Scientists discover key factor in brain cancer resistance

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Researchers at the NFCR Center for Cancer System Informatics at MD Anderson Cancer Center have discovered a key factor that may explain drug resistance in glioblastoma (GBM), the most common and deadliest form of brain cancer.

GBM accounts for 17% of all brain tumors, and over 10,000 new cases of GBM are diagnosed in the US each year. Unfortunately - since there are no effective, long-term therapies available - survival is typically less than 17 months.

Approximately 50% of GBMs are known to have mutations in a gene called EGFR. However, treatments targeting the mutated EGFR protein have so far been relatively unsuccessful. This new research, supported in part by the National Foundation for Cancer Research, may explain why.

Under the direction of Wei Zhang, Ph.D., researchers at the NFCR Center for Cancer System Informatics at MD Anderson Cancer Center have discovered a key role played by another protein, called IGFBP2, in regulating the action of EGFR.

"Most treatments target EGFR on the surface of the cancer cell," said Dr. Zhang, "but our research shows that IGFBP2 actively moves the EGFR target to the nucleus, where it is beyond the reach of the drug treatment. That means that IGFBP2 appears to be an escape mechanism, allowing GBM cells to become resistant to EGFR-targeted therapy."

Armed with this new knowledge, researchers can now move to develop strategies to target EGFR and IGFBP2 together. Unlike other targets associated with EGFR, IGFBP2 is only expressed in brain cancer cells, not normal adult brain cells, making it an attractive possible target for new GBM therapies. Even more exciting, the potential new therapies may effectively treat cancers other than GBM, as IGFBP2 and EGFR are both known to be activated in prostate, breast, and lung cancers, as well.

"We are very proud of Dr. Zhang, and of the many discoveries he and his team have made at the NFCR Center for Cancer System Informatics at MD Anderson Cancer Center," said NFCR CEO Franklin Salisbury, Jr. "This research brings renewed hope for desperately-needed treatments, not just for GBM patients, but for patients with other types of cancer as well. This has always been the focus of NFCR - Research for a Cure."

These findings are published in the April 20, 2015 issue of journal *Oncogene*. The first author of the paper is graduate student Corrine Chua who is receiving her PhD this May.

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