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Protein FGL2 may have potential as therapy target for brain cancer

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Blocking FGL2, a protein known to promote cancer, may offer a new strategy for treating brain cancer, according to a study at The University of Texas MD Anderson Cancer Center.

FGL2 (fibrinogen-like protein 2) is commonly expressed in brain cancer tumors and promotes cancer development through suppressing the immune system in several ways, say scientists who demonstrated that it achieves this through manipulation of the proteins, PD1 and CD39.

"It is well known that cancer evades immune surveillance by exploiting a series of editing mechanisms to avoid immune detection and eradication," said Shulin Li, Ph.D., professor of Pediatrics. "One such mechanism is to hijack an immune cell's checkpoints, subverting the immune system and allowing tumor growth."

FGL2 modulates the immune system's "brakes" called checkpoints, as well as immune suppressive cells that stop the immune system's natural attack on cancer cells. Li and fellow co-investigator, Amy Heimberger, M.D., professor of Neurosurgery found that FGL2 acted as a key "switch" to prevent tumors from being detected by the immune system.

The team's results were published in the May 13, 2015 issue of the *Journal of the National Cancer Institute*.

The study, using mouse models, data from The Cancer Genome Atlas (TCGA) and human tumor samples, found that FGL2 increased tumor

growth in mice by enhancing immune checkpoint gene expression. The research team neutralized the protein by using an anti-FGL2 antibody.

"The average survival time in mice treated with the antibody was significantly longer than those receiving an alternative control antibody," said Heimberger. "Interestingly, four of 17 mice treated with FGL2 antibody were completely tumor free."

Through TCGA data, the study team also found an association between levels of FGL2 expression and tumor aggressiveness. The results revealed that patients who had higher levels of FGL2 expression experienced a lower overall survival rate than patients with less FGL2 expression.

While the team reported on new understandings regarding FGL2's role in immune suppression, there remains much still to be studied. These include a better understanding of the cellular signaling pathway, crucial to developing an effective anti-FGL2 therapy and learning exactly how the protein influences tumor progression.

Provided by University of Texas M. D. Anderson Cancer Center