

## New Model Suggests Role of Low Vitamin D in Cancer Development

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In studying the preventive effects of vitamin D, researchers at the Moores Cancer Center at the University of California, San Diego, have proposed a new model of cancer development that hinges on a loss of cancer cells' ability to stick together. The model, dubbed DINOMIT, differs substantially from the current model of cancer development, which suggests genetic mutations as the earliest driving forces behind cancer.

"The first event in cancer is loss of communication among cells due to, among other things, low vitamin D and calcium levels," said epidemiologist Cedric Garland, DrPH, professor of family and preventive medicine at the UC San Diego School of Medicine, who led the work. "In this new model, we propose that this loss may play a key role in cancer by disrupting the communication between cells that is essential to healthy cell turnover, allowing more aggressive cancer cells to take over."

Reporting online May 22, 2009 in the *Annals of Epidemiology*, Garland suggests that such cellular disruption could account for the earliest stages of many cancers. He said that previous theories linking vitamin D to certain cancers have been tested and confirmed in more than 200 epidemiological studies, and understanding of its physiological basis stems from more than 2,500 laboratory studies.

"Competition and natural selection among disjointed cells within a tissue compartment, such as might occur in the breast's terminal ductal lobular unit, for example, are the engine of cancer," Garland said. "The DINOMIT model provides new avenues for preventing and improving the success of cancer treatment."

Garland went on to explain that each letter in DINOMIT stands for a different phase of cancer development. "D" stands for disjunction, or loss of intercellular communication; "I," for initiation, where genetic mutations begin to play a role; "N" for natural selection of the fastest-reproducing cancer cells; "O" for overgrowth of cells; "M" for metastasis, when cancer cells migrate to other tissues, where cancer can kill; "I" refers to involution, and "T" for transition, both dormant states that may occur in cancer and potentially be driven by replacing vitamin D.

While there is not yet definitive scientific proof, Garland suggests that much of the evolutionary process in cancer could be arrested at the outset by maintaining vitamin D adequacy. "Vitamin D may halt the first stage of the cancer process by re-establishing intercellular junctions in malignancies having an intact vitamin D receptor," he said.

According to Garland, other scientists have found that the cells adhere to one another in tissue with adequate vitamin D, acting as mature epithelial cells. Without enough vitamin D, they may lose this stickiness along with their identity as differentiated cells, and revert to a stem cell-like state.

Garland said that diet and supplements can restore appropriate vitamin D levels, and perhaps help in preventing cancer development. "Vitamin D levels can be increased by modest supplementation with vitamin D3 in the range of 2000 IU/day," he noted.

The researchers noted that many studies show an apparent beneficial effect of vitamin D and calcium on cancer risk and survival of patients with breast, colorectal and prostate cancer. However, there are some studies that have not found such benefit, especially when taking smoking, alcohol and viruses into account. While more research needs to be done, Garland recommends that individuals should have their vitamin D level tested during an annual check up.

Garland and his colleagues have published epidemiological studies about the potential preventive effects of vitamin D for some two decades. Last year, his team showed an association between deficiency in sunlight exposure, low vitamin D and breast cancer. In previous work, they showed associations between increased levels of vitamin D3 or markers of vitamin D and a lower risk for breast, colon, ovarian and kidney cancers.

Other authors on the study include Edward D. Gorham, Sharif B. Mohr and Frank C. Garland, UC San Diego.

The Moores UCSD Cancer Center is one of the nation's 41 National Cancer Institute-designated Comprehensive Cancer Centers, combining research, clinical care and community outreach to advance the prevention, treatment and cure of cancer. For more information, visit <http://health.ucsd.edu/cancer>

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