

## High cholesterol levels increase prostate tumor growth

A study scheduled for publication in the April 1 2005 issue of the *Journal of Clinical Investigation* (<http://www.jci.org/>) found that a high level of cholesterol in the blood speeds the growth of prostate tumors by altering chemical signaling patterns within the cells. The finding helps explain the results of epidemiologic studies that have established an association between prostate cancer risk and having high cholesterol levels or consuming a Western style diet, as well as those that have found a lower risk of prostate cancer in men taking drugs that reduce cholesterol.

Researchers at Children's Hospital Boston led by Michael Freeman, PhD, who is the program director of the hospital's Urological Diseases Research Center, injected human prostate cancer cells into mice and elevated their cholesterol by dietary means. They observed that the outer cell membranes experienced an accumulation of cholesterol, particularly in lipid rafts, which are cholesterol structures that aggregate and disaggregate like icebergs. This accumulation was found to activate a cell-survival pathway known as Akt, which is believed to be a prostate cancer pathway, allowing the tumor cells to resist apoptosis, or programmed cell death.

Although having high cholesterol was not linked to the risk of developing new cancers in the animals, after six weeks tumor incidence in mice receiving injected cancer cells more than doubled and tumors were much larger.

In another experiment, the cholesterol-reducing drug simvastain was added to cells in vitro. Simvastain was found to inhibit the Akt pathway, increase programmed cell death and arrest the growth of tumors. Adding cholesterol to the cell membranes halted the drug's benefit.

Dr Freeman stated, "Our study opens up a new paradigm in thinking about how cancer might be controlled pharmacologically by manipulating cholesterol. Our data support the notion that cholesterol-lowering drugs -- which are widely used and fairly safe -- might be effective in prevention of prostate cancer, or as an adjunctive therapy."

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Protocol

### **Prostate cancer**

There are studies that show that dietary fat increases tumor growth rates in an animal model of human prostate cancer (PC). In a mouse model of PC involving androgen-sensitive human prostatic adenocarcinoma cells (LNCaP cells), mice fed a 40.5% fat diet had mean tumor weights more than 2 times greater than mice fed a 21% fat diet. The 40.5% fat diet approximates that found in the average American male diet, which has been determined to be 36%.

The slower tumor growth associated with the low-fat diet occurred even after the formation of measurable tumors when the diets were changed from 40% fat to 21% fat. Serum PSA levels also were highest in the 40.5 kcal% fat group and lowest in another group fed only 2.3 kcal% fat.

Measures to prevent PC must be a routine part of the counsel that general practitioners and internists give their patients. Selenium intake of at least 200 mcg a day should be a consideration in the prevention of PC. Low plasma selenium is associated with a four- to fivefold increased risk of PC. In addition, levels of plasma selenium also decrease with age, resulting in middle-aged to older men being at a higher risk for low selenium levels. Ideally, baseline levels of selenium should be obtained before beginning routine selenium supplementation. It would make sense to begin such a micronutrient and mineral assessment at age 25 and perhaps every 10 years thereafter.

Research studies have shown that vitamin E reduces growth rates of PCs resulting from a high fat diet. Tumor growth rates were highest in the animals fed a 40.5%-kcal fat diet (the typical American diet). Tumors in animals fed 40.5%-kcal fat plus vitamin E were the same as those fed a 21.2%- kcal fat diet (an ideal fat level).