

Letter from the Lab



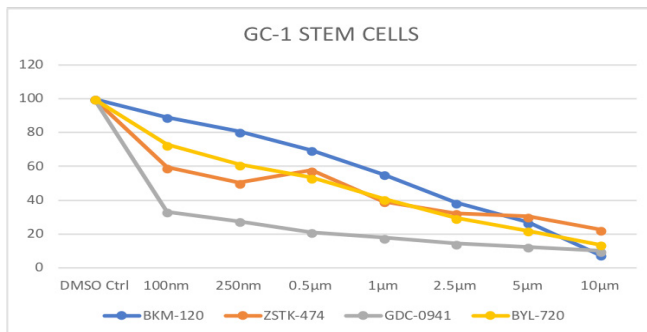
Welcome to the gliomatosis cerebri (gc) "Letter from the Lab." This is the first in a series of regular lab communications specific to progress being made in studying gliomatosis cerebri* at the Children's Brain Tumor Project, Weill Cornell Medicine.

At the Children's Brain Tumor Project, we have a dedicated lab team that has been working with various tissue samples from GC patients that were donated over the past seven years with the goal of identifying mutations that can be better targeted with customized treatment.

The process can be long and arduous, but the results are very rewarding. Upon tumor donation, the tissue is sent for DNA and RNA sequencing so we can better understand the genetic footprint and identify mutations. As a next step, we attempt to grow a cell line from the tumor tissue. A cell line is a permanently established cell culture that will proliferate indefinitely given appropriate fresh medium and space, meaning, we can replicate tumor growth repeatedly in order to conduct various types of tests.

Establishing a cell line is very difficult and often unsuccessful, therefore I am proud to report that the Children's Brain Tumor Project has successfully established four cell lines from gliomatosis cerebri tumor tissue that was collected straight from the OR. These include both stem cell lines and differentiated cell lines. A differentiated cell line is made up of single gc cancer cells that are adherent and less aggressive. This is an incredible accomplishment, and it means our research is better informed because both cell line types (stem cell and differentiated) give us different insight into the behavior of the tumor.

These cell lines have opened many different doors for investigation. Our team is able to explore and better understand the genomics of these tumors. We are identifying mutations, and testing the cells invitro in order to identify agents that we can target against those mutations. For example, these charts show the results from testing four different P13K inhibitors against three different gc cell lines.



Although these results appear promising, we know that drugs can show tremendous progress invitro yet fail to perform invivo. Therefore we are advancing into the next phase of testing the most promising agents discovered via xenograft mouse models.

We have recently seen success using gc stem cells to grow tumors in several mouse models, and we have confirmed active tumor growth via MRI. This is another tremendous advancement in gc research that has not been accomplished in any other lab. The CBTP lab currently has several viable mouse models under observation.

As we observe the intracranial tumor growth, the lab team has simultaneously created successful flank models, meaning, gc tumors are successfully growing subcutaneously (under the skin) in the mouse models. All of these avatars are important as we advance into the next phase of testing new agents against gliomatosis cerebri in order to discover effective new treatment options!

We have come so far, but there is still so much work to be done. Our dedicated team of scientists and clinicians are passionate about finding a cure for gliomatosis cerebri, and we thank our donors for enabling us to do so.

With my deepest gratitude,

Jeffrey P. Greenfield, MD, PhD

*Gliomatosis cerebri (GC) is a rare, highly aggressive brain cancer that is very resistant to treatment. GC is commonly identified by its diffuse infiltration of the brain with thread-like malignancies that spread very quickly affecting various areas of the cerebral lobes and surrounding brain tissue, making them very difficult to remove with surgery or treat with radiation.