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CNS CANCER

NEW OPTIONS FOR GLIOBLASTOMA

Glioblastoma muliforme (GBM) is the most common and aggressive brain cancer in adults. The standard of care includes surgery and radiation or chemotherapy but even after these aggressive treatments, prognosis is very poor. Two recent studies have finally provided some options to improve survival of patients with GBM.

In the first study, a group of researchers led by Franzisca Michor had used an iterative combined theoretical and experimental approach to predict the efficacy of different radiation schedules. This approach was based on the fact that GBM has a dynamic heterogeneity of differentiation states that might allow some cells to survive radiation and rapidly acquire a resistant phenotype. Michor explains that "a mathematical model of this plasticity could be used to enhance radiation therapy. Our model identifies the fraction of cells able to acquire radioresistance and also the temporal constraint of this process." On the basis of this model, the researchers determined an optimal radiation schedule that was able to improve survival in a mouse model of GBM. "These findings may have broad implications for improving radiation therapy and provide a framework for future optimization of cytotoxic treatment delivery," concludes Michor.

Beyond the optimization of radiotherapy, a promising result for patients with GBM comes from the identification of stage-specifc embryonic antigen-4 (SSEA-4) as a potential therapeutic target. In this second study, Wong and colleagues found that SSEA-4 is the major glycolipidic marker expressed in brain tumours as well as in 13 other cancers (such as pancreatic, prostate or breast cancers). Specifically, they reported that SSEA-4, although not present in normal brain tissue, is highly expressed in 69% of human GBM. Wong explains that "the monoclonal antibody against SSEA-4 was shown to be effective in killing the GBM cells *in vitro* … and was also able to reduce the size of the tumour in mice". These findings could lead to a better therapy for this disease, but also provide a new therapeutic direction for the other cancer types that uniquely express the SSEA-4 glycolipid.

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Original articles Leder, K. *et al.* Mathematical modeling of PDGF-driven glioblastoma reveals optimized radiation dosing schedules. *Cell* doi:10.1016/j.cell.2013.12.029 | Lou, Y. *et al.* Stage-specific embryonic antigen-4 as a potential therapeutic target in glioblastoma multiforme and other cancers. *Proc. Natl Acad. Sci. USA* doi:10.1073/pnas.1400283111