

Study provides comprehensive look at brain cancer treatments

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Led by the Translational Genomics Research Institute (TGen) and UC San Francisco (UCSF), a comprehensive genetic review of treatment strategies for glioblastoma brain tumors was published today in the Oxford University Press journal *Neuro-Oncology*.

The study, *Towards Precision Medicine in Glioblastoma: The Promise and The Challenges*, covers how these highly invasive and almost-always-deadly brain cancers may be treated, reviews the continuing challenges faced by researchers and clinicians, and presents the hope for better treatments by harnessing the power of the [human genome](#).

The study also describes a pioneering clinical trial underway for 15 patients at UCSF, guided by TGen research, in which an individual patient's genomic profile is used to offer treatment recommendations to an expert, multidisciplinary panel.

"This study thoroughly explores how we arrived at the current standard-of-care, and how—through cutting-edge genomic technologies—we might find better answers for these patients who need our help today," said Dr. Jeffrey Trent, TGen President and Research Director and the study's senior author.

Funded by The Ben & Catherine Ivy Foundation, the study is one of several simultaneous and coordinated efforts seeking to uncover the molecular source of this deadly [brain cancer](#) with the goal of prolonging survival of [glioblastoma](#) patients.

"Despite pivotal advances in the characterization of genomic mutation in glioblastoma, targeted drug agents have so far shown minimal effect in [clinical trials](#), and patient survival remains poor," said Dr. Michael D. Prados, the Charles B. Wilson, MD, Endowed Chair in Neurological Surgery at UCSF,

and one of the study's co-lead authors.

One of the major difficulties in treating [brain tumors](#) is finding drugs that can penetrate the blood-brain barrier, which buffers the brain from the rest of the body's blood-circulatory system. Located along capillaries, the blood-brain barrier protects the brain from rapid changes in the body's metabolic conditions and minimizes exposure to molecules that are toxic to neurons in the brain.

"This study outlines strategies for overcoming past failures, primarily by applying targeted combination therapies that match the tumors' genetic changes with drug compounds that can reach the central nervous system," said Dr. Sara Byron, Research Assistant Professor in TGen's Center for Translational Innovation, and the study's other co-lead author.

Another major challenge in treating glioblastoma is its intrusive penetration into adjoining tissues, which prevents the complete surgical removal of the tumors from the brain, even with follow-up radiation and chemotherapy: "It is this invasive, infiltrative disease component that is the ultimate cause of recurrence, resistance and death," the study says.

"All patients will continue to show tumor growth and progression because of rapidly proliferating infiltrative disease remaining after surgery," according to the study. "Effective treatment for glioblastoma remains an unmet need."

The only FDA-approved drugs to treat glioblastoma are temozolomide, nitrosoureas, and bevacizumab.

In the clinical trial begun at UCSF, multiple biopsies are performed on each patient at the time of surgery in different regions of the brain tumor. That is followed by extensive genome-wide profiling, leading to a selection of drugs that would target the brain cancer and diffuse regions of the lesion that

cannot be removed by surgery.

Drug selection is individualized, and multiple FDA-approved agents (up to four) allowed. "Rules" for drug selection are implemented, using the specialized drug pharmacopeia designed for this trial. The drugs are chosen carefully, considered with knowledge about the ability of the drug to reach the brain and the patient's past treatment history and concomitant therapies, with the assistance of multi-specialty, multi-institutional molecular tumor board that drafts a report to the treating physician.

In addition, "Small, informative, tissue-based clinical trials that take into account the individual molecular features of patients and provide early 'go' or 'no go' decisions are needed and should be prioritized over unselected, large, population-based strategies," the study recommends.

A separate clinical trial that follows this path, also guided by TGen genomic research, is underway at Barrow Neurological Institute. This clinical trial also is funded by The Ben & Catherine Ivy Foundation. For more about this clinical trial, go to: <http://www.tgen.org/home/news> and click on March 10, 2015.

"These studies, and their associated clinical trials, have the potential to lift our knowledge of glioblastoma to an unprecedented new level," said Catherine Ivy, President of The Ben & Catherine Ivy Foundation. "Developing drug compounds that breach the blood-brain barrier and are effective against tumors would fulfill one of the medical community's most critical unmet needs, and boost the hopes of [brain](#) tumor patients everywhere."

Provided by The Translational Genomics
Research Institute

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