Women With Variants in 'CLOCK' Gene Have Higher Risk of Breast Cancer

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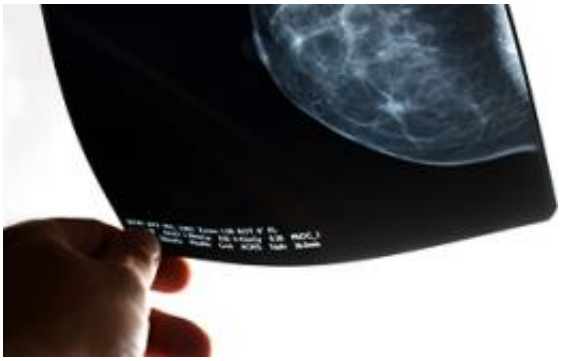

(PhysOrg.com) -- A Yale University-led team of researchers has demonstrated for the first time that variants in a gene responsible for regulating the body's circadian rhythm may lead to breast cancer. The study appears as an OnlineFirst publication of the journal *Cancer Research*.

Previous studies have shown that prolonged disruption of circadian cycles - for example working the "night shift" - may negatively affect cellular function, putting women at increased risk of breast cancer. However, the biological mechanisms for this association remain poorly understood. The Yale team showed that genetic and epigenetic changes in the "CLOCK" gene, which is a key component of the molecular circadian regulatory system and enhances the expression of a variety of

genes, may trigger breast cancer susceptibility.

Epigenetic variants are those that influence gene regulation without altering the DNA code directly. The Yale team found that there was significantly less methylation (a chemical process that often leads to decreased gene expression) in the promoter region (which facilitates gene transcription) of the CLOCK gene in breast cancer patients, compared to the same region in cancer-free individuals.

According to the study's principal investigator, Yong Zhu, Ph.D., associate professor of epidemiology and public health at Yale School of Medicine, "The next step will be to determine whether environmental factors, such as exposure to light at night, have the ability to induce epigenetic alterations, such as those we observed in the CLOCK promoter. This would provide a specific mechanism by which environmental circadian disruption could influence breast cancer risk in women."

The Yale team found that the CLOCK gene is overexpressed in breast cancer tumor tissue, and that there was an even greater effect in women with estrogen and progesterone receptor-negative tumors, which is a more aggressive form of breast cancer. "Future research will focus on understanding whether the circadian genes play a role in breast cancer by influencing hormone regulation, or whether other cancer pathways are perhaps more relevant," Zhu said.

Provided by Yale University