Vitamin D can decrease -- or increase -- breast cancer development and insulin resistance

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In mice models of breast cancer, researchers at the Georgetown Lombardi Comprehensive Cancer Center, a part of Georgetown University Medical Center, found that vitamin D significantly reduced development of estrogen receptor-positive (ER+) breast cancer both in lean and obese mice, but had no beneficial effect in estrogen receptor-negative (ER-) cancer. In fact, obese mice destined to develop ER- breast cancer were clearly worse off than lean ER- mice if they were given vitamin D in their diet.

The researchers, who will present their study at the American Association for Cancer Research (AACR) 102nd Annual Meeting 2011, also found that vitamin D reversed insulin resistance in obese mice, no matter which breast cancer subtype they later developed. In lean mice, however, there was no evidence that vitamin D increased insulin sensitivity.

"Use of vitamin D supplementation is clearly tricky. In the many studies that have been done studying the effect of vitamin D in different cancer types, there is no straight link between use and benefit," says the study's lead investigator, Leena Hilakivi-Clarke, Ph.D., a professor in the Department of Oncology.

For example, in the colon, vitamin D seems to reduce the risk of cancer development, but it may not have any effect on later stage colon cancer.

There is also concern that vitamin D may increase the risk of prostate, esophagus and pancreatic cancer. In work she has conducted in endometrial cancer, Hilakivi-Clarke found that although vitamin D was not beneficial in lean mice, in obese animals it reverses both early and advanced stages of the cancer.

"This is not a vitamin that should be taken lightly," she cautions. "People need sufficient amounts because it has beneficial effects for overall health that have nothing to do with preventing cancer. But for those who want to boost their use of vitamin D, it is important that they have their individual levels tested by a physician, and that they discuss their desire to use supplements."

IMPACTS OF VITAMIN D INTAKE IN MICE MODELS (findings in Hilakivi-Clarke lab)

	Lean mice	Obese mice
ER+ breast cancer	Risk reduced	Risk reduced
ER- breast cancer	Dose dependent benefit	No benefit
Insulin resistance	No benefit	Reversed
Endometrial cancer	No benefit	Risk reduced

IN HUMANS

Colon cancer Reduces risk of development; No effect on later stage cancers

Pancreatic, esophageal, prostate cancers Potentially increases risk

In their ER- breast cancer study, the researchers fed lean mice two doses of vitamin D - 15 or 20 K international units [IU] VD3 - from puberty onset onwards for 24 weeks. They found that the lower dose (15 K IU) of VD3 significantly reduced mammary tumor incidence as well as time

for tumors to develop in lean mice, when compared to mice that were fed control diet. A higher dose (25K IU) was used in mice fed the obesity-inducing diet because vitamin D becomes trapped in fatty tissue and thus is reduced in the blood stream, Hilakivi-Clarke says. Obese mice destined to develop ER- cancer that were given vitamin D developed the highest incidence of breast cancer.

In their ER+ breast cancer, only the higher vitamin D dose (20K IU) was used. This dose significantly reduced breast tumor incidence in lean mice, compared to control or obese animals. Additionally, obese mice fed vitamin D developed fewer tumors than obese mice not supplemented with it, says Hilakivi-Clarke.

In both mouse models of breast cancer, obese mice developed insulin resistance, and vitamin D supplementation reversed it. However, vitamin D in lean mice tended to reduce insulin sensitivity in both mouse models, she says.

The researchers are currently studying possible mechanisms by which vitamin D may reverse obesity induced increase in breast cancer and insulin resistance, and preliminary results suggest vitamin D reverses the action of genes which promote inflammation, cell proliferation and survival, and this might involve epigenetic modifications.

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