

Researchers develop approach for identifying tumor targets when genetic drivers are unknown

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Ependymoma is a type of brain tumor that is resistant to chemotherapy. While genomic sequencing has provided molecular targets and resulted in precision oncology therapies for many cancers, effective targets for ependymomas have remained elusive. Dr. Stephen Mack, assistant professor of pediatrics – oncology and new faculty member at Baylor College of Medicine and Texas Children's Hospital, and colleagues have developed a framework for discovering targets in ependymomas, and other cancer that lack known genetic drivers, thereby also providing insights into treatment strategies. The study appears in *Nature*.

"Ependymoma is the third most common cancer type in children, and there are no current targeted therapies available. Even with surgery and radiation, the more aggressive tumors will keep coming back," said Mack. "Traditional genomic sequencing revealed that these tumors are relatively silent, meaning mutations in the DNA are few. However, we found changes in the way the DNA is folded and packed and how the genes are regulated."

The research team developed a more in depth approach to find the actively transcribed genes that play a role in [tumor](#) formation, as opposed to identifying mutations alone. A specific process in the tumor's epigenome, called histone acetylation, tells genes to turn on or off, thereby regulating the action of the DNA. The team assayed the markers for this process in the ependymoma tumor type and found that the [genes](#)

are highly active in tumor development.

"This is an important strategy to develop because we are looking at gene regulation specifically as a new approach to targeted therapy for cancers in which there are no known [molecular targets](#)," said Mack. "It can act as a complimentary tool to [genomic sequencing](#) to identify potential targets, and could later be useful in developing drug treatment plans."

"As a neurosurgeon, it is very frustrating to operate on babies with [ependymoma](#), and then not have any effective chemotherapy. This new approach to finding effective chemotherapies discovered by Dr. Mack offers a new way forward in this very difficult disease that affects the youngest members of our society," said Dr. Michael Taylor, neurosurgeon and senior scientist in the Program in Stem Cell and Developmental Biology at the Hospital for Sick Children in Toronto.

More information: Stephen C. Mack et al. Therapeutic targeting of ependymoma as informed by oncogenic enhancer profiling, *Nature* (2017). [DOI: 10.1038/nature25169](https://doi.org/10.1038/nature25169)

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