Treatment that 'switches off' cancer cells and limits growth could make aggressive brain tumor easier to treat

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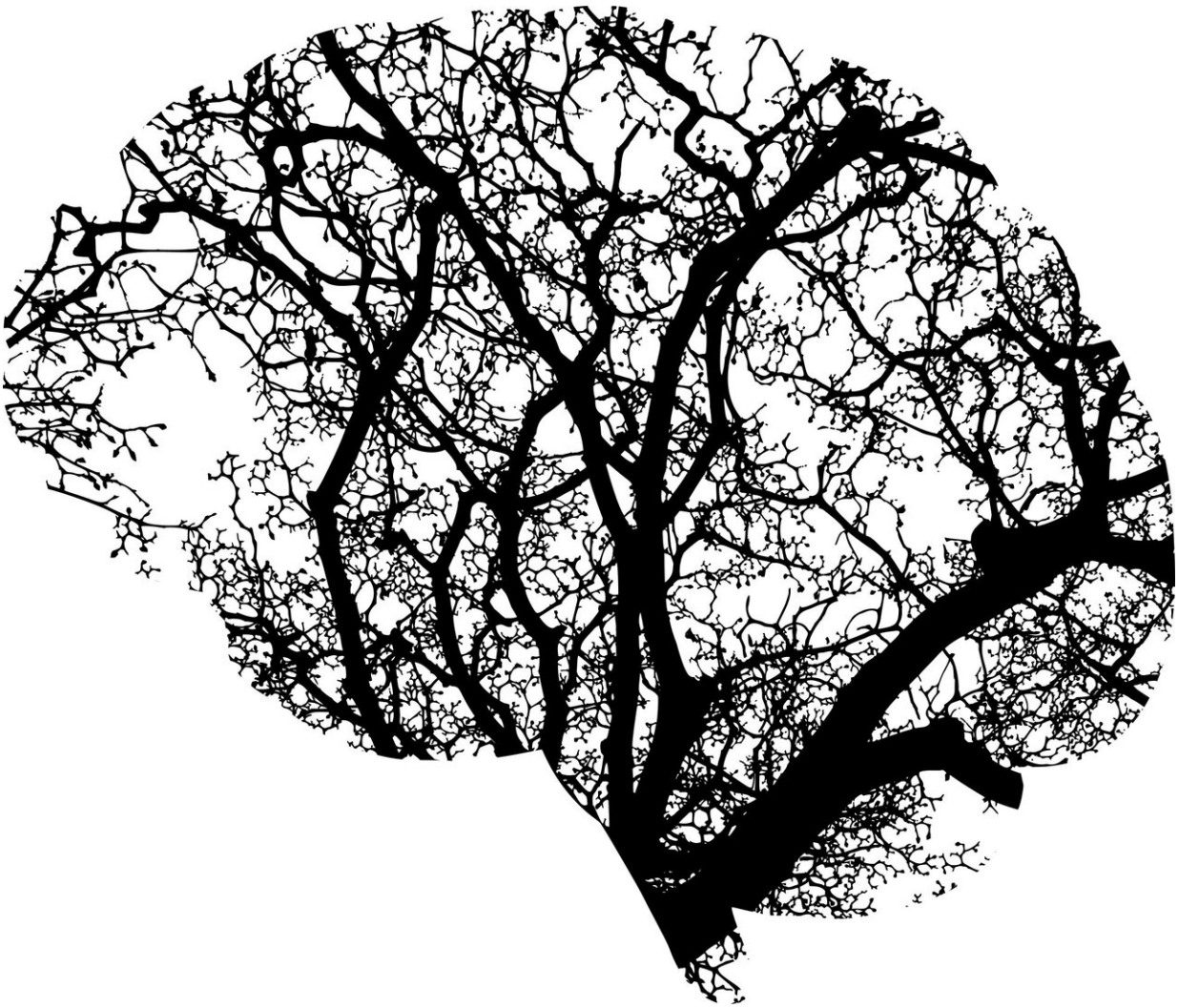

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Researchers believe they may have found a way to strengthen possible treatments for glioblastoma and reduce the speed at which the aggressive tumor progresses.

Glioblastoma is the most common primary brain tumor in adults, and because it is often resistant to treatment, the most fatal too.

But researchers at the University of Sussex have now provided some hope by demonstrating the potential impacts of differentiation therapy, which can effectively "switch off" the malignant properties of cancerous cells and limit tumor growth.

A new study published in the journal *Oncogene* suggests that an inhibitor drug that targets a particular cell protein could refine therapeutic strategies against glioblastoma, making them more effective.

Professor of Cancer Cell Signalling Georgios Giamas and doctoral researcher Rosemary Lane at the University of Sussex worked with researchers from Imperial College London; the Royal College of Surgeons and Beaumont Hospital in Dublin, Ireland; Sun Yat-Sen University in Guangzhou, China; and Genentech and the University of Southern California, in the U.S.

Their research focused on differentiation therapy, a method in which malignant cells are "switched" into a more benign composition using drugs. The cells then divide and grow more slowly, limiting tumor growth.

Professor Georgios Giamas explained, "By slowing or limiting the growth of tumor cells, we essentially make glioblastoma an easier target for more conventional strategies, including surgery and chemotherapies."

In the study, the researchers tested different drugs that belong to a

family of proteins called "kinases." They identified an inhibitor that targets a particular protein (PDGFR), and by altering the expression of downstream targets, it is able to switch glioblastoma cancer cells and glioblastoma cancer stem cells into neuronal-like cells and ultimately reduce their proliferation and invasion abilities.

Furthermore, through in-vivo studies, the team then showed that treatment with this particular drug improved the effect of temozolide (TMZ), the main chemotherapeutic drug used to treat brain cancers like glioblastoma.

Professor Giamas said, "New treatment options are urgently needed for glioblastoma, and over recent years, differentiation therapy has been proposed as an alternative bringing new hope to researchers, medical professionals and patients alike.

"We've not only identified a potential drug which limits the tumor growth by effectively 'switching off' their malignant characteristics, but also demonstrated an improved effect on an existing chemotherapeutic cancer drug.

"As a result, we believe that differentiation therapy holds great promise as a treatment option which could greatly benefit glioblastoma patients in the future and improve their quality of life during the treatment stages. But, as ever, more research is now needed to explore this area further."

More information: Rosemary Lane et al, PDGF-R inhibition induces glioblastoma cell differentiation via DUSP1/p38MAPK signalling, *Oncogene* (2022). DOI: 10.1038/s41388-022-02294-x

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