Brain Tumour Foundation of Canada – Studentship Final Report
Robyn L. McClelland

Summary of Work

This project sought to examine two different chemical inhibitors on differing types of medulloblastoma cells. Within a medulloblastoma tumour, there are cells with different features. Some cells are very mobile, and therefore can spread through brain tissue very easily. Other cells divide very quickly and thus can make a brain tumour grow. A smaller population of cells are able to start a whole tumour from just one cell. These cells are called the tumour initiating, or stem, cells. Current therapies for medulloblastoma, including radiation and chemotherapy, target the most quickly growing cells. Unfortunately, these therapies aren't as effective on the migrating or stem cell populations. My project sought to explore two chemical inhibitors, cyclopamine and Compound X γ-secretase inhibitor, and their effects on various subtypes of medulloblastoma cells.

Much of the work done for this project involved titrating appropriate concentrations in order to examine the effects of these potential chemotherapeutic agents, without killing all the cells. Various functional assays to test differ properties of the cells (ie: cell division, self-renewal) were performed. Changes in expression of important Shh pathway genes were also examined in response to chemical treatment.

Previous work in the lab determined that cells expressing a cell surface marker called CD271 act as progenitor cells. They are able to provide the tumour with bulk, and are slightly less self-renewing than stem cells. When treated with Compound X γ-secretase inhibitor, these cells actually appeared to become more stem like, with higher levels of self-renewal. Preliminary results showed that medulloblastoma cells that were more stem-like (that is, not expressing the CD271 cell surface receptor) were more sensitive to KAAD-cyclopamine. Though these results are preliminary and require further investigation, it suggests that the heterogeneity of medulloblastoma tumours would be best treated with combination chemotherapy, rather than a single chemotherapeutic agent.

My Experience

It was a privilege to be able to continue the work I performed in my undergraduate honours project with Dr. Werbowetski-Ogilvie. I am truly thankful to the Brain Tumour Foundation of Canada, and all of its supporters, for enabling this research to happen. Since beginning research on medulloblastoma in my undergrad, I always imagined that I would end up in the field. Upon getting accepted to medical school, I've explored various ways I could continue to stay involved with brain tumour treatment and/or research. My recent medical school experiences, combined with two summers of research have led to my interest in the field of neurosurgery. Ultimately, I would like to become a pediatric neurosurgeon, and have an opportunity to treat medulloblastoma firsthand.

Publications

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McClelland, R. (2014) *Investigating the role of selective pathway antagonists in highly self-renewing medulloblastoma subpopulations.* B.Sc (Med) Thesis. University of Manitoba: Canada.

1. Liang L*, Aiken C*, McClelland R, Coudière Morrison L, Remke M, Del Bigio MR, Taylor M, **Werbowetski-Ogilvie T**. 2015. Functional characterization of novel biomarkers for subtype-specific medulloblastoma cell phenotypes. *These authors contributed equally to this work. ***Under revision, Oncotarget***.