy-induced peripheral neuropathy,” says Brenner. Peripheral neuropathy—damage to neurons outside the brain and spinal column—is a side effect of many chemotherapeutic agents; neuropathy frequently limits the chemotherapy dose a patient is able to tolerate. But test tube experiments show that neurons are protected from damage by NR.

So maybe Brenner didn’t discover a fountain of youth. And maybe years of further experimentation will be required before NR is ready for clinical application. But a vitamin that might foil the side effects of chemotherapy or mitigate some of the diseases associated with aging: that appears to be no empty promise.

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