Aspirin may interact with cells' DNA modifications to alter breast cancer outcomes

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New findings suggest that women with specific DNA characteristics in certain areas of the genome may live longer if they take aspirin before they are diagnosed with breast cancer. Published early online in

CANCER, a peer-reviewed journal of the American Cancer Society, the findings point to the need for studies on the potential of aspirin to prevent or treat breast cancer in some individuals.

It is often unclear why some patients benefit from a particular therapy while others do not. In some cases, gene sequences play a role, but in other cases, chemical modifications to DNA may be important. The latter are termed epigenetic changes, and they include a process called DNA methylation.

Tengteng Wang, Ph.D., MSPH, and her mentor Marilie Gammon, Ph.D., of the University of North Carolina at Chapel Hill, wondered whether DNA methylation may influence the effects of aspirin in patients with breast cancer. The team examined DNA methylation in breast tumor tissues—including at DNA sites that control the expression of 13 breast cancer-related genes—and also in cells circulating in patients' blood. The study is the first to examine the effect of DNA methylation on the association between aspirin use and mortality in women with breast cancer.

In the study of 1266 women who were diagnosed with breast cancer during the 1996-1997 period, 476 died from any cause and 202 died specifically from breast cancer by the end of 2014. In women who used aspirin, the risk of dying from any cause and the risk of dying from breast cancer was lower among those whose DNA was not methylated in the region that controlled expression of the breast cancer-related BRCA1 gene. Other methylation patterns related to aspirin use and mortality were also observed.

The authors noted that the findings could help identify individuals who may benefit from aspirin after a breast cancer diagnosis due to their cells' DNA methylation profile. Future research should consider a more comprehensive DNA methylation profile in order to better characterize

women who are at risk.

"Consideration of DNA methylation profiles as potential modifiers of the aspirin-mortality association may provide new insights on the underlying biological mechanisms on aspirin use in relation to mortality after breast cancer diagnosis," said Dr. Wang. "Our findings, if confirmed, may also impact clinical decision-making by identifying a subgroup of patients, using epigenetic markers, for whom pre-diagnosis aspirin use impacts subsequent mortality, and may help refine risk reduction strategies to improve survival among women with breast cancer," added Dr. Gammon.

In an accompanying editorial, Kristen Malecki, Ph.D., MPH, of the University of Wisconsin-Madison, noted that the findings support the importance of research examining interactions between epigenetics and low-cost therapies such as aspirin. According to Dr. Malecki, "The study by Wang et al. shows that beyond gene-environment interactions, epigenetic and environment interactions also exist, and suggest that DNA methylation could in the future help to support the identification of individuals for whom treatment may or may not be successful.

More information: "Pre-diagnosis aspirin use, DNA methylation, and mortality after breast cancer: a population-based study," *CANCER* (2019). DOI: 10.1002/cncr.32364

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