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Final Report – Brain Tumour Foundation of Canada Studentship

What We Currently Know:

Due to your continued generosity over the past two summers I was given the opportunity to study and dissect the heterogenous nature of the most aggressive form of brain tumour known as Glioblastoma multiforme (GBM). Every year about 1000 Canadians are diagnosed with GBM and the 5-year survival rates are determined to be less than 10%. Previous literature contends that certain populations of cells within a tumour mass are drivers of GBM progression and they are known as Brain Tumour Initiating Cells (BTICs). Physiologically, these cells possess immature properties of normal neural stem cells. Therefore, they are not only capable of expansion and maintenance of the tumour mass but are also speculated to be involved in tumour initiation. These BTICs are highly resistant to contemporary drug treatments, radiation and can form tumours rapidly when transplanted into *in vivo* models.

Based on genetic information, GBM is grouped into three subtypes. This indicates that all GBM tumours are not exactly the same. With my research, we were motivated to look at GBM from another angle, specifically the cell surface markers. Understanding which specific BTIC populations within a GBM heterogeneous mass are driving tumour progression or drug resistance would be of utmost importance. Therefore, utilizing fluorescence activated cell sorting and magnetic bead sorting of the heterogeneous samples obtained from GBM patients, we were able to derive individual BTIC populations marked with well characterized surface molecules. Past data supports that when these markers are present on the surfaces of cells they are associated with characteristics like proliferation and drug resistance. With these subsequent populations, we then looked at different markers of proliferation and aggressiveness. In our research we discovered interesting correlations between a unique cell cycle regulator, Spy1 (or RINGO as named by other groups), and the markers tested for. Upon over-expressing Spy1 levels in low Spy1 populations we found that proliferation, aggressiveness, and therapy resistance increased. We have also begun *in vivo* studies of the certain populations derived from cell sorting and hope to continue these models in the future. With the different cell surface markers, I established a BTIC bank which will allow for further research into what role these populations play in tumours and will allow me to further dissect the role of Spy1 in GBM *in vitro* and *in vivo*.

Future Directions:

Our research suggests that Spy1 plays a role in tumour aggressiveness and drug resistance; however, further analysis must be completed. Firstly, I would like to complete a drug efflux assay and correlate the results with obtained drug response data. Additionally, we could observe how effective contemporary therapy is against the different populations *in vitro* and *in vivo*. A spectrum of *in vitro* assays could also be completed within organoids which provides a more relevant environment to the human brain. Lastly, the laboratory has been working on a Spy1 knockdown/knockout that can be applied to cell populations that contain high levels of Spy1 expression. We can then apply a knockdown of cell populations that are initially high in Spy1 and observe the effects, possibly leading to a new therapeutic target. Sorting out the heterogeneous tumours creates innumerable possible studies and hopefully we can establish different collaborations to attack GBM from multiple perspectives.

Personal Impact of this Award:

Throughout the past two summers I have grown immensely and every lesson and experience I've had will stick with me throughout my whole life. Researching in Dr. Porter's laboratory, under the wing of my passionate and supportive supervisor, Dr. Lubanska, has been extremely rewarding. I have gained so much valuable knowledge about molecular biology and have been able to apply it in real life situations. Researching in the laboratory has provided me with learning experiences that the classroom never could.

From learning the ropes in the first summer to being able to independently design my own experiments I have become very diligent, patient, and careful with my research. Research has taught me to think critically and to be able to work with likeminded individuals; promoting collaborations and sparking novel ideas. The studentship has provided me with the tools to excel in any career I wish to pursue in the future.

Furthermore, the Brain Tumour Foundation of Canada Studentship I received was generously donated by the Taite Boomer Foundation and, during each experiment I conducted I thought of the individuals afflicted by cancer and their hope towards research. This studentship and the story behind the funding motivated me to perform to the best of my ability and I truly hope my work will benefit future research. Lastly, I would like to wholeheartedly thank Brain Tumour Foundation of Canada and the Taite Boomer Foundation for providing such a fulfilling opportunity to many students like myself.