

Breast inflammation is key to cancer growth, researchers say

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It took 12 years and a creation of a highly sophisticated transgenic mouse, but researchers at Kimmel Cancer Center at Jefferson have finally proven a long suspected theory: Inflammation in the breast is key to the development and progression of breast cancer.

In the December 15 issue of <u>Cancer Research</u>, the scientists say they can now definitively show that an inflammatory process within the breast itself promotes growth of breast cancer stem cells responsible for tumor development.

They also demonstrate that inactivating this inflammation selectively within the breast reduced activity of these stem cells, and stopped breast cancer from forming.

"These studies show for the first time that inactivating the NFKB inflammatory pathway in the breast epithelium blocks the onset and progression of breast cancer in living animals," says Richard G. Pestell, M.D., Ph.D., Director, Kimmel Cancer Center and Chairman of Cancer Biology.

"This finding has clinical implications," says co-author Michael Lisanti, Leader of the Program in Molecular Biology and Genetics of Cancer at Jefferson. "Suppressing the whole body's inflammatory process has side effects. These studies provide the rationale for more selective antiinflammatory therapy directed just to the breast."



Dr. Pestell and his colleagues show the "canonical" NFKB pathway promotes breast <u>cancer development</u>: the first "insult" is provided by the HER2 <u>oncogene</u>, which then activates NFKB (nuclear factor kappa-light-chain-enhancer of activated <u>B cells</u>). NFKB turns on inflammation via tumor-associated <u>macrophages</u> (TAM), which produce <u>tumor growth</u> promoting factors.

Although inflammation, mediated by NFKB, has long been thought to be important in breast cancer development, the theory had been untestable because NF- κ B is essential to embryonic development, Dr. Pestell says. "When you try to knock out NFKB genes in mice, they die."

He addressed this problem by creating a mouse in which the inflammatory system within the adult animal's normal breast could be regulated. This allows selective inactivation of NFKB in different cell types and took 12 years to accomplish, Dr. Pestell says. "These mice have five co-integrated transgenes."

The mice are programmed to develop <u>breast cancer</u>, but the researchers found that if they selectively blocked inflammation just in the breast, tumors would not develop. "This is a very novel finding," Dr. Pestell says.

They then demonstrated that this inactivation also reduced the number of cancer stem cells in the breast. "That told us that inflammation, through the action of NF- κ B, is important to the growth and activity of cancer stem cells," Dr. Pestell says. "The transgenic mice are a new technology that can be used by the scientists and the pharmaceutical industry to understand the role of NFKB in different diseases including heart disease, neurodegeneration and other cancers."

Provided by Thomas Jefferson University



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