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REPORT

New Promise for Cancer Prevention and Treatment

Newly published research confirms that nutrients such as ECGC (a green tea polyphenol), resveratrol, and indole-3-carbinol (I3C) are potent cancer inhibitors and may be valuable in both preventing and treating the disease. The findings were the focus of the "Nutritional Genomics and Proteomics in Cancer Prevention Conference" held in Bethesda, MD, and sponsored by the National Cancer Institute, the National Institutes of Health, and the American Society for Nutritional Sciences. The conference findings were featured in The Journal of Nutrition (July 2003).

Green Tea and Resveratrol Inhibit Cancer Cell Growth

Prostate cancer is the second leading cause of cancer death in men in the US. Just as cigarette smoking is linked to lung cancer, prostate cancer is linked to diet, with meat, meat fat, and dairy products strongly implicated in prostate cancer.[1-3] By contrast, Asian men have a much lower incidence of prostate cancer, and researchers tie these lower rates to the Asian diet, which emphasizes rice, soy, and tea rather than meat and dairy products.

American meat and dairy products come from cows treated with steroid drugs that are banned in Europe. These synthetic mixtures of estrogen, testosterone, and other hormones, which are implanted in the cows in the weeks before slaughter, are designed to accelerate growth and weight gain. When put in a petri dish with cancer cells, these drugs do the same thing to the cells—they accelerate their growth.[4]

Treating cows with growth implants increases levels of a growth factor known to promote cancer cell growth.[5,6] At the Bethesda conference, University of Wisconsin researchers reported finding a polyphenol in green tea (ECGC) that suppresses the growth factor.[7,8] When rodents with actively growing prostate cancer were fed the equivalent of six cups of green tea a day, no metastasis occurred, overall survival was greater, and tumor-free survival was longer. In a separate study, a microarray test of 250 prostate cancer genes showed that ECGC significantly affected 25 genes that could influence cancer growth.[9]

Researchers at New York Medical College reported on a study that examined the impact of beef fat on the genes of normal prostate tissue in rats. They found that a diet containing beef fat increases the activity of genes promoting cancer and decreases the activity of genes suppressing cancer. The genes affected by beef fat include a gene that suppresses inflammation, a gene that could allow cells to escape growth control, and a gene that promotes invasion of cancer cells.[10]

The University of Wisconsin researchers also reported that ECGC from green tea reduces levels of cancer-enhancing enzymes. One (5a-reductase) promotes baldness, body hair, benign prostatic hyperplasia (BPH), and cancer. Another, known as ornithine decarboxylase, is critical for cell growth. Having too much of this enzyme is dangerous in the prostate gland, which has the body's highest levels of inflammation-promoting cyclooxygenase (COX) and largest supply of cell building blocks.[11] ECGC lowered levels of ornithine decarboxylase and also suppressed the enzyme proteasome, which protects cancer cells from apoptosis (cell death) by the body's normal processes. Levels of proteasome are decreased in the serum of green tea drinkers. The Wisconsin researchers concluded: "Taken together, our studies and the data from other laboratories suggest that green tea and its constituents induce apoptosis, inhibit cell growth, arrest the progression of the cell cycle, inhibit angiogenesis and metastasis, and importantly, inhibit prostate tumor growth in an animal model in which prostate cancer progresses as in humans."

Researchers from the M.D. Anderson Cancer Center (Houston, TX) reported on the impact of resveratrol—a polyphenol found in wine, grapes, peanuts, and mulberries—on single cells of prostate cancer.[12] Their study adds to the growing body of data on resveratrol's powerful and diverse anti-cancer effects. Resveratrol inhibits each stage of prostate cancer by a different means. It blocks growth-promoting hormones in prostate cancer cells,[13] halting their growth and inducing cell destruction. Resveratrol also has strong anti-inflammatory effects that lower the risk of cancer and help stop the spread of the disease if it develops.[14] Inflammation promotes cancer and suppressing it lowers the risk of cancer. The researchers concluded by proposing resveratrol as the leading candidate in prostate cancer prevention, based on its cancer-inhibiting properties.

The M.D. Anderson researchers are addressing the problem of aggressive, hormone-unresponsive prostate cancers, which invariably arise after treatment of the first, hormone-responsive cancer. These cancers involve the activation of an enzyme that enables growth. The Anderson researchers conclude that resveratrol indirectly interferes with this enzyme, and they propose resveratrol as a prostate cancer preventive agent as well as an adjuvant therapy for treatment of advanced disease.

I3C Enhances Genistein's Cancer-Fighting Capabilities

Research on new phyto-based cancer therapies is moving beyond single compounds to combinations of nutrients. In one of the first studies of its kind, researchers at North Shore-Long Island Jewish Research Institute, Albert Einstein College of Medicine, St. Johns University, and Oregon State University report that genistein, a phytochemical almost entirely derived from soybeans, enhances the anti-cancer effects of indole-3-carbinol (I3C).[15] I3C is a plant compound found in vegetables such as broccoli, cabbage, mustard, kale, and cauliflower. Studies show that people who eat a lot of these cruciferous vegetables have the lowest risk of various types of cancer, including lung, stomach, colon and rectal,[16] breast,[17] and prostate.[18,19] Both I3C and genistein are established anti-cancer nutrients.

This research produced exciting new results concerning the apoptosis of breast cancer cells and the blocking of estrogen. When the researchers put I3C or DIM (diindolylmethane, one of the products produced by the breakdown of IC3) together with genistein in amounts comparable to those in food or supplements, and then added it to breast cancer cells (both with and without estrogen receptors), 40% of cells underwent apoptosis or cell death, and the amount of I3C/DIM required was cut by about two-thirds.

The researchers also investigated the combination's impact on estrogen's ability to promote cell growth. I3C blocked the hormone's effects by about 25%, genistein blocked it by about 55%, and the two compounds together blocked estrogen by about 90%. The effect was synergistic rather than additive—that is, the two work in tandem, though how this occurs is not presently known.

I3C and DIM Work Synergistically to Stop Cancer

Only about one-third of all breast cancers are estrogen receptor positive, and only about half of those respond to the estrogen blocker tamoxifen. Even then, tamoxifen resistance eventually will develop. Two-thirds of breast cancer cases cannot be treated with tamoxifen to begin with. Currently, broad-spectrum chemotherapy is the preferred treatment for breast cancer, and while frequently effective, a therapy tailored to breast cancer, especially the non-estrogen type, is needed. Researchers at the University of California-Berkeley report that I3C is potentially such a therapy.[20]

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The new research shows that I3C and its breakdown product DIM work synergistically to stop the growth of breast cancer cells, with I3C inhibiting a cancer-related gene (the gene for Cdk-6 kinase) that DIM does not. DIM and I3C both kill breast cancer cells.[21] But maximum cell-killing effect occurs when both compounds are present. While I3C and DIM each have unique effects on genes that control the multiplication of cancer cells, they share some effects in common that have been dubbed “overlapping effects.” Life Extension advises its members to take I3C rather than DIM, as I3C naturally breaks down into DIM and other products that may have unknown beneficial effects. Taking DIM offers the benefits of only the one compound.

I3C stops breast cancer cells from multiplying through a unique, partly unknown pathway. Its effects against various types of breast cancer are so promising that the University of California researchers state: “In the case of estrogen-nonresponsive MDA-MB-231 cells, indole treatment (I3C) inhibited proliferation under conditions in which the antiestrogen tamoxifen had no effect, which suggests that a wider range of breast cancer cells responds to indoles than estrogen antagonists.” Their research adds to the growing evidence that I3C may form the basis of a powerful new therapy for breast cancer treatment. Its efficacy in prevention already has been established.[22-25]

Italian researchers recently created an artificial product from natural I3C that has twice the strength in estrogen-receptor-negative breast cancer cells.[26] It inhibits the same critical enzyme (Cdk6 kinase) as I3C, but instead of activating the p21 tumor suppressor gene, it activates another known as p27. The researchers intend to pursue the “tetramer” they created as a drug. Preliminary evidence shows that it does not harm normal cells.

Cancer Research Continues to Advance

Despite some setbacks and negative findings, the trend in nutrition and cancer research is overwhelmingly positive. The Bethesda conference demonstrated that research is moving beyond the idea that eating fruits and vegetables helps prevent cancer, to identifying which compounds in plant food are cancer-preventing agents. Research is now focusing on how —not whether—phyto-compounds inhibit cancer cell growth.

Nutrition and cancer researchers who attended the conference are more and more investigating the interactions of cancer-preventing compounds and proposing sophisticated new research to bring all the new findings together. They contend that a new kind of scientific review is needed to evaluate the potential of anti-cancer modalities to work together synergistically, with geneticists and nutritionists working in tandem. They note that cancer survivors need to be utilized as valuable sentinels of cancer prevention, and that the notion that a nutrient may be more effective at one stage of cancer than at another should be considered.

Researchers hope that these and other new developments—such as the use of sophisticated new computer models and imaging systems—will bring them that much closer to finally winning the war on cancer.

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