



A 10 Year Retrospective

imagine 09/10

The Annual Scientific Report of
The Arthur and Sonia Labatt Brain Tumour Research Centre
at The Hospital for Sick Children



Dr. James Rutka, Co-Director

MESSAGE FROM DR. JAMES RUTKA

This past year has been characterized by several new advances in the field of brain tumour research. Once again, we are pleased that several of these have been made within the Arthur and Sonia Labatt Brain Tumour Research Centre (BTRC).

Michael Taylor's team has discovered that the paediatric brain tumour known as "medulloblastoma" is actually comprised of four separate diseases (*J Clin Oncology 2010*). Annie Huang's team discovered an association between amplification of a chromosome 19q13.41 microRNA polycistron and aggressive supratentorial primitive neuroectodermal tumors (*Cancer Cell 2009*), and that silencing of thrombospondin-1 is critical for Myc-induced metastatic phenotypes in medulloblastoma (*Cancer Res 2010*). Cynthia Hawkins and Uri Tabori showed that p53 mutations predict for a universally poor survival in children with medulloblastoma (*J Clin Oncol 2010*). Peter Dirks wrote a seminal review on microRNAs and parallel stem cell lives (*Cell 2009*). Gelareh Zadeh demonstrated a role for angiopoietin-2 in regulating growth and vascularity in astrocytomas (*J Oncol 2010*). Ab Guha's team used iTRAQ analysis to show that the loss of collapsing response mediator Protein1 promotes the invasion of human gliomas expressing EGFRvIII (*Cancer Res 2009*). Jane McGlade's group demonstrated that Numb regulates post-endocytic trafficking and degradation of Notch-1 (*J Biol Chem 2009*). And finally, my research group identified the SFRP family of WNT inhibitors which function as tumor suppressor genes in medulloblastoma (*Oncogene 2010*).

We are pleased to provide this summary of the progress made within the BTRC for 2009-10. We hope you will appreciate our enthusiasm for and dedication to the field of brain tumour research as you read through the pages of this year's scientific report.



Dr. Ab Guha, Co-Director

THE LABATT BTRC – A 10 YEAR RETROSPECTIVE

Few of us would have predicted the power of the generous philanthropic gifts of Arthur and Sonia Labatt which helped us establish the Labatt BTRC more than 10 years ago. We now find ourselves in over 15,000 sq feet of bench and workspace with 10 principal investigators (PIs) who are engaged as independent scientists pursuing their research efforts on paediatric and adult brain tumours. Our current space on the 11th floor of the Medical and Related Sciences (MaRS) building at the corner of College and Elizabeth Streets is newly renovated and completely equipped with tissue culture rooms, cell imaging facilities, workspace for graduate and post-doctoral students, a conference room, and a major equipment room. The laboratory space is fashioned on an open concept theme where bench modules are placed side-by-side, fostering the collaboration of researchers from different laboratories. This is a far cry from where we started 10 years ago on the 3rd floor of the Elizabeth McMaster Building with 4,000 sq feet and four PIs. As excited and pleased as we are with our current space, all of us are enthusiastic about the prospect of moving into the new SickKids Research Institute Tower. The Tower, located at the corner of Bay and Elm Streets which is now under construction and scheduled to be completed in the next three years. Stay tuned as we keep you informed in the future about our transition to the new SickKids Research Tower.



In 1997, Arthur and Sonia Labatt generously donated \$5 million in research funding to be used for the study of the molecular biology of human brain tumours. In 2006, the Labatts more than doubled their original commitment to the BTRC. Their tremendous philanthropic gift has served as the catalyst which has led to the incredible growth and success of the Centre. We are truly indebted to the Labatts for their vision in supporting brain tumour research at The Hospital for Sick Children, the University Health Network, and the University of Toronto.

ABOUT THIS SPECIAL 10 YEAR RETROSPECTIVE ISSUE

In 2008, we celebrated our 10th anniversary of operations within the Labatt BTRC. In honour of this event, a gala was held in the MaRS Conference centre. Accordingly, this edition of “Imagine” captures the scientific achievements that have been made over the past decade. In this issue, we continue to highlight the major accomplishments that have taken place within the BTRC during this past year, but we also outline the evolution of our Centre over the past 10 years. As tribute to their dedication and hard work over the past decade, we have asked the original four scientists, Dr’s McGlade, Guha, Dirks and Rutka, to predict where they envision the Labatt BTRC and research in the field of brain tumours to be in the next 10 years.

The front and back covers of this special 10 year retrospective visually chronicles the progress we have made since the inception of the Labatt BTRC. We hope you will enjoy the opportunity we have taken to reflect upon our past while we look forward with equal enthusiasm to the future.



PRINCIPAL INVESTIGATORS AT THE BTRC



Left to right: Dr. Michael Taylor, Dr. Uri Tabori, Dr. Ab Guha, Dr. Jane McGlade, Dr. Annie Huang, Dr. Peter Dirks, Dr. Cynthia Hawkins and Dr. James Rutka (Missing Dr. Sidney E. Croul, Dr. Gelareh Zadeh and Dr. Todd Mainprize)



ABOUT THE BTRC LOGO

The Arthur and Sonia Labatt Brain Tumour Research Centre logo was created at the time of the grand opening of the centre in January 1999. The logo depicts a dove, symbolizing hope, carrying a twig in its beak. The twig is actually a piece of double-stranded DNA representing molecular medicine. The logo symbolizes the mandate of the BTRC: Hope through molecular medicine.





DR. JAMES RUTKA

Co-Director, The Arthur and Sonia Labatt Brain Tumour Research Centre, Principal Investigator

When a child is diagnosed with a brain tumour the family is faced with a potentially catastrophic experience. Our vision for the next ten years is to change this experience into one of hope and reassurance. Currently, the therapy for most childhood brain tumours is physical removal by surgery followed by a combination of radiation and/or chemotherapy.

While we have seen improved survival and have had successful outcomes, the children often suffer severe side effects that can persist for a lifetime. Coupled with this, the most common reason for treatment failure is due to recurrence of the tumour because some of the tumour cells have escaped by migrating outwards from the initial site prior to surgical removal.

One of the main research interests of our lab is to understand at the genetic and molecular level how tumour cells move and invade areas outside of the original tumour site. In recent years we have discovered several proteins in a pathway that are overactive in migrating tumour cells. With the recent advances in genomic analyses, we can profile a very small amount of tumour DNA within hours. We speculate that within 10 years we can examine patient blood samples or tumour samples directly at the time of surgery to rapidly evaluate which genes are abnormally active in the tumour. Armed with this information, we can then tailor our treatment to the individual patient and use only the therapeutics that will be beneficial to the patient. We anticipate that targeting one gene or pathway at a time is likely not going to be fully effective, therefore we envision in the future using a combination therapy approach to target multiple levels of the migration machinery.

Currently we are also working on new delivery approaches to ensure that therapeutics reach tumour cells specifically. In the next 10 years, we hope to use these markers on the outside of the tumour cells to specifically deliver the treatments to only cancer cells and not normal cells nearby, thereby significantly reducing side effects. Taken together, our 10 year plan is to focus our research efforts on finding new ways to identify tumour specific targets within the individual patient and use this information to deliver an ideal combination therapy that will stop tumour growth and invasion with minimal deleterious side effects on the child.

STAFF OVER THE DECADE

- Kotaro Akaishi *Fellow*
- Mylene Bouget *Technician*
- Jong Hee Chang *Fellow*
- Arnold Etame *Grad Student*
- Brian Goldbourn *Technician*
- Mustafa Guduk *Fellow*
- Sherri-Lynn Hubbard *Technician*
- Jason Hwang *Fellow*
- Stacey Ivanchuk *Grad Student*
- Ian Kamaly *Fellow*
- Chinatsu Kasuga *Fellow*
- Dong-Seok Kim *Fellow*
- Paul Kongkham *Grad Student*
- Tomohiko Kouhata *Fellow*
- John Kuo *Fellow*
- Andrew Liang *Fellow*
- James Loukides *Clinical Technician*
- Todd Mainprize *Grad Student*
- Michelle Mastronardi *Technician*
- Soma Mondal *Grad Student*
- Juan Moreno *Fellow*
- Shoichi Nagai *Fellow*
- Paul Northcott *Technician*
- Sara Onvani *Grad Student*
- Hirokatsu Osawa *Fellow*
- Aurelia Peraud *Fellow*
- Young-Shin Ra *Fellow*
- Amit Ray *Fellow*
- Andres Restrepo *Technician*
- Fredericke Rutten *Overseas Volunteer*
- Bodour Salhia *Grad Student*
- Ho-Jun Seol *Fellow*
- Christian Smith *Associate*
- Mandeep Tamber *Grad Student*
- Michael Taylor *Grad Student*
- Yuzo Terakawa *Fellow*
- Shigeo Ueda *Fellow*
- Wouter van Furth *Fellow*
- Adrienne Weeks *Grad Student*
- Raafat Yahya *Fellow*
- Naoki Yokota *Fellow*

FUNDING OVER THE DECADE

- | | |
|---|---|
| b.r.a.i.n.child | NCIC (National Cancer Institute of Canada) |
| Canadian Cancer Society Research Institute | Ontario Cancer Research Network |
| CIHR (Canadian Institutes of Health Research) | Pediatric Brain Tumor Foundation of the United States |
| Katie's Kids for the Cure | Rochelle Sherwood Endowment Fund |
| Labatt BTRC Endowment Fund | Terry Fox New Frontiers |
| Laurie Berman Fund for Brain Tumour Research | The Wiley Fund |
| Megan's Walk | |

PUBLICATIONS OVER THE DECADE: 85

WEBSITES OF INTEREST

- www.sickkids.ca/Research/Rutka-Lab/index.html
- www.sickkids.ca/AboutSickKids/Directory/People/R/James-Rutka.html
- www.pbtfus.org/

DR. AB GUHA

Co-Director, The Arthur and Sonia Labatt Brain Tumour Research Centre, Principal Investigator

Management of nervous system tumors affecting the Central Nervous System (CNS) and Peripheral Nervous System (PNS) is multi-disciplinary. As a neurosurgeon-scientist working with other members of BTRC and research community, we bring clinical questions to the laboratory towards understanding the biology, origin and altered regulatory mechanism(s) of tumors. We utilize a variety of model systems from cell lines: tumors implanted in mice and mice which have been genetically altered to spontaneously form tumors and operative specimens. Tumor research is somewhat of a long-journey, however, if not ventured will not yield significant in-roads to our understanding and ultimate goal of making significant improvements for our patients.

My lab studies malignant gliomas (the most common CNS tumors in adults) and neurofibromas/schwannomas/malignant peripheral nerve system tumors (the most common adult PNS tumors). We use the breadth of model systems briefly listed above. In gliomas, we have made and continue to make transgenic mouse models to study the role and interaction and also discover new genetic alterations that are relevant in human gliomas and their origin. We are investigating the effect of the tumor microenvironment on the molecular alterations and thereby growth and resistance to therapies of gliomas. Specifically, we are interested in how gliomas metabolize sugar differently, how it recruits various angiogenic and survival factors differentially in varying tumor regions. Biomarkers, which can be detected in the blood, are an area of interest because they aid with the diagnosis, molecular make-up, prognosis, treatment choice and monitoring treatment response of gliomas.

In PNS tumors we are interested in genetic alterations and aberrant signalling molecules which are involved in PNS tumor growth. An area of special interest is understanding the cognitive alterations that arise in syndromes such as Neurofibromatosis-1 which are also associated with PNS tumors. This area is of high clinical significance, without much understanding of underlying molecular mechanisms(s).

In summary, my lab will continue to pursue mechanism at the molecular genetic level that lead to the formation, growth and therapeutic resistance of nervous system tumors in a collaborative manner. The ultimate goal is that some of our findings will eventually translate to better therapies for our patients.

FUNDING OVER THE DECADE

American Cancer Research Society

Arraybiopharm

Canadian Cancer Society Research Institute

Childhood Brain Tumor Foundation

CIHR (Canadian Institutes of Health Research)

Cleveland Clinic Foundation

Donald Whitewood

Heart and Stroke Foundation of Ontario

Labatt BTRC Endowment Fund

National Brain Tumor Foundation

National Institutes of Health

NCIC (National Cancer Institute of Canada)

NSERC

Ontario Cancer Research Network

Ontario Ministry of Health

Physicians' Services Incorporated

Sherring-Plough Virtual National Bank

US Army Department of Defense



STAFF OVER THE DECADE

Sameer Agnihotri *Grad Student*

Alenoosh Albertvartanian *Grad Student*

Anandh Balasubramaniam *Postdoc*

Vedant Arun *Grad Student*

Suhail Asrar *Postdoc*

Karolyn Au *Grad Student*

Priya Bhola *Grad Student*

Kelly Burrell *Technician*

Sabrina De Girolamo *Grad Student*

Hao Ding *Postdoc*

Aaron Gajadhar *Grad Student*

Sabiha Gardezi *Co-op Student*

Deepak Kamnasaran *Postdoc*

Zia Karim *Technician*

Nelson Lau *Technician*

Johann Micallef *Grad Student*

Tadashi Miyagawa *Fellow*

Joydeep Mukherjee *Postdoc*

Diana Munos *Grad Student*

Ajay Pandita *Associate*

Baoping Qian *Technician*

Gayatri Shangari *MSc Student*

Nesrin Sabha *Assistant*

Alenoush Varkarian *Grad Student*

Heather Vogel *Technician*

Qingzia Wei *Postdoc*

Joseph Wiley *Grad Student*

Amparo Wolf *Grad Student*

Stacey Woods *Technician*

Oliver Yeung *Technician*

Gelareh Zaden *Grad Student*

Cindy Zhang *Assistant*

PUBLICATIONS OVER THE DECADE: 67

WEBSITES OF INTEREST

www.sickkids.ca/Research/Guha-lab/index.html

www.sickkids.ca/AboutSickKids/Directory/People/G/Abhijit-Guha.html

www.sontagfoundation.org/display.aspx?page=home



DR. JANE MCGLADE

Senior Scientist, Principal Investigator

Brain tumors arise as a consequence of a multi-step process in which control over cell fate, and behaviours such as growth and migration are lost. In a normal cell, these properties are regulated by signals that come from the surrounding tissue and neighbouring cells. Signals are interpreted by receptors that pass the signal on to circuitry inside the cell which is made up of networks of proteins that control cell behaviour. The purpose of our research is to understand how these protein networks control normal cell behaviour and function and how specific proteins within a network are altered in cancer cells. We hope that understanding these processes can provide the basis for new strategies and a rationale for drug design in the development of new treatments for brain tumors. Over the last several years we have identified and described new protein networks that control the activity of cell receptors, and recently we have discovered that alterations in these proteins is associated with brain tumors. We have also discovered a new protein network that controls the shape and migratory behaviour of cells. Our goal over the next 10 years is to use advanced proteomic approaches to map these protein networks in brain tumors and put screening techniques to identify small molecules and drugs that can return these signaling networks to their normal activity.

STAFF OVER THE DECADE

Andrea Angus, *Technician*
Kaylee Barber, *Co-op student*
Sally Benn, *Postdoc*
Donna Berry, *Technician*
Christophe Debonneville, *Postdoc*
Sascha Dho, *Associate*
Emily Griffiths, *Postdoc*
Jonathon Krieger, *Grad Student*
Kimberly Lau, *Grad Student*
Irene Leung, *Grad Student*
Larissa Lontos, *Grad Student*
Michael Loreto, *Grad Student*
Melanie McGill, *Postdoc*
Fabio Morgese, *Postdoc*
Jenny Nie, *Postdoc*
Ben Pakuts, *Grad Student*
Brittany Prevost, *Grad Student*
Renu Sarao, *Technician*
Rachel Shaye, *Technician*
Nancy Silva, *Postdoc*
Dan Simoncic, *Grad Student*
Christian Smith, *Grad Student*
Cheryl Wolting, *Grad Student*
Stacey Woods, *Grad Student*
Leanne Wybenga-Groot, *Postdoc*

FUNDING OVER THE DECADE

b.r.a.i.n.child
Canadian Cancer Society Research Institute
Cancer Research Society
CIHR (Canadian Institutes of Health Research)
Foundation Fighting Blindness
Labatt BTRC Endowment Fund
Leukemia Research Fund of Canada
NCIC (National Cancer Institute of Canada)

PUBLICATIONS OVER THE DECADE: 52

WEBSITES OF INTEREST

www.sickkids.ca/Research/McGlade-Lab/index.html
www.sickkids.ca/AboutSickKids/Directory/People/M/Jane-McGlade.html
riweb.sickkids.on.ca/facultyOffice/



HIGHLIGHTS FROM PREVIOUS ISSUES OF IMAGINE

2000 – 2001 First edition of Imagine
2001 – 2002 Dr. Annie Huang joins the BTRC as Principal Investigator
2003 Dr. Peter Dirks discovers the relation between stem cells and brain tumours
2003 – 2004 Dr. Michael Taylor joins as Principal Investigator
2004 – 2005 Dr Cynthia Hawkins joins as Principal Investigator
2005 – 2006 Dr. Uri Tabori joins as Principal Investigator
2006 Labatt BTRC moves to the MaRS complex
2007 Historic signing of new philanthropic gift to SickKids and BTRC by the Labatts

DR. PETER DIRKS

Scientist, Principal Investigator

Our laboratory has been taking a stem cell view of brain tumors. Our research supports that brain tumors can be thought of as an aberrant or uncontrolled stem cell system. Within the tumor mass, there are small numbers of tumor cells endowed with stem cell properties which drive the growth of the tumor. These generate more tumor stem cells and tumor cells that form the bulk of a tumor mass, but do not contribute to tumor growth. Our research strongly supports that tumor stem cells are the key drivers of brain tumor growth and the critical targets for treatment. There remains much to learn, as research in this area is in its early days. We predict that by continuing to apply stem cell concepts and methodologies to brain tumor research we will accelerate new and exciting discoveries.

Our current research is intensively focused on unlocking the secrets of brain tumor stem cells. We want to be able to precisely identify these cells, understand the molecular machinery that determines their behaviour, and shut them down with treatment. In 10 years, we hope to be able to acquire a clearer picture of the tumor stem cell from each patient's tumor to enable us to deliver a curative individualized therapy. Today, we may not be able to cure a brain tumor without targeting its tumor stem cell, but tomorrow, we hope to offer patient specific tumor stem cell treatment.

FUNDING OVER THE DECADE

b.r.a.i.n.child

California Institute of Regenerative Medicine

Canadian Cancer Society Research Institute

Canadian Research Society

CIHR (Canadian Institutes of Health Research)

Genome Canada Competition

Jack Michael Baker Fund

Jessica Durigon Family (Jessica's Footprint)

Labatt BTRC Endowment Fund

NCIC (National Cancer Institute of Canada)

Networks of Centres of Excellence

OICR (Ontario Institute of Cancer Research)

Pediatric Brain Tumor Foundation of
the United States

Robert Capotosto Family

Stem Cell Network

PUBLICATIONS OVER THE DECADE: 25

WEBSITES OF INTEREST

www.sickkids.ca/Research/Dirks-Lab/index.html

www.sickkids.ca/AboutSickKids/Directory/People/D/Peter-Dirks.html

www.cancer.ca/Canada-wide/Cancer%20research/Meet%20our%20researchers/Dr%20Peter%20Dirks.aspx?sc_lang=en



STAFF OVER THE DECADE

Kevin Au, *Technician*

Tzvi Aviv, *Postdoc*

Caroline Brandon, *Grad Student*

Ian Clarke, *Technician*

Phedias Diamandis, *Grad Student*

Sonam Dolma, *Grad Student*

Mia Enarsson, *Foreign Observer*

Jeremy Graham, *Technician*

Kevin Graham, *Postdoc*

Victoria Gratl, *Grad Student*

Renee Head, *Technician*

Takuichiro Hide, *Fellow*

Jenny Ho, *Postdoc*

Leanne Jamieson, *Grad Student*

Lillian Lee, *Technician*

Jen Li, *Technician*

Erick Ling, *Grad Student*

Kathy Nethry-Brokk, *Technician*

Rohita Sharma, *Postdoc*

Sheila Singh, *Grad Student*

Mizuhiko Terasaki, *Fellow*

Ryan Ward, *Grad Student*

Koichi Yoshikawa, *Fellow*

HIGHLIGHTS CONTINUED

- 2007 Dr. Michael Taylor first Canadian to receive a Sontag Foundation Award as a Distinguished Scientist
- 2007 – 2008 Dr. Gelareh Zadeh joins as Principal Investigator
- 2008 Labatt BTRC at SickKids becomes an Institute of the Pediatric Brain Tumor Foundation of the US
- 2008 – 2009 Dr. Todd Mainprize joins as Principal Investigator
- 2010 Michael Taylor and colleagues discover that medulloblastoma is comprised of 4 separate variants



DR. ANNIE HUANG

Scientist, Principal Investigator

Brain tumours, the most common solid malignancies of childhood, differ from other solid malignancies in that they rarely metastasize outside of the central nervous system. Despite this relatively “restricted” pattern of progression, metastatic brain tumours are therapy resistant. Due to the devastating growth and neurocognitive consequences of the best current treatment which includes radiation, there is much interest in identifying molecular pathways that specify metastatic behaviour in malignant paediatric brain tumours, in order to ultimately develop more effective and less toxic tumour therapy.

Dr. Huang’s lab is interested in cellular and molecular mechanisms that underlie tumour progression in central nervous system primitive neuro-ectodermal tumours (PNET), which are the most frequent group of paediatric malignant brain tumours. Current projects involve use of high resolution genomic tools such as SNP microarrays and ChiP-on-chip technology to define novel genes and pathways associated with aggressive PNET phenotypes.

A major interest in the lab is to determine how c-Myc, a potent oncoprotein, specifies aggressive phenotypes in cerebellar PNET/medulloblastoma. To investigate the molecular basis of this association the lab has focused on identifying Myc protein interactors and target genes with key contributions to Myc-mediated transformation in medulloblastoma cells. Recently, a novel family of Myc interacting and co-transforming proteins, the JPO proteins, which are overexpressed in metastatic medulloblastoma was identified. Characterization of the role of JPO proteins and other novel Myc partners/targets in medulloblastoma/PNET pathogenesis is the focus of ongoing work.

LABORATORY PERSONNEL

Tiffany Chan, *Master’s Student*
Daniel Picard, *Master’s Student*
David Shih, *Master’s Student*
Tara Spence, *PhD Student*
Limei Zhou, *Research Associate*

RESEARCH SUPPORT

Brain Tumor Society, Children’s Brain Tumor Foundation U.S., CIHR, Eli-Lilly – Cancer Care Ontario, Labatt BTRC Endowment Fund, NCIC

WEBSITE OF INTEREST: www.sickkids.ca/Research/Huang-lab/index.html



DR. MICHAEL D. TAYLOR

Scientist, Principal Investigator

Dr. Taylor’s laboratory hopes to use the tools of forward and reverse genetics to better understand the underlying biology of medulloblastoma and ependymoma, two of the most common malignant paediatric brain tumours.

In forward genetic approaches, the normal cells that are thought to give rise to a cancer are perturbed in a systemic fashion in an attempt to determine which genes or signalling pathways promote malignant transformation. By randomly over-expressing genes in the cellular precursor of medulloblastoma, the lab hopes to determine which genes are important to the initiation, maintenance and progression of medulloblastoma. This sort of functional genomic approach has recently been made feasible by the completion of the mouse genome project.

In reverse genetics, primary human tumours are studied in an attempt to determine the genetic events that lead to transformation. The Taylor lab is using a number of genome-wide techniques to identify novel tumour suppressor genes and oncogenes important in the pathogenesis of medulloblastoma and ependymoma.

Through an understanding of the genetic basis of brain tumours, it is hoped that novel, rational therapeutics may be developed that are more effective and less toxic than existing therapies. It is hoped that synergism between forward and reverse genetic approaches will allow for key genes important in brain tumour biology to be identified.

LABORATORY PERSONNEL

Adrian Dubuc, *PhD Student*
Livia Garzia, *Postdoc*
Jessica Lui, *Technician*
Stephen Mack, *PhD Student*
Paul Northcott, *Postdoc*
John Peacock, *Technician*
Adi Rolider, *Postdoc*
Zueyuan Shang, *Technician*
Alexander Unterberger, *Postdoc*
Xiaochong Wu, *Postdoc*
Yuan Yao, *PhD Student*

RESEARCH SUPPORT

American Brain Tumor Association, CIHR, Labatt BTRC Endowment Fund, NCIC, NIH, Sontag Foundation

WEBSITE OF INTEREST: www.sickkids.ca/Research/Taylor-lab/index.html

DR. CYNTHIA HAWKINS

Scientist, Principal Investigator

Dr. Hawkins' laboratory focuses on genetic and proteomic markers for prognostication and therapy guidance in paediatric brain tumours including medulloblastoma, astrocytoma and ependymoma. Traditionally, medulloblastomas have been classified on the basis of their appearance into different pathological types, but with poor correlation between categories and outcome.

Dr. Hawkins' laboratory developed a clinical-biologic model to predict survival in medulloblastoma. Although this goes beyond previous studies in differentiating those children with a good versus a poor prognosis, Dr. Hawkins' laboratory aims to acquire more detailed knowledge of the biology of medulloblastomas in order to tailor therapy to the particular biology and predicted behaviour of an individual patient's tumour. Genome-wide approaches are being used to better understand the genes important for development of paediatric astrocytoma. Potential targets are then verified at the RNA and then protein level using tissue microarrays. In ependymoma, Dr. Hawkins' laboratory has found that expression of telomerase, a protein important for continued cell division, can predict outcome in paediatric ependymoma more effectively than clinical prognostic factors and is investigating its potential as a therapeutic target for these tumours.

DR. URI TABORI

Scientist, Principal Investigator

Dr. Tabori's lab is a translational lab aimed at transforming basic biology and clinical observations to improve prognostication and to find novel treatments for children with brain tumours. His lab focuses on mechanisms that control tumour progression and resistance to therapy. The lab is also focusing on tumours that have low and high grade components such as paediatric gliomas and neuroblastoma. Using these models, we plan to understand how tumours stop progressing, and to expand our knowledge of the specific pathways that control this unique behaviour. Specifically, we have shown that replicative and oncogene induced senescence may be the most important prognostic and predictive factors in some paediatric glial neoplasms. We are currently exploring the role of telomere maintenance inhibitors as novel therapies for higher grade paediatric gliomas such as neuroblastomas and glioblastomas which progress relentlessly.

Additionally, we are investigating how these and other mechanisms confer tumour radioresistance on the one hand, and host (patients) sensitivity to such toxic therapies on the other. We hope to be able to tailor future doses of radiation and develop agents which will enhance or reduce radiotherapy-related damage.

We are involved in exploring the interaction of cancer genetics and genetics with paediatric brain tumours through the role of germline and somatic mutations in TP53 and other genes in childhood gliomagenesis.



LABORATORY PERSONNEL

Pawel Buczkowicz, *Master's Student*
Andrew Morrison, *Technician*
Eugene Tam, *Co-op Student*
Maryam Zarghooni, *Postdoc*

RESEARCH SUPPORT

b.r.a.i.n.child, Brain Tumor Society, CIHR,
C17 Research Network

WEBSITE OF INTEREST: www.sickkids.ca/Research/hawkins-lab/index.html



LABORATORY PERSONNEL

Pedro Castelo-Branco, *Postdoc*
Tatiana Lipman, *PhD Student*
Erin Walker, *Postdoc*
Cindy Zhang, *Associate*
Natalya Zhokova, *Technician*

RESEARCH SUPPORT

Brain Tumor Society, CCS, CIHR

WEBSITE OF INTEREST: www.sickkids.ca/Research/tabori-lab/Index.html



DR. GELAREH ZADEH

Scientist, Principal Investigator

Dr. Zadeh's overall research goal is to gain a better understanding of the molecular regulators of tumour angiogenesis in response to ionizing radiation (IR) in order to improve the therapeutic benefit of radiation therapy (RT) for brain tumours. Her central hypothesis is that ionizing radiation modulates molecular regulators of tumour angiogenesis. She has two inter-related research aims to investigate her hypothesis. Her first aim focuses on understanding the molecular mechanisms that regulate bone marrow progenitor cells (BMPCs) and in specific endothelial progenitor cell's (EPCs) contribution in response to IR in both normal and tumour related vasculature.

The lab focuses on establishing the temporospatial response of BMPCs following IR in normal subcutaneous and intracranial tissue in addition to intracranial tumours. Her second aim is to identify the mechanisms and sequence of therapeutics targeting tumour angiogenesis concurrent with IR in order to identify the most efficacious therapeutic combination for treatment of malignant astrocytomas. She uses three principal anti-angiogenic strategies: VEGF-TRAP, Pharmaceutical inhibitors of angiogenesis and lastly, a novel strategy using radiation-activated angiogenic and anti-angiogenic genes of interest in collaboration with Dr. Scott, UK. In order to carry out these experiments, she takes advantage of a wide range of molecular biology, molecular imaging, molecular physics and angiogenesis techniques in collaboration with other groups.

LABORATORY PERSONNEL

Caroline Chung *Postdoctoral Fellow*
Kelly Burrell *Research Technician*

RESEARCH SUPPORT

Labatt BTRC Endowment Fund,
University Health Network (UHN)



DR. TODD MAINPRIZE

Scientist, Principal Investigator

Dr. Mainprize has two main areas of research interest. In his first area of interest, Dr. Mainprize is collaborating with scientists at Sunnybrook Health Science Centre to investigate the utility of MR-guided Focused Ultrasound in the treatment of primary and metastatic brain tumours. This novel modality can be used to safely and reversibly disrupt the blood-brain barrier allowing for better delivery of chemotherapeutic agents to a tumour. Focused Ultrasound can target and destroy tumour cells with millimeter accuracy and may be a radiation-free alternative to radiosurgery. In his second area of interest, he is investigating the various pathway dysregulations in meningiomas with the hopes of developing more effective treatments for recurrent and higher grade tumours.



DR. SIDNEY E. CROUL

Scientist, Principal Investigator

Dr. Croul's primary research interest is the role that cell surface adhesive molecules play in the tendency of certain central nervous system tumors, particularly medulloblastoma, to undergo leptomeningeal dissemination. This spread across the surface of the brain and spinal cord is associated with significant morbidity and mortality. The identification of these molecules may help to predict which patients are at risk for leptomeningeal dissemination at an earlier and more treatable stage than is presently possible. Recognition of cellular pathways which are activated by this spread may also help to design more effective and less toxic therapies than are currently available.

LABORATORY PERSONNEL

Donya Aref, *Masters Student*
Conner Moffat, *Technician*

RESEARCH AWARDS

Grant Miller Foundation,
University of Toronto, b.r.a.i.n.child

GRADUATES OF THE LABATT BTRC THIS YEAR



Kelsey Bertrand, MSc

The Role of Cell Adhesion Genes in the Pathogenesis of Medulloblastoma.



Caroline Brandon, MSc

Wnt Signaling in human neural stem cells and brain tumour stem cells.



Phedias Diamandis, PhD

Chemical genetic interrogation of neural stem cell: Phenotype and function of neurotransmitter pathways in normal and brain tumour initiating neural; precursor cells.



Kimberly Lau, PhD

Function and regulation of the cell fate determinant Numb in polarized epithelial cells.



Erick Ling, PhD

Using Notch Pathway Blockade to Define Human Glioblastoma Stem Cell Heterogeneity and Sensitivity to Neuronal Lineage Commitment.



Larissa Liontos, PhD

Role of the SRC-like adaptor proteins, SLAP and SLAP-2, in dendritic cell development and signaling.



Paul Northcott, PhD

Genomic Characterization of Medulloblastoma.



Ryan Ward, PhD

Identification of cancer stem cells in mouse models of brain tumors.



Ampro Wolfe, PhD

Hexokinase 2 is a key mediator of aerobic glycolysis promoting tumour growth in Glioblastoma Multiforme.



Cheryl Wolting, PhD

Development and Implementation of Gene Ontology Cluster Analysis of Protein Array Data.

GRADUATES OVER THE DECADE

Peter Dirks

Caroline Brandon, MSc
Phedias Diamandis, PhD
Victoria Gratl, MSc
Leanne Jamieson, MSc
Eric Ling, PhD
Sheila Singh, PhD
Ryan Ward, PhD

Ab Guha

Lilyana Angelov, MSc
Priya Bhola, MSc
Matthias Feldkamp, PhD
Johann Micallef, PhD
Gayatri Shangari, MSc
Joseph Wiley, MSc
Amparo Wolfe, PhD
Stacey Woods, MSc
Gelareh Zadeh, PhD

Annie Huang

Kyle Lee, MSc

Jane McGlade

Kimberly Lau, PhD
Irene Leung, PhD
Larissa Liontos, PhD
Stanley Liu, PhD
Michael Loreto, MSc
Melanie McGill, PhD
Ben Pakuts, MSc
Dan Simonic, PhD
Christian Smith, PhD
Cheryl Wolting, PhD

Michael D. Taylor

Kelsey Bertrand, MSc
Karen Zilberberger, MSc

James Rutka

Stacey Ivanchuk, PhD
Soma Mondal, PhD
Paul Northcott, PhD
Bodour Salhai, PhD
Michael D. Taylor, PhD

VISITING FELLOWS



JONG HEE CHANG

I graduated from Yonsei University College of Medicine in Seoul, Korea, in 1991, where I completed the four-year neurosurgical resident program and 2-year clinical fellowship. I then undertook a research fellowship at Washington University in St. Louis in February of 2003. I returned to Seoul in 2003 and am a staff neurosurgeon in the Brain Tumor and Neurooncology Section of Yonsei University Hospital.

My clinical work is largely focused on the management of brain tumours such as gliomas, metastases and meningiomas in adult patients. I am particularly interested in image-guided surgery and brain mapping using awake surgery. In my work I often felt ill-equipped and realized the limitation of current treatment modalities while I was treating gliomas patients. In order to better treat patients with malignant brain tumours, I felt it was necessary to gain some training in basic research of brain tumours in order to extend my knowledge about tumour biology and the development of therapeutics in neurooncology. I have been working as a research fellow under the supervision of Dr. James Rutka since February 2010. I am pleased to have the opportunity to pursue this training at the Brain Tumour Research Centre (BTRC). The BTRC is one of the most up-to-date and organized brain tumour research centres in the world. I believe my year long experience at BTRC will be a life-changing experience for me.



LIVIA GARZIA

I received a degree in medical biotechnology from the University of Naples in Italy in 2002. I then went on to pursue my PhD in life sciences at the Open University in Cambridge, UK. My research has been focused on two nervous system tumours – medulloblastoma and neuroblastoma – in which I studied altered non-coding RNAs involved in the disease pathogenesis. I have always been interested in how basic research can impact the outcome of severe diseases like paediatric brain cancers. I have always felt that better integration between clinicians and researchers and new tools to improve the tumours therapy is extremely important. Dr. Taylor's exciting new model of medulloblastoma which recapitulates the progression of the human pathology inspired me and I am thrilled to be starting a research fellowship in his group to study and improve this genetic model of medulloblastoma. I believe that our research will provide the scientific community with a new powerful tool to develop new anti-cancer drugs and treatments.



SHOICHI NAGAI

I joined the BTRC in September 2008. Prior to joining SickKids I was engaged in clinical neurosurgery work at Totama University Hospital in Japan. My work was focused on the treatment of adult malignant brain tumours, including glioma, primary central nervous system lymphoma and metastatic brain tumours. I pursued my PhD at the Brain Research Institute, Niigata University, Japan, studying molecular biology, with a specific focus on malignant gliomas. My thesis was on NF-kappaB. I am pleased to have the opportunity to pursue both a clinical and research career in tumours as it gives me the ability to understand clinical problems and address them through research. Since joining the BTRC I have spent my time studying regulatory molecules for the dynamics of the actin cytoskeleton under Dr. Rutka. Through this research I hope to understand the molecular mechanism of glioma invasion.

XIAOCHONG WU

In 1995 I won a Swedish Institute Scholarship and attended the Lund University in Sweden. With a food biochemistry background from China, my research in Sweden focused on the mutagenicity of processed food. It was at Lund University that I was prompted to switch my interest to the field of cancer research. In 1996, I move to Houston, Texas to pursue my PhD in molecular cell biology and cancer biology at the Graduate School of Biomedical Sciences, University of Texas at Houston.

I left Texas in the summer of 2006 to join Dr. Michael Taylor's laboratory at SickKids as a postdoctoral fellow. Over the past four years, I have come to appreciate the closeness, enthusiasm, and collaborative spirit of the international neurooncology community. In comparison to many other malignant diseases, paediatric neurooncology is both fascinating, and under-served.

My research is focused on using mouse models to study the link between the normal development of the brain, and the formation and progression of paediatric brain tumours.



JUNKOH YAMAMOTO

I have been working as a research fellow at BTRC under the supervision of Dr. Rutka since September, 2009. I am a graduate of Hamamatsu University School of Medicine in Japan. I entered the training program in neurosurgery at Hamamatsu University School of Medicine in 1996. During my residency, I achieved a PhD in photodynamic therapy for malignant glioma, specializing in the pathogenesis of cytotoxic effect in singlet oxygen. I received my Japanese Neurosurgical Board in 2002 and worked as an assistant professor of Clinical Neurosurgery at the University of Occupational and Environmental Health in Japan with an interest in the biology of human brain tumours. Currently, I am investigating molecular mechanisms in malignant glioma, in particular the role of the interleukin-13 receptor in glioma.



YUZO TERAOKA

I have worked in Dr. James Rutka's laboratory at the Arthur and Sonia Labatt Brain Tumour Research Centre at SickKids since April 2010. I recently took part in a research project to investigate the genes related to the development and tumorigenesis of medulloblastoma.

I graduated from Osaka City University Graduate School of Medicine in 1999 and finished a residency program in neurosurgery in 2005. Following completion of my residency, I worked as a general neurosurgeon, mainly treating patients with cerebrovascular diseases. During this period, I was also engaged in clinical studies concerning the neuro-imaging of brain tumours with positron emission tomography (PET) and in neurophysiological experiments with magnetoencephalography (MEG) at the Osaka City University Hospital.

The Osaka City University Hospital is one of the leading hospitals in Japan which focuses on treating patients with brain tumours. However, this hospital has not yet organized a brain tumour research team in our department. I applied to Dr. Rutka's laboratory to learn skills and techniques necessary for basic research using a molecular biological approach which I hope I can bring back to my team in Japan. I am pleased and excited about the opportunity to gain knowledge and experience in Dr. Rutka's laboratory.





A 10 YEAR HISTORY OF GUEST SPEAKERS TO THE BTRC

2001

David Louis, MGH Harvard University - Thursday, October 25

2002

David James, Mayo Clinic - Tuesday, June 18

2003

E. Antonio Chioocca, Harvard Medical School - Thursday, October 16

2004

Paul Muller, St. Michael's Hospital - Thursday, November 25

Steven C. Clifford, University of Newcastle, - Thursday, June 17

Wan Lam, British Columbia Cancer Agency - Thursday, October 28

2005

Donna Senger, University of Calgary - Wednesday, February 9

Uri Tabori, The Hospital for Sick Children - Thursday, April 28

Marc Symons, Feinstein Institute for Medical Research - Thursday, October 27

2006

Kazuo Tabuchi, Saga University Nabeshima - Monday, February 20

Sohail Ahmed, Centre for Molecular Medicine Singapore - Wednesday, June 28

Charles Eberhart, Johns Hopkins University School of Medicine - Thursday, December 14

2007

Bernie Maria, Darby Children's Research Institute - Monday, May 7

Lara Shayne Collier, University of Minnesota - Wednesday, May 9

Johanthan Finlay, Children's Hospital Los Angeles - Thursday, May 10

Hai Yan, Comprehensive Cancer Center Duke University - Thursday, May 24

Enrique Torchia, St. Jude Children's Research Hospital - Wednesday, June 6

Janusz Rak, Montreal Children's Hospital - Thursday, December 6

2008

Donna Senger, Clark H. Smith Brain Tumor Research Center - Monday, January 28

Arnab Chakravarti, Harvard Medical School - Wednesday, January 30

Anindya Bagchi, Cold Springs Harbor - Wednesday, March 12

Santosh Kesari, Brigham and Women's Hospital - Thursday, March 27

Linda L. Restifo, University of Arizona Brain Institute Cognitive Science - Wednesday, April 2

Kumar Somasundaram, Indian Institute of Science - Monday, August 25

Dr. John Bell, University of Ottawa - Wednesday, October 1

Stefan Pfister, German Cancer Research Center - Thursday, November 27

Daniel Fults, University of Utah School of Medicine - Thursday, December 11



12TH ANNUAL LABATT BTRC ACADEMIC LECTURESHIP 2010

This year's guest speaker was Dr. Waldemar Debinski, Professor of Neurosurgery, Director, Brain Tumor Center of Excellence at Wake Forest University at Winston-Salem, North Carolina. The topic of his lecture was "Will We Score a Bull's Eye in Targeting GBM?"



Dr. Waldemar Debinski



Left to right: Dr. Eric Bouffet, Dr. James Rutka and Dr. Waldemar Debinski



Left to right: Dr. Ab Guha, Dr. Todd Mainprize, Dr. Jane McGlade, Dr. Uri Tabori, Dr. Gelareh Zadeh, Dr. James Rutka, Dr. Waldemar Debinski, Dr. Cynthia Hawkins and Dr. Annie Huang

BTRC GUEST LECTURERS 2009-2010

Friday April 17, 2009 *Stretch-Regulated Membrane Traffic in Bladder Umbrella Cells*, Gerard Apodaca, PhD Departments of Medicine and Cell Biology and Physiology University of Pittsburgh

Thursday February 25, 2010 *Epigenetic changes on the way from neural progenitor to paediatric ependymoma*, Tim Van Meter, PhD, Virginia Commonwealth University

Thursday April 8, 2010 *Children are not small adults: Molecular pathways in paediatric astrocytomas*, Nada Jabado, MD, PhD, Department of Pediatrics Montreal Children's Hospital McGill University Health Centre

Wednesday April 28, 2010 *Criminal Intent: What normal progenitors cells teach us about the biology of brain tumors*, Rob Wechsler Reya, PhD, Duke Institute for Brain Sciences, Pharmacology & Cancer Biology

Thursday June 3, 2010 *An unfinished story of glioblastoma stem cell self-renewal*, Sadhan Majumder, PhD, Department of Cancer Genetics/Department of Neuro-Oncology, MD Anderson

Thursday July 15, 2010 *To Live or Let Die: Understanding how to therapeutically target survival and death pathways in cancer*, Spencer Gibson, PhD, Provincial Director, Research CancerCare Manitoba

PREVIOUS BTRC ANNUAL ACADEMIC LECTURERS

1999 Robert Martuza, MD
Professor and Chairman,
Department of Neurosurgery,
Georgetown University
Director of Georgetown Brain Tumor Center

2000 Gregory Cairncross, MD
Vice President, Cancer Care Ontario –
Southwest Region
Chair, Department of Oncology,
University of Western Ontario

2001 David Kaplan, PhD
Professor, Department of Neuroscience
McGill University
Director of Brain Tumour Research Centre,
Montreal Neurological Institute

2002 Charles Stiles, PhD
Department of Microbiology and
Molecular Genetics Harvard Medical School
The Dana-Farber Cancer Institute

2003 Luis Parada, PhD
Director, Center for Developmental Biology
at the University of Texas Southwestern
Medical Center

2004 Eric Holland, MD, PhD
Associate Professor, Neurosurgery,
Neurology & Cell Biology Memorial
Sloan-Kettering Cancer Center

2005 Darell Bigner, MD, PhD
Edwin L. Jones, Jr. and Lucille Finch Jones
Cancer Research Professor
Director, Pediatric Brain Tumor Foundation
Institute at Duke
Deputy Director, Duke Comprehensive
Cancer Center

2006 Webster Cavenee, PhD
Director of the Ludwig Institute
for Cancer Research
Professor of Medicine at the
University of California at San Diego

2007 David H. Gutmann, MD, PhD
Professor Department of Neurology
Washington University School of Medicine

2008 Henry Brem, MD, PhD
Director of Neurosurgery Harvey Cushing
Professor of Neurosurgery
Professor of Oncology and Ophthalmology
at Johns Hopkins University

2009 Joe Costello, PhD
Assistant Professor of Neurological Surgery
Chair in Molecular Neuro-Oncology UCSF

STUDENT AWARDS

Vedant Arun

Princess Margaret Hospital
Foundation Graduate Fellowship
Margaret and Howard Gamble
Research Grant
Vivekanada Graduate Prize

Tzvi Aviv

Terry Fox Post-doc Fellowship

Tiffany Chan

Restracomp
Hilda and William Courtney
Clayton Paediatric Research Fund
OSOTF Frank Fletcher
Memorial Fund

Julia Diabio

NSERC Canada Graduate Scholarship

Adrian Dubuc

CIHR Vanier Scholarship

Arnold Etame

Wilder Penfield Fellowship from
the Congress of Neurosurgeons

Stephen Mack

CIHR Vanier Award

Brittany Prevost

NSERC Canada Graduate Scholarship

Nancy F. Silva-Gagliardi

Restracomp

Xiaochong Wu

American Brain Tumor Association
Fellowship Award
AACR-Bristol-Myers Squibb
Oncology Scholar-IN-Training Award

Maryam Zarghooni

Restracomp

THE YEAR IN REVIEW

GRANTS HELD 2009 - 2010

DR. JAMES RUTKA

Canadian Institutes of Health Research – *Molecular Targeting of the Rho-GTPase Pathway in Human Astrocytoma*

National Cancer Institute of Canada – *The Role of Aberrant HGF/c-Met Signaling in Medulloblastoma*

Pediatric Brain Tumor Foundation of the United States – *An Analysis of Isochromosome 17q in paediatric medulloblastoma*

Brain Tumour Foundation of Canada – *Characterization of nanoparticle delivery across the blood brain barrier*

DR. AB GUHA

National Cancer Institute of Canada – *Tissue factor in tumor progression, angiogenesis*

Canadian Institutes of Health Research – *Microenvironment induced molecular heterogeneity in glioblastoma multiforme (GBM)*

Brain Tumor Society of North America – *Role of LAPs in Gliomas*

b.r.a.i.n.child – *Embryonic Stem Cell Based Models of Low Grade Glioma*

National Cancer Institute of Canada – *The Role of Oncogene-Containing Microvesicles in Tumor Angiogenesis*

Canadian Institutes of Health Research – *Glioblastoma Multiforme Biomarkers*

Canadian Institutes of Health Research – *From Tumors to Blood: Biomarker-Based Diagnostics, and Implications in Prognostics and Therapeutics of Glioblastoma Multiforme*

b.r.a.i.n.child – *Role of a Novel NF1 – LRPPRC Interaction in RNA Granule Transport*

DR. JANE MCGLADE

National Cancer Institute of Canada – *Role of the endocytic adaptor protein Numb in normal development and cancer*

Foundation Fighting Blindness – Canada – *Role of mammalian CRB1 in retinal morphogenesis and degeneration*

The Leukemia and Lymphoma Society of Canada – *Role of the GADS adaptor protein in BCR-Abl induced leukemogenesis*

Canadian Institutes of Health Research – *Role of the SLAP adaptor proteins in ubiquitin dependent regulation of receptor tyrosine kinases*

Canadian Cancer Society Research Institute – *Role of the E3 ligase LNX2 in Wnt signaling, cell polarity and cancer*

Foundation Fighting Blindness – Canada – *Role of the CRB1-EPB41L5 complex in retinal degeneration*

Canadian Institutes of Health Research – *Function and regulation of Numb isoform expression in cancer*

DR. PETER DIRKS

Canadian Institutes of Health Research – *Therapeutic Opportunities to Target Tumor Initiating Cells in Solid Tumors*

National Cancer Institute of Canada – *Defining Cancer Stem Cell and Clonal Heterogeneity in Mouse Brain Tumors*

Canadian Institutes of Health Research – *Asymmetrical Self Renewal in Normal and Cancer Stem Cells of the Human Brain*

Ontario Institute of Cancer Research – *Screening Brain Cancer Stem Cells*

Ontario Institute of Cancer Research – *Characterization of Brain Cancer Stem Cells*

National Cancer Institute of Canada – *Understanding the human brain tumorigenic process: focus on cancer stem cells*

DR. MICHAEL D. TAYLOR

National Cancer Institute of Canada – *The role of aberrant HGF/cMET signaling in medulloblastoma*

Ontario Institute for Cancer Research, Cancer Stem Cell Initiative – *CNS group*

Canadian Institutes of Health Research – *Role of Histone Lysine Methylation in Medulloblastoma and Cerebellar Development*

National Institutes of Health, United States – *Medulloblastoma and Metastases*

David Pitblado 'New Ideas' Cancer Research Fund, The Hospital for Sick Children – *Zebrafish as a novel, tractable model of metastatic medulloblastoma*

DR. ANNIE HUANG

Canadian Institutes of Health Research – *Discovery and characterization of C19MC a novel oncogenic miRNA locus in malignant brain tumors*

National Brain Tumor Society – *Genetic alterations converge on cell adhesion pathways in childhood Spnet*

Canadian Cancer Society Research Institute – *Biochemical and genetic analyses of JPO2, a novel of c-Myc interacting protein*

DR. URI TABORI

New Ideas' Cancer Research Funds, Comprehensive Cancer Centre – *Examining the Relationship Between White Matter Integrity and the Speed of Neural Processing in Healthy Children and Children with Brain Tumours*

Canadian Institutes of Health Research – *The neuro-protective effects of exercise in children treated with cranial radiation for brain tumors*

Canadian Institutes of Health Research – *Combined telomerase inhibition and drug screen as novel therapies for tumor initiating cells in paediatric nervous system tumors*

b.r.a.i.n.child – *A novel classification for childhood low grade gliomas*

The Comprehensive Cancer Centre Grant – *Determination of the extent and role of monoallelic gene expression in low and high grade paediatric brain tumors*

b.r.a.i.n.child – *Prediction of tumor resistance and normal brain sensitivity to cranial irradiation in paediatric brain tumors*

Ontario Institute of Cancer Research – *Combined telomerase inhibition and drug screen as novel therapies for tumor initiating cells in paediatric nervous system tumors*

Pediatric Brain Tumor Foundation of the United States – *Predictors of functional and neuro-cognitive outcomes in long term survivors of paediatric low grade gliomas*

Canadian Institutes of Health Research – *Prognostic and therapeutic implications for telomere maintenance and telomerase inhibition in paediatric high grade gliomas*

b.r.a.i.n.child – *Genetic determinants of predisposition to childhood brain tumor initiation and progression*

b.r.a.i.n.child – *Establishment of a Comprehensive Genetic Bank for Children with Brain Tumors*

DR. CYNTHIA HAWKINS

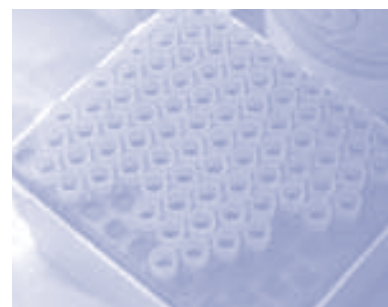
Canadian Institutes of Health Research – *GATA4 and GATA6 Transcription Factors in Gliomagenesis*

National Brain Tumor Society – *Genome-wide profiling of paediatric diffuse intrinsic pontine glioma*

The Physicians' Services Incorporated – *Filaminopathy: Unravelling a new paediatric seizure disorder*

C17 Research Network – *Thalamic Brain Tumours in Canada in the MRI era*

Canadian Institutes of Health Research – *Telomerase in Paediatric Ependymoma – Its Role as a Novel Prognostic Marker and Potential New Therapy*





ENDOWMENT FOUNDERS

Arthur and Sonia Labatt

MAJOR DONORS

From Endowments to Directed Funding to Bequests, the Arthur and Sonia Labatt Brain Tumour Research Centre has received funding from Major Donors since its inception. These major funding sources have been central to the establishment and continued success we strive for in our research.

Jack Michael Baker Fund

Laurie Berman Fund for Brain Tumour Research

Jonathan Hill Research Fund

Rochelle Sherwood Endowment Fund for Brain Tumour Research

The Wiley Fund

Bequest from the Estate of Eric Yolles

Jessica's Footprint



NEW FUNDRAISING

Each year new groups join forces to help children with brain tumours. We would like to acknowledge the recent efforts of these two groups.

Suri's Smile

C. R. Younger Foundation



PAST AND PRESENT FUNDRAISING EVENTS

Over the years we have been honoured to receive funding from a diverse group of donors. We would like to take this time to recognize the support we have received. By assisting our work in volunteerism and financial support, you are enabling us to have the tools necessary to help us propel child health research forward for future generations.

Amy's Shining Star

B Strong Fund

b.r.a.i.n.child Golf Tournament

b.r.a.i.n.child Summerfest

Blading for b.r.a.i.n.child

BUNZL "Ripple of Hope" Golf Tournament

Care for Kids Golf Classic

E1 Entertainment

Golf for Grace

Imagine the Cure

Jonathan Hill Memorial Golf tournament

Keisuiikai Medical Corporation

Laughing with the Ladybugs

Lifebeat

Maritimes b.r.a.i.n.child

Meagan's Walk: Creating a Circle of Hope

• Meagan's Walk Dinner and Dance Gala

• Meagan's Walk Golf and Spa Fundraiser

Montana/Big Star Annual Golf tournament

Rigatoni for Research

Salon Collage

The Daniel Bertoia Family Fund -

Skate with Daniel

Tali's Fund

Team Brother Bear

Walk for Grace

Wiley Buzz-off



A SPECIAL THANK YOU

We would also like to thank the individuals who took the time to contribute to the Arthur and Sonia Labatt Brain Tumour Research Centre over the last ten years. Your donations are truly appreciated and are being used to further our goals.



FELLOWS OVER THE DECADE

Past Foreign Fellows and Students

Kotaro Akaishi *Japan*
 Mia Enarsson *Sweden*
 Anandh Galasubraman *India*
 Mustafa Guduk *Turkey*
 Takuichiro Hide *Japan*
 Jason Hwang *South Korea*
 Ian Kamaly *U.K.*
 Chinatsu Kasuga *Japan*
 Dong-Seok Kim *South Korea*
 Tomohiko Kouhata *Japan*
 John Kuo *USA*
 Mei Hua Li *China*
 Andrew Liang *Taiwan*
 Terasaki Mizuhiko *Japan*
 Tadashi Miyagawa *Japan*
 Juan Moreno *Cuba*
 Shoichi Nagai *Japan*
 Yukiko Nakahara *Japan*
 Jing Nie *China*
 Hirokatsu Osawa *Japan*
 Aurelia Peraud *Germany*
 Young-Shin Ra *South Korea*
 Amit Ray *Wales/India*
 Fredericke Rutten *Netherlands*
 Young Seo *Japan*
 Ho-Jun Seol *South Korea*
 Mizuhiko Terasaki *Japan*
 Shigeo Ueda *Japan*
 Wouter van Furth *Netherlands*
 Raafat Yahya *Lebanaon*
 Naoki Yokota *Japan*
 Koichi Yoshikawa *Japan*

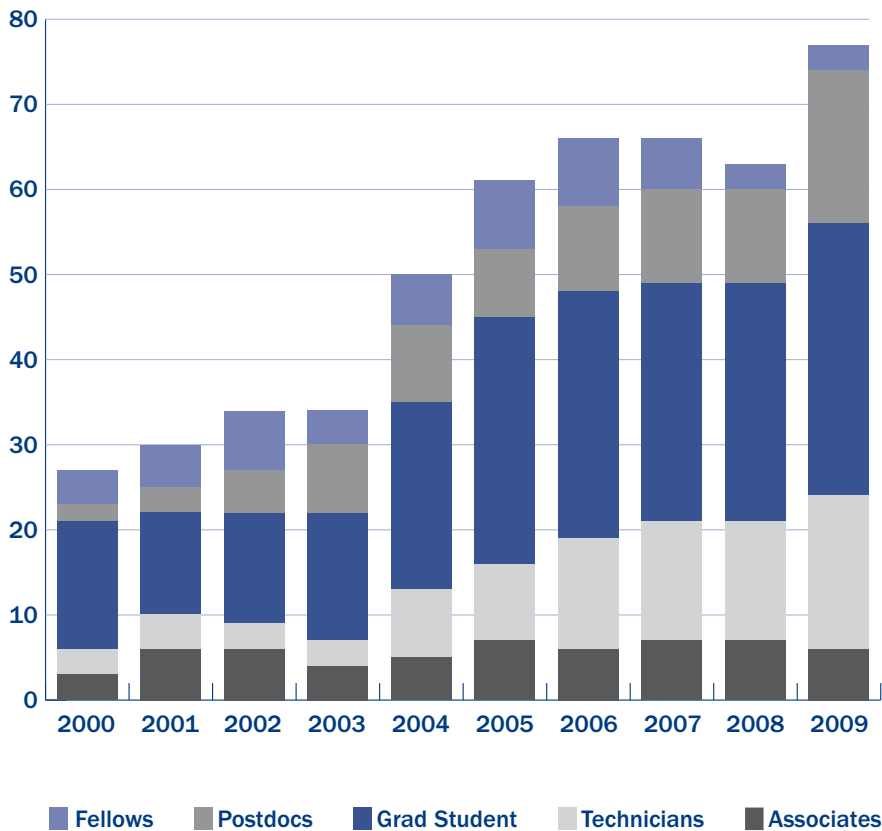
Visiting Professor

Wiesia Grajkowska *Poland*

ADVISORY BOARD OF THE ARTHUR AND SONIA LABATT BRAIN TUMOUR RESEARCH CENTRE

Sonia and Arthur Labatt, *Benefactors*
 Dr. Robert S. Bell, *CEO, University Health Network*
 Dr. David Berman, *Scientific Advisor*
 Helen Berman, *Benefactor*
 Ted Garrard, *President and CEO, SickKids Foundation*
 Mary Jo Haddad, *CEO, The Hospital for Sick Children*
 Dr. Christopher Paige, *Director of Research, OCI/PMH*
 Dr. Janet Rossant, *Chief of Research, SickKids Research Institute*
 Dr. Catharine Whiteside, *Dean, Faculty of Medicine*
 Dr. Jim Wright, *Surgeon-in-Chief, The Hospital for Sick Children*

EDUCATION AT THE BTRC OVER THE DECADE



PUBLICATIONS

2009

Agnihotri S, Wolf A, Picard D, Hawkins C, Guha A. GATA4 is a regulator of astrocyte cell proliferation and apoptosis in the human and murine central nervous system. *Oncogene* 2009;28:3033-46.

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Mack SC, Taylor MD. The genetic and epigenetic basis of ependymoma. *Childs Nerv Syst* 2009.

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PUBLICATIONS

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HARRISON, L.M., L.
 The Annual Report of
 The Arthur and Sonia Labatt
 Brain Tumour Research Centre
 at The Hospital for Sick Children
 2004 - 2005



Imagine

Introduction

"Research of the brain has long been considered among the most difficult of human sciences to study. The progress made in recent years has been rapid and exciting, especially in the past few decades despite advances in surgery, chemotherapy and radiation therapy. We believe that further advances in the diagnosis and management of pediatric brain tumours will only come when it comes to large groups with rare genotypes and increased numbers of cancer patients. We are fortunate to have assembled a "think tank" in molecular biology from past few years. Since the discovery of DNA was fundamentally Watson and Crick in 1953, as the first period of about four decades, we have gone from knowing the structure of DNA and the genetic code to creating over 1000 genes in animal gene therapy, producing many of these genes have had success including from

research. Such interdisciplinary advances in the care of patients with brain tumours would not have been possible without the complementary advances in technology in molecular biology including gene cloning, sequencing and mapping the polymerase chain reaction (PCR), gene transfer and sequencing analysis. The identification of oncogenes and tumour suppressor genes as contributors to human brain tumours has led to a number of strategies by which these tumours can be rationally be prevented.

Research continues to be critically important to create the "next" technology" good for patients with brain tumours. We are on the verge of significant breakthroughs in the treatment of pediatric brain tumours with targeted drugs. A critical area of continued research, genotyping, stem cell research has direct impact on the Arthur and Sonia Labatt Brain Tumour





Acknowledgement

We would like to acknowledge the generous support of the Research Institutes and Foundations of The Hospital for Sick Children and the University Health Network in the establishment of The Arthur and Sonia Labatt Brain Tumour Research Centre. Special thanks to b.r.a.i.n.child for generously supporting ongoing research projects.

To learn more about The Arthur and Sonia Labatt Brain Tumour Research Centre, visit www.sickkids.ca/research/BTRC.

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