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New tool gives deeper understanding of glioblastoma

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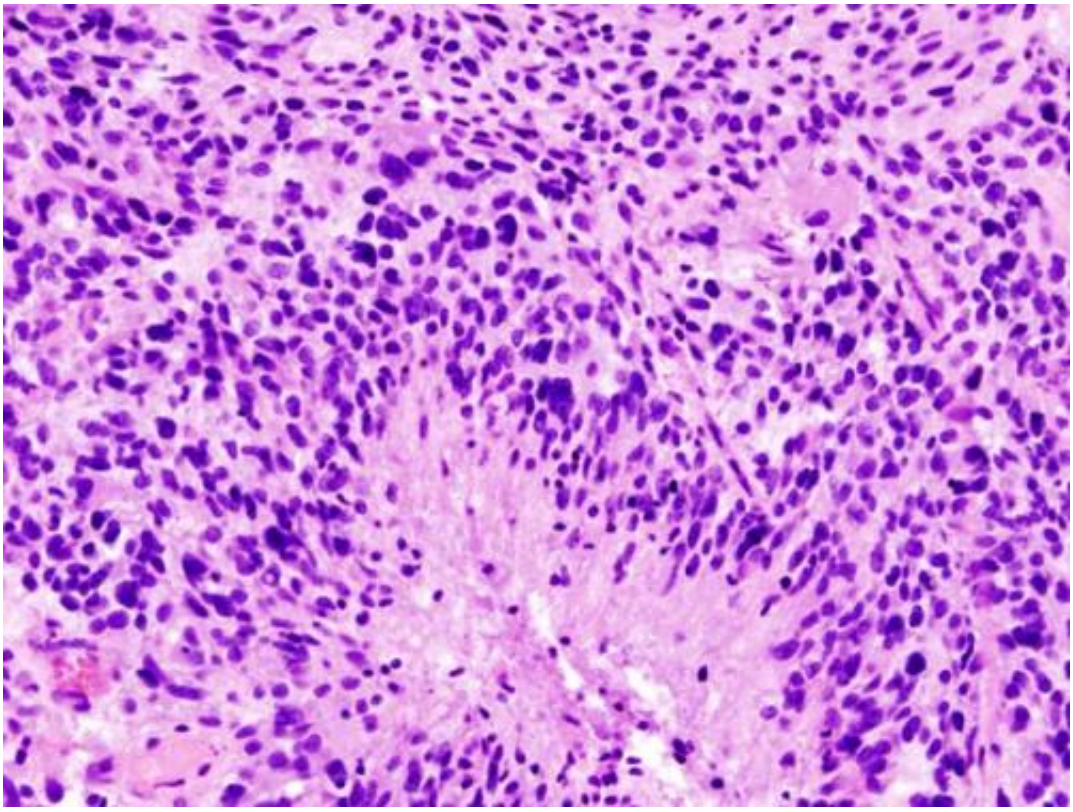

Glioblastoma (histology slide). Credit: Wikipedia/CC BY-SA 3.0

Researchers in the lab of Charles Danko at the Baker Institute for Animal Health have developed a new tool to study genetic "switches" active in glioblastoma tumors that drive growth of the cancer. In a new paper in *Nature Genetics*, they identified key switches in different types of tumors, including switches linked to how long a patient survives.

Glioblastoma is an aggressive cancer that forms in the brain or spinal cord. "It's a devastating disease, and there are no good treatment options," said lead author Tinyi Chu, a graduate fellow in Danko's lab. Even when patients undergo treatment, most survive just 15 months post-diagnosis.

In the new study, Danko's group partnered with colleagues at the State University of New York Upstate Medical University to analyze 20 glioblastoma samples from its tissue bank.

"A lot of diseases, including cancer, fundamentally are defects in how our genes are used, not necessarily in the genes themselves," said Danko, assistant professor of biomedical sciences. Genes make up only two percent of our genome. Switches called transcription factors bind to the genome to turn those genes on and off, which trigger the cellular changes that cause disease.

To analyze the tumors, the researchers used a technique called ChRO-seq that creates a map of which switches are active and which genes they turn on. Co-author Hojoong Kwak, Cornell assistant professor of molecular biology and genetics, initially invented ChRO-Seq as a graduate student at Cornell University, and collaborated with Danko's group to develop the new application.

Using ChRO-seq data, the team was able to classify the glioblastomas into subtypes, based on which particular switches were active in the different tumors compared to healthy brain tissues. They also identified three switches that will be tested in larger studies to determine their ability to predict which patients will survive longer with the disease, including two switches whose connections were previously unknown.

Chu is now analyzing an even larger group of glioblastomas to link patient survival and treatment outcomes with the active switches in each

tumor. He hopes the results could inform personalized treatment plans for patients or help to develop new therapies in the future.

The new technique studies not only cancer, but many other diseases caused by malfunctions in gene regulation, such as certain types of heart or autoimmune diseases. "ChRO-seq gives you a lot of information about what switch is turning on a tumor or a diseased cell," said Danko. "It gives you a starting point to think about how you can shut that switch off."

More information: Tinyi Chu et al, Chromatin run-on and sequencing maps the transcriptional regulatory landscape of glioblastoma multiforme, *Nature Genetics* (2018). DOI: 10.1038/s41588-018-0244-3

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