BACKGROUNDER

Stand Up 2 Cancer Canada – Cancer Stem Cell Dream Team

On February 4, 2016 (World Cancer Day), Stand Up to Cancer Canada and partners announced a new Cancer Stem Cell Dream Team to attack brain cancer in children and adults. The pan-Canadian team of researchers will receive $11.7 million in funding from Genome Canada and the Canadian Institutes of Health Research, through the Cancer Stem Cell Consortium, the Ontario Institute for Cancer Research, and Stand Up to Cancer Canada. This project is one of two projects funded as a result of the Stand Up 2 Cancer Canada Dream Teams – Inaugural "Call for Ideas." The project is led by Dr. Peter Dirks of The Hospital for Sick Children and co-led by Dr. Samuel Weiss of the University of Calgary.

Targeting Brain Tumour Stem Cell Epigenetic and Molecular Networks

Brain cancer is a largely incurable disease affecting adults and children. The five-year survival rate for adults with glioblastoma, the most common form of brain cancer, is below 10 percent, and treatment options are limited. For children, in whom many glioblastomas are inoperable, the outlook is also dismal with brain cancers killing more U.S. and Canadian children than any other pediatric cancer.

In cancer, individual tumours can actually contain more than one type of cancer cell. Researchers are learning rapidly about the biological differences between cancer cell subtypes and how they contribute to tumour growth and the effectiveness of anti-cancer drugs. It is now apparent that a small fraction of the total number of tumour cells, called cancer stem cells, are the key to tumours getting started and growing back after initial response to drugs. Stem cells are immature cells that mature into an adult cell type, like a liver cell or a nerve cell, a process that is essential to normal development. In tumours, however, cancer stem cells do not mature; instead they continually regenerate and grow, sustaining the tumour. And it takes only a few cancer stem cells, maybe even just one, to start the process of tumour growth and regrowth.

The Stand Up To Cancer Canada Cancer Stem Cell Dream Team brings together a pan-Canadian group of outstanding leaders across multiple scientific and clinical disciplines who will focus their attention on brain tumours that have the worst outcomes – glioblastomas in adults and children and posterior fossa ependymomas in infants. Members of this Dream Team, as well as others in the field, have found that these tumours contain brain tumour stem cells (BTSCs). While similar to nerve stem cells that mature during normal brain development, abnormal programming in BTSCs allows them to drive tumour relapse (when the tumours grow back) and drug resistance. The Dream Team's goal is to understand the abnormalities in BTSCs so that they can identify vulnerabilities that can be used to develop new drugs that are effective against brain cancers.

To achieve this goal, the Dream Team will take a three-pronged approach to understanding and targeting brain cancer stem cells that resist treatment and fuel tumour regrowth. Their first approach is to perform a detailed analysis of BTSCs taken from 70 different patient glioblastomas or ependymomas and grown in the laboratory. They will use cutting-edge technology to understand the full biological profile of these cells – from changes in the cells' genetic codes to epigenetic programs that control when genes are turned on or off to alterations in the way the cells metabolize nutrients. Their second approach will be to screen a collection of chemicals on the same BTSCs for potential new drugs and drug combinations that are effective against these cells. Finally, while they are learning about the biology of BTSCs and screening for new compounds, the Dream Team will test five new potential drugs that they have already identified as very promising, by testing them in laboratory mice to find out which drugs or drug combinations might kill glioblastomas or ependymomas. The Dream Team hopes to bring new drugs for brain cancer into clinical trials in the third and fourth years of their research funding.

By understanding the cancer stem cells that drive brain cancer relapse and drug resistance, the Dream Team hopes to change the outlook for adults and children with brain cancer from a deadly disease with few viable treatment options and no realistic chance of a cure, to a reality where safe and effective drugs are available to combat these devastating cancers.