

## Plant Compound Reduces Breast Cancer Mortality

**Many studies suggest that hormone-like plant compounds called phytoestrogens have a cancer protective effect. Scientists of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) have now been the first to provide evidence that in postmenopausal breast cancer patients these substances also lower the risk of developing metastasis or secondary tumors and dying by up to 40 percent.**

Phytoestrogens are plant compounds which, in the human body, can attach to the receptors for the female sexual hormone estrogen and which are taken in with our daily diet. A number of findings have attributed a cancer protective effect to these plant hormones. At DKFZ, a team headed by Prof. Dr. Jenny Chang-Claude summarized the results of several studies in a meta-analysis last year and showed that a diet rich in phytoestrogens lowers the risk of developing breast cancer after menopause. Now the Heidelberg researchers wanted to find out whether phytoestrogens also have an influence on the course of breast cancer. Prior investigations on this topic had provided contradictory results.

The most important type of phytoestrogens in our Western diet are lignans, which are contained in seeds, particularly flaxseeds, as well as in wheat and vegetables. In the bowel, these substances are turned into enterolactone, which is absorbed by the mucous tissue and which was determined by the Heidelberg researchers as a biomarker in the patients' blood.

From 2002 to 2005, the DKFZ researchers used the MARIE study to take blood samples of 1,140 women who had been diagnosed with postmenopausal breast cancer. After a mean observation time of six years, they related enterolactone levels to clinical disease progression.

The result: Compared to the study subjects with the lowest enterolactone levels, the women with the highest blood levels of this biomarker had an approximately 40 percent lower mortality risk. When the scientists additionally took account of the incidence of metastasis and secondary tumors, they obtained a similar result: Women with the highest enterolactone levels also had a lower risk for such an unfavorable disease progression.

"We now have first clear evidence showing that lignans lower not only the risk of developing postmenopausal breast cancer, but also the mortality risk," says Jenny Chang-Claude. There had been prior studies to determine the lignan intake by means of dietary surveys. But the results of such surveys are often unreliable and, in addition, there are big differences in the way individuals actually process the plant substances into effective metabolic products. Therefore, the Heidelberg team chose the more reliable measurement of biomarkers.

However, Chang-Claude narrowed down the result: "The result was significant only for the group of tumors that have no receptor for the estrogen hormone (ER-negative tumors). This gives reason to suspect that enterolactone protects from cancer not only by its hormone-like effect." Indeed, studies of cells and animals had already provided evidence suggesting that the substance also has an influence on cancer growth irrespective of estrogen. Thus, it promotes cell death and inhibits sprouting of new blood vessels.

"In order to find out whether enterolactone also inhibits the aggressiveness of estrogen receptors in estrogen-positive tumors, we would need to expand this study to include much larger groups of women," said Jenny Chang-Claude. Moreover, the scientist firmly emphasized: "By eating a diet that is rich in wholemeal products, seeds and vegetables,

which is considered to be health-promoting anyway, everybody can take in enough lignans. At the present time, we can only discourage people from taking any food supplements.”

Phytoestrogens have been the subject of intense scientific debates in past years. On the one hand, the results of several studies of cells as well as epidemiological findings suggest that they have a cancer protective effect. Another observation that may be interpreted in this direction is that Asian women are less frequently affected by breast cancer. Their soy-rich diet contains large amounts of another type of phytoestrogens, isoflavones. On the other hand, scientists fear that isoflavones might imitate the growth-promoting properties of real hormones and, thus, accelerate hormone-dependent tumors such as breast cancer and prostate cancer. “It has not yet been finally determined whether lignans in the body imitate the hormone effect or, on the contrary, counteract it,” says Jenny Chang-Claude. “Our studies will help achieve more clarity in this important question, which also concerns our daily diet.”

Katharina Buck, Alina Vrieling, Aida Karina Zaineddin, Susen Becker, Anika Hüsing, Rudolf Kaaks, Jakob Linseisen, Dieter Flesch-Janys, and Jenny Chang-Claude: Serum Enterolactone and Prognosis of Postmenopausal Breast Cancer. *Journal of Clinical Oncology*, 2011, DOI: 10.1200/JCO.2011.34.6478

The German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ), employing over 2,500 staff members, is the largest biomedical research institute in Germany. More than 1,000 scientists are working to investigate the mechanisms of cancer development, identify cancer risk factors and develop new strategies for better cancer prevention, more precise diagnosis and effective treatment of cancer patients. In addition, the staff of the Cancer Information Service (KID) provides information about this widespread disease for patients, their families, and the general public. DKFZ is funded by the German Federal Ministry of Education and Research (90%) and the State of Baden-Wuerttemberg (10%) and is a member of the Helmholtz Association of National Research Centers.

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