Is College Really Worth the Money?

rd.com

Reader's Digest

The New Pill That Can End Aging

PAGE 70

Faith Hill & 12 Stars
Country Music Takes Over

PAGE 88

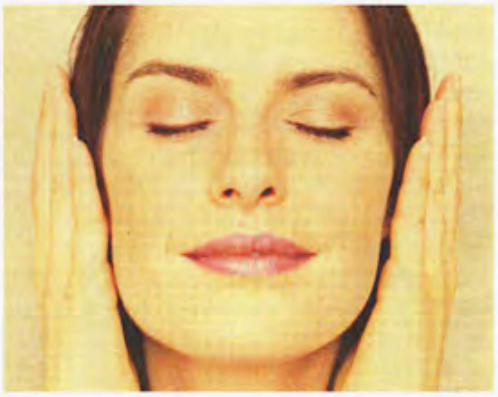
Stalked!
Amazing Animal Attacks

PAGE 162

November 2003 $2.99

PLUS Good at Giving: The Best Charities ▪ Nick of Time Rescues ▪ More Weird Science

America's Worst Judges: Our Annual Survey



The End of Aging

Breakthrough science may keep us all from growing old

BY AMY ELLIS NUTT FROM THE STAR-LEDGER

WE HUMAN BEINGS are the only animals capable of contemplating our own demise. We mourn, we memorialize, we philosophize and we pray. And when it happens on rare occasions that we "cheat" death, we believe, just for a moment, in immortality.

Today scientists are tempting fate in ways never before imagined as they demystify the secrets of longevity. Biochemist Bruce Ames believes that nutrients can repair damaged cells and make them "young" again. Molecular biologist Judith Campisi is studying how to keep cells from aging.

Both believe that while there may be no actual Fountain of Youth or scientific Dorian Gray in a bottle, reversal of aging and an extended life span are now on the horizon.

AT 74, BRUCE AMES looks every bit the part of an elderly gent, with his white hair, bifocals and quaint bow tie. Ames is a big idea man. Genes. Cancer. Nutrition. And now aging. He has published more than 450 articles and is becoming one of the most frequently cited scientists on the planet. "I told a colleague recently that 1 was doing the best work in my career," says Ames, who is a professor of biochemistry at the University of California at Berkeley, "and he looked at

PHOTOGRAPHED BY IRAIDA ICAZA

me and said, 'Bruce, you've been telling me that for 30 years.' I guess that means my enthusiasm genes are undamaged."

AMES WOULD KNOW if they were. Damaged genes have been his business for half a century. In the 1950s, Ames was a researcher at the NIH. His research ultimately proved that genes damaged by certain chemicals often give rise to cancer. By the 1970s, the "Ames test" was the world's most widely used method for identifying potential carcinogens in everything from clothing to hair dye to pharmaceuticals.

Ames has a penchant for mixing plaids; at the same time, his mind is relentlessly mixing and matching ideas. "It's just problem-solving:' he says of his methodology. "If you have two odd facts in your head and suddenly they fit together, you see a new way of explaining something."

Two odd events kept jangling about in Ames's head: the rise in cancer and the increase in free radicals with age. Free radicals are molecular miscreants that create havoc inside cells by stripping other molecules of vital electrons. Was there a direct link between free radicals and aging? he wondered.

Ames began by looking at mitochondria, where free radicals are produced. Mitochondria are tiny structures inside cells that act like furnaces, manufacturing most of the energy that is used by the body. Mitochondria are spectacularly efficient. Of the oxygen consumed by an average cell, the mitochondria convert 95 percent to help turn food into fuel. Every time we breathe, we're giving a boost to our cells.

During that process, however, mitochondria sometimes "misplace" electrons. Like money flying out the back of a Brink's truck careening around a corner, these electrons-now called free radicals-scatter around inside cells, bonding indiscriminately with other molecules. This mischief is called oxidation, and it allows free radicals to become chromosomal rototillers, mangling DNA at will.

Too many free radicals create a kind of cellular pollution that shoots down our energy levels. Too much damaged DNA causes cell mutation (which can cause cancer) and cell death. Both are signs of aging. In 1990 Ames and his colleagues at the University of California at Berkeley announced that they'd discovered twice as much free radical damage in tissues of two-year-old rats as in two month-old rats. Ames's team had found a crucial link between oxidation, DNA mutation and age: Free radical oxidation doesn't just rise with aging-it causes it. The more that mitochondria "leak" free radicals, the more those radicals end up damaging the mitochondria, which in turn leak even more free radicals.

This vicious cycle gets worse as we get older. It is the ultimate biological irony: The thing we most need to live oxygen-is the very thing killing us. Regarding his own biological clock,

Ames, surprisingly, has been something of a slacker. He likes to joke that he gets his exercise by "running" experiments, "skipping" the controls and "jumping" to conclusions. His wife of 40 years, biochemist Giovanna Ferro Luzzi, heard the joke for the 50th time recently and exacted her revenge: "She got me a personal trainer."

Ames says he has time for only about an hour a week with the trainer, but Giovanna insists they walk the two miles to their favorite Italian restaurant, Oliveto, for lunch at least three times a week.

Visiting his wife's native country in the mid-I990s, Ames saw that a dietary supplement known as acetyl-L-carnitine, or ALCAR, was sweeping Italy. It was being marketed as a pick-me-up, and Ames understood why: ALCAR is a natural biochemical that helps cells produce energy. He suspected ALCAR might slow, or even reverse, aging, and began feeding it to his old rats. They loved the stuff. Within weeks, they appeared re-energized.

There was a problem, however. The ALCAR did not lower the level of free radicals. Ames decided to add another supplement to his rats' diets, the antioxidant alpha lipoic acid.

"With the two supplements, these old rats got up and did the Macarena," said Ames. "The brain looked better; they were full of energy." It was the equivalent of making an 8O-year-old person look and act middle-aged. In 1999, Ames and a colleague, Tory Hagen, founded the Juvenon company in order to sell the energy formula.

The pill, available over the Internet, includes 200 milligrams of alpha lipoic acid and 500 milligrams of acetyl-L carnitine, but the two nutrients can be purchased at any health food store.

"I don't want to over-hype it," cautions Ames, who has no financial stake in the company. "We have to wait for the results of the human trials."

The ultimate irony: The thing we need most to live—oxygen—is what's killing us.

Right now, Ames and his researchers are studying whether the pill can improve circulation in cardiovascular patients by relaxing blood vessels, thereby possibly reducing the risk of heart attack or stroke. Ames takes a dose of his own supplement twice a day. "I'm very optimistic."

The ultimate irony: The thing we need most to live-oxygen-is what's killing us.

IN HER BASEMENT OFFICE in Berkeley, Judith Campisi sits on the edge of a chair and speaks with a wide-eyed enthusiasm usually reserved for first year graduate students. Piles of papers rise from the floor like unsteady chimneys,

We age not because our cells die but because they stop dividing.

some nearly as tall as the four foot-ten scientist. Campisi is a senior molecular biologist at Lawrence Berkeley National Laboratory. An expert in the genetics of aging, she believes that altering genes to extend life span may not be far off.

Campisi, 54, is a proponent of the "double-edged sword" theory of aging: The same cellular process that keeps us healthy in.our youth also causes our bodies to age in later years.

Her research focuses on the telomere, a structure containing a repeated DNA sequence that is found on both ends of every chromosome in the human body. In 1990, Calvin Harley, now the chief scientist at Geron, a biopharmaceutical company, discovered that as cells divide, the telomeres of the new cells are shorter.

Later, it was shown that in some cells the telomeres also got shorter with age. When telomeres become too short, they send a signal to the cell to stop dividing, and a natural state called senescence ensues. Campisi believes the primary function of senescence is to fight off cancer.

"Senescent cells are not dead;' she says. "They're perfectly alive, but what they can never, ever do again is divide. And if you can't divide, you can't form a tumor."

Campisi's research has shown that the longer we live, the more senescent cells our bodies accumulate, and it's those cells, she says, that may play a leading role in making us look and feel old-causing wrinkles, failing eyesight and chronic inflammation.

If she can prove this hypothesis, Campisi will have identified one of the main contributors to aging: We age not because our cells die, but because they stop dividing and start to malfunction.

"One thing we've learned;' she says, "is that you don't want cells to not 'senesce' at all, because then you have cancer. What would be great would be to have some of the senescent cells

die, so they don't accumulate with age. That's what we're working on."

Research, says Campisi, is a lot like one of her favorite pastimes, cooking. A little of this, a little of that-the best meals are unplanned, the result of intuition and experimentation. "I consider recipes advisory only," she says.

Likewise in her research, Campisi enjoys creating her own path, pursuing solutions not with a sprinter's speed but at an ambler's pace, taking the time to search familiar territory for missed clues. "I just start doing this random walk," she says, "and eventually I wind up where I need to go."

SOME SCIENTISTS, such as Jay Olshansky, a professor in the school of public health at, the University of Illinois at Chicago, express caution. The co-author of The Quest for Immortality, Olshansky says: "When we survive into old age, just as with automobiles and race cars, things can start to go wrong."

Robert Lanza, medical director of Advanced Cell Technology in Worcester, Mass., shares this view. "You can achieve immortality at the cellular level, but I don't see how it would be practical in extending life span," he says. "Humans hit a wall at 120 years.

"There's no question that in two or three decades we'll be able to replace every part of the human body," Lanza continues. "But we're like tires. There are just so many times you can be patched up." Ames and Campisi remain optimistic. Both share the belief that a delay of aging is within our grasp. Someday, they say, we may all enjoy a very long and healthy extended middle age.

For current resources on looking and feeling your best, check out rd.com/wellness.