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Study finds gene associated with aggressive skin cancer

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The loss of a gene known as INPP5A could predict the onset, and track the progression, of an aggressive type of skin cancer, according to a study published today by the Arizona Cancer Center, Mayo Clinic and the Translational Genomics Research Institute (TGen).

Targeting INPP5A could provide physicians with better ways to prevent and treat cutaneous squamous cell carcinoma, or SCC, a skin cancer that often spreads to other parts of the body, according to a scientific paper published today in the journal *Cancer Prevention Research*.

"Loss of INPP5A can be detected in most primary SCC tumors and even in actinic keratoses, or AK, the earliest stage in SCC development," said Aleksandar Sekulic, M.D., Ph.D., an Assistant Professor of Dermatology at Mayo Clinic in Arizona, and the study's lead author. "Importantly, further reduction of INPP5A was detected as a subset of SCC tumors progressed from primary to metastatic stage."

More than 1 million non-melanoma skin cancers are diagnosed annually in the U.S., making these the most common type of cancer and the fifth most costly cancer type in the Medicare population, those Americans age 65 and older. The vast majority of non-melanoma skin cancers are basal cell carcinoma and SCC.

"At present, our ability to assess who is at risk for SCC and our ability to treat the disease, especially in its aggressive forms, is clearly inadequate," said Dr. Jeffrey Trent, President and Research Director of

TGen and one of the study's authors. "Without question, additional investigations into INPP5A are warranted. Studies like this are critical if we are to ever get a handle on this all-too-common type of skin cancer."

The study used TGen's advanced genomic technologies to analyze 40 skin tissue samples that ranged from normal skin to highly invasive SCC. Specifically, researchers used a technique called high-resolution array-based comparative genomic hybirdization to identify genetic deletions in a portion of DNA that normally harbors the INPP5A gene.

INPP5A, or inositol polyphosphate-5-phosphatase, interacts within the chemical pathways of cells to limit their proliferation, suggesting that this gene may play a key role as a tumor suppressor. In other studies, the loss of genetic material in the chromosome that includes INPP5A has been associated with brain tumors and leukemias.

Genetic mutations contribute to the development and progression of cancer by either stimulating cells to multiply too rapidly, or interfering with normal processes that allow them to die off, according to the paper, Loss of Inositol Polyphosphate-5-Phosphatase is an Early Event in Development of Cutaneous Squamous Cell Carcinoma.

"Understanding the precise mechanisms of INPP5A loss, and exploring the connection between INPP5A and uncontrolled cellular proliferation, could provide us with new insights," said Dr. Michael Bittner, Co-Director of TGen's Computational Biology Division, and the study's senior author. "Continuing studies could lead to new drug targets that could contribute to better treatments for patients with SCC, and some day perhaps even help prevent this type of skin cancer."

Tissue samples and research collaborations for the study were provided by: the University of Arizona's Arizona Cancer Center in Tucson; the Southern Arizona Veterans Affairs Health Care System in Tucson;

Loyola University Medical Center in Chicago; and Mayo Clinic.

Dr. David S. Alberts, Director of the Arizona Cancer Center, is the Principal Investigator for a cancer prevention grant from the National Institutes of Health, which provided the main funding for the study.

"Observed deletions in INPP5A represents a highly selected, non-random genetic event in SCC, giving researchers confidence that this is a biomarker with great potential for clinical study and patient benefit," said Dr. Alberts, another author of the paper and a Regents Professor of Medicine, Pharmacology, Nutritional Science and Public Health at the University of Arizona College of Medicine.

Provided by The Translational Genomics Research Institute