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Researchers identify three single-driver genetic alterations that occur in neuroepithelial tumors

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The St. Jude Children's Research Hospital – Washington University Pediatric Cancer Genome Project (PCGP) has identified critical driver genes that account for disease-related alterations in a range of uncommon low-grade neuroepithelial tumors. These diverse brain tumors grow slowly and are found in some children and young adults, many of whom have a history of epilepsy. The study describing the genetic alterations has just been published online in the journal *Acta Neuropathologica*. The study represents an extension of the authors' earlier PCGP analysis of common low-grade gliomas published in *Nature Genetics* in 2014.

The researchers identified three single-driver genetic alterations known as *BRAF*, *FGFR* and *MYB* that occur at high frequency in these types of tumors and which correspond to the pathologic features of the disease. The findings offer improved options not only for characterization and diagnosis of these low-grade neuroepithelial tumors but also for new treatment options.

"Low-grade neuroepithelial tumors are varied, and some types are rare, particularly those associated with chronic epilepsy. Until now, genetic alterations driving the growth of many of these rare tumors have largely been unknown," said corresponding author David Ellison, M.D., Ph.D., St. Jude Department of Pathology chair, the study's principal investigator. "Our findings have shown that many of the tumors we studied are caused by relatively few key genetic alterations, some of which have new drug therapies in development."

The researchers conducted next-generation DNA sequencing of samples from tumors obtained from 91 patients who had an average age of 10 years. Whole-genome, whole-exome and transcriptome sequencing revealed that 78 percent of these low-grade neuroepithelial tumors could be pinned down to single alterations in the *BRAF*, *FGFR* or *MYB* genes.

Overall survival of patients with common low-grade neuroepithelial tumors is good mainly because such tumors occur in locations amenable to surgical removal. However, a significant number of the less common types of low-grade neuroepithelial tumors are more challenging to remove surgically and may lead to long-term illness and premature death. Therapeutic options are already being tested in clinical trials that target the effects of some of the driver genes identified in the study. This may lead to new treatment options.

Increasingly, the profiling of genetic alterations is being incorporated into the diagnosis of many types of disease. "Our genetic analysis should help the diagnosis of low-grade neuroepithelial tumors that present similar cytological features," said co-author Richard K. Wilson, Ph.D., director of The McDonnell Genome Institute at Washington University School of Medicine in St. Louis. "Genome sequencing allows us to have more information for each tumor type and can help in classifying some of the tumors that are less amenable to study by other diagnostic methods."

Source:
St. Jude Children's Research Hospital