

Team identifies drug that could limit the spread of deadly brain tumors

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In a significant breakthrough, the Translational Genomics Research Institute (TGen) has identified a drug, propentofylline or PPF, that could help treat patients with deadly brain cancer.

In a study published today in the *Journal of NeuroOncology*, TGen researchers report that PPF works to limit the spread of glioblastoma multiforme, or GBM—the most common [primary tumor](#) of the brain and central nervous system—by targeting a protein called TROY.

In addition, TGen laboratory research also found that PPF increases the effectiveness of a standard-of-care chemotherapy drug called temozolomide (TMZ), and radiation, to treat glioblastoma.

"We showed that PPF decreased glioblastoma cell expression of TROY, inhibited glioma cell invasion, and made [brain cancer](#) cells more vulnerable to TMZ and radiation," said Dr. Nhan Tran, Associate Professor and head of TGen's Central Nervous System Tumor Research Lab.

An advantage of small-molecule PPF—which has been previously used in clinical trials in an attempt to treat Alzheimer's disease and dementia—is that it can penetrate the blood-brain barrier and reach the tumor. And, the FDA has already approved it.

"Our data suggests that PPF, working in combination with TMZ and radiation, could limit glioblastoma invasion and improve the clinical

outcome for brain tumor patients," said Dr. Tran, the study's senior author.

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

"GBM is one of the most aggressive of all cancers and it affects people of all ages," said Catherine (Bracken) Ivy, founder and president of The Ben & Catherine Ivy Foundation. "Funding research focused on helping patients survive longer is critical, and studies such as this advance our goal of not only improving treatments for brain cancer, but eventually finding a cure."

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 insidious cancer invasion also limits the effectiveness of chemotherapy drugs and radiation therapy.

TGen found that PPF works to limit the spread of glioblastomas by targeting and knocking down the expression of the TROY protein. TGen researchers have linked TROY to the cellular mechanisms that enable glioblastomas to invade normal brain cells, and resist anti-cancer drugs.

"New therapeutic strategies that target the molecular drivers of invasion are required for improved clinical outcome," said Dr. Harshil Dhruv, a TGen Research Assistant Professor and lead author of the study.

"Propentofylline may provide a pharmacologic approach to targeting TROY, inhibiting cell invasion and reducing therapeutic resistance in glioblastomas."

One of the fundamental challenges in treating brain cancer with drugs is what is known as the blood-brain barrier that separates circulating blood

from the brain extracellular fluid in the central nervous system. This barrier works to protect the brain from toxins. However, this security system is so effective at protecting the brain that it prevents many life-saving drugs—all but some small molecules—from being able to treat cancer and other diseases of the brain.

As a result, there has been little progress in recent decades in finding new effective treatments for GBM. Median survival for newly diagnosed GBM patients is only 14.6 months. Only 5 percent of patients survive more than 5 years.

"Clinical trials revealed that PPF can cross the blood-brain barrier, and has minimal side effects," Dr. Tran said. "PPF could be easily translated to the clinic as an adjuvant therapy in combination with standard of care treatment for GBM patients."

More information: Harshil D. Dhruv et al. Propentofylline inhibits glioblastoma cell invasion and survival by targeting the TROY signaling pathway, *Journal of Neuro-Oncology* (2015). [DOI: 10.1007/s11060-015-1981-0](https://doi.org/10.1007/s11060-015-1981-0)

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