

Genome sequencing uncovers therapy for rare brain tumor

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A microscopic image of chordoid glioma. Credit: University of California, San Francisco

Brain tumors are among the deadliest forms of cancer, due in large part to their sensitive location and the challenge of performing surgery to remove them. New research led by David Solomon, MD, Ph.D., an assistant professor in the Department of Pathology at UC San Francisco, provides much-needed targeted treatment options for patients whose tumors cannot be surgically removed.



Using tumor genome sequencing, Solomon identified the first potential targeted drug to treat chordoid gliomas, a rare type of <u>brain cancer</u> that develops within the third ventricle, a fluid-filled pocket that helps cushion the brain. Although these tumors are slow-growing, their proximity to the hypothalamus – a critical brain region involved in hormone production – makes chordoid gliomas difficult and potentially deadly to remove.

In the study, published on Feb. 23, 2018, in *Nature Communications*, Solomon's team sequenced the genomes of 13 chordoid glioma tumors and identified a single mutation in one gene, PRKCA, that was consistent across all 13 samples. PRKCA is part of a key growth pathway, called MAP kinase, that is turned off in normal brain <u>cells</u>. The mutation in PRKCA activates this MAP kinase pathway, causing the cells to divide dangerously and form a tumor.

While PRKCA is not yet known to be mutated in any other type of cancer, Solomon says most human tumors activate this same growth pathway via one genetic mechanism or another.

Because the MAP kinase pathway is so commonly implicated in cancer, drugs that target it are already available and approved by the FDA. The researchers tested trametinib, a drug used to treat melanoma, on brain cells with the PRKCA mutation. The drug effectively stopped <u>tumor</u> growth in cells carrying the mutation. Solomon is now working with neuro-oncologists at UCSF Medical Center to set up a nationwide clinical trial for patients with chordoid gliomas.

Solomon says identifying the genetic signatures of cancers may reveal their vulnerabilities and ways to stop them. "Precision medicine for cancer is based on identifying the DNA alterations that are behind the tumor. Then we can figure out what that DNA alteration does inside the cells to cause the tumors to form," he says. "Once we know that, then we



can predict drugs to give to inhibit the activated pathways and stop the <u>tumor</u> growth."

More information: Benjamin Goode et al. A recurrent kinase domain mutation in PRKCA defines chordoid glioma of the third ventricle, *Nature Communications* (2018). DOI: 10.1038/s41467-018-02826-8

Provided by University of California, San Francisco

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