



## SU2C Canada Cancer Stem Cell Dream Team

### “Targeting Brain Tumour Stem Cell Epigenetic and Molecular Networks”

#### 6 Month Progress Update – June 2016

**Funding:** \$11,790,000 CAD

**Funding Awarded:** October 2015

#### Dream Team Members

##### **Dream Team Leader:**

- Peter B. Dirks, MD, PhD, The Hospital for Sick Children, Toronto, Ontario

##### **Dream Team Co-leader:**

- Samuel Weiss, PhD, Hotchkiss Brain Institute, Calgary, Alberta

##### **Principals:**

- Michael D. Taylor, MD, PhD, The Hospital for Sick Children, Toronto, Ontario
- Nada Jabado, PhD, Research Institute of the McGill University Health Centre, Montreal, Quebec
- Cheryl H. Arrowsmith, PhD, University of Toronto, Toronto, Ontario
- Michael Salter, MD, PhD, The Hospital for Sick Children, Toronto, Ontario
- Marco A. Marra, PhD, BC Cancer Agency, Vancouver, British Columbia
- Mathieu Lupien, PhD, Princess Margaret Cancer Centre, Toronto, Ontario
- Amy A. Caudy, PhD, University of Toronto, Toronto, Ontario
- Trevor J. Pugh, PhD, Princess Margaret Cancer Centre, Toronto, Ontario
- Gary D. Bader, PhD, University of Toronto, Toronto, Ontario
- Michael D. Tyers, PhD, University of Montreal, Montreal, Quebec

##### **Advocates:**

- Wendy Marie Durigon, Guelph, Ontario

#### Fast Facts on Brain and Central Nervous System Tumors

- There are nearly 100 different types of brain tumors and most are not linked with any known risk factor and have no obvious cause.
- Brain and central nervous system tumors are the most common cancer-related cause of death in children.
- Approximately three of four children with brain tumors survive at least 5 years after being diagnosed.
- In adults, the 5 year survival rate varies depending on the type of brain tumor and the age of patient.



## Summary

Malignant brain tumors remain deadly, incurable diseases. Recent biomedical advances have identified some driving mutations and epigenetic alterations. Although targeted therapies have been promising, there is a lack of translational efficacy and the standard of care remains the same: post-surgery chemotherapy and radiation. To address this barrier in bench to bedside translation, the SU2C Canada Cancer Stem Cell Dream Team will study the brain tumors of and develop new treatments for adults diagnosed with glioblastoma and for children diagnosed with pediatric glioblastoma and the posterior fossa subtype A of ependymoma. Members of this Dream Team previously discovered that at the root of these brain tumors lies a relatively small population of cells that are uniquely able to grow the whole tumor, and these cancer cells are especially skilled at evading therapy. When patients undergo surgery and chemotherapy/radiation to treat their tumors, this tumor subpopulation, known as brain tumor cancer stem cells, survives the therapy and regrows the tumor causing a relapse in the patient.

The overall goal of the pan-Canadian team of experts is to understand the special characteristics of these cells, in terms of identity and behavior. To accomplish this, the Team is taking a three-tiered approach: 1) cancer stem cells from the tumors of 70 patients will be studied to dissect the properties of the cancer stem cells that are shared and those that are unique to the individual patient tumors; 2) a panel of drugs will be tested on these tumors to find promising candidates and understand the mechanisms by which they effectively target these cells and their molecular programs; and 3) drug testing will also be performed in pre-clinical mouse models to predict efficacy in human patients.

Taking a multi-disciplinary approach, this Dream Team will provide new biological insights into brain tumor stem cell biology, providing a promising avenue to solving a problem that has been long enough without a solution.

## Status update

### **6 months:**

In the first 6 months of this contract, the Team has made considerable progress in all aspects of the project.

- The Team has nominated the first 20 of 70 patient tumors to undergo all brain tumor stem cell characterization.
  - They have started to investigate the genetic and functional characteristics of these cells across tumors and have identified key commonalities of the brain tumor stem cell state.
- Drug screening efforts have already led to the identification of two promising drugs, which are now being studied by Team members in unique experimental models.
- The Team has formed an academic-industry partnership with 8 top pharmaceutical companies.
- The clinical trial protocol is underway and they have secured free drug (Vidaza) from CelGene.