# Stopping tumors in their path

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Glioblastoma (GBM) is the most common and deadly form of primary malignant brain cancer accounting for approximately 15% of all brain tumours and occurring mostly in adults between the ages of 45 and 70. The aggressive recurrent nature of this cancer is only temporarily contained by combined surgery, chemotherapy and radiation treatment. The recurrence of GBM is usually fatal, resulting in an average patient survival time of less than two years. A new study from the Montreal Neurological Institute and Hospital – The Neuro - at McGill University, published in *Nature Communications*, identifies two specific key players in the growth of GBM.

A GBM tumour contains a complex combination of different cell types, including 'stem-like' cells that are able to initiate brain tumour growth, even when present in very small numbers. These cells, known as brain-tumour initiating cells (BTICs), are believed to be among the cells that can re-initiate GBM if they are not completely eradicated through surgery, radiation and chemotherapy. Thus, BTICs represent an important therapeutic target for GBM treatment strategies.

"We wanted to find out how GBM-derived BTICs are able to initiate a tumour with the ultimate goal of preventing the re-growth of this deadly form of brain cancer," says Dr. Stefano Stifani, neuroscientist at The Neuro and senior investigator on the paper. "What we found is that by impairing the activity of two transcription factors (proteins that control gene expression), termed FOXG1 and TLE, we can significantly reduce the ability of BTICs to give rise to brain tumours." The researchers studied brain tumour growth in an in vivo mouse model using human

GBM-derived BTICs. This approach provides what is called an in vivo environment that closely resembles the original human brain tumours. The demonstration that the FOXG1 and TLE proteins are important for the tumour-forming ability of human GBM-derived BTICs has long-term implications because FOXG1 and TLE control the expression of numerous genes. Identifying the genes whose expression is controlled by FOXG1 and TLE is expected to provide further information on the mechanisms involved in GBM tumourigenesis. In the long term, researchers hope to identify multiple important regulators, in order to find new potential therapeutic targets to impair the tumourigenic ability of BTICs.

"The implication of transcription factors FOXG1 and TLE in the tumour-forming ability of BTICs opens the door to possible strategies to block tumour growth – a major advance in the fight against GBM."

The Neuro's Brain Tumour Program sees 3500 patients annually, and performs on average 450 tumour procedures per year. These procedures include surgeries for brain cancers such as GBM and other gliomas, as well as meningiomas, vestibular schwannomas, pituitary adenomas, metastases, among others.

This research, which was supported by the Canadian Institutes of Health Research and the Cancer Research Society, highlights the benefits of The Neuro's integrated model – where clinicians collaborate closely with researchers, to significantly advance neuroscience and clinical care for patients with neurological disease.

Provided by McGill University