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In The NEWS

Life Extension Foundation Sponsors Highly Promising Breast Cancer Trial

According to the National Cancer Institute, more than 40,000 women will die of breast cancer this year, while nearly 180,000 new cases of the dread disease will be diagnosed.¹ Over the course of a lifetime, one in eight women will receive such a diagnosis.² Breast cancer is an all-too-prevalent disease that seems to touch every American sooner or later. These patients are our mothers, sisters, wives, daughters, friends, and co-workers. But despite these grim statistics, there's ample reason for hope. Advances are being made, victories won.

NOVEL TREATMENT

For example, Life Extension Foundation is pleased to report that it's funding highly promising research that has already yielded remarkably encouraging preliminary results. Principal investigator, Dr. Richard Ishmael—with colleague Dr. Steven Hamilton—has completed a Phase I trial using two existing chemotherapeutic drugs for the treatment of stage IV breast cancer. Administered in a novel alternating dose protocol, the drugs docataxel and gemcitabine show great promise.

Stage IV is the grim term used to describe breast cancer that has spread beyond the breast; often to the bones, lungs, liver, or brain. It's considered largely incurable, with a mere 7% five-year survival rate. According to Medline Plus (US National Library of Medicine), "For stage IV cancer, the goal is to improve symptoms and prolong survival. However, in most cases, stage IV breast cancer cannot be cured."²

DR. ISHMAEL AND COLLEAGUES HOPE TO REWRITE THAT PROGNOSIS.

The doctors investigating this novel approach are not reinventing the wheel, but instead are carefully building and expanding upon previous research, which demonstrate that docataxel and gemcitabine could kill some breast cancer cells, some of the time. Suspecting that subtle alterations in how these drugs are administered—at what times and in which doses—might significantly affect their impact on cancer cells, the doctors devised experiments on cancer cells growing in culture to determine an optimized treatment regimen. Eventually they found that when these drugs are administered alternately (but not simultaneously), at specific doses, they exert a synergistic effect. That is to say, their effectiveness against cancer cells is greater than that exerted by either drug alone, or even in combination.

SEEKING ADDITIONAL PATIENTS

Moving from the laboratory to the clinic, the investigators enrolled stage IV breast cancer patients in a Phase I trial, and fine-tuned the doses and treatment schedule until optimum results were obtained. A further benefit of this protocol is a reduction in side effects and overall toxicity. The team, which now includes additional oncologists in the Oklahoma City area, is currently treating more women in an ongoing Phase II trial, and they are seeking new subjects.

Although the trial is in the early stages, impressive results have already been obtained. *"The first patient...has had a complete response,"* writes collaborator Dr. Orn Adalsteinsson. Dr. Ishmael concurs. *"[This protocol] is unique. There are a lot less side effects; it's better tolerated...We've had very, very good results."* So far only one of nine patients has failed to respond. Four have experienced a "complete response." With additional patients, Dr. Ishmael hopes to be able to report soon that the protocol's results are nothing short of extraordinary. *"Dr. Ishmael is one of the most effective oncologists in the US,"* says Dr. Adalsteinsson. *"He has been very successful."*

Potential subjects with early stage IV breast carcinoma (first relapse or metastatic presentation) wishing to volunteer for inclusion in this trial should contact Nurse Coordinator Angie Miller at Cancer Treatment Center of Oklahoma, 230 N. Midwest Blvd. Midwest City, OK 73110 or by calling (405) 737-8455. Alternately, you may e-mail Dr. Ishmael at ishdr@aol.com. This study is being funded by a grant from the Life Extension Foundation

Reference

1. Available at: <http://www.cancer.gov/cancertopics/types/breast>. Accessed May 25, 2007.
2. Available at: <http://www.nlm.nih.gov/medlineplus/ency/article/000913.htm>. Accessed May 25, 2007.

DHEA Holds Potential in Breast Cancer Management

Dehydroepiandrosterone (DHEA) may offer a new method of treatment for estrogen and progesterone receptor-negative breast cancers.

*Researchers examined the effects of DHEA-sulfate (a metabolite of DHEA) on three lines of androgen-sensitive breast cancer cells. When DHEA is orally ingested, some of it converts to DHEA-sulfate in the body. In this study, when DHEA-sulfate was administered with an aromatase inhibitor, the cancer cells were induced to commit suicide.

Combining DHEA-sulfate with an aromatase inhibitor may thus offer a new therapeutic strategy for individuals fighting certain types of breast cancers. Breast cancer patients should consult with their treating oncologist before supplementing with DHEA.

—Elizabeth Wagner, ND

Reference

- * Hardin C, Pommier R, Calhoun K, Muller P, Jackson T, Pommier S. A new hormonal therapy for estrogen receptor-negative breast cancer. *World J Surg.* 2007 May;31(5):1041-6.

Rhodiola Offsets Effects of Stress



The herb *Rhodiola rosea* has long been valued as a potent adaptogen (agent that strengthens the body's response to stress) and has traditionally been used to improve mental and physical performance. New findings in rodents confirm rhodiola's ability to offset stress-induced anxiety, depression, and loss of appetite.^{1,2}

In one study, a single oral dose of rhodiola produced significant antidepressant and anti-anxiety effects in stressed mice. "This study...confirms many preclinical and clinical studies indicating the adaptogenic and stimulating effects of...*R. rosea*," wrote the researchers.¹

In a second study, physical and psychological stressors caused laboratory rats to stop eating. Rhodiola administration reversed the animals' loss of appetite. Control animals, which were either free-feeding or food deprived, did not change their eating behavior in response to rhodiola, indicating that the herb "...is able selectively to attenuate stress-induced anorexia."²

Rhodiola thus has broad spectrum potential to alleviate a number of human miseries, including hospital-induced appetite suppression that causes so many confined patients to become malnourished.

—Dale Kiefer

Reference

1. Perfumi M, Mattioli L. Adaptogenic and central nervous system effects of single doses of 3% rosavin and 1% salidroside *Rhodiola rosea* L. extract in mice. *Phytother Res.* 2007 Jan;21(1):37-43.
2. Mattioli L, Perfumi M. *Rhodiola rosea* L. extract reduces stress- and CRF-induced anorexia in rats. *J Psychopharmacol.* 2007 Jan 26; [Epub ahead of print].

Daily Aspirin Use Reduces Cancer Risk



Daily intake of adult-strength aspirin reduces the overall incidence of cancer, according to a large study published by the American Cancer Society.* The decade-long study examined data from nearly 150,000 older men and women. Long-term (five or more years) daily use of adult-strength aspirin (>325 mg) was associated with a significantly lower overall incidence of cancer in men. Women also experienced a lower overall incidence of cancer.

Aspirin-using men and women experienced a 32% reduction in the incidence of colorectal cancer versus non-aspirin users. The risk reduction in prostate cancer, at 19%, was also statistically significant. Breast cancer rates declined by 17% among aspirin-using women, but the decline failed to achieve statistical significance.

“Long-term daily use of adult-strength aspirin may be associated with modestly reduced overall cancer incidence in populations among whom colorectal, prostate, and breast cancers are common,” concluded the researchers.

—Dale Kiefer

Reference

* Jacobs EJ, Thun MJ, Bain EB, Rodriguez C, Henley SJ, Calle EE. A large cohort study of long-term daily use of adult-strength aspirin and cancer incidence. *J Natl Cancer Inst.* 2007 Apr 18;99(8):608-15.

Vitamin D Deficiency Lowers Physical Performance in Older Adults



Older adults with low blood levels of vitamin D display decreased physical performance and hand grip strength, according to a recent study.* For some time, scientists have proposed that vitamin D may play an essential role in musculoskeletal function.

Investigators measured blood levels of 25-hydroxyvitamin D and assessed physical performance such as walking speed and hand grip strength in 976 men and women age 65 and older. The researchers found that 75% of the women and 51% of the men had low vitamin D levels. Twenty-nine percent of the women and 14% of the men were classifiable as vitamin D deficient. Physical performance and grip strength of adults with low vitamin D levels was 5% to 10% below those who had vitamin D levels within the normal range.

These findings suggest that ensuring optimal blood levels of vitamin D may be an essential strategy for protecting older adults against future disability.

—Robert Gaston

Reference

* Houston DK, Cesari M, Ferrucci L, et al. Association between vitamin D status and physical performance: The InCHIANTI Study. *J Gerontol A Biol Sci Med Sci.* 2007 Apr;62(4):440-6.

FDA drops the ball on Avandia® warning

The FDA came under renewed criticism recently, when it was revealed that warnings by its own safety committee regarding a popular diabetes drug were ignored by the regulatory agency. FDA safety staff had recommended that prescribing information for the type 2 diabetes drug, Avandia® (rosiglitazone), should include a so-called “black box” warning—the FDA’s most dire alert—indicating that the drug might put some patients at increased risk of congestive heart failure. But the FDA ignored that recommendation.

Instead, the warning is buried on line 351 of the label, noted Senator Charles Grassley (R-IA), whose staff investigated the FDA’s inaction. The investigation was prompted by the publication of an analysis of the drug’s cardiovascular risk profile in the prestigious *New England Journal of Medicine* in May. In that analysis, researchers from the Cleveland Clinic concluded, “Rosiglitazone was associated with a significant increase in the risk of myocardial infarction and with an increase in the risk of death from cardiovascular causes.”*

Reference

* Nissen SE, Wolski K. Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes. *N Engl J Med.* 2007 May 21; [Epub ahead of print]

Depression Linked to Diabetes in Older Individuals



Symptoms of depression are associated with an increased risk of type 2 diabetes among older adults, according to the results of a new study.* Researchers at Northwestern University followed 4,681 adults age 65 and older for a decade, measuring symptoms of depression annually, and monitoring changes in blood sugar at two- to four-year intervals. All subjects were free from diabetes at the beginning of the study.

Investigators found that a single incidence of depressive symptoms was associated with an increased risk of developing diabetes. Subjects with the highest depression scores were 50% more likely to develop diabetes than those with the lowest scores. Subjects who were treated with antidepressant drugs were not at increased risk of diabetes, but it remained unclear

whether or not treating depression affected diabetes risk.

—Dale Kiefer

Reference

* Carnethon MR, Biggs ML, Barzilay JI, et al. Longitudinal association between depressive symptoms and incident type 2 diabetes mellitus in older adults: the cardiovascular health study. *Arch Intern Med.* 2007 Apr 23;167(8):802-7.

Green Tea Antioxidant May Fight Rheumatoid Arthritis

The green tea antioxidant epigallocatechin-3-gallate (EGCG) offers hope as a treatment for rheumatoid arthritis, according to a recent presentation by University of Michigan scientists at the Experimental Biology 2007 meeting in Washington, DC.¹ Rheumatoid arthritis is a potentially debilitating condition characterized by inflammation and the degeneration of joint tissues. Earlier studies have documented the antioxidant and anti-inflammatory effects of EGCG and have suggested its potential role in fighting conditions such as cancer, diabetes, and Alzheimer's disease.²

In the recent study, joint tissue cells from adults with rheumatoid arthritis were cultured with or without EGCG. They were then exposed to the pro-inflammatory cytokine interleukin-1 beta, an immune system protein that instigates joint damage in rheumatoid arthritis. EGCG-treated cells were inhibited from producing several inflammatory compounds that are associated with joint tissue destruction. As expected, cells that were not pretreated with EGCG produced damaging inflammatory compounds.

"EGCG may be of potential therapeutic value in regulating the joint destruction in [rheumatoid arthritis]," concluded the scientists.³

—Dale Kiefer

Reference

1. Available at: <http://www.news-medical.net/?id=24333>. Accessed May 15, 2007.
2. Zaveri NT. Green tea and its polyphenolic catechins: medicinal uses in cancer and noncancer applications. *Life Sci.* 2006 Mar 27;78(18):2073-80.
3. Available at: <http://www.cbsnews.com/stories/2007/04/30/health/webmd/main2743971.shtml>. Accessed May 15, 2007.

Salk Scientists Find Gene Linking Calorie Restriction with Longevity



For decades, researchers have repeatedly shown that calorie restriction results in an up to 40% extension of life span. This effect is not explained by a simple reduction in metabolic rate or slower growth rate; until now, scientists have puzzled over the specific mechanisms by which calorie restriction may extend life.

Researchers at the Salk Institute for Biological Studies in La Jolla, California, recently announced that they have identified a gene in adult worms undergoing near-starvation that is specifically involved in life span extension.* The gene corresponds to a family of genes found in mammals which regulates adults' energy usage. Published in *Nature*, this groundbreaking finding may pave the way for new treatments aimed at extending life span in humans and

delaying the onset of age-related maladies—without the hardship of calorie restriction.

—Dale Kiefer

Reference

* Panowski SH, Wolff S, Aguilaniu H, Durieux J, Dillin A. PHA-4/Foxa mediates diet-restriction-induced longevity of *C. elegans*. *Nature*. 2007 May 2; [Epub ahead of print]

Melatonin Supplementation May Delay, Improve Menopause Symptoms

Italian researchers report they may have discovered a “cause-effect relationship” between declining levels of melatonin and the onset of menopause.* Produced by the pineal gland deep within the brain, melatonin is known for its role in promoting sleep and regulating circadian (about one day) cycles.

The researchers investigated whether nightly melatonin supplementation could modify women's output of reproductive hormones in women ages 42-62. Women took 3 mg melatonin or placebo each night for six months, and their levels of melatonin and a variety of other hormones were repeatedly monitored. Besides uncovering a possible link between the decline of melatonin and the onset of menopause, researchers also found that melatonin can restore menstrual cycles and fertility in perimenopausal (within a few years of the onset of menopause) and menopausal women. “The six-month treatment with [melatonin] produced a remarkable and highly significant improvement of thyroid function, positive changes of [reproductive hormones] towards more juvenile levels, and abrogation of menopause-related depression,” concluded researchers.

—Dale Kiefer

Reference

* Bellipanni G, Di Marzo F, Blasi F, Di Marzo A. Effects of melatonin in perimenopausal and menopausal women: our personal experience. *Ann N Y Acad Sci.* 2005 Dec;1057:393-402.

Single Fast-Food Meal Increases Blood Pressure



A single high-fat fast-food meal causes an increase in blood pressure, according to a study published in the *Journal of Nutrition*.*

On two separate occasions, researchers at the University of Calgary fed thirty healthy participants with normal blood pressure either a breakfast from McDonald's® containing 42 grams of fat or a low-fat meal containing only 1 gram of fat. The meals contained equal amounts of sodium. The participants were then exposed to various stressors in the laboratory. After consuming the high-fat meal, the participants' systolic and diastolic blood pressures, as well as total peripheral resistance, were significantly higher, compared to measurements taken after the low-fat meal.

“Our findings suggest that even a single high-fat meal can result in an exaggerated response to stress,” researcher Dr. Tavis Campbell told *Life Extension*. While it is well-known that long-term intake of fatty foods increases cardiovascular disease risk, this study demonstrates that just one unhealthy meal can have a negative effect on health.

—Marc Ellman, MD

Reference

* Jakulj F, Zernicke K, Bacon SL, et al. A high-fat meal increases cardiovascular reactivity to psychological stress in healthy young adults. *J Nutr.* 2007 Apr;137(4):935-9.

Topical Nutrients Improve Common Skin Complaint

Topical application of the nutrients N-acetyl glucosamine and niacinamide helps reduce skin hyperpigmentation, according to a recent report in the *Journal of Cosmetic Dermatology*.* Hyperpigmentation (dark spots on the skin) frequently occurs in aging skin as a result of sun exposure. Scientists have speculated that N-acetyl glucosamine (a stabilized form of glucosamine) and

niacin-amide (a B vitamin) might promote a more even skin tone by reducing the production of melanin, the skin's natural pigment.

Caucasian women applied a lotion containing 2% N-acetyl glucosamine with 4% niacinamide or niacinamide alone to half the face, and a control lotion to the other half, twice daily for eight weeks. The combination of N-acetyl glucosamine with niacinamide was more effective than niacinamide alone.

Gary Goldfaden, MD, member of the American Academy of Dermatology and founder of Cosmesis Skincare told Life Extension, "The combination of these two novel ingredients has proven to be a breakthrough in creating more healthy and youthful appearing skin."

—Dayna Dye

Reference

* Bissett DL, Robinson LR, Raleigh PS, et al. Reduction in the appearance of facial hyperpigmentation by topical N-acetyl glucosamine. *J Cosmet Dermatol.* 2007 Mar;6(1):20-6.

Magnesium Protects Against Inflammation, Endothelial Dysfunction

Healthy women who consume more magnesium are less prone to inflammation and endothelial dysfunction than those who do not, according to Harvard University scientists.* Inflammation and endothelial dysfunction often precede atherosclerosis and diabetes, and are involved in metabolic syndrome. Previous research suggests that magnesium intake may decrease the features of metabolic syndrome.

Researchers examined 657 participants in the Nurses' Health Study. Blood samples collected between 1989 and 1990 were analyzed for markers of inflammation and endothelial function. Dietary questionnaires completed by the subjects in 1986 and 1990 were assessed on the dietary intake of magnesium and other nutrients.

Higher intake levels of magnesium were associated with lower levels of C-reactive protein (a marker of inflammation) and E-selectin (a marker of endothelial dysfunction).

"These observed associations, albeit generally modest, may represent a pathophysiologic mechanism for the [multiple] effects of magnesium intake on the features of the metabolic syndrome and its associated chronic diseases," the authors concluded.

—Dayna Dye

Reference

* Song Y, Li TY, van Dam RM, Manson JE, Hu FB. Magnesium intake and plasma concentrations of markers of systemic inflammation and endothelial dysfunction in women. *Am J Clin Nutr.* 2007 Apr;85(4):1068-74.

Zelnorm® Sales Suspended Due to Increased Risk of Cardiovascular Events



Novartis Pharmaceuticals Corp. announced its decision to voluntarily suspend sales of its anti-constipation drug, Zelnorm® (tegaserod maleate), at the request of the Food and Drug Administration (FDA). The drug had been on the market for slightly less than five years.

Marketed as a treatment for the relief of chronic constipation and constipation associated with irritable bowel syndrome (IBS), Zelnorm® was found to be associated with an increased risk of "cardiovascular ischemic events." According to Novartis, a retrospective analysis of clinical trial data involving more than 18,000 patients revealed, "a statistically significant imbalance in the incidence of cardiovascular ischemic events in patients taking Zelnorm® compared to those taking placebo. These events included myocardial infarction, stroke, and unstable angina pectoris."*

Life Extension reminds its readers that it is possible to obtain relief of constipation, often within an hour, by taking two or more teaspoons of buffered vitamin C powder on an empty stomach. Some people with irritable bowel

syndrome that results in chronic, dull pain and bowel spasms find relief with an enteric-coated peppermint/caraway oil preparation called Regimint™.

—Dale Kiefer

Reference

* Available at: http://www.pharma.us.novartis.com/newsroom/pressReleases/releaseDetail.jsp?PRID=2021&usertrack.filter_applied=true&Novald=3350119485402711127. Accessed March 31, 2007.

Cruciferous Vegetables Fight Prostate Cancer



Cruciferous vegetable-derived phytonutrients called isothio-cyanates provide a two-pronged approach in slowing prostate cancer growth, according to a presentation by Dr. Shivendra Singh at the American Association for Cancer Research's meeting in Los Angeles.* Cruciferous vegetables, which includes broccoli, cauliflower, and cabbage, have demonstrated anticancer effects in numerous studies over the past several decades. Isothiocyanates, compounds that are formed when the vegetables are cut or chewed, may be responsible for some of these benefits.

Dr. Singh's previous work showed that mice implanted with human prostate tumors showed reduced cancer growth after receiving phenethyl-isothiocyanate (PEITC) for 31 days. In the current study, Dr Singh's team found that PEITC inhibited angiogenesis (the formation of new blood vessels that allows tumors to grow and spread, or metastasize) in cultured prostate cancer cells.

"Angiogenesis is a major issue in cancer metastases," Dr. Singh noted. "Our results provide promising preliminary evidence that constituents of many edible cruciferous vegetables may slow down, or even halt, this process."

—Dayna Dye

Reference

* Available at: http://www.eurekalert.org/pub_releases/2007-04/uops-nic041607.php. Accessed May 16, 2007.

Needle Biopsy Benefits Outweigh Risks



Many people worry that needle biopsy procedures—such as those used to sample lung or breast tumors—could contribute to cancer spread or metastasis. Yet it appears that this worry is largely groundless, as recently reported in the New York Times.¹

According to radiologist Dr. David Yankelevitz of New York-Presbyterian/Weill Cornell hospital in New York, "With any biopsy of any organ, you do loosen some cells, and some do get into the bloodstream, but very rarely do they stick and implant. If you were causing Stage 1 tumors to spread by putting in a needle, you would expect the long-term survival would be lower, but in fact we found no difference at all."^{1,2}

"The reason you do a biopsy in the first place is that you don't want to do surgery... for a benign condition. A biopsy can reduce the chance of an operation for someone who doesn't need one, which is a much greater risk."¹ A 1998 study found that among approximately 68,000 needle biopsies, there were eight metastases along the needle track, a rare risk that was deemed "random and unavoidable."³

—Elizabeth Wagner, ND

Reference

1. Ray CC. Q & A: Needle Biopsy Risk. New York Times. March 27, 2007.

2. Wisnivesky JP, Henschke CI, Yankelevitz DF. Diagnostic percutaneous transthoracic needle biopsy does not affect survival in stage I lung cancer. Am J

Fish Oil and Exercise Combo Reduces Body Fat, Improves Cardiovascular Health



Fish oil supplementation helps reduce body fat and improve cardiovascular health, according to a recent study.* When combined with regular exercise, the healthful benefits of fish oil are amplified.

Australian researchers examined the effects of fish oil and exercise, alone or in combination, on body composition and cardiovascular health. Approximately 80 overweight men and women were randomly assigned to one of four groups. Subjects blindly took either six grams of fish oil per day, or six grams placebo (sunflower) oil. One group assigned to each oil treatment also exercised in a prescribed fashion three times weekly. Supplementation and/or exercise continued for three months.

Tests performed at six and 12 weeks indicated that fish oil supplementation and exercise alone both improved body composition and several key indicators of cardiovascular health. When

supplementation and regular exercise were combined, the beneficial effects were even greater.

—Dale Kiefer

Reference

* Hill AM, Buckley JD, Murphy KJ, Howe PR. Combining fish-oil supplements with regular aerobic exercise improves body composition and cardiovascular disease risk factors. Am J Clin Nutr. 2007 May;85(5):1267-74.

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