BIOGRAPHICAL SKETCH

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NAME: Michael David Taylor

eRA COMMONS USER NAME (credential, e.g., agency login): TAYLORMD

POSITION TITLE: Professor /Senior Scientist

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE	Completion Date MM/YYYY	FIELD OF STUDY
University of Western Ontario, London, Ontario	M.D.	1994	Medicine (*cum laude*)
University of Toronto, Ontario	FRCS	2003	Neurosurgery
University of Toronto, Ontario	PhD	2002	Molecular Genetics of Paediatric Brain Tumours
St Jude Children's Research Hospital, Memphis, Tennessee	Post Doc	2003-2004	Cancer Genomics
University of Toronto	Post Doc	2004-2005	Functional Genomics

A. Personal Statement

As a practicing pediatric neurosurgeon/clinician scientist, my research focuses on using tools from human genetics/genomics, and from mouse models to better understand the biology of pediatric brain tumors, particularly medulloblastoma and ependymoma. As someone who is comfortable in both the clinic and at the bench, I have a great deal to offer in the development of translational research for brain tumor research. I have previously described a number of the genetic events that are thought to drive the pathogenesis of medulloblastoma. More recently my laboratory has developed functional genomic mouse models of medulloblastoma to help better interpret our genomic studies of human medulloblastoma. I am the creator, and principal investigator of the **M**edulloblastoma **A**dvanced **G**enomics **I**nternational **C**onsortium (MAGIC), through which I have collected >2200 frozen medulloblastomas from >90 high quality pediatric neuro-oncology centers from around the world. My clinical expertise, research experience in the field, and my current resources uniquely position me to contribute to studies on medulloblastoma and ependymoma.

B. Positions and Honors

Positions and Employment (current as of September 2019)

2004-present Staff Neurosurgeon, The Hospital for Sick Children
2004-2010 Assistant Professor, Department of Surgery, University of Toronto
2004-2012 Scientist, Program in Developmental Biology, the Hospital for Sick Children
2010-2013 Associate Professor, Department of Surgery, University of Toronto
2012-present Senior Scientist, Program in Developmental and Stem Cell Biology, Hospital for Sick Children
2013-present Professor, Department of Surgery and Department of Laboratory Medicine and Pathobiology, University of Toronto

Selected Honors

2004 Peter A. Steck Memorial Award
2004 Canadian Institutes of Health Research Clinician Scientist Award, Phase I
2004 Best Individual Investigator Award, AANS/CNS Brain Tumor Satellite Symposium
2004 Pediatric Brain Tumor Foundation Award at Society for Neuro-Oncology (SNO) meeting

2005 American Brain Tumor Association, Emily Dorfman Foundation for Children Fellowship
2005 Schweiszguth Prize, International Society of Pediatric Oncology (SIOP)
2007 Elsie W. Crann Award, University of Toronto
2007 Canadian Institute of Health Research, Clinician-Scientist Award, Phase II
2007 Sontag Foundation, Distinguished Scientist Award
2008 Bernard Langer Surgeon-Scientist Award. Department of Surgery, University of Toronto.
2008 Canada's Top 40 under 40 award
2009 Canadian Cancer Society Award. Young Investigator Award in Biomedical Science
2010 Royal College of Physicians and Surgeons of Canada Gold Medal Award in Surgery
2010 Canadian Institute of Health Research, Clinician-Scientist Award, Phase II - Renewal
2011 George-Armstrong Peters Prize in Surgery, University of Toronto
2013 Garron Family Endowed Chair in Childhood Cancer Research, Hospital for Sick Children
2015 Canadian Cancer Society William E. Rawls Prize for 2015
2016 Lister Prize in Surgery. University of Toronto 2016
2016 Voynick Award in Neuro-Oncology 2016. Yale University
2016 Guha Award in Neuro-Oncology 2016. Society for Neuro-Oncology
2016 Zulch Prize in Basic Neuroscience 2016. Max Planck Society
2019 H. Richard Winn, MD Prize. The Society of Neurological Surgeons
2019 The Distinguished Oliver Smithies Lecture. McLaughlin Centre of the University of Toronto
2019 Fellow and Member of the Royal Society of Canada

C. Contributions to Science

Total (August 11, 2020):	**Citations: 37,097**	**h-index: 96**	**i10 index: 300**
Last five years:	**Citations: 26,150**	**h-index: 81**	**i10 index: 278**

1) Discovery that Medulloblastoma is a Heterogeneous Entity Comprised of Distinct Diseases
Northcott et al J. Clin. Oncol. 2011, Taylor et al. Acta Neuro. 2012, Shih et al. J. Clin. Oncol. 2014, Ramaswamy et al. Neuro- Oncology 2015, Cavalli et al. Cancer Cell 2017, Vladoiu et al. Nature 2019.

We demonstrated, and it is accepted by the World Health Organization, that medulloblastoma (MB) comprises four distinct diseases, each with their own epidemiology, and response to therapy. Globally, clinical trials stratify patients based on this classification. Subgroup affiliation is now part of the standard of care for MB patients at SickKids and we have trained clinicians/scientists around the globe to make this highly available. We also recently showed that the MB, are a disorder of early brain development, a finding which provides an explanation for the peak incidence in early childhood.

2) Discovery of Novel Medulloblastoma Oncogenes and Tumour Suppressor Genes.
Northcott et al. Nature 2012. PMID: 22832581. Northcott et al. Nature Genetics 2009. PMID: 1927076. Taylor et al. Nature Genetics 2002. PMID: 12068298. Huang et al. Nature Neuroscience 2015 PMID: 26258683.

We have described and characterized a number of somatic and germline mutations that are drivers in subgroups of medulloblastoma. These driver events are useful for modeling the disease, and as targets for rational therapy.

3) Discovery of molecular distinct subgroups of ependymoma brain tumors from different parts of the central nervous system that are biologically distinct, likely arise from radial glial cell progenitor cells.
Taylor et al. Cancer Cell 2005. PMID: 16226707. Johnson et al. Nature 2010. PMID: 20639864. Witt et al. Cancer Cell 2011. PMID: 21840481. Mack et al. Clinical Cancer Research 2015. PMID: 25957288.

Ependymoma can arise at all levels of the nervous system, and was thought to arise from post-mitotic cells of the ependymal. We have shown that in fact, ependymomas arise from radial glial cells (CNS progenitors), and that there are several distinct molecular subgroups of ependymoma with widely variant biology and outcomes. The next round of clinical trials for ependymoma are all accounting for these molecular subgroups.

4.) Discovery of clinically significant heterogeneity in metastatic and recurrent medulloblastoma.

Wu et al. Nature 2012. PMID: 22343890. Ramaswamy et al. Lancet Oncology 2013. PMID: 24140199. Wang et al. Acta Neuropathologica 2015. PMID: 25689980. Garzia et al. Nature 2016, PMID: 26760213. Morrissy et al., Nature Genetics 2017, PMID: 28394352

Current *modus operandi* are to discover and validate novel targets for therapy on untreated primary tumors, and then to take novel agents to clinical trials and test them on patients with highly treated, recurrent, metastatic disease. This approach is doomed to failure, as we have shown that children die from metastases rather than the primary tumor, that metastases are vastly different from the primary tumor, and that recurrent disease has undergone extensive clonal divergence from the untreated primary tumor. These findings necessitate re-biopsy at recurrence for targeted therapy, and considering temporal and spatial heterogeneity when studying medulloblastoma to develop novel therapies.

5.) Discovery and delineation of the importance of epigenetic mechanisms in childhood brain tumors.
Mack et al. Nature 2014. PMID: 24553142. Hovestadt et al. Nature 2014. PMID: 24847876. Leprivier et al. Cell 2013. PMID: 23706743. Dubuc et al. Acta Neuropathologica 2013. PMID: 23184418. Mack et al. Nature 2017. PMID: 29258295.

Both medulloblastoma and ependymoma have a paucity of recurrent somatic mutations, particularly SNVs. Due to a lack of somatic genetic targets, alternatives must be found. We have shown in a number of publications that non-genetic, particularly epigenetic mechanisms (both DNA CpG methylation and histone post-translational modifications) are important in medulloblastoma and ependymoma biology, and might serve as novel targets for rational therapy.

URL to published work: https://www.ncbi.nlm.nih.gov/myncbi/michael.taylor.2/bibliography/public/

D. Research Support *(Ongoing and Recent Research Support)*
National Institute of Health (NIH) Multi-Investigator R01
Co-PI: Michael Taylor (with Robert Wechsler-Reya and William Weiss) **Funding Period**: 2017-2022
Title: Heterogeneity Amongst Metastases in Children with Medulloblastoma: Focusing on the Real Problem
Summary: This grant supports research in which we study the genetic events in Group 4 medulloblastomas.

National Institute of Health (NIH) Multi-Investigator R01
Co-PI: Michael Taylor (with William Weiss) **Funding Period**: 2018-2023
Title: Prevention and treatment of lethal metastases in group 3 medulloblastoma
Summary: This grant supports studies in which we study the genetic events in both human and murine Group 3 subgroup of medulloblastoma in both the primary tumor and its metastases.

Canadian Institutes of Health Research (CIHR) Terry Fox New Frontiers Program, Project Grant
PI: Michael Taylor (S. Egan, J. Woodgett and E. Zacksenhaus) **Funding Period**: August 2014 to July 2019
Title: Killing the Hydra: Genetic Dissection of Actionable Targets Required for Maintenance of Metastatic Disease.
Summary: This grant supports studies that look for genetic events that are shared by both the primary tumor and its metastases, and attempts to find targets in Shh medulloblastoma that will address both compartments simultaneously. The predominant pathway focused on for study in Shh MB is the PI3 Kinase pathway.

St. Baldrick's Foundation-Stand Up To Cancer Pediatric Dream Team Translational Cancer Research Grant (Renewal)
Dream Team Leaders: John Maris and Crystal Mackall **Funding Period:** 2017-2021
Michael Taylor is a Dream Team member (Co-PI)
Title of Grant: Immunogenomics to Create New Therapies for High Risk Childhood Cancers.
Summary: This is a large group grant that proposes to integrate genomics with immunotherapy to create novel immunotherapeutics to target childhood cancers, including brain tumors. There is absolutely no overlap with the current proposal.

Cancer Research Society
Principal Investigator: Michael D Taylor **Funding Period:** September 2014 - August 2016

Title: Defining the Subgroup Specific Epigenetic Landscape of Medulloblastoma
Summary: For this recent grant from the CRS we outline a series of experiments to look at tumors that have mutations in the genes that lay down or erase H3K27 and H3K4 methylation such as MLL2, MLL3, and UTX. We propose to study samples with and without pathway mutations by ChIP-Seq to attempt to determine the effects of mutations in these genes on the tumor's epigenome - again, no overlap with the current proposal.

Canadian Cancer Society Research Institute (*Co-funded by Brain Canada)
Principal Investigator: Michael Taylor **Funding Period:** February 2015 - January 2020
Title: Molecular heterogeneity drives the clinical behaviour of childhood medulloblastoma
Summary: Determine intertumoral heterogeneity among MBs, and develop biomarkers that identify subgroups and subtypes of MB that will allow us to tailor, target, and stratify therapy

Ontario Institute for Cancer Research (OICR) - Translational Research Initiative (**Brain Cancer Translational Research Initiative)**
PI: Michael Taylor and Peter Dirks (with **Co-Principal Investigators:** Bret Pearson; Daniel Schramek; David Stojdl; Gary Bader; Ian Scott; Jüri Reimand; Ken Aldape; Mathieu Lupien; Sheila Singh; Stephane Angers; Sunit Das; Trevor Pugh; Xi Huang) **Funding Period**: July 2017 - June 2021
Title: Cellular and Genetic Heterogeneity as a Therapeutic Hurdle and Opportunity for Ontarians with Brain Cancer.
Summary: This is a large group proposal aimed at discovering targets for treatment of brain cancers and developing and testing compounds so that brain cancers can be better targeted therapeutically.

Canadian Institutes of Health Research (CIHR) Foundation Award
PI: Michael Taylor **Funding Period**: July 2017 - June 2024
Title: Heterogeneity through space and time drive the clinical behaviour of childhood medulloblastoma.
Summary: A project based on compelling preliminary data showing that medulloblastoma metastasizes through the blood to form tumours on the brain surface. The main objective is to demonstrate that CCL2/CCR2 signalling drives haematogenous dissemination of MB, and that this can be targeted therapeutically.

V-Foundation Pediatric Cancer-Translational Award
PI: Michael Taylor, **Co-PI:** William Weiss **Funding Period:** November 2017 – November 2020
Title: Targeting Circulating Metastatic Cells as a Novel Approach for Cancer Therapy
Summary: A project aimed at discovering the detailed mechanisms which are enabling metastases through the circulatory system. Here we are looking closely at the differences between the original tumours and the metastases to predict if a tumour can become metastatic.

Genome Canada / Canadian Institutes of Health Research - LSARP
Team Leaders: Nada Jabado, Michael Taylor, Jacek Majewski **Funding Period:** April 2018-August 2022
Title: Tackling Childhood Brain Cancer at the root to improve survival and quality of life.
Summary: The goal of this large group project is to improve survival and quality of life for all children and young adults with brain tumours. The research aims to inform the selection and validation of more efficient drugs tailored to specific patients with deadly and severely debilitating cancers.

Cancer Research United Kingdom (CRUK)
PI: Richard Gilbertson, **Co-PI:** Michael Taylor **Funding Period:** July 2019 – June 2023
Title: The New Roads Team – Innovative Approaches to Curing Brain Tumours
Summary: This large collaborative research programme is focused on producing a sea change in brain tumour treatment by markedly accelerating understanding of the normal and malignant brain, and exploiting this understanding to produce safe and effective therapies.