BIOGRAPHICAL SKETCH

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NAME: Tamra Werbowetski-Ogilvie

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

POSITION TITLE: Associate Professor

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 *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Western Ontario, London, ON, Canada	HBSc	06/2000	Biology
McGill University, Montreal, QC, Canada	PhD	03/2006	Neuroscience
McMaster University, Hamilton, ON, Canada	PDF	10/2010	Stem Cell Biology

A. Personal Statement

I have made significant contributions to the underlying cellular and molecular mechanisms regulating stem cell function and heterogeneity in medulloblastoma (MB), the most common primary malignant pediatric brain tumor. As an independent investigator since November 2010, I have acquired 6 million in operating and infrastructure funds to support my research and have established collaborations with world-renowned experts in brain tumor and stem cell biology. My laboratory specializes in the characterization of the cellular and molecular mechanisms regulating medulloblastoma (MB) progression, with a focus on the processes that are common between normal stem cells and MB cells. We have discovered central regulators of self-renewal (Nature Communications, 2020, Molecular Oncology, 2018, Disease Models & Mechanisms, 2015; Stem Cells, 2012) and potential diagnostic biomarkers for MB (Cancer Research, 2018). We routinely utilize model systems, some of which I first developed (Nature Biotechnology, 2009; Stem Cells, 2012), that most closely represent the human condition, including primary MB cells from patient tumors, MB-like cells derived from human neural precursor cells and mouse models where these cells are implanted into the cerebellum.

B. Positions and Honors

Positions and Employment

2005-2010 Post-doctoral Fellow, McMaster Stem Cell and Cancer Research Institute, McMaster University
2010-2017 Assistant Professor, Biochemistry & Medical Genetics, Regenerative Medicine Program, University of Manitoba
2012-present Adjunct Professor Department of Physiology & Pathophysiology, University of Manitoba
2012-present Scientist, Children's Hospital Research Institute of Manitoba (CHRIM)
2017-present Associate Professor, Biochemistry & Medical Genetics, Regenerative Medicine Program, University of Manitoba

Committees and Review Panels

2011 Estonian Science Foundation (ESF): Grant Reviewer
2011 Canadian Cancer Society Research Institute (CCS-RI) Innovation Grants: External Reviewer
2011 Manitoba Health Research Council (MHRC) Postdoctoral Fellowships Committee: Scientific Officer

2012	Terry Fox New Frontiers in Cancer (CIHR/Terry Fox Research Institute): Program and Project Grant Review Committee, Scientific Officer
2012	Canadian Cancer Society Research Institute (CCS-RI) Impact Grants: Review Panel Member
2012-2014	Manitoba Health Research Council (MHRC): Postdoctoral Fellowships Review Committee Member
2015-2016	Alberta Innovates Health Solutions (AIHS) Postgraduate Fellowship Review Committee Member
2016	Research Manitoba New Investigator Operating Grants Review Committee
2016	Canada Foundation for Innovation (CFI): John R. Evans Leaders Fund, Reviewer
2016-present	Canada Research Chairs Tier II program, Reviewer
2016-present	Research Councils UK, Medical Research Council, External Reviewer for Operating Grants Competition
2017	Barrow Neurological Institute, Phoenix Arizona, Promotion/retention/tenure applications, Reviewer
2017	The French National Cancer Institute Integrated Research Action Programme (PAIR) in Pediatric Oncology, Reviewer
2017-present	Canadian Institute of Health Research (CIHR), Project Grant Competition, Fall 2017-present, Cancer Progression and Therapeutics panel, Reviewer or Scientific Officer
2017-present	Canada Research Chars Tier I program, Reviewer
2020	Austrian Science Fund. Grant Reviewer

Honors

2002-2005	CIHR Doctoral Research Award, McGill University. Supervisor: Dr. Rolando Del Maestro
2007- Declined	CIHR Post-doctoral Fellowship
2007-2010	NCIC Post PhD Research Fellowship, McMaster University. Supervisor: Dr. Mick Bhatia
2008	NCIC Harold E. Johns Fellowship Award for highest-ranking post-doctoral fellow in Canada, 2007 NCIC competition, McMaster University. Supervisor: Dr. Mick Bhatia
2010	McMaster University FHS Postdoctoral Fellow Publication Award, for Werbowetski-Ogilvie et al., Nature Biotechnology, 2009. McMaster University. Supervisor: Dr. Mick Bhatia.
2011	Canadian Cancer Society Research Institute (CCS-RI), Junior Investigator Grant Panel Travel Award
2011-present	Canada Research Chair Tier II in Neurooncology & Human Stem Cells Renewed: July 2017. University of Manitoba.
2017	Nominee: YMCA/YWCA Women of Distinction Award, Manitoba
2020	Outstanding reviewer recognition by CIHR College of Reviewers

C. Contribution to Science
(Articles selected from 35 peer-reviewed publications, book chapters and reviews)

1. *The functional role of CD271/p75NTR in SHH medulloblastoma*

Liang L, Coudière Morrison L, Tatari N, Stromecki M, Fresnoza A, Porter CJ, Del Bigio MR, Hawkins C, Chan J, Taylor MD, Ramaswamy V*, Werbowetski-Ogilvie TE*. 2018. CD271+ cells are diagnostic and prognostic and exhibit elevated MAPK activity in SHH medulloblastoma. *Cancer Research.* 78 (16) 4745-4759.

Liang L*, Aiken C*, et al. 2015. Functional characterization of novel biomarkers for subtype-specific medulloblastoma cell phenotypes. *Oncotarget*, 6(36): 38881-38900.

We discovered that the neurotrophin receptor CD271 or p75NTR is a novel regulator of stem/progenitor cell function in SHH medulloblastoma. This led to our recent findings demonstrating that CD271 is also a novel potential diagnostic marker and cells bearing the CD271 “mark” are therapeutic targets in SHH medulloblastoma. These preclinical studies, which combine extensive bioinformatics analyses in patient samples with the most biologically relevant *in vitro* and orthotopic *in vivo* models, have also revealed a novel role for the MEK inhibitor selumetinib in regulating SHH medulloblastoma progression both *in vitro* and *in vivo*. Our work provided the first evidence that the MEK/ERK pathway is a therapeutic target in human SHH medulloblastoma. Both studies were supported by my 5-year CIHR operating grant (2014-2019).

2. Characterizing the role of OTX2 in regulating self-renewal and differentiation of highly aggressive Group 3 and Group 4 medulloblastoma

***Zagozewski J, et al., 2020. An OTX2-PAX3 signaling axis regulates Group 3 medulloblastoma cell fate. Nature Communications*. July 20; 11(1):3627. doi: 10.1038/s41467-020-17357-4.**

Stromecki M, et al. 2018. Characterization of a novel OTX2-driven stem cell program in Group 3 and Group 4 medulloblastoma. *Molecular Oncology* 2018. Apr;12(4):495-513.

Kaur R, et al., 2015. OTX2 exhibits cell context-dependent effects on cellular and molecular properties of human embryonic neural precursors and medulloblastoma cells.
***Disease Models & Mechanisms,* 8(10): 1295-1309.**

OTX2 overexpression is a molecular hallmark of Group 3 MB. We discovered that OTX2 is a master regulator of stem cell fate in Group 3 MB thus expanding the scope of OTX2's regulatory role beyond cell cycle. Our studies have also revealed novel druggable targets downstream of OTX2 that open up previously unexplored avenues for pursuit of new targeted therapies. This work was supported by an Innovation Grant from the Canadian Cancer Society Research Institute (CCSRI) (2012-2014), bridge funding from CIHR (Fall 2016 Project Grant competition) and an Innovation Grant from Alex's Lemonade Stand Foundation, USA (2017-2019).

3. Coudière Morrison L *, McClelland R *, et al., 2013. Deconstruction of medulloblastoma cellular heterogeneity reveals differences between the most highly invasive and self-renewing phenotypes. Neoplasia, 15(4): 384-398.

This study from my laboratory dissected heterogeneity within medulloblastoma cell cultures and suggested that successful treatment of pediatric brain tumors requires concomitant targeting of a spectrum of transitioning self-renewing and highly infiltrative cell subpopulations. Moreover, this work suggests that drugs targeting cells in the migratory or invasive state may not abrogate the putative cancer stem cells in a state of higher self-renewal.

4. Human embryonic stem cells (hESCs) as a human cancer model

Werbowetski-Ogilvie TE*, Coudière Morrison L, Fiebig-Comyn A, Bhatia M*. 2012. In vivo generation of neural tumors from neoplastic pluripotent stem cells models early human pediatric brain tumor formation. * denotes co-corresponding authorship
***Stem Cells*. 30(3): 392-404.**

Werbowetski-Ogilvie TE, et al., 2009. Characterization of human embryonic stem cells with features of neoplastic progression.
***Nature Biotechnology.* 27:91-97.**

human embryonic stem cells as a cancer model: Our *Stem Cells* paper was the first study to describe the use of human embryonic stem cell (hESC) derivatives as a model system for studying the molecular mechanisms contributing to pediatric brain tumor progression. Specifically, neural precursors from a starting population of neoplastic hESCs resemble Group 3 and 4 medulloblastomas *in vitro* and *in vivo*. These neoplastic hESCs were first characterized in my 2009 *Nature Biotechnology* paper during my time as a postdoctoral fellow. In this study, we described the first set of functional "litmus tests" to identify a transformed hESC in culture. Prior to this publication, studies in this area were limited to karyotypic analysis.

5. Werbowetski-Ogilvie TE, et al., 2006. Inhibition of medulloblastoma cell invasion by Slit.
***Oncogene* 25(37) 5103-5112.**

This study from my PhD highlights my experience with studying axon guidance signaling in the context of medulloblastoma. This work demonstrated the functional significance of the axon guidance cue SLIT2 to medulloblastoma cell motility. Very few studies to date have linked axon guidance genes to medulloblastoma progression, and it is fortuitous that we have discovered a potential novel role for axon guidance genes in self-renewal of the most aggressive medulloblastoma cell types (Stromecki et al., 2018).

Complete List of Published Work in PubMed:
https://www.ncbi.nlm.nih.gov/pubmed/?term=werbowetski-ogilvie

https://www.ncbi.nlm.nih.gov/pubmed/?term=werbowetski+t

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

1. Canadian Institutes of Health Research Project Grant 10/2020-09/2025
Novel therapeutic targets for Group 3 medulloblastoma stem cells
The goal of this project is to identify the OTX2-mediated regulatory pathways and networks associated with the most aggressive Group 3 medulloblastomas.
Role: PI

2. CancerCare Manitoba Foundation Multidisciplinary Team Grant 07/2020-06/2023
Exploring the Regulatory Role of Medulloblastoma Stem Cells
The goal of this project is to identify the molecular pathways regulating self-renewal and differentiation in medulloblastoma stem cells from the most aggressive Group 3 subgroup.
Role: PI

3. CancerCare Manitoba Foundation 07/2019-06/2021
Combinatory therapies for SHH medulloblastoma
The goal of this project is to evaluate novel, targeted therapies in combination with MEK inhibition as potential treatments for SHH medulloblastoma.
Role: PI

4. Rally Foundation for Pediatric Cancer Research 07/2019-06/2021
Combinatory therapies for SHH medulloblastoma
The goal of this project is to evaluate novel, targeted therapies in combination with MEK inhibition as potential treatments for SHH medulloblastoma.
Role: PI

5. Canada Research Chair (CRC) Tier II in Neuro-oncology and human stem cells 11/2011-06/2022
Identification of new molecular targets that regulate brain tumor progression
The overall goal of this 5-year renewable program grant is to identify novel therapeutic targets for the treatment of the most common type of primary malignant pediatric brain tumor, medulloblastoma.
Role: PI

Completed Research Support

1. Alex's Lemonade Stand Foundation Innovation Grant 10/2017-09/2019
Characterization of novel OTX2-semaphorin gene signaling pathways regulating the "grow and go" arms of highly aggressive medulloblastomas
The goal of this project is to characterize novel signalling pathways regulated by OTX2 in the most highly malignant Group 3 and Group 4 medulloblastoma.
Role: PI

2. Natural Sciences and Engineering Research Council of Canada (NSERC) 04/2013-03/2019
Investigating the role of Lin28A in human embryonic neural lineage function
The overall goal of this study is to functionally characterize the role of Lin28A in regulating the balance between self-renewal and differentiation during normal neurodevelopment.
Role: PI

3. Canadian Institutes of Health Research Operating Grant 04/2014-03/2019
Functional characterization of novel biomarkers for subtype-specific medulloblastoma cell phenotypes
The overall goal of this study is to functionally characterize newly identified biomarkers in SHH medulloblastoma cells and to determine their role *in vitro* and *in vivo*.
Role: PI

4. Canadian Institutes of Health Research Project Grant 04/2017-09/2017

Characterization of novel OTX2-semaphorin gene signaling pathways regulating the "grow and go" arms of highly aggressive medulloblastomas
The goal of this project is to characterize novel signalling pathways regulated by OTX2 in the most highly malignant Group 3 and Group 4 medulloblastoma.
Role: PI

5. Canadian Institutes of Health Research Project Grant 09/2016-08/2017
Targeting the regulation of subtypes of autophagy in cell survival and death to develop novel treatment strategies for glioblastoma
The goal of this project is characterize the role of autophagy in the most highly aggressive adult brain tumor, glioblastoma.
PI: Dr. Spencer Gibson
Role: Co-PI

6. The University Collaborative Research Program (UCRP)/ 01/2016-31/2017
Department of Biochemistry & Medical Genetics
Investigating chromosomal instability in ovarian cancer stem cells
The overall goal of this project is to evaluate chromosome instability in putative ovarian cancer stem cell populations derived from cell lines and patient samples.
PI: Dr. Mark Nachtigal
Role: Co-PI

7. Children's Hospital Research Institute of Manitoba/Kenzie's Kauze 07/2016-06/2017
Delineating the OTX2 regulatory network: Targeting the "grow and go" arms of the most aggressive medulloblastomas
The goal of this study is to identify and fully characterize the role of novel OTX2-target genes in regulating self-renewal or stem cell function and cell motility in the most highly aggressive medulloblastomas.
Role: PI

8. Canadian Cancer Society Research Institute (CCSRI) Innovation Grant. 02/2012-01/2014
Using human embryonic stem cells to understand early molecular events during pediatric brain tumorigenesis
The goal of this study was to use human embryonic stem cells and their neural derivatives to identify novel early molecular events leading to pediatric medulloblastoma progression.
Role: PI

9. Children’s Hospital Research Institute of Manitoba (CHRIM) 06/2013-05/2014
The role of CD271/p75NTR in medulloblastoma tumorigenesis
The goal of this study was to investigate the role of CD271/p75NTR in medulloblastoma progression *in vivo*.
Role: PI

10. Research Manitoba Establishment Grant 07/2011-06/2014
Identification of new molecular targets that regulate malignant brain tumor progression
The goal of this study was to identify new molecular targets that regulate medulloblastoma and glioblastoma brain tumor progression using both *in vitro* and *in vivo* models.
Role: PI

11. Research Manitoba Operating Grant 07/2013-06/2015
Investigating the role of Lin28A during early human neurodevelopment and pediatric brain tumorigenesis
The major goal of this project was to use human embryonic stem cells and their neural derivatives to characterize the role of Lin28A in medulloblastoma progression.
Role: PI