Brain Tumour Foundation of Canada Final Report
Targeting Bevacizumab resistance via LIVE-mediated vascular mimicry in Glioblastoma

The objective of my project was to further elucidate the role of LIVE1 in Glioblastoma Multiforme (GBM), as well as its relationship with the anti-angiogenesis agent, Bevacizumab.

Working with glioma stem cells (GSCs), we determined that the GliNS1 cell line expressed the most LIVE1. Since vascular cells can differentiate into either endothelium (cells lining blood vessels) or pericytes (cells wrapped around endothelium), immunofluorescence staining for endothelium and pericyte markers was done on GliNS1 xenograft control tissue and LIVE1 knockdown. This experiment showed reduced pericyte coverage in the LIVE1 knockdown mouse model, indicating that LIVE1 plays a role in pericyte formation, contributing to blood vessel formation to the tumour.

Bevacizumab is an antibody against VEGF-A, vascular endothelial growth factor A, and it is used in various cancers, as well as a treatment for recurrent GBM. However, it does not have a significant impact on patient survival as they experience resistance. Base level VEGF-A secretion was determined for GSCs, which showed that they produce high levels of VEGF-A. Cells were then stimulated with VEGF, which increased LIVE1 expression. Next, cells were treated with Bevacizumab (B20-4.1.1), which did not significantly increase LIVE1 expression. This suggests that LIVE1 and Bevacizumab function by a separate mechanism in their impact on blood vessel formation.

The next steps for this project would be further study the signaling pathway of Bevacizumab, to determine whether there is a common interaction point of it with LIVE1. This project can further the understanding of the impact of non-coding RNA on tumour growth, and by determining the true signaling pathways, will introduce new ways of treating brain tumours.

I am extremely grateful for having been awarded the Brain Tumour Foundation of Canada Research Studentship and having the opportunity to contribute to Glioblastoma research as part of Dr. Das' team at the Hospital for Sick Children. This award has had a significant impact on my personal and professional growth. Being responsible for my own project, with all of its successes and obstacles, I learned to be patient, resilient and to persevere, as well as to celebrate the little victories as they come. Throughout my two summer terms, I learned many molecular biology techniques, such as RNA extraction and q-RT-PCR, as well as broader research techniques, like consulting literature, planning experiments, and writing about my findings. Moreover, I saw first-hand the interconnectedness of research and medicine, and was able to contribute to research that will hopefully positively impact patients with this brutal disease in the near future. This experience has further intensified my interest in research and the skills I have developed will assist me on my path to becoming a clinician-scientist.

I would like to thank my supervisor Dr. Sunit Das and the team for their continuous support, mentorship and teaching throughout my studentship. I would also like to share my

gratitude for the Brain Tumour Foundation of Canada, the Taite Boomer Foundation and all of the donors, who make this studentship possible and advance the fight against cancer.