Study Describes Novel Model of Skin Cancer

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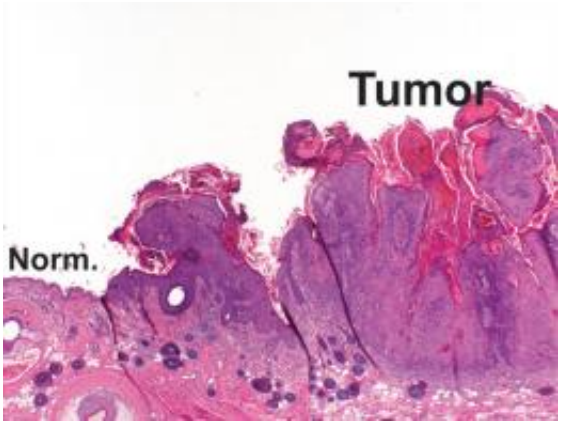

Normal skin (Norm) with adjacent squamous cell carcinoma (Tumor). Credit: John T. Seykora, MD, PhD, University of Pennsylvania School of Medicine

(PhysOrg.com) -- Scientists at the University of Pennsylvania School of Medicine have developed a new model of skin cancer based on the knowledge that a common cancer-related molecule called Src kinase is activated in human skin-cancer samples.

“Our previous work demonstrated that Src kinases are activated in human squamous cell carcinomas of the skin. We modeled these observations by increasing the expression of the gene Fyn, a member of Src family of proteins, in mouse skin,” explains senior author John T. Seykora MD, PhD, assistant professor of Dermatology. In addition, prior work by the Seykora lab on a related protein called Srcasm, discovered by him in 2002, suggested that Srcasm may function as an anti-

oncogene, a molecule that keeps others in check in order to control cell growth.

In this proof-of-principle study, published this month in *Cancer Research*, the authors found that genetically engineered mice expressing a K14-Fyn transgene develop precancerous lesions and invasive squamous cell carcinomas (SCCs) spontaneously in 5 to 8 weeks. Skin SCCs are the second most common form of cancer, with greater than 250,000 cases annually in the US, leading to approximately 2,500 deaths.

This study demonstrates that Fyn is a potent oncogene in skin. When Srcasm levels are raised in the mouse skin cancer model, tumor formation is dramatically inhibited showing that Srcasm functions as an anti-oncogene.

The findings highlight an important relationship between Fyn and Srcasm—Fyn encourages growth, while Srcasm inhibits it. “When this system malfunctions, it’s like stepping on the gas and taking off the brakes on cell growth,” explains Seykora. “Adding Srcasm back to the system lowers Fyn levels and restores order.”

Analysis of human skin tumor samples confirmed that Srcasm levels are decreased and Src kinase activity is increased. The authors conclude that one potential means of combating skin cancer would be to inhibit Src kinases and/or increase Srcasm levels.

This work may have broader relevance as Src kinases are one of the longest studied oncogenes and are activated in many types of human cancer, including colon and breast cancer. This study provides insight into how Src kinases are activated in human cancers. Further study of this model may provide insights into treating carcinomas that have increased Src kinase activity.

Future work will involve determining how Srcasm levels are decreased in skin tumors to promote cell growth. In addition, topical compounds will be tested using this model to determine if they may be useful in treating skin cancer in people.

Provided by University of Pennsylvania School of Medicine (news : web)