

Elusive gene mutations found for malignant brain tumor

August 4 2011

A discovery by scientists at Duke University Medical Center and Johns Hopkins University could increase the chances for an effective combination of drug therapy to treat the second most common type of brain tumor.

For years scientists have been looking for the primary cancer genes involved in the development of oligodendrogliomas. Scientists knew the two chromosomes that held the probable [mutations](#), but not the particular gene information.

Now scientists at Duke and Johns Hopkins have discovered the most likely [genetic mutations](#) that researchers have been hunting for on [chromosomes](#) 1 and 19. These genes were difficult to find until the technology improved, said Hai Yan, M.D., Ph.D., Duke associate professor of pathology and co-corresponding author of the study.

"The team used whole genome sequencing technology so that no genes would be excluded, and we found to our surprise that one gene, on chromosome 19, was mutated in six out of the seven initial tumor specimens we sequenced," Yan said. "A mutation frequency of 85 percent is very high."

The study was published in the Aug. 4 ahead-of-print issue of the journal *Science*.

"Whenever we find genes mutated in a majority of tumors, it is likely

that the pathway regulated by that gene is critical for the development and biology of the tumor," says Nickolas [Papadopoulos](#), Ph.D., co-corresponding author and associate professor of oncology at the Johns Hopkins Kimmel Cancer Center.

The finding of two additional new genes involved in oligodendrogliomas increases the chances for an effective combination drug therapy for the tumor, Yan said. He envisions a combination cocktail of drugs similar to the combination-drug treatments taken by HIV patients that would target different pathways involved in cancer, and assist in reducing the chance of relapsing, increasing odds of success.

The genes they identified are tumor suppressor genes. The cancer-related pathways that involve these genes could become targets for future treatments, Yan said.

"Tumor suppressor genes like the ones we found, CIC or FUBP1, won't be targeted directly by small molecules, because the mutated gene products result in loss of function, but the pathways that these genes are involved in could be targeted," Yan said.

"Another very important feature is that the genes could be used as biomarkers to distinguish this type of cancer from other types of [brain tumors](#)."

The researchers found CIC on chromosome 19 and FUBP1 on chromosome 1 based on an initial study of seven oligodendrogliomas; they found six mutations and two mutations, respectively, in the seven tumors. Further study of 27 more of these tumors showed that there were 12 and three mutations of CIC and FUBP1, respectively. The two genes were rarely mutated in other types of cancers, indicating that they are oligodendroglioma-specific [genes](#).

These tumors also contained a glioma (brain tumor) gene mutation identified earlier by Yan and colleagues, the IDH mutations.

Provided by Duke University Medical Center

Citation: Elusive gene mutations found for malignant brain tumor (2011, August 4) retrieved 26 April 2024 from

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