Study targets SGEF protein in treating glioblastoma brain tumors

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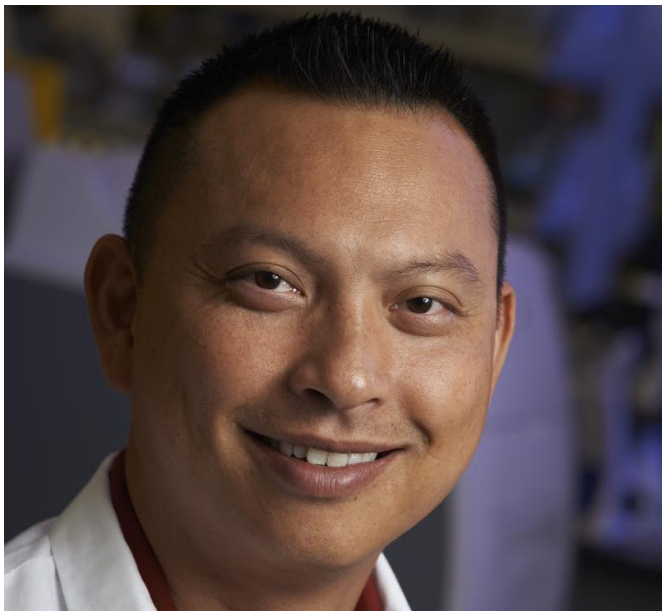

Dr. Nhan Tran, is Associate Professor and head of TGen's Central Nervous System Tumor Research Lab and the study's senior author. Credit: TGen

The Translational Genomics Research Institute (TGen) has identified a protein called SGEF that promotes the survival of glioblastoma tumor cells and helps the cancer invade brain tissue.

TGen researchers identified SGEF as a target for new brain cancer therapies in a study published today by *Molecular Cancer Research*, a journal of the American Association for Cancer Research, the world's largest professional organization dedicated to advancing cancer research.

Glioblastoma multiforme, or GBM, is the most common primary tumor of the brain and central nervous system. One of the primary treatments for glioblastoma is surgical removal of the tumor. However, because of the aggressive way glioblastomas invade surrounding brain tissue, it is impossible to remove all parts of the tumors, and the cancer eventually returns and spreads.

This study found that SGEF also plays a role in how glioblastoma tumors develop resistance to treatment. Following surgery, GBM is treated with radiation and the standard-of-care chemotherapy drug called temozolomide (TMZ),

"We need to identify the genetic and cellular-pathway signaling mechanisms that make brain tumors resistant to treatment," said Dr. Nhan Tran, Associate Professor and head of TGen's Central Nervous System Tumor Research Lab. "And the role of SGEF in promoting chemotherapeutic resistance highlights this previously unappreciated protein. Importantly, this also suggests that SGEF could be a new candidate for development of targeted therapeutics," said Dr. Tran, the study's senior author.

This study was funded, in part, by The Ben & Catherine Ivy Foundation.

"Contributing to the progress, TGen studies are helping uncover the mysteries behind glioblastoma," said Catherine (Bracken) Ivy, founder and president of the Arizona-based Ben & Catherine Ivy Foundation. "This research is fundamental to helping patients survive longer and critical to our goal of improving treatments, and eventually finding a cure."

The ability of cancer cells to survive is influenced by the proteins that regulate cellular pathways involved in promoting how cells grow, replicate and spread, as well as whether cells will die when exposed to anti-cancer drugs. Radiation and drug treatment of GBM can lead to DNA damage. This study shows that SGEF promotes cancer cell survival in response to TMZ treatment by allowing tumor cells to rapidly repair the damaged DNA that otherwise would lead to cell death.

"Our study shows that SGEF may have an important role in helping cells survive injury—known as the pro-survival cellular signaling response—including injury to common drugs used to treat brain cancer such as TMZ," said Dr. Shannon Fortin Ensign, the study's lead author.

"The roles of invasion and survival are interconnected in the promotion of disease progression," said Dr. Fortin Ensign, a former researcher at TGen who now is a resident in Internal Medicine at Scripps Green Hospital in La Jolla, Calif. "SGEF presents a novel hub in the interrelated axes of tumor cell invasion and survival."

The study, SGEF is Regulated via TWEAK/Fn14/NF-?B Signaling and Promotes Survival by Modulation of the DNA Repair Response to Temozolomide, was published online today by AACR's *Molecular Cancer Research*.

Provided by The Translational Genomics Research Institute