

Researchers find more clues to causes of breast cancer

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Publishing in the current issue of The Journal of Biological Chemistry (Vol. 286, No 43), researchers at Moffitt Cancer Center in Tampa, Fla., have discovered additional mechanisms of "Akt" activation and suggest a component of that activation mechanism - inhibitor of nuclear factor kappa-B kinase subunit epsilon (IKBKE) - could be targeted as a therapeutic intervention for treating cancer.

Akt, also known as protein kinase B, is one of about 500 protein kinases in the human genome. Kinases are known to regulate the majority of cellular pathways. Akt modifies other proteins chemically and regulates cell proliferation.

"Recent evidence suggests that IKBKE is an oncogenic kinase that participates in malignant transformation and tumor development," said Moffitt senior researcher and lead author Jin Q. Cheng, Ph.D., M.D.

"Our study identified Akt as a bona fide substrate of IKBKE and IKBKE direct activation of Akt independent PI3K and revealed a functional link between IKBKE and Akt activation in [breast cancer](#)."

Cheng's lab studies a variety of genetic alterations and their molecular mechanisms in both ovarian and breast cancer, particularly on their effect on the molecules that are regulated by Akt and the small molecule inhibitors of Akt.

"We found that inhibition of Akt suppresses IKBKE's oncogenic transformation," said Cheng. "This is significant because overexpression

of IKBKE and activation of Akt has been observed in more than 50 percent of human cancers. Akt inhibitors targeting PH domain do not have inhibitory effect on IKBKE-induced Akt."

The researchers experimented with a variety of inhibitors currently being used in clinical trials.

The laboratory study utilized breast cancer cell lines from received from patient donors at Moffitt and cell lines received from Harvard University and Johns Hopkins University. The work was supported by a National Institutes of Health grant and a grant from the James and Esther King Biomedical Research Program.

Provided by H. Lee Moffitt Cancer Center & Research Institute

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