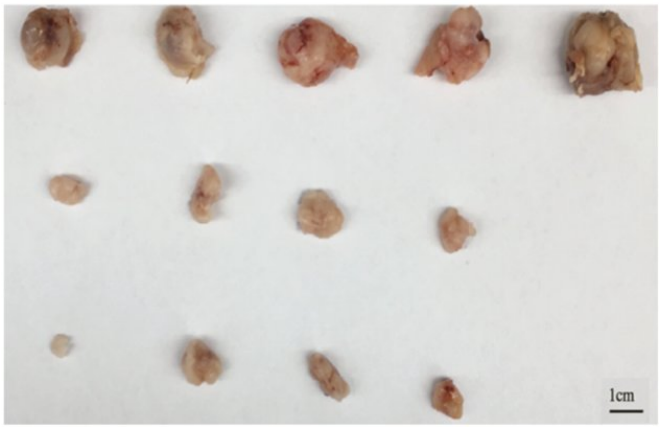
Scientists target glioma cancer stem cells, which could improve patient survival

5 February 2018



This photo illustrates the effect of secretion inhibitors on the growth of high-grade glial tumors in mice. The top row show tumors grown in the absence of secretion inhibitors and bottom two rows show tumors grown in the presence of secretion inhibitors. Credit: Damian Almiron Bonnin

Glioblastoma multiforme is the most common and aggressive primary brain tumor and has one of the worst survival rates of all cancers. Despite surgery, radiation and chemotherapy, these tumors virtually always become resistant to therapy and eventually recur. The cancer stem cells within these tumors are thought to be important drivers of resistance and recurrence. Researchers at Dartmouth's Norris Cotton Cancer Center, led by Damian A. Almiron Bonnin, MD-PhD candidate of the Mark Israel laboratory, are devising strategies to target glioma stem cells which could significantly improve patient survival.

"The presence of glioma stem cells within high-grade gliomas is one of the reasons they are so difficult to treat," says Almiron Bonnin. "In this study, we have successfully identified a secretion-mediated pathway that is essential for the survival of glioma stem cells within aggressive brain tumors."

Multiple studies suggest that these cancer stem cells resist therapy and give rise to recurrences. "To put it simply, if you eliminate most of the tumor with standard treatments, but leave even one cancer stem cell behind, that cell could, in theory, give rise to an entire new tumor," says Almiron Bonnin. "Therefore, making sure these cells are being effectively targeted is an important goal of cancer research." The team is using their understanding of the mechanism by which these cells are maintained within brain tumors to develop new and potentially more effective approaches to treating high-grade brain tumors. Their strategy of utilizing drugs that target glioma stem cells may increase the effectiveness of chemotherapy agents in brain tumors and ultimately prolong the survival of patients with this type of tumor. The team's work, "Secretion-mediated STAT3 activation promotes self-renewal of glioma stem-like cells during hypoxia" was recently published in *Oncogene*.

Pharmacological blockade of the identified pathway leads to a noticeable reduction in tumor growth. Computational studies suggest that the use of these pharmacological agents may significantly increase the survival of patients with this type of tumor. "Being able to target the cancer stem cells within these tumors, like we did here, could potentially improve response to current chemotherapies and prevent recurrences, which would translate into an increase in patient survival rates," says Almiron Bonnin.

Almiron Bonnin's study will lead to a better understanding of cancer mechanisms (drug resistance) that will hopefully translate into improved clinical therapies for the treatment of high-grade gliomas. Looking ahead, Almiron Bonnin's team is finalizing the preclinical experiments that are necessary to pursue a clinical trial that will test drugs that target glioma stem cells of patients diagnosed with this type of incurable tumor.

More information: D A Almiron Bonnin et al, Secretion-mediated STAT3 activation promotes self-renewal of glioma stem-like cells during hypoxia, *Oncogene* (2017). DOI: 10.1038/onc.2017.404

Provided by Dartmouth-Hitchcock Medical Center