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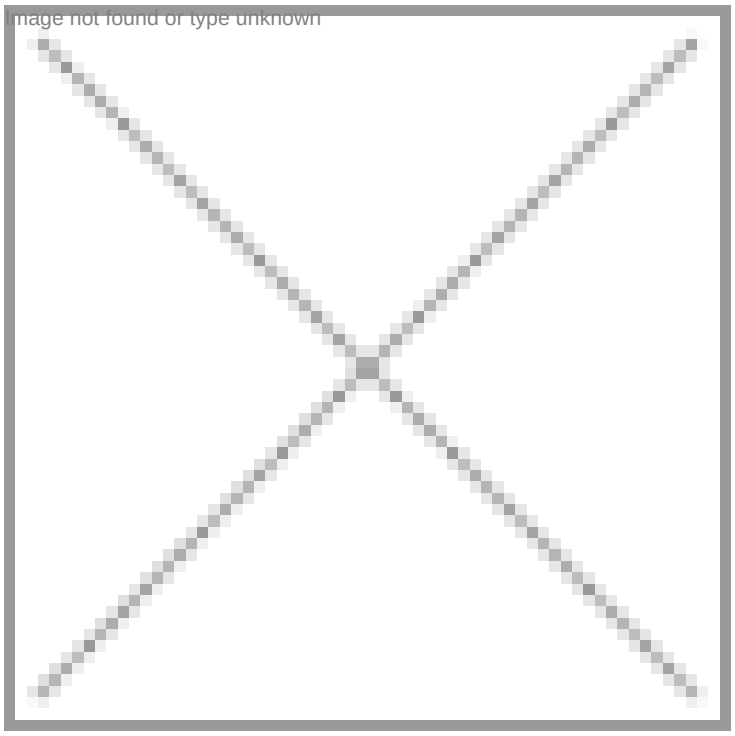
The secret of longevity

12 February 2004 | News



The secret of longevity

"Eat less and live longer". This principle now has the backing of science. Latest research says that in order to lead a long and healthy life calorie intake needs to be reduced. Calorie restriction extends life span in a wide spectrum of organisms and has been shown to delay the onset or reduce the incidence of many age-related diseases, including cancer and diabetes. Shedding light on why drastically restricting calorie intake prolongs life span in some organisms, MIT researchers have reported that lowering the level of a common coenzyme activates an anti-aging gene in yeast.

MIT Biology Professor Leonard P Guarente had earlier discovered that calorie restriction activates the silenced information regulator (SIR2) gene, which has the apparent ability to slow aging during the low-calorie diet. This gene makes a protein called Sir2, which is normally activated by the coenzyme molecule NAD. Guarente has shown that SIR2 is integrally tied to extending life span in yeast and in the roundworm. And significantly humans carry a similar gene.

The present study probed how Sir2 is activated by calorie restriction. The researchers found that a coenzyme related to NAD, called NADH (nicotinamide adenine dinucleotide) inhibits Sir2 by blocking the action of NAD. During calorie restriction, levels of NADH decline in cells. This decrease in NADH allows NAD to better activate Sir2 and thereby extend life span.

NADH is a coenzyme or enzyme helper is present in all living cells. (An enzyme is a protein that works like a catalyst in the body to prompt chemical changes; for instance, turning food into energy.) NADH, an activated form of the B vitamin niacin, helps produce energy through a series of chemical reactions in the cell. These findings have been reported in the January 1

issue of Genes and Development.

"These findings provide a simple model for activation of Sir2 and extension of life span by calorie restriction," the researchers said. "Our findings suggest that the NAD/NADH ratio can serve a critical regulatory function, determining the life span of yeast mother cells. A reduction in this nucleotide activates Sir2 to extend the life span in calorie restriction."

Guarente also found that respiration in yeast cells under calorie restriction goes up, not down. "A high respiration rate is intimately connected with calorie restriction in yeast," he said. "A high respiration rate activates SIR2. When respiration goes up, NADH goes down and SIR2 goes up. When SIR2 goes up, longevity happens."

Though it still remains to be proved that whether these findings about yeast and NADH will relate to the extension of life span in mammals by calorie restriction. But all the same, no harm in going slow on calories.

Targeted tumor treatment

Taking cue from nature, scientists at the Weizmann Institute, Israel, have developed an innovative method for selectively killing cancer cells in mice using allicin, a chemical that occurs naturally in garlic.

Allicin, which gives garlic its distinctive aroma and flavor, is as toxic as it is pungent. It has been shown to kill not only cancer cells but also the cells of disease-causing microbes and even healthy human body cells. Fortunately for our body's cells, allicin is highly unstable, and breaks down quickly once ingested. However, the rapid breakdown and undiscriminating toxicity presented twin hurdles to creating an allicin-based therapy.

The key to scientists' success was the development of a unique, two-step system for delivering the cancer-wrecking chemical straight to the tumor cells.

Scientists at the Weizmann Institute's biological chemistry department designed an ingenious delivery method that works with the pinpoint accuracy of a smart bomb. Their findings were reported in the December issue of Molecular Cancer Therapeutics.

The method parallels the way allicin is synthesized in nature. Not present in whole, unbroken cloves of garlic, allicin is the product of a biochemical reaction between two substances stored apart in tiny, adjoining compartments within each clove. The two are an enzyme, alliinase, and a normally inert chemical called alliin. When the clove is damaged or broken, the membranes separating compartments are ruptured and rapid allicin production follows.

The scientists realized that if doses of allicin could be repeatedly generated in this way at the site of the tumor, the highest concentration of the toxic molecules would be available for killing cancer cells.

To zero in on the targeted tumor, scientists took advantage of the fact that most types of cancer cells exhibit distinctive receptors on their surfaces. An antibody that is "programmed" to recognize the tumor's characteristic receptor is chemically bound to the enzyme, alliinase. Injected into the bloodstream, the antibody seeks out these cells, and lodges itself and its passenger enzyme on the tumor cells. The scientists then inject the second component, alliin, at intervals. When it encounters the alliinase, the resulting reaction turns the normally inert alliin molecules into lethal allicin molecules, which penetrate and kill the tumor cells. Due to the precise delivery system, neighboring, healthy cells remain intact.

Using this method, the team succeeded in blocking the growth of gastric tumors in mice. The scientists observed that the method could work for most types of cancer, as long as a specific antibody can be customized to recognize receptors unique to the cancer cells. The technique could prove invaluable for preventing metastasis following tumor surgery.

Instant stem cells

Extract stem cells from the bone marrow, dehydrate and pack them. Then wherever and whenever required, rip the packet open, mix water and use them!

Just like the "ready to eat" instant foods, scientists are actively working towards perfecting the technique of creating instant stem cells. Cell biologists at University of California Davis have shown for the first time that mesenchymal stem cells (MSCs) can be dehydrated for storage and activated for possible use in future stem cell therapies.

Researchers at the university are developing ways to desiccate and store mesenchymal stem cells (MSCs). These stem cells can be isolated from adult bone marrow and have the potential to produce bone, cartilage, muscle, fat, and even neural

tissue. The hope is to use MSCs clinically for tissue engineering and regenerative medicine. However, this goal will be feasible only if MSCs are available in a form that is easily and reliably transported, stored and used. The Davis researchers proposed that desiccation might be the best approach, and tested ways to make a stable dry mesenchymal stem cell product.

Ann Oliver and colleagues of Center for Biostabilization, University of California Davis, air-dried the stem cells until their water content was in the range of 17-25 percent. Remarkably, the desiccated cells maintained 20-50 percent viability, which is the highest viability ever achieved in cells desiccated to this degree, the researchers said.

Strikingly, the dried and rehydrated cells were also metabolically active suggesting they are capable of cell division. Since mammalian cells need their water, and usually die when dehydrated, so to protect cells during dehydration, protective substances are delivered into the cells. Oliver and her team soaked the stem cells in an anti-freeze sugar called trehalose. This is a sugar found in extremely high concentrations in organisms that can naturally survive drying and is a protective compound.

This is the first step in making stem cell therapy a practical reality. But a real breakthrough will be if 80-90 percent of the cells can be revived after several weeks on the shelf. This will make handling stem cells easier and take the scientists one step closer towards clinical MSC treatment.