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**IN THE NEWS****Folate Counters Depression Tied to High Homocysteine**

In a study of nearly 6,000 adults in Norway, researchers found that participants with the highest homocysteine levels were nearly twice as likely to be depressed as those with the lowest homocysteine levels.\*

The researchers also found that people with a certain gene that alters folate metabolism and leads to a relative folate deficiency are much more likely to suffer depression. Folate, a B vitamin, helps to break down homocysteine in the body.

In their article published in the Archives of General Psychiatry, the researchers noted, “clinical studies have shown an inverse relationship between folate status and depression” and previous research has shown “enhanced antidepressant response with folic acid supplementation.”

“Folate is a vitamin involved in a number of metabolic processes in the body,” lead study author Ingvar Bjelland, MD, told Life Extension. “Lack of folate or disturbed folate metabolism is involved in serious fetal malformations, disturbances in the formation of red blood cells, development of cancer

and cardiovascular illness, and dementia and peripheral nerve damage. Folate and its metabolism also are most probably involved in depression.”

—Marc Ellman, MD

\* Bjelland I, Tell GS, Vollset SE, Refsum H, Ueland PM. Folate, vitamin B12, homocysteine, and the MTHFR 677C->T polymorphism in anxiety and depression: the Hordaland Homocysteine Study. Arch Gen Psychiatry 2003 Jun;60(6):618-26.

**DHA Inhibits Melanoma Cell Growth in Lab Test**

Docosahexaenoic acid (DHA), an omega-3 polyunsaturated fatty acid, stopped the growth of some melanoma cell lines in a laboratory test, according to a study published in the journal Cancer Research.\*

Melanoma is a potentially deadly skin cancer. Scientists predict that one in 75 Americans born today will develop malignant melanoma during their lifetimes. If discovered early, melanoma can be cured; however, if melanoma is allowed to spread deeper into tissue and metastasize, the five-year survival rate is only about 10%.

Previous research has shown that omega-6 polyunsaturated fatty acids act as stimulators and long-chain omega-3 polyunsaturated fatty acids act as inhibitors of development and progression of

many human cancers, including melanoma.

To investigate the effect of omega-3 fatty acids on melanoma growth, scientists at the Institute for Cancer Prevention and New York Medical College in Valhalla, NY, exposed 12 different, rapidly growing human metastatic melanoma cell cultures in the laboratory to DHA. Cell growth in more than half of the melanoma cell lines was inhibited with increasing concentrations of DHA.

Lead researcher Dr. Anthony Albino told Life Extension that a good omega-3 to omega-6 fatty acid ratio seems to be important in preventing many diseases, including a range of cancers. “Clearly, the single most important risk factor for melanoma and other forms of skin cancers is excessive sun exposure, but the fact that diet may impact both the etiology and progression of a number of cancers seems fairly correct,” said Dr. Albino.

—Marc Ellman, MD

\* Albino AP, Juan G, Traganos F, et al. Cell cycle arrest and apoptosis of melanoma cells by docosahexaenoic acid: association with decreased pRb phosphorylation. *Cancer Res.* 2000 Aug 1; 60(15):4139-45.

## Antioxidants Offset Alcohol's Brain Cell Damage

Antioxidants appear to counteract brain cell damage caused by alcohol in rats, according to a study published in the *Proceedings of the National Academy of Sciences*.

Researchers at Cornell University's Weill Medical College in New York found that rats fed a liquid diet containing moderate amounts of ethanol for six weeks had a 66.3% decrease in the number of new neurons and a 227-279% increase in cell death in the dentate gyrus as compared to rats fed an alcohol-free diet. The dentate gyrus is part of the brain's hippocampus, an integral part of our memory systems.

"While neurons continue to develop, alcohol causes the new cells to die off before they mature," lead researcher Dr. Daniel Herrera explained to *Life Extension*. "This damage, we proposed, may be caused by oxidative stress."



This hypothesis appears to be accurate, as the antioxidant ebselen appeared to counteract the effects of alcohol in the rats' brains. "Rats that were co-administered ethanol and ebselen had neither a reduction in new cells nor increased cell death," said Herrera. The researchers believe that antioxidants may help reduce the cognitive deficits seen in alcoholics, as well as in other neurodegenerative diseases.

"[Ebselen] or similar compounds could be used in the treatment of cognitive impairment seen in alcoholic patients and possibly in other disorders where adult neurogenesis may be affected," stated the researchers.

—Marc Ellman, MD

\* Herrera DG, Yague AG, Johnsen-Soriano S, et al. Selective impairment of hippocampal neurogenesis by chronic alcoholism: protective effects of an antioxidant. *Proc Natl Acad Sci U S A.* 2003 Jun 24;100(13):7919-24. Epub 2003 Jun 05.

## IN THE NEWS

### Resveratrol Extends Cell Survival and Life Span



Rodents, worms, flies, and yeast cells live longer when fed a low-calorie diet, which protects mammals against age-related diseases, including cancer. In May, researchers reported the first known genetic link between environmental stress and a longer life span in yeast.\*

Triggered by salt, heat, or caloric restriction, a yeast “longevity gene” was found to stimulate the activity of Sir2, an enzyme that belongs to the sirtuin family of enzymes known to extend the life span of yeast and worms.

Now, a group from Pennsylvania’s Biomol Research Laboratories has found a way to duplicate the benefits of caloric restriction in yeast cells by polyphenols, antioxidants that are found in vegetables, olive oil, fruit, and wine, and whose levels in plants increase in response to stress. The findings, reported in August in the journal *Nature’s* advanced online edition, show that polyphenols

prompt yeast cells and human cells to prepare for harsh conditions by switching to a life-extending survival program that mimics caloric restriction. This occurs by a mechanism other than their antioxidant action—activation of the sirtuin family, the SIRT2 protein in yeast and SIRT1 protein in humans.

The most potent activator of sirtuins is resveratrol, found in grapes, wine, and peanuts. In yeast, resveratrol mimics caloric restriction by stimulating the SIRT2 enzyme, increasing the stability of DNA, and extending the life span of the yeast cells by 70%.

In experiments with human cells, resveratrol activated a similar pathway that enabled 30% of the cells to survive exposure to radiation, compared to 10% of untreated cells. Little is known about the human SIRT2, except that it switches off p53, a growth-regulating protein that plays a role in programmed cell death. Increasing survival through the activation of SIRT1 and SIRT2 by polyphenols may allow cells time to repair damage, thereby extending their life span.

—Carmia Borek, PhD

\* Howitz KT, Bitterman KJ, Cohen HY, et al. Small molecule activators of sirtuins extend *Saccharomyces cerevisiae* life span. *Nature*. 2003 Sep 11;425 (6954):191-6. Epub 2003 Aug 24.

### Ginkgo Biloba May Slow Glaucoma’s Progression

A small study of patients with normal tension glaucoma indicates that ginkgo biloba may slow the progression of the disease.

Glaucoma is an eye disease in which damage to the optic nerve leads to progressive peripheral vision loss. This loss can be measured with specialized visual field testing. In most glaucoma cases, the pressure inside the eye (intraocular pressure) is elevated; in people with “normal tension glaucoma,” however, optic nerve damage occurs despite normal intraocular pressures.

In an effort to determine whether ginkgo biloba affects visual field loss in patients with normal tension glaucoma, Italian researchers recruited 27 patients with visual field loss from normal tension glaucoma and divided them into two groups.\* The first group received 40 mg of ginkgo biloba extract in pill form three times a day for four weeks, followed by a washout period of eight weeks, and then four weeks of placebo treatment comprising similar-appearing pills that did not contain ginkgo biloba. The second group received the placebo pills first, and then the ginkgo biloba extract after the washout period. On average, patients performed significantly better in visual field testing after receiving the ginkgo biloba extract than after receiving the placebo.



“Our results suggest that ginkgo biloba extract can effect an improvement in preexisting visual field damage in some individuals with normal tension glaucoma,” the researchers wrote in their article published in the journal *Ophthalmology*.

“Ginkgo biloba extract has numerous properties that theoretically should be beneficial in treating non-intraocular pressure-dependent mechanisms in glaucoma. Its multiple beneficial effects, including increased ocular blood flow, and its antioxidant activity, platelet activating factor inhibition, nitric oxide inhibition, and neuroprotective activity combine to suggest that ginkgo

biloba extract could play a major role in the treatment of glaucoma.”

—Marc Ellman, MD

\* Quaranta L, Bettelli S, Uva MG, Semeraro F, Turano R, Gandolfo E. Effect of ginkgo biloba extract on preexisting visual field damage in normal tension glaucoma. *Ophthalmology* 2003 Feb;110(2):359-62; discussion 362-4.

## Broccoli May Be Tops in Health-Promoting Benefits

Cruciferous vegetables such as cauliflower, brussels sprouts, cabbage, and kale are powerful anti-cancer agents, but among this group, broccoli may contain the most life-extending nutrients. Rich in vitamins and fiber, broccoli also boasts special ingredients that promote good health and prevent disease.

Broccoli is unusually rich in phytochemicals that fight cancer, including indoles, isothiocyanates, and glucoraphanin, which the body converts to sulforaphane. These substances can prevent carcinogens from damaging cell DNA and causing various forms of cancer.



Indoles can reduce the risk of breast cancer by stimulating enzymes that weaken the female hormone estrogen. Isothiocyanates, which are up to 100% higher in young broccoli sprouts than in adult broccoli stalks,<sup>1</sup> stimulate glutathione S-transferase and other enzymes that prevent carcinogens from entering the cells. And sulforaphane can stimulate the production of phase II enzymes that are powerful carcinogen detoxifiers.

Since 1992, pharmacology professor Paul Talalay and his group at Johns Hopkins University have been studying broccoli's cancer-fighting properties. Their research has demonstrated that sulforaphane can prevent breast and colon cancer in mice and also destroy *Helicobacter pylori*, the bacteria linked to gastritis, stomach ulcers, and stomach cancer (the second most common form of cancer).<sup>2</sup>

Containing generous amounts of such vital nutrients as calcium, manganese, beta carotene, vitamin C, and vitamin K, broccoli's health benefits are undiminished by cooking; in fact, heat actually appears to increase indoles in broccoli.

An average serving of cooked broccoli has more vitamin C than an orange and as much calcium as an eight-ounce glass of milk, while an average broccoli spear has three times the fiber of a slice of wheat bread. Broccoli sprouts have as much glucoraphanin as a pound and a quarter of cooked broccoli. Those looking for a vegetable packed with essential nutrients and life-extending components may want to reach first for the broccoli.

—Donna Caruso

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### References

1. Fahey JW, Zhang Y, Talalay P. Broccoli sprouts: an exceptionally rich source of inducers of enzymes that protect against chemical carcinogens. *Proc Natl Acad Sci U.S.A.* 1997 Sep; 94(19):10367-72.
2. Fahey JW, Haristoy X, Dolan PM, et al. Sulforaphane inhibits extracellular, intracellular, and antibiotic resistant strains of *Helicobacter pylori* and prevents benzo[a]pyrene-induced stomach tumors. *Proc Natl Acad Sci U.S.A.* 2002 May 28;99(11):7610-5

## IN THE NEWS

### Western Diet May Increase Prostate Cancer Risk



Prostate cancer is 10 times more common in the US than in Japan, and new research suggests that the typical high-fat American diet may be to blame.

To confirm this hypothesis, researchers examined 50 Japanese men with prostate cancer who had undergone removal of the prostate. Half of the participants lived in Nagoya, Japan, while the other half lived in Los Angeles, CA. In other words, all the men had similar genetic backgrounds, but different dietary habits and lifestyles. The researchers examined the removed prostates, as well as blood and urine samples from all the participants. They also interviewed the men and reviewed their medical records.

Their findings suggest that Japanese men who live in the US have much poorer dietary habits than their native Japanese counterparts, as they were on average heavier, had more body fat, and had five times more triglycerides in their blood than the native Japanese men.

Furthermore, laboratory examinations of removed prostates from the two groups indicated that the cancer's DNA was arranged differently in the two samples, suggesting that diet may affect the genetic composition of the cancerous prostates.

These findings were presented at the American Urological Association meeting in Chicago on June 30, 2003. The abstract was also published in the May 2003 Journal of Urology. The results are currently being prepared for publication in a medical journal.

—Marc Ellman, MD

### Phytoestrogens Shown to Lessen Endometrial Cancer Risk

Endometrial cancer is associated with prolonged exposure to estrogens without cyclic exposure to progesterone. Isoflavones in soybeans and lignans in flax have weak estrogenic effects, and by binding to estrogen receptors in cells block estrogen's ability to promote cell division that may lead to cancer.



In a study published in the Journal of the National Cancer Institute, researchers at the Northern California Cancer Center report a link between phytoestrogen intake and a reduced risk of endometrial cancer.\* Investigators collected data on food consumption from 500 women, 35 to 79 years old, who were diagnosed with endometrial cancer, documenting their food intake one year prior to diagnosis.

These were compared to 470 matched controls. The questionnaire included the intake of three classes of phytoestrogens in food: isoflavones (including genistein and daidzein), coumestans, and lignans.

Isoflavone and lignan intake was inversely related to the risk of endometrial cancer: the highest consumption of isoflavones (about 2.7 mg or more) and lignans (about 0.2 mg or more) reduced endometrial cancer risk by approximately half compared to controls. Postmenopausal women showed the most benefit. The protection by phytoestrogens, previously observed for soy intake, suggest that phytoestrogens in soy are the compounds responsible for the associated cancer preventive effects.

—Carmia Borek, PhD

\* Horn-Ross PL, John EM, Canchola AJ, Stewart SL, Lee MM. Phytoestrogen intake and endometrial cancer risk. J. Nat. Cancer Inst 2003 Aug 6;95 (15):1158-64.

### New Studies Support Silicon's Role in Bone Formation

Two recent studies in the medical journal Bone support the theory that silicon, the second most abundant element in the Earth's

crust, plays an important role in bone formation.

In the first study, researchers found that silicon (as orthosilicic acid) may have a stimulatory effect on bone formation in the human body.<sup>1</sup> “Orthosilicic acid at physiologic concentrations stimulates collagen type 1 synthesis in human osteoblast-like cells and enhances osteoblastic differentiation,” the researchers reported.

In another study, scientists found that dietary silicon was associated with greater bone mineral density in approximately 3,000 American men and pre-menopausal women, but not in post-menopausal women.<sup>2</sup> According to the researchers, these findings are “consistent with [silicon’s] role in bone formation rather than in preventing bone resorption. Orthosilicic acid appears to be an important nutrient with anabolic effects on bone.”

In an interview with Life Extension, researcher Dr. Ravin Jugdaohsingh of St. Thomas’ Hospital in London said, “silicon is a major component of the human diet, the intake of which has greatly been reduced due to modern food processing and refining, water treatment and purification, and the growth of vegetables under hydroponic conditions. Animal studies have shown that silicon is important for normal growth and development, specifically with skeletal growth.



“Currently, nearly all treatments for osteoporosis (or low bone mass) work by reducing the breakdown of bone, but none, with the exception of parathyroid hormone, actually increase bone formation (i.e., make new bone). Silicon could thus provide a new type of therapy for low bone mass or osteoporosis by increasing bone formation. Silicon has also been linked to atherosclerosis, having anti-atherosclerotic properties, and with connective tissue (i.e., skin, hair, and nails), and thus may have a wider beneficial role in human health.”

—Marc Ellman, MD

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## References

1. Reffitt DM, Ogston N, Jugdaohsingh R, et al. Orthosilicic acid stimulates collagen type 1 synthesis and osteoblastic differentiation in human osteoblast-like cells in vitro. *Bone*. 2003 Feb; 32(2):127-35.
2. Jugdaohsingh R, et al. Silicone intake is a major dietary determinant of bone mineral density in men and premenopausal women of the Framingham offspring cohort. *Bone*. 2003 May; 32(5):S192.

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