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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	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. My current research is heavily focused on the metastases of brain tumors, monitoring circulating tumor cells over time and the effects of current therapies and inflammatory responses on the metastatic process. The overall goal being to drive novel adjuvant therapies into the clinic to treat patients suffering from these devastating diseases.

Ongoing and recently completed projects that I would like to highlight include:

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.

Genome Canada / Canadian Institutes of Health Research - LSARP
Team Leaders: Nada Jabado, Michael Taylor, Jacek Majewski **Funding Period:** April 2018-April 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.

Citations:
Skowron P, Farooq H, Cavalli FMG, et al. The transcriptional landscape of Shh medulloblastoma. **Nat Commun.** 2021 Mar 19;12(1):1749. doi: 10.1038/s41467-021-21883-0. PubMed PMID: 33741928; PubMed Central PMCID: PMC7979819.

Michealraj KA, Kumar SA, Kim LJY, et al. Metabolic Regulation of the Epigenome Drives Lethal Infantile Ependymoma. **Cell.** 2020 Jun 11;181(6):1329-1345.e24. doi: 10.1016/j.cell.2020.04.047. Epub 2020 May 22. PubMed PMID: 32445698.

Donovan LK, Delaidelli A, Joseph SK, et al. Locoregional delivery of CAR T cells to the cerebrospinal fluid for treatment of metastatic medulloblastoma and ependymoma. **Nat Med.** 2020 May;26(5):720-731. doi: 10.1038/s41591-020-0827-2. Epub 2020 Apr 27. PubMed PMID: 32341580; NIHMSID: NIHMS1696196.

Suzuki H, Kumar SA, Shuai S, et al. Recurrent noncoding U1 snRNA mutations drive cryptic splicing in SHH medulloblastoma. **Nature.** 2019 Oct;574(7780):707-711. doi: 10.1038/s41586-019-1650-0. Epub 2019 Oct 9. PubMed PMID: 31664194; PubMed Central PMCID: PMC7141958.

Vladoiu MC, El-Hamamy I, Donovan LK, et al. Childhood cerebellar tumours mirror conserved fetal transcriptional programs. **Nature.** 2019 Aug;572(7767):67-73. doi: 10.1038/s41586-019-1158-7. Epub 2019 May 1. PubMed PMID: 31043743; PubMed Central PMCID: PMC6675628.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments:

2023-present Professor, Departments of Pediatrics-Hematology/Oncology and Neurosurgery-Pediatrics at Baylor College of Medicine (BCM)

2023-present Director, Pediatric Neuro-Oncology Research Program at Texas Children's Hospital (TCH)

2023-present Adjunct Scientist, Program in Developmental and Stem Cell Biology, Hospital for Sick Children

2013-present Professor, Department of Surgery, Department of Laboratory Medicine and Pathobiology, University of Toronto

2012-2022 Senior Scientist, Program in Developmental and Stem Cell Biology, Hospital for Sick Children
2004-2022 Staff Neurosurgeon, The Hospital for Sick Children
2010-2013 Associate Professor, Department of Surgery, University of Toronto
2004-2010 Assistant Professor, Department of Surgery, University of Toronto
2004-2012 Scientist, Program in Developmental Biology, the Hospital for Sick Children

Honors:

2021 49th Fondation ARC Leopold Griffuel Award (co-awarded with Professor Stefan Pfister, Heidelberg)
2021 AACR Team Science Award (Team Co-Leaders: Crystal L. Mackall and John M. Maris, MDT one of ten principal investigators on the team)
2019 Fellow and Member of the Royal Society of Canada
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 Adam Balinsky Lecturer Hospital for Sick Children, Toronto, Canada.

2019 Sutow Award and Lectureship in Pediatric Oncology. M.D. Anderson Cancer Center
2019 The Marion Walker Honourable Lectureship in Neurosurgery, Salt Lake City, Utah
2018 Mr. Otto Lien Da Wong Visiting Prof. in Neuro-oncology, Dept. of Surgery, Chinese University HK
2017 17th Annual Invited Rosomoff Visiting Professor in Neurosurgery, University of Miami.
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
2015 Canadian Cancer Society William E. Rawls Prize for 2015
2013 Garron Family Endowed Chair in Childhood Cancer Research, Hospital for Sick Children
2011 George-Armstrong Peters Prize in Surgery, University of Toronto
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
2009 Canadian Cancer Society Award. Young Investigator Award in Biomedical Science
2008 Bernard Langer Surgeon-Scientist Award. Department of Surgery, University of Toronto.
2008 Canada's Top 40 under 40 award
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
2005 American Brain Tumor Association, Emily Dorfman Foundation for Children Fellowship
2005 Schweiszguth Prize, International Society of Pediatric Oncology (SIOP)
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

C. Contributions to Science

Complete List of Published Work in MyBibliography:
Total (January 10, 2022): Citations: 56,293 h-index: 113 i10 index: 374
Last five years: Citations: 32,963 h-index: 90 i10 index: 333
URL to published work: https://www.ncbi.nlm.nih.gov/myncbi/michael.taylor.2/bibliography/public/

1) Discovery that Medulloblastoma is a Heterogeneous Entity Comprised of Distinct Diseases
Northcott et al J. Clin. Oncol. 2011. PMID: 20823417, Taylor et al. Acta Neuro. 2012. PMID: 22358457, Shih et al. J. Clin. Oncol. 2014. PMID: 24493713, Ramaswamy et al. Neuro- Oncology 2015. PMID: 25605817, Cavalli et al. Cancer Cell 2017. PMID: 28609654, Vladoiu et al. Nature 2019. PMID: 31043743, Skowron et al., Nat Commun. 2021. PMID: 33741928.

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.