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Researchers identify genetic alterations that make a type of brain cancer more aggressive

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Among the cancerous brain tumors, 70 percent are astrocytomas. Fatal in as many as 90 percent of cases, astrocytomas originate in the largest and most numerous cells in the central nervous system, called astrocytes because of their star shape.

A study conducted by biologist Valeria Valente, a researcher at São Paulo State University in Brazil, with support from the São Paulo Research Foundation (FAPESP), explores the mechanisms that make astrocytomas so aggressive and seeks ways to customize treatment to patient needs.

The study identified the genetic alterations with the most potential to promote aggressiveness, pointing to possible prognostic biomarkers and genes that could be candidate therapeutic targets. "We discovered a very strong correlation between alterations in the expression of astrocytoma cell repair genes and patient survival prognosis," Valente said.

The study focused on glioblastomas, the most aggressive of the four subtypes into which the World Health Organization (WHO) classifies astrocytomas. Patients with this type of tumor survive 14 months on average.

"The point was to characterize the cellular alterations that promote the aggressive behavior of glioblastomas, tumors with a very high mortality rate. They're practically untreatable owing to their aggressiveness and their location in the brain," Valente explained. The study was published

in *Tumor Biology*.

Valente and her team worked on astrocytoma cells collected from 55 patients submitted to surgical resection for tumor removal at the general hospital of the University of São Paulo's School of Medicine of Ribeirão Preto (FMRP-USP), looking for gene expression signatures associated with patient survival time.

The samples analyzed included cells from 42 glioblastomas (grade IV) and from 12 astrocytomas (six grade III and six grade II), which are still fatal but much less aggressive—patient survival can reach five years.

"In these comparisons, we found 19 genes with significantly altered expression. It was diminished in some genes, but in most cases, it was greatly augmented. Some genes were expressed as much as 100 times more highly in tumor tissue than healthy tissue," Valente said.

"We then defined gene expression signatures representing these alterations, in isolation and in all possible combinations, and investigated whether there was a correlation between the presence of the signature and patient survival."

The search was conducted using publicly available data from a much larger set of cases, giving the study statistical strength. Once they had detected the genetic signatures in the samples, they separated the patients into two groups according to the presence or absence of a specific signature.

The researchers found the average survival time for each group and identified signatures that correlated with shorter prognoses, establishing a methodology capable of predicting the aggressiveness of the disease based on the presence of each gene signature. "An alteration in just one gene could correlate with a worse prognosis," Valente said. "We

developed a strategy to correlate gene signatures with tumor behavior. This can be used to predict patient prognosis and drive the development of novel therapies."

Until a cure is found for the most aggressive astrocytomas, the priority for oncologists is to detect their existence as early as possible so that treatment by surgery, radiation or chemotherapy can begin rapidly and patient survival can be prolonged.

More information: Juliana Ferreira de Sousa et al. Expression signatures of DNA repair genes correlate with survival prognosis of astrocytoma patients, *Tumor Biology* (2017). DOI: 10.1177/1010428317694552

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