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Gene found to play a suppressor role in skin cancer development

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Researchers at the Burnham Institute for Medical Research (Burnham Institute) have provided genetic evidence that Activating Transcription Factor 2 (ATF2) plays a suppressor role in skin cancer development. ATF2 is a protein that regulates gene transcription, which is the first step in the translation of genetic code, in response to extracellular stresses such as ultraviolet light and ionizing radiation. This function of ATF2 in stress and DNA damage response suggests that it may also play a role in the formation of tumors.

Previous studies led by Ze'ev Ronai, Ph.D. have suggested an important role of ATF2 in melanoma development and progression. In this new study, published in this week's issue of Proceedings of the National Academy of Sciences of the United States of America, the Ronai laboratory, in collaboration with Nic Jones, Ph.D. from the University of Manchester UK, used a mouse model that expresses a transcriptionally inactive form of ATF2 in skin cells (keratinocytes). When the mice were subjected to chemically mediated skin carcinogenesis, tumors appeared faster and more frequently. These findings reveal that loss of ATF2 transcriptional activity in skin exposed to carcinogens enhances skin tumor formation, suggesting a tumor suppressor role for ATF2 in keratinocytes.

"Important support for the finding comes from the analysis of tumor samples from human patients with non malignant skin cancer," states Dr. Ronai. "Unlike the strong nuclear expression of ATF2 in normal skin, squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) samples

exhibit a significantly reduced nuclear staining for ATF2."

The analysis of human skin cell carcinomas are also consistent with the reduced expression of ATF2 found in the papillomas that developed in the wild-type animals in this study, supporting the notion that ATF2 needs to be inactivated to support skin tumor development.

The group also identified ATF2 as an upstream regulator of genes including Presenilin1 (PS1), Notch1, and â-catenin, all of which have previously been reported to be involved in skin tumor development; thus providing an example of a mechanism by which ATF2 functions as a tumor suppressor.

Source: Burnham Institute