

## Researchers discover potential new target for treating glioblastoma

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Dr. Ralf Kittler, with the Eugene McDermott Center for Human Growth and Development, and Dr. Robert Bachoo, with the Annette G. Strauss Center for Neuro-Oncology, are part of UT Southwestern's precision medicine campaign in neuro-oncology. Credit: UT Southwestern Medical Center

Scientists have found a way to inhibit the growth of glioblastoma, a type of brain cancer with low survival rates, by targeting a protein that drives growth of brain tumors, according to research from the Peter O'Donnell Jr. Brain Institute and Harold C. Simmons Comprehensive Cancer Center.

"These findings change our fundamental understanding of the molecular basis of glioblastoma, and how to treat it," said co-senior author Dr. Robert Bachoo, Associate Professor of Neurology and Neurotherapeutics, Internal Medicine, and with the Annette G. Strauss Center for Neuro-Oncology at UT Southwestern Medical Center. "We may have identified a set of critical genes we can target with drugs that are shared across nearly all glioblastomas."

The study, <u>published</u> in *Cell Reports*, represents research from UT Southwestern's precision

medicine campaign in neuro-oncology.

For the past decade, patients diagnosed with glioblastoma have been treated with the current standard of care regimen: surgery followed by chemotherapy and radiation. This regimen improves median survival by an average of four to six months, followed by recurrence of the tumor. There are currently no successful therapies available to treat glioblastoma patients when the tumor recurs. Five-year survival rates are around 5 percent.

Faced with these prospects, the brain tumor research and clinical communities turned to genetic studies to guide possible treatment strategies.

"Our work shows that the gene mutations which the pharmaceutical industry and clinicians have been focusing on are essential only for starting tumor growth. Once the tumor has advanced to the stage where patients seek treatment, these mutations are no longer required for continued tumor growth; they are in effect redundant," said Dr. Bachoo, a member of the Simmons Cancer Center and O'Donnell Brain Institute, who holds the Miller Family Professorship in Neuro? Oncology. Previously, proteins called drivers of glioblastoma; however, drugs that inhibit

receptor tyrosine kinase were considered the these proteins have not been effective in treating this type of cancer.

"We learned that, instead, it is neurodevelopmental transcription factors (master proteins that regulate the activity of hundreds of genes during normal brain development), which are reactivated to drive the growth of glioblastoma. We can inhibit these transcription factors and prevent further tumor growth with the chemotherapy drug mithramycin, a drug that has not been in clinical use for years due to its side effects," said co-senior author Dr. Ralf Kittler, Assistant Professor of Pharmacology in the Eugene McDermott Center for Human Growth and



Development. "Our discovery has the potential for the development of a new therapy that may increase survival time for glioblastoma patients."

Dr. Kittler, a member of the Simmons Cancer Center and the Cecil H. and Ida Green Center for Reproductive Biology Sciences, is a Cancer Prevention and Research Institute of Texas (CPRIT) Scholar in Cancer Research and John L. Roach Scholar in Biomedical Research.

The researchers caution that repurposing mithramycin, which is known to cause liver toxicity in some patients, with safer and more effective treatments for brain tumor patients may take years.

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