Marin County's high breast cancer rate may be tied to genetics

August 8 2012

(Medical Xpress) -- Marin County, California has one of the highest rates of breast cancer in the world, a fact that scientists know has nothing to do with the land itself but with some other, unknown factor.

A new study that analyzed mouth buccal cell samples stored frozen at the University of California, San Francisco (UCSF) suggests what this factor may be: a genetic trait present among women within the county's predominantly white population.

In an article published online this week by the Journal of the American College of Surgeons, which will appear in the November 2012 print issue, surgeon scientist Kathie Dalessandri, MD, FACS and colleagues at UCSF and the company InterGenetics, Inc. in Oklahoma City describe how, in a small, retrospective pilot study involving buccal cells from 338 women living in Marin, slight variations within the DNA of a human gene for vitamin D receptor were associated with breast cancer risk.

"While the findings must be validated in a much larger, prospective study," Dalessandri warned, "we found that women who were at high risk for breast cancer were 1.9 times more likely to have a specific vitamin D receptor variation than the general population."

A larger, collaborative prospective study in Marin County is ongoing, spearheaded by the Marin County Department of Health and Human Services (www.marinwomensstudy.org). This study includes an examination of breast cancer risk on a scale involving thousands of

women.

For now, Dr. Dalessandri said, there is no clear-cut advice on the level of vitamin D needed for breast cancer prevention, but variations in the Vitamin D receptor may be an important modulator of risk. The discovery does not rule out that there may be other factors involved in the elevated breast cancer risk in Marin County, said Dalessandri, but it gives an important clue moving forward.

After More than a Decade, New DNA Secrets

The first major study to look at the question of why women in Marin County are at higher risk for breast cancer was led by UCSF cancer epidemiologist Margaret Wrensch, MPH, PhD and Georgianna Farren and colleagues from Marin Breast Cancer Watch.

Published in 2003, that study compared 285 women with breast cancer in Marin with 286 local women who did not have the disease, and examined traditional risk factors such as risk of breast cancer based on a woman's at the time of diagnosis of breast cancer, age when menstruation began, age at first live birth, history of breast cancer in first degree relatives, history of breast irradiation, history of benign breast biopsies, and use of hormone replacement therapy that may have accounted for the difference—as well as environmental, lifestyle and nutritional factors.

One important conclusion of that study was that there was nothing about the land itself that was causing breast cancer. A woman's risk of developing breast cancer did not increase according to the amount of time she spent in Marin County. The study also found that women with cancer were more likely to report drinking two or more drinks per day than women without cancer who had lived the same amount of time in Marin County and had the same other risk factors.

The cell samples from the 2003 study had been kept frozen for future research use by UCSF's John Wiencke in his Molecular Epidemiology Laboratory within the UCSF Department of Neurological Surgery. That allowed Dalessandri and her colleagues to collect DNA from the samples were analyzed using new technology developed by Eldon Jupe PhD, of InterGenetics, Inc., and colleagues in recent years.

The technology is an algorithm named OncoVue, a polyfactorial risk model (PFRM) that scores breast cancer risk based on particular genetic variations within the vitamin D receptor and other genes. Looking blindly at the DNA of some 338 Caucasian women from the original study—164 who had breast cancer and 174 who did not—Jupe and his colleagues applied the algorithm and found that it was highly accurate in predicting risk in the Marin County study. The women predicted at highest risk of breast cancer by the algorithm were analyzed to determine the strongest genetic factors contributing to the risk.

They found a genetic variation, known as the Vitamin D Receptor Apa1 A2/A2 homozygous polymorphism, was associated with elevated risk of breast cancer in Marin County women—64 percent of the women at high risk of breast cancer had the genetic trait compared to 34 percent in the overall population, a significant 1.9 fold difference.

If genetic variations in the vitamin D receptor prove to be causally linked to breast cancer, that may help pave the way for new ways to prevent or treat the disease through vitamin D supplementation—though any such approaches would have to prove safe and effective in clinical trials, which can take years to reveal impact.

Other work looking at the factors that might explain the elevated breast cancer risk in Marin County includes the Breast Cancer and the Environment Research Program, a national study coordinated by UCSF investigator Robert Hiatt in the Department of Epidemiology and

Biostatistics and the San Francisco Coordination Center. This study is exploring environmental factors that may lower the age of pubertal onset, known to be a risk factor for breast cancer. The local study is being conducted under the leadership of Lawrence Kushi of Kaiser Permanente in Northern California and comprises girls from Marin, San Francisco and Alameda counties recruited from Kaiser Permanente member families prior to puberty and followed to maturity.

More information: The article, "Vitamin D Receptor Polymorphisms and Breast Cancer Risk in a High-Incidence Population: A Pilot Study" by Kathie M Dalessandri, Rei Miike, John K Wiencke, Georgianna Farren, Thomas W Pugh, Sharmila Manjeshwar, Daniele C DeFreese and Eldon R Jupe, appears in the November, 2012 issue of the *Journal of the American College of Surgeons*. See: dx.doi.org/10.1016/j.jamcollsurg.2012.06.413

Provided by University of California, San Francisco