Brain Tumour Foundation of Canada Research Studentship Final Report – Colin Maslink

During the past two summers, we have made significant progress in our evaluation of MRI-guided focused ultrasound (MRIgFUS) as a potential treatment for diffuse intrinsic pontine glioma (DIPG).

Firstly, we have demonstrated that MRIgFUS is a safe and well-tolerated treatment when used to achieve blood-brain barrier (BBB) disruption in the brainstem of healthy rats. No cardiorespiratory or neurological deficits were noted and no microscopic damage to the brainstem was found.

Next, we have observed that doxorubicin, when compared to other traditional chemotherapeutics, is the most cytotoxic agent against our *in vitro* DIPG cell lines. We have also shown that with MRIgFUS, we can deliver a 40 fold greater quantity of doxorubicin into the brainstem compared to doxorubicin administration without MRIgFUS. Thus, doxorubicin is a very promising chemotherapeutic to use in combination with MRIgFUS.

We are also making progress in the establishment of two DIPG mouse models for use in evaluating MRIgFUS: (1) The genetically engineered mouse model (GEMM) involves mice growing tumours with the specific genetic mutations seen in DIPG, and (2) the patient-derived xenograft (PDX) model grows tumours with cells derived from DIPG patients. Both of these models will allow us to test MRIgFUS in the unique genetic and cellular context of DIPG. To date, we have demonstrated successful growth of brainstem tumours in the PDX model and development of the GEMM is in progress.

In summary, we have demonstrated that MRIgFUS is both safe and feasible to use in the region of the brainstem. We have also found that doxorubicin is both potently cytotoxic against DIPG cells and is much more effectively delivered to the brainstem when combined with MRIgFUS. Once our DIPG mouse models are finalized, we will be able to evaluate MRIgFUS in combination with doxorubicin in the treatment of brainstem tumours, assessing both changes in tumour size as well as overall survival.

Impact of Award

Receiving this Studentship has had a profound impact on me, both personally and professionally. Firstly, I have been able to gain valuable lab experience and develop necessary research skills that I can carry forward in a career as a clinician-scientist. This includes learning the rationale and protocol of different molecular techniques, such as Western blots, genotyping, and RNA extractions, as well as learning the broader theoretical concepts behind developing models and experiments for preclinical neuro-oncology research. I've also been able to observe how much thoughtfulness, patience, and collaboration goes into designing and performing this research.

Gaining exposure to neuro-oncology research has also peaked my interest even further in pursuing this field clinically. This comes not only as a result of being involved in carrying out this research, but also by being able to form meaningful mentoring relationships with other members of this field, which have positively impacted me and which I will carry forward with me.

It is with the utmost and sincerest gratitude that I thank Dr. Rutka, Saira Alli, and all the members of the Rutka Lab for their guidance and support, to Brain Tumour Foundation of Canada for this opportunity, and to the Turek family for their generosity in making this experience possible.