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Brain Canada Foundation

Canadian Cancer Society / Société canadienne du cancer

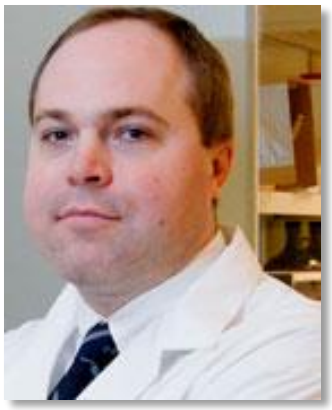
The Research - Dr. Michael Taylor

Annual Progress Report: Dr. Michael Taylor, Hospital for Sick Children
Brain Tumour Foundation of Canada Pediatric Brain Cancer Impact Grant
Canadian Cancer Society and Brain Canada

Molecular heterogeneity drives clinical behaviour of childhood medulloblastoma:

About the research

Dr. Taylor studies the molecular genetics factors of medulloblastoma and ependymoma, two of the most common malignant pediatric brain tumours. He has previously discovered that medulloblastoma is not one disease, but four, each with a different genetic footprint. Now, Dr Taylor aims to find a way to predict the aggressiveness of these different cancer subtypes. Knowing how each tumour changes in response to treatment will help physicians identify which children have high-risk cancers requiring the most aggressive treatments, versus those that can receive a gentler regimen that could spare them lifelong effects of treatment.



Dr Taylor's work will impact the treatment, long-term survival and quality of life for medulloblastoma patients

What we've learned so far, thanks to you!

Studies conducted by Dr Taylor and his team indicate that medulloblastoma has a much higher degree of difference between tumours than anticipated. Initially, the research community believed that there were 4 subtypes of this disease; due to Dr Taylor's work this past year there now appear to be at least 10 different types of the disease.

More about this project

This study uses patient samples that are collected at surgery to look at the very specific genetic events that have occurred and caused the cancer/tumour. In the lab, Dr Taylor and his team worked on mice with medulloblastoma. The mice underwent tumour resection and then were treated with repeated cycles of the chemotherapy drugs cisplatin and cyclophosphamide, both widely used to treat medulloblastoma in children. After chemotherapy treatment, several genes involved in DNA repair were identified in both recurrent tumours and metastases, suggesting that deregulation of response to DNA damage caused by chemotherapy leads to chemoresistance.

In this first year of the project, the team has developed a highly reproducible single cell RNA sequencing method which has shown to be extremely consistent. Being able to sequence single cells to determine genetic alterations is a very important methodology that will enable the team to more quickly determine the heterogeneity in medulloblastoma and move the findings to the clinic.

Using bioinformatic techniques, the team analyzed each of the 4 subgroups of medulloblastoma. Analysis combined with clinical information enabled them to define clinically relevant subtypes in the 4 subgroups.

With these and future findings, Dr Taylor aims to be able to classify the difference between medulloblastoma tumours so that treatment can be focused according to a patient's specific needs.

"I would like to say thank you to our donors. This very generous grant gives me the opportunity to recruit high-quality individuals and plan more ambitious experiments with greater horizons in mind. Instead of aiming for small goals, we're aiming for big goals so that we can make big changes in the lives of Canadian kids with cancer."

Dr Michael Taylor

Impact and Relevance

Dr Taylor's work will have direct impact on the treatment, long-term survival and quality of life for patients with medulloblastoma. The overall objective is to identify low risk subtypes of medulloblastoma subgroups, and discover and validate biomarkers to identify these patients in a clinical setting. This will allow for clinical trials of de-escalation of therapy to minimize the catastrophic effects of therapy on a child's developing brain.

Single Greatest Impact on Fundamental Knowledge in Cancer Research

Recurrent medulloblastoma is a devastating disease with almost universal mortality despite highly aggressive therapy. It has always been assumed that recurrent medulloblastoma is highly similar at a molecular level to the tumour at diagnosis. However, Dr Taylor's preliminary data shows that the tumour has greatly changed at the time of recurrence. This is critically important because all clinical trials of experimental therapy for medulloblastoma are delivered at the time of recurrence. Confirming divergence of the biology of this cancer at recurrence would explain the high failure rate of clinical trials, offer a solution to design effective trials of rational therapy and have a profound impact on medulloblastoma patients around the world.

If you would like to learn more about the Brain Tumour Foundation of Canada Pediatric Brain Cancer Impact Grant, please visit **www.braintumour.ca/ImpactGrant**

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