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In The **News**

Lovastatin shows potent anti-cancer effects

In 1997, The Life Extension Foundation published a protocol suggesting that cancer patients ask their oncologist to consider prescribing the drug lovastatin (80 mg a day) as an adjuvant therapy. This recommendation was based on scientific studies indicating that lovastatin interfered with the cancer cell growth cycle and might be synergistic with conventional therapies in inducing apoptosis (programmed cell death). Since 1997, a number of studies have substantiated the potential benefit of lovastatin in treating a wide range of cancers. In a new study published in the journal *Clinical Cancer Research* (January 2001), lovastatin demonstrated pronounced effects in inducing cancer cell apoptosis in certain types of cancer. The scientists who conducted this study showed that lovastatin worked particularly well in the following cancer cells: acute myeloid leukemia, neuroblastoma, squamous cell carcinoma of the cervix, juvenile monomyelocytic leukemia, head and neck squamous cell carcinoma, medulloblastoma and rhabdomyosarcoma. In discussing the results of their most recent research, the scientists pointed to a previous five-year study on 745 people taking lovastatin (to reduce their high cholesterol) that showed that these subjects had a lower than expected incidence of cancer. Most interesting was that in this group of 745 people taking lovastatin for 5-years, the incidences of prostate and breast cancer was as expected, whereas there were no cases of lovastatin-sensitive cancers observed. The scientists suggested that these findings indicated that lovastatin may prevent certain types of cancer from developing in the first place. In this study published in *Clinical Cancer Research*, the scientists noted that "lovastatin has the potential as an immediate, novel therapeutic approach in the treatment of these responsive tumors. Lovastatin induced a specific apoptotic response in these tumor cells within achievable therapeutic range and it (lovastatin) has a proven record in the clinic as a safe and effective drug." The scientists related a case history of a patient with acute myeloid leukemia treated at their institution using lovastatin at the high dose of 2 milligrams per kilogram of body weight per day for 52 consecutive days. For a person weighing 154 pounds, this would mean a daily dose of lovastatin of 140 mg. The patient taking this high-dose lovastatin demonstrated control of leukemic blast counts that lasted more than six months after cessation of treatment.

There are now Phase I clinical trials scheduled to evaluate the toxicity and efficacy of low-dose lovastatin in the treatment of recurrent acute myeloid leukemia, head and neck squamous cell carcinomas, and cervical cancer. The Life Extension Foundation does not recommend that members enter these Phase I clinical trials, as they will restrict the use of other synergistic cancer therapies and may use a dose of lovastatin too low to provide optimal benefit. Instead, members should ask their doctor to prescribe a higher dose lovastatin and have a complete blood chemistry test performed every two weeks for the first two months of therapy to make sure lovastatin is not causing liver or muscle damage. Monthly blood chemistry tests should be done as long as high dose lovastatin is used.

Previous studies have indicated that lovastatin and other fat-soluble "statin" drugs are also effective against pancreatic, colon, liver and thyroid tumors. There are several mechanisms of action that have been proposed for lovastatin's anti-cancer actions, including suppressing the over-expression of the RAS oncogene and interfering with the mevalonate pathway used by some cancer cells in the G1 phase of the cell cycle. Lovastatin (sold under the trade name Mevacor) is one fat-soluble "statin" drug available by prescription. Other fat-soluble statin drugs include Zocor and Lipitor. The popular cholesterol-lowering drug called Pravachol is a water-soluble "statin" that may not work as well against cancer as the fat-soluble "statin" drugs. For further information on the use of "statin" drugs to treat cancer refer to the Cancer (Adjuvant) Treatment section of the book *Disease Prevention and Treatment* or view this protocol on the Foundation's website at www.lef.org



Japanese researchers have reported that the benefits of soy may include psychological well-being. Women who eat soy products are less anxious, fearful and depressed, according to a new study. All the women who participated were healthy, and none were on hormone replacement therapy. The beneficial effects of soy may be due to its estrogen-like actions. Genistein, a component of soy, interacts with estrogen and GABA receptors in the brain. Information was obtained from 103 Japanese women, average age 54. The women then completed the Center for Epidemiologic Studies Depression (CES-D) Scale and the psychological part of the General Health Questionnaire (GHQ). Women who ate the most soy scored the best on these tests. Neither estradiol nor sex hormone binding globulin correlated with mood, but dehydroepiandrosterone did. DHEA, as it is known, was also higher in the study participants who were happier. It's unknown whether there is a correlation between soy and DHEA, but previous studies have shown a positive effect of DHEA on mood in older people.



DHEA is an androgen-type hormone that is converted to both estrogen and testosterone. Testosterone increases libido in some women. Estrogen replacement therapy (drug therapy) has proven beneficial in enhancing mood in some older women. According to a meta-analysis published in 1999, "At this time, estrogen therapy [synthetic estrogen drugs] for the treatment of depression in peri and postmenopausal women may be useful, but confirmatory studies are still lacking." The possible benefits of drug therapy should be weighed against the risks and side effects, which are substantial.

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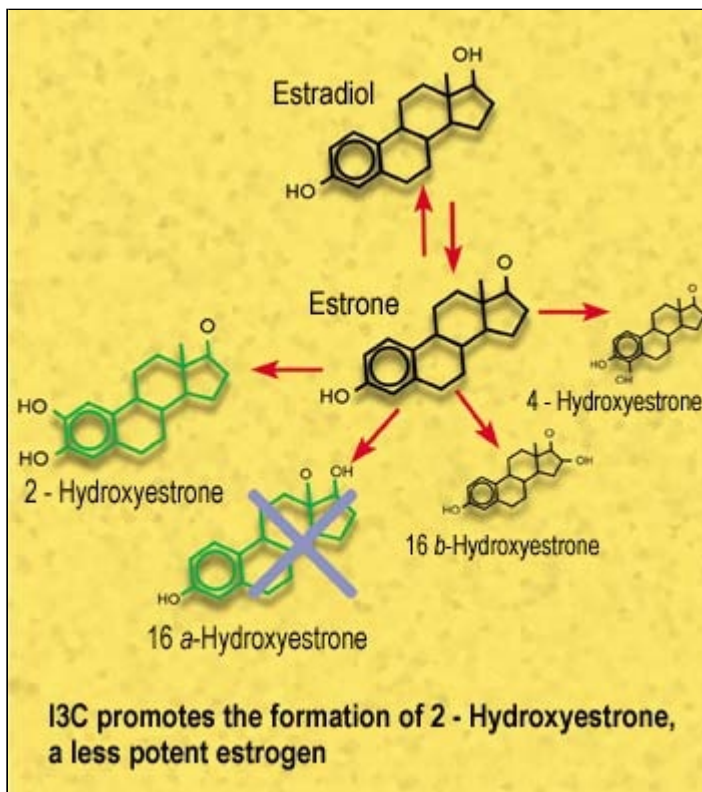
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I3C and breast cancer

A new study confirms that invasive breast cancer is less likely to occur when the body converts estrogen a certain way. The study reports a 40% reduction in risk when the body metabolizes estrogen into the less potent 2-hydroxyestrone instead of 16a-hydroxyestrone. These metabolites have important differences, one being that 16a-hydroxyestrone has stronger estrogenic activity than 2-hydroxyestrone which is a weak form of estrogen. The more 2-hydroxyestrone a woman has in her body, the less likely she will have the strong 16a-hydroxyestrone that can drive cancer growth. The findings are based on data from 144 Italian women with breast cancer out of 10,000 who participated in a study on how hormones and diet might cause the disease. 16a-hydroxyestrone is higher in women with breast cancer, and correlates with a greater incidence of mammary tumors in mice.

One of the things that changes the way estrogen is metabolized is indole-3-carbinol (I3C), a substance in cruciferous vegetables such as cabbage, cauliflower and broccoli. I3C has been purified, and is sold as a supplement. In studies where the supplement is used, I3C causes an increase in the amount of 2-hydroxyestrone. That in turn, puts a damper on cancer growth encouraged by 16a-hydroxyestrone. I3C doesn't affect 16a-hydroxyestrone directly. Studies show that I3C can also reduce DNA damage caused by heterocyclic amines (cancer-causing molecules that arise when meat is cooked), and cigarette smoke. It also inhibits the formation of 4-hydroxyestrone which is carcinogenic. In cancer cells, it induces apoptosis (cell death), and stops the cell cycle. In mice, I3C prevents cervical cancer caused by papilloma virus. It may also affect the growth of prostate cancer (although studies have not been done). A male hormone, 16a-hydroxytestosterone, is transformed through the same mechanism as 16a-hydroxyestrone in women.



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