



*imagine* 08<sup>09</sup>

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 many significant scientific advances in the field of brain tumour research. We are pleased that some of these have been made within the The Arthur and Sonia Labatt Brain Tumour Research Centre (BTRC). Dr. Taylor's team discovered that multiple recurrent genetic events converge on the epigenetic regulation of the medulloblastoma genome (Nature Genetics 2009). Continuing with his seminal research in the field of cancer stem cells, Dr. Dirks and his team discovered a method of growing brain tumour stem cells that are suitable for testing in chemical and drug screens (Cell Stem Cell 2009). The Rutka lab team discovered a novel tumour suppressor gene, *SPINT2*, in medulloblastoma (Cancer Research 2008). Dr. McGlade's team further characterized the role of the protein, Numb, in the Notch signaling pathway (J Biol Chem 2009), and she was a collaborator on a study which described a novel group of epithelial polarity proteins (Nature 2009). Dr. Guha's team showed that the drug, Gleevec, can be used to stop the growth of human schwannomas (Cancer Research 2009).

We are pleased to provide this summary of the progress made within the BTRC for 2008-09. We hope you will appreciate our enthusiasm 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

## CONTINUED GROWTH AND DEVELOPMENT OF THE BTRC

Scientists and clinicians from The Hospital for Sick Children (SickKids) and from the University Health Network (UHN) within the University of Toronto (U of T) teaching hospitals come together at the BTRC to study human brain tumours. The BTRC fosters excellence in brain tumour research, amalgamating the expertise of scientists, clinician-investigators and physicians in a virtual laboratory environment at U of T. A stimulating research environment has been created allowing scientists to share ideas, resources and equipment in an atmosphere conducive to achieving excellence in molecular neuro-oncology research, scientific publications and translational research.

Thanks to another generous gift from Arthur and Sonia Labatt this past year, the BTRC endowment fund has increased to more than \$10 million. This increase in the BTRC endowment fund and addition of new principal investigators (PIs), Todd Mainprize and Gelareh Zadeh, has facilitated the expansion of the BTRC facilities and transition to the 11th floor of the Medical and Related Sciences (MaRS) building at the corner of College and Elizabeth Streets. The laboratory space at MaRS is newly renovated and comprises more than 10,000 square feet of bench workspace, equipment rooms, tissue culture rooms, imaging facilities, workspace for students and postdoctoral fellows, and offices for the principal investigators. 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. Since the BTRC was founded in 1999, the number of PI's has doubled from four to ten, and our research space has more than doubled.

This past year, several new grants were awarded to the BTRC PI's. Dr. McGlade received a new grant from the Canadian Institutes of Health Research (CIHR), the Canadian Cancer Society Research



### FRONT COVER

*Left to right, back row:* Vanessa Speranza, Krystal Kulbaba, Likam Kyanzaire, Dr. James Rutka, Matthew Mcfarlane, Charlotte Pape, Matthew Buccieri, Wyatt McKinnon, Ryland Correa.  
*Left to right, front row:* Evan Martin, Dawson Dominick, Tobin Haas.

### BACK COVER

Tobin Haas, Dawson Dominick and Evan Martin with Dr. James Rutka.

Institute (CCSRI) and the Leukemia and Lymphoma Society of Canada. Dr. Rutka was awarded a three-year CCSRI grant to study the role of the HGF/cMet signaling pathway in medulloblastoma. Dr. Dirks received a five-year grant from the CIHR to study asymmetric cell division in normal and cancer stem cells. Dr. Huang received a grant from the Children’s Brain Tumor Foundation to study paediatric supratentorial primitive neuroectodermal tumours. Dr. Taylor received a grant from the CIHR to study the role of amplified oncogenes in paediatric ependymomas. And Dr. Tabori received grants from the Pediatric Brain Tumor Foundation (PBTf) of the United States, and the CIHR for his work on telomere maintenance and telomerase inhibition.



This year marks a special year for researchers in the BTRC, as Drs. Rutka, Taylor, and Dirks submitted a proposal to the PBTf that earned them the designation of an “Institute” of the PBTf. As an Institute, the Researchers in the Labatt BTRC will be working closely with two other U.S. Institutes – Duke University, and the University of California San Francisco. Please see page 10 for more details regarding the PBTf Institutes.



Accordingly, grant capture and peer review publications in high-impact scientific journals are at an all time high. The BTRC thanks the Labatt family and all the donors who have given so generously to ensure that the BTRC can continue to grow and develop well into the future.

#### ABOUT THE BTRC LOGO

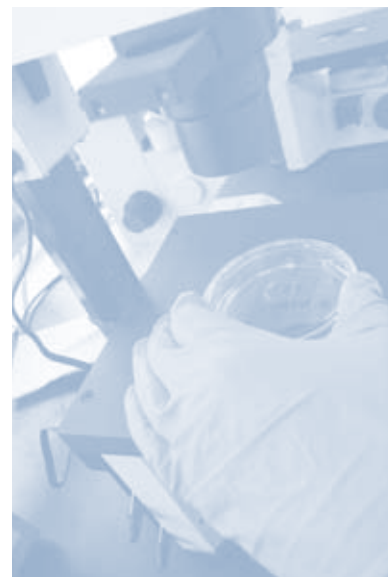
The Arthur and Sonia Labatt Brain Tumour Research Centre logo was created at the time of the grand opening of the centre in January 1999. The logo depicts a dove, symbolizing hope, carrying a twig in its beak. The twig is actually a piece of double-stranded DNA representing molecular medicine. Hence,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



#### 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





## DR. JAMES RUTKA

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

Dr. Rutka's laboratory has been studying the cytoskeleton as a means to increase our understanding of the mechanisms by which astrocytoma cells grow, adhere to surrounding substrates and invade normal brain tissue. Current studies are aimed at investigating how cytoskeletal matrix interactions lead to the profound cellular changes we have observed through a detailed analysis of cell cycle gene alterations, metalloproteinase and inhibitor secretion and ultrastructural cytoskeletal relationships. Recent emphasis has been placed on the small Rho-GTPases as potential targets for inhibiting astrocytoma invasiveness.

In a second project, Dr. Rutka's lab has focused on genetic and epigenetic alterations that occur in paediatric medulloblastoma. His lab has previously shown the importance of the sonic hedgehog signalling pathway in medulloblastoma with the discovery of a novel human gene, *Suppressor of Fused*, which is inactivated in the tumours of many children with this disease. Recently, he has used genome- and epigenome-wide searches with SNP-chip array platforms on large numbers of tumour samples to find additional pathways that are involved in the origins of medulloblastoma. One of these is the HGF/cMet signaling pathway which is actively being investigated in the lab at this time.

### LABORATORY PERSONNEL

Christian Smith *Research Associate*  
Paul Kongkham *PhD Student*  
Adrienne Weeks *PhD Student*  
Shoichi Nagai *Postdoctoral Fellow*  
Ho Jun Seol *Postdoctoral Fellow*  
Arnold Etame *PhD Student*  
Sara Onvani *M.Sc. Student*  
Andres Restrepo *Research Technician*  
James Loukides *Clinical Research Technician*

### RESEARCH SUPPORT

NCIC, CIHR, Ontario Cancer Research Network, Pediatric Brain Tumor Foundation of the United States



## DR. AB GUHA

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

Dr. Guha and his colleagues have shown that activated Ras is functionally relevant in human astrocytomas. Blockade of Ras signalling leads to decreased glioma growth. This activation is not only found within human gliomas, but also peripheral nerve tumours. Ras and other signalling pathways are activated by aberrant growth factor receptors in gliomas, such as the epidermal growth factor receptor (EGFR). Using state-of-the-art technologies, in collaboration with MDSProteomics, Dr. Guha's lab is investigating Ras and other signalling pathways utilized by these receptors to promote growth of gliomas. It is hoped that drugs being investigated in the Guha lab to inhibit these receptors or their signalling pathways, will be ultimately efficacious in the clinic.

Another area of interest for the laboratory is the study of angiogenic factors. Brain tumours remain among the most angiogenic tumours known to man. In particular, vascular endothelial growth factor (VEGF) and angiopoietins and their receptors are angiogenic specific and aberrant in human gliomas and peripheral nerve tumours. Dr. Guha's laboratory is studying how VEGF and angiopoietins stimulate and interact to promote angiogenesis, how they are regulated in normoxia and hypoxic conditions, as well as pharmaceutical inhibition in pre-clinical models to determine if they are relevant clinical therapeutic targets.

### LABORATORY PERSONNEL

Zia Karim *Research Associate*  
Kelly Burrell *Research Technician*  
Joydeep Mukherjee *Postdoctoral Fellow*  
Amparo Wolf *PhD Student*  
Sameer Agnihotri *PhD Student*  
Aaron Gajadhar *PhD Student*  
Diana Munoz *PhD Student*  
Vedant Arun *M.Sc. Student*

### RESEARCH SUPPORT

Arraybiopharm, Childhood Brain Tumor Foundation, CIHR, NBTF, NCIC, U.S. Army DOD

## DR. JANE MCGLADE

*Senior Scientist, Principal Investigator*

Dr. McGlade's research is directed towards understanding the molecular changes which occur during the process of malignant cell transformation. Work in the lab involves several aspects of signal transduction and the identification and characterization of novel signalling molecules.

Recently, Dr. McGlade has focused specifically on one class of cytoplasmic adapter molecules and the role they play in the localization, integration and co-ordination of signalling cascade components within two distinct signalling paradigms. It is hoped that this work will have broad implications in terms of understanding temporal and spatial organization of mitogenic signal transduction pathways, as well as the process of asymmetric cell division and epithelial cell polarity in mammals.

The long-term goal of this work is to define the molecular processes which regulate the formation and activation of signalling complexes and how disruption of this regulation can lead to cell dysfunction and malignant disease.

## DR. PETER DIRKS

*Scientist, Principal Investigator*

Dr. Peter Dirks' research program's long-term goal is to determine if a normal neural stem cell or progenitor cell is transformed into a brain tumour. Two approaches are being used to study this question. One approach involves a study of primary human brain tumours to determine if stem cell populations exist in brain tumours.

Our question: is there a small population of cancer cells in a brain tumour that uniquely has the ability to maintain the tumour? Dr. Dirks' lab has recently isolated and characterized a repopulating cell from human brain tumours of different phenotypes that expresses neural stem cell markers and has stem cell-like behaviour in vitro. This subpopulation of tumour cells could be considered as cancer stem cells, because they share properties with normal stem cells and because they are necessary for maintaining tumour growth in vitro.

The second approach involves a study of the key determinants of proliferation and self-renewal in normal neural stem cells. The focus is on the sonic hedgehog signalling pathway, as it is perturbed in primary human brain tumours (medulloblastomas), and because it has been shown to be critically important for normal brain development.

Preliminary studies suggest that different Shh pathway members play important and distinct roles in neural stem cell proliferation and self-renewal. A better understanding of how this pathway functions in normal neural stem cells may help us to better understand brain tumour proliferation and self-renewal.



### LABORATORY PERSONNEL

Donna Berry *Research Associate*  
Sasch Dho *Research Associate*  
Renu Sarao *Project Manager*  
Kimberly Lau *PhD Student*  
Nancy Silva *Postdoctoral Fellow*  
Larissa Liontos *PhD Student*  
Emily Griffiths *Postdoctoral Fellow*  
Cheryl Wolting *PhD Student*  
Jon Krieger *PhD Student*  
Christopher Smith *PhD Student*  
Fabio Morgese *Postdoctoral Fellow*

### RESEARCH SUPPORT

CIHR, NCIC, Foundation Fighting Blindness – Canada



### LABORATORY PERSONNEL

Ian Clarke *Research Associate*  
Jeremy Graham *Research Technician*  
Renee Head *Research Technician*  
Lillian Lee *Research Technician*  
Kathy Nethry-Brookx *Research Technician*  
Phedias Diamandis *PhD Student*  
Kevin Graham *Postdoctoral Fellow*  
Erick Ling *PhD Student*  
Ryan Ward *PhD Student*  
Tzvi Aviv *Postdoctoral Fellow*  
Caroline Brandon *M.Sc. Student*  
Sonam Dolma *PhD Student*  
Mia Enarsson *Research Fellow*

### RESEARCH SUPPORT

CIHR, Networks of Centres of Excellence  
Stem Cell Network, NCIC, Genome Canada  
Competition, OICR



## 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), 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

Daniel Picard *PhD Student*  
Limei Zhou *Research Associate*  
David Shih *M.Sc. Student*  
Tiffany Chan *M.Sc. Student*  
Johnny Ng *Student*

### RESEARCH SUPPORT

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



## 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

Paul Northcott *PhD Student*  
Joanna Radowski *Research Technician*  
Jessica McLeod *Research Technician*  
Xueyuan Shang *Research Technician*  
John Peacock *Research Technician*  
Adrian Dubuc *PhD Student*  
Kelsey Bertrand *M.Sc. Student*  
Stephen Mack *PhD Student*  
Yuan Yao *PhD Student*  
Livia Garzia *Postdoctoral Fellow*  
Xiachong Wu *Postdoctoral Fellow*  
Gabriel Fung *Student*

### RESEARCH SUPPORT

Sontag Foundation, CIHR, American Brain Tumor Association, NCIC

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

They are also involved in a group effort exploring the interaction of cancer genetics and the genetics with paediatric brain tumours. This is done by exploring the role of germline and somatic mutations in TP53 and other genes in childhood gliomagenesis.



### LABORATORY PERSONNEL

Andrew Morrison *Research Technician*  
Pawel Buczkwicz *M.Sc.*  
Maryam Zaghooni *Postdoctoral Fellow*  
Eugene Tam *Student*

### RESEARCH SUPPORT

Brainchild, CIHR, Brain Tumor Society,  
C17 Research Network



### LABORATORY PERSONNEL

Cindy Zhang *Research Associate*  
Nataliya Zhukova *Research Technician*  
Pedro Castelo-Branco *Postdoctoral Fellow*  
Erin Walker *Postdoctoral Fellow*

### RESEARCH SUPPORT

CCS, CIHR, Brain Tumor Society



## DR. GELAREH ZADEH

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.

Dr. Zadeh's lab approach focuses on establishing the temporospatial response of BMPCs following IR in normal subcutaneous and intracranial tissue in addition to intracranial tumours. Her second aim focuses on identifying 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 finally 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 her laboratory and work in collaboration with other groups.

### LABORATORY PERSONNEL

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

### RESEARCH SUPPORT

Labatt Endowment  
University Health Network – UHN



## DR. TODD MAINPRIZE

Dr. Mainprize has two main areas of research interest. He 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.

## 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*



## 11TH ANNUAL BTRC LECTURESHIP 2009

This year's guest speaker was Dr. Joe Costello PhD, Assistant Professor of Neurological Surgery, Chair in Molecular Neuro-Oncology at University of California at San Francisco. The topic of his lecture was "Genome-Epigenome Interactions in Normal Cells and Cancer."



**Dr. Joe Costello**



## BTRC GUEST LECTURERS

**Monday January 28, 2008** *Glioma invasion: A role for p75NTR*, Dr. Donna Senger, PhD, Assistant Professor, Clark H. Smith Brain Tumour Research Centre, Southern Alberta Cancer Research Institute, University of Calgary

**Wednesday March 12, 2008** *Quest for the 1p36 tumor suppressor*, Dr. Anindya Bagchi, PhD, Scientist, Cold Spring Harbor, Woodbury, New York

**Thursday March 27, 2008** *Role of Olig2 in human gliomagenesis*, Santosh Kesari, PhD, Brigham and Women's Hospital, Neurology, Division of Neuro-Oncology, Boston, Massachusetts

**Wednesday April 2, 2008** *A novel fascin bioassay allows bidirectional drug screening for gliomas and brain-development disorders*, Dr. Linda L. Restifo, MD, PhD, Professor, Neurobiology, Neurology Member, Evelyn F. McKnight Brain Institute, Cognitive Science, University of Arizona, Tucson, Arizona

**Monday August 25, 2008** *Identification of diagnostic, prognostic and therapeutic markers of astrocytoma*, Dr. Kumar Somasundaram, PhD, Associate Professor, Indian Institute of Science, Bangalore, India

**Wednesday October 1, 2008** *Viruses for Cancer Therapeutics*, Dr. John Bell, Senior Scientist, Cancer Therapeutics, Ottawa Health Department of Medicine and Biochemistry, Microbiology & Immunology, University of Ottawa, Ottawa, Ontario

**Thursday November 27, 2008** *Molecular genetics of pediatric brain tumours – translation of basic science into clinics*, Stephen Pfister, Department of Pediatric Oncology, Hematology, and Immunology, German Cancer Research Center, Heidelberg, Germany

**Thursday December 11, 2008** *Somatic Cell Gene Transfer to Model Medulloblastoma in Mice*, Dr. Daniel Fufts, Department of Oncological Sciences, University of Utah School of Medicine

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

## VISITING LECTURESHIP

### PREVIOUS BTRC ACADEMIC GUEST LECTURERS

**1999 Dr. Robert Martuza**  
*Professor and Chairman,  
Department of Neurosurgery, Massachusetts  
General Hospital, Harvard University*

**2000 Dr. Gregory Cairncross**  
*Professor of Neurology, Director,  
London Regional Cancer Centre,  
University of Western Ontario*

**2001 Dr. David Kaplan**  
*The Montreal Neurological Institute,  
McGill University*

**2002 Dr. Charles Stiles**  
*Dana Farber Cancer Institute at  
Harvard Medical School, Professor,  
Department of Microbiology and  
Molecular Genetics*

**2003 Dr. Luis Parada**  
*Southwestern Medical Center at  
the University of Texas at Dallas*

**2004 Dr. Eric Holland**  
*Associate Professor, Neurosurgery,  
Neurology and Cell Biology at  
Memorial Sloan-Kettering Cancer Center*

**2005 Dr. Darell Bigner**  
*Director, Pediatric Brain Tumor Foundation  
Institute, Duke University Comprehensive  
Cancer Center*

**2006 Dr. Webster Cavenee**  
*Director, Ludwig Institute for Cancer  
Research, University of California  
at San Diego*

**2007 Dr. David H. Gutmann**  
*Professor, Department of Neurology,  
Washington University School of Medicine*

**2008 Dr. Henry Brem**  
*Harvey Cushing Professor of Neurosurgery,  
and Professor of Oncology and  
Ophthalmology, Johns Hopkins University*

## PEDIATRIC BRAIN TUMOR FOUNDATION (PBTF) VISITS THE LABATT BTRC, MARCH 12, 2009

### PEDIATRIC BRAIN TUMOR FOUNDATION OF THE UNITED STATES FUNDS BTRC RESEARCHERS AT THE INSTITUTE LEVEL:

This past year, the PBTF awarded Drs. Rutka, Taylor, and Dirks a three-year grant at an “Institute-level” for their project entitled “The Role of Isochromosome 17q in Pediatric Medulloblastoma.” In their proposal, the BTRC researchers will determine how isochromosome 17q, the most common genetic abnormality in medulloblastoma, causes this tumour to form. According to Dr. Rutka, “Funding by the PBTF at the Institute Level will ensure that our exciting work on medulloblastoma can continue at a rapid pace, and that we can collaborate more closely with our colleagues at Duke University and the University of California San Francisco. We are truly honoured, and deeply appreciative of becoming an Institute of the PBTF”

In March 2009, Executive Directors of the PBTF, Mike and Dianne Traynor came to Toronto and performed a site visit of the BTRC. They toured the facilities, interviewed several scientists and took part in a photo-shoot with childhood brain tumour survivors at SickKids and the BTRC. The accompanying photo montage highlights the visit of the Traynors to the BTRC.





**IN MEMORIAM, MIKE TRAYNOR, 1939 – 2009**

It is with great sadness that we report that following a severe respiratory illness in August-September 2009, Mike Traynor, President, PBTF and co-founder of the Ride for Kids passed away on September 12, 2009. He was 70 years old. Mike and his wife, Dianne, began the Ride for Kids program in 1984. Their success with this program led to the formation of the PBTF in 1991. Since its inception, the PBTF has granted

more than \$50 million for research and family support programs. The PBTF has also helped establish the Central Brain Tumor Registry, and has funded the journal, Neuro-Oncology. Motorcycling was Mike's enduring passion. It is perhaps not surprising then that he combined his love of motorcycling with his strong desire to help children with brain tumours. To this day, the Ride for Kids program, which raises funds to support initiatives to fight this devastating disease, remains one of the most successful charities in the United States. Members of the BTRC send their sincere condolences to Dianne Traynor and the Traynor family.

## STUDENT AWARDS

### MCGLADE

Leanne Wybenga-Groot  
CIHR Postdoctoral Fellowship

Cheryl Wolting  
NCIC Terry Fox Studentship

Kimberly Lau  
Ontario Graduate Scholarship

Jon Krieger  
U of T Faculty of Medicine Award  
Peterborough K. M. Hunter Studentship

Christopher J. Smith  
Vanier Graduate Scholarship

### RUTKA

Adrienne Weeks  
NCIC Fellowship

Paul Kongkham  
Thomas P. Morley Prize  
Division of Neurosurgery

Canadian Brain Tumour Consortium  
Young Investigator Award

Gallie-Bateman Prize for Surgical Research,  
Department of Surgery

### DIRKS

Erick Ling  
Hilda and William Courtney Clayton  
Paediatric Research Fund.

Tzvi Aviv  
OICR-Terry Fox Post-doctorate Fellowship

Ryan Ward  
CIHR CGS Studentship

### GUHA

Vedant Arun  
James F. Crothers Family Fellowship

Aaron Gajadhar  
James F. Crothers Family Fellowship

Joydeep Mukherjee  
Exceptional Research Trainee Award,  
SickKids Research Institute

Ontario Post Doctoral Fellowship  
(Ministry of Research and Innovation)

American Brain Tumor Association  
Basic Research Fellowship for two years

## THE YEAR IN REVIEW

### NEW GRANTS AWARDED IN 2009

#### DR. JAMES RUTKA

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

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

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

#### DR. AB GUHA

**U.S. Army Department of Defense Concept Award** – *Protein Expression profile of NF1 deficient Schwann cells*

**National Brain Tumor Foundation** – *Regional variation in Inhibitors of Apoptosis (IAPs) in GBMs and their role in apoptosis and therapeutic resistance*

#### National Cancer Institute of Canada:

- *Tissue factor in tumor progression, angiogenesis*
- *The Role of Oncogene-Containing Microvesicles*
- *Functional Analysis of GATA6 in Human Gliomas: A Novel Tumor Suppressor Gene Identified from Genetically Engineered Murine (GEM) Glioma Model by Gene-trapping*

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

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

**Ontario Institutes for Cancer Research** – *CSC group grant to UHN and SickKids*

**Radiation Therapy Oncology Group** – *GATA4 and GATA6 as Prognostic Indicators of Glioblastoma Multiforme Patients*

#### DR. JANE MCGLADE

#### Canadian Institutes of Health Research:

- *Role of adaptor proteins in hematopoietic cell signaling*
- *LNX family ubiquitin ligases in cellular signaling and polarity*
- *Role of the SLAP adaptor proteins in ubiquitin dependent regulation of receptor tyrosine kinases*

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

#### DR. PETER DIRKS

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

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

**Genome Canada** – *Identification of Pathways Regulating Survival and Development of Cancer and Cancer Stem Cells*

## **DR. MICHAEL D. TAYLOR**

**Canadian Institutes of Health Research** – *Characterization of Amplified Oncogenes in Pediatric Ependymoma*

**National Cancer Institute of Canada** – *Mutation of Neuronal Differentiation Genes in Medulloblastoma*

**Sontag Foundation** – *Multiple Genetic Events Converge to Target Histone 3 Lysine 9 Methylation in Pediatric Medulloblastoma*

**b.r.a.i.n.child** – *Creation of Novel Transgenic Mouse Model of Ependymoma*

**Ontario Institute for Cancer Research, Cancer Stem Cell Initiative**

## **DR. ANNIE HUANG**

**Brain Tumor Society** – *Characterization of cell adhesion pathways in childhood supra-tentorial PNET*

**Phase 2, Eli Lilly Canada – Cancer Care Ontario, Clinician Scientist Award** –

*Characterization of a novel family of Myc protein interactors and their role in medulloblastoma transformation*

**Children's Brain Tumor Foundation U.S.** – *Genomic analyses of paediatric supratentorial primitive neuroectodermal tumors*

**National Cancer Institute of Canada** – *Biochemical and genetic analyses of JPO2, a novel c-Myc oncogene interacting protein*

## **DR. URI TABORI**

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

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

**Pediatric Brain Tumor Foundation U.S.** – *Predictors of functional and neuro-cognitive outcomes in long term survivors of pediatric low grade gliomas*

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

### **b.r.a.i.n.child:**

- *Genetic determinants of predisposition to childhood brain tumour initiation and progression*
- *Establishment of a Comprehensive Genetic Bank for Children with Brain Tumours*
- *Prediction of tumour resistance and normal brain sensitivity to cranial irradiation in pediatric brain tumours*

## **DR. CYNTHIA HAWKINS**

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

**National Cancer Institute of Canada** – *GATA6: A Novel Tumour Suppressor Gene in Human Gliomas Identified From Mouse Glioma Models by Gene-trapping*

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

**Brain Tumor Society** – *The Biologic and Prognostic Role of Replicative and Oncogene Induced Senescence in Pediatric Low Grade Gliomas*

**C17 Research Network** – *Evaluation of Biomarkers in Relation to Recurrence Rate in Childhood Ependymoma*

## **STUDENT AWARDS**

### **HUANG**

**Tiffany Chan**

OSOTF Frank Fletcher Memorial Fund

Hilda and William Courtney Clayton Paediatric Research Fund Award

**Daniel Picard**

University of Toronto Fellowship – Laboratory Medicine and Pathobiology

**David Shih**

RESTRACOMP

### **TAYLOR**

**Xiaochong Wu**

American Brain Tumor Association Fellowship Award

American Association for Cancer Research Scholar-in-Training Award

**Livia Garzia**

American Brain Tumor Association Basic Research Fellowship

**Yuan Yao**

NSERC Alexander Graham Bell Canada Graduate Scholarship

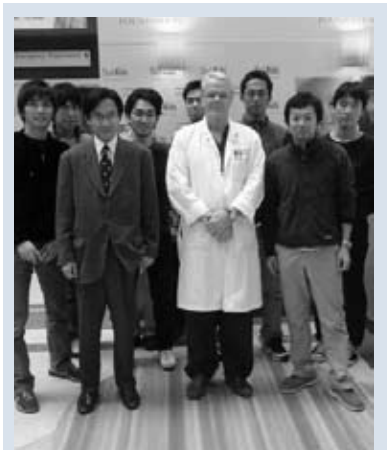
### **HAWKINS**

**Pawel Buczowicz**

University of Toronto Fellowship Award

Ryerson University Dean's Award of Excellence





Dr. Kazuhito Matsuzawa and Dr. Rutka with doctors from Keisuikai Medical Corporation

## MAJOR DONORS

### JACK MICHAEL BAKER FUND

Brian and Erin Baker have established a fund to further research on cancer stem cells in brain tumours. This donation is in honour of their son, Jack Michael Baker.

### LAURIE BERMAN FUND FOR BRAIN TUMOUR RESEARCH

Established in 2002 by Helen and Joe Berman in memory of their son, Laurie, this fund provides ongoing support for graduate students, postdoctoral research fellows, lab equipment and supplies. The fund also enables neurosurgical nurses to attend the annual Canadian Neurological Sciences Federation meeting.

### NATHALIE CROSBIE ENDOWMENT FUND

The Nathalie Crosbie Endowment Fund was created in 1998 by Jolie Lin and Ian Crosbie to support paediatric brain tumour research at SickKids. The fund is now fully endowed and enables scientists at the BTRC to perform research on medulloblastoma, the most common malignant brain tumour in children.

### JONATHAN HILL FUND

In 1997, Jonathan Hill, a vivacious, charismatic boy with an infectious smile, an irresistible charm, a beloved son and nephew, lost his courageous battle to a brain tumour at the age of eight. At the same time, two of his cousins were fighting their own battles and both are survivors. Why? Mostly because of the tireless efforts of doctors and researchers who were able to develop life-saving treatments for their particular cancers. Paediatric cancer research has come a long way, and has resulted in treatments that improve the quality of life for children with cancer, and even produced higher cure rates. The Jonathan Hill Fund will specifically assist research in the areas of brain tumours and leukemia, two of the most common childhood cancers. This fund will help future children afflicted with cancer beat the odds and help keep Jonathan's memory alive.

### ROCHELLE SHERWOOD FUND FOR BRAIN TUMOUR RESEARCH

Judy Stein-Korte and Carl Korte have given generously to establish a fund to support research in the BTRC in honour of Judy's sister, Rochelle, who was diagnosed with a brain tumour. This endowment fund will be used to support ongoing research projects on esthesioneuroblastoma, medulloblastoma and primitive neuro-ectodermal tumours.

### THE WILEY FUND IN BRAIN TUMOUR RESEARCH

Established in 2001 by Averil and Joe Wiley in honour of their son, Andrew, who was cared for by Dr. Rutka. This fund supports the ongoing research projects of two PhD students, and two postdoctoral research fellows.

### BEQUEST FROM THE ESTATE OF ERIC YOLLES

A bequest has been received from the estate of Eric Yolles to be used for furthering research in the BTRC.

### DONATION FROM KEISUIKAI MEDICAL CORPORATION

On March 15-16, 2009, Dr. Kazuhito Matsuzawa, former BTRC visiting post-doctoral researcher, visited SickKids and the BTRC with seven young doctors from the Keisuikai Medical Corporation in Japan. Currently Dr. Matsuzawa is the Chief of Neurosurgery at Nadogaya Hospital in Chiba. He and a medical contingent from Japan enjoyed a tour of the facilities and SickKids. In honour of their visit to Toronto, Dr. Makoto Yamazaki, President of Keisuikai Medical Corporation, made a generous donation to the BTRC. We thank Dr. Yamazaki for his support for the BTRC, and we thank Dr. Matsuzawa for his return visit to Toronto.

## ANNUAL FUNDRAISING EVENTS

**Rigatoni for Research** is a family style event that was created to honour the memory of young Christopher Douthart. In the event's 10-year history over 1.6 million dollars was raised for research and equipment at The Arthur & Sonia Labatt Brain Tumour Research Centre. Kathy and Danny Douthart, the founders of Rigatoni for Research, refer to the BTRC as their beacon of hope and a place where their dreams can rest.

**Bunzl Canada** has been an exemplary corporate citizen, whose dedication to b.r.a.i.n.child and SickKids Foundation is unwavering. John & Leanne Howlett, Michelle Fletcher and the entire team at Bunzl and their supporters have made it their mission to help transform the lives of children and their families with brain tumours. They have fundraised through their Ripple of Hope Golf Tournament and in the most recent years through their unique event Blading for b.r.a.i.n.child.

**Larry and Gloria Sdao** are proud supporters of b.r.a.i.n.child and SickKids Foundation. They host annual fundraisers in an effort to make a difference in the health and well-being of children in Canada and around the world.

**Laughing with the Ladybugs** is a tribute event that celebrates the wonderful life of Kathryn Peeters. The Peeters family hosts this event in their hometown of Omemee, celebrating the milestone of Kathryn's diagnosis and her life with a brain tumour. Kathryn has an incredible spirit and infectious passion for life, not to mention a vast adoration of ladybugs.

**Amy's Shining Star** continues to make a difference by supporting brain tumour research in memory of Amy Beacock through a biennial gala. Since the inception of this family event, Sue Beacock-Scott and Debbie and Trish Barnett, have engaged their community and raised over \$114,000 in support of b.r.a.i.n.child and SickKids Foundation.

**Care for Kids** one of the oldest community partners of SickKids Foundation. They are committed to helping children and families affected by brain tumours through their annual golf tournament. Larry Naccarato and Peter Eliopoulos keep up their crusade to make an impact at SickKids through their philanthropic endeavours.

**Meagan's Walk:** Creating a Circle of Hope: In 2001, when five-year-old Meagan Bebenek lost her life to brainstem glioma, her mother, Denise, established Meagan's Walk: Creating a Circle of Hope. Through her own family's experience, Denise learned that brain tumours are the leading cause of cancer-related death in young people, age 20 and under. Meagan's Walk raises hope and awareness about brain tumours and has now contributed more than \$1.6 million to SickKids, which hosts the only facility in Canada dedicated to paediatric brain tumour research. The original and signature event, Meagan's Walk on Mother's Day, is for all ages and abilities, and continues to grow larger each year. Beginning at Ontario Place, and following a 5km. route, the event culminates with participants joining hands in a human "hug" around SickKids, a clear signal to those within that they need not journey alone. Meagan's Walk also hosts an annual gala, golf and spa day and is the beneficiary of many community events. By fostering a culture of scientific discovery and care, Meagan's Walk helps improve the understanding of brain tumours, leading to new therapies, and improved treatments and cure rates for young brain tumour patients. Meagan's Walk brings hope to those who need our support and encourages all in our community to make a difference for the health of our children.

**Tali's Fund:** Tali's Fund raises money for research projects in the BTRC. In 2009, Tali's Fund sponsored in part a research project in Dr. Huang's lab on identifying the biological predictors of Atypical Teratoid/Rhabdoid (ATRT) tumours.





**Salon Collage Fundraiser:** Salon Collage co-owner Sandro Macri had bracelets created to sell to family, friends and salon clients to raise money for the BTRC. On June 30, Salon Collage presented Dr. Rutka with a \$10,000 cheque in honour of Mr. Macri's daughter's surgery at SickKids.

**Jessica's Footprint – A Walk in the Park:** on March 21, 2002, parents Wendy and Rob Durigon and big sister Alyssa happily brought home two-day-old Jessica from Guelph General Hospital. Exactly one year later, on March 21, 2003, Wendy, Rob and Alyssa returned home from SickKids in Toronto without Jessica because she had died from a cancerous brain tumour. To celebrate her life, her family organized Jessica's Footprint, a five-kilometre, family-oriented walk held in her hometown of Guelph. This year marked the fourth anniversary of the walk and the outstanding support of the Guelph community who continue to rally around the Durigons and help them in their fundraising efforts. To date, close to \$800,000 has been raised to support the BTRC and hopefully, some day, find a cure so no parent has to lose their child to this horrible disease.



**Grace's Walk:** Ian Stanley and Lesley Compagnon began a walk for their daughter, Grace, while she was still alive, shortly after her diagnosis in 2005. The walk has been held annually since then and they have also added an annual golf tournament to their yearly fundraising activities. Grace's fund has raised \$130,000 since its inception in 2005.



**E1 Entertainment** is considered Canada's home entertainment products warehouse and has chosen the b.r.a.i.n.child program at SickKids for the proceeds that are raised at the annual E1 Entertainment's Golf Fore Charity Tournament. In 2008, they donated \$10,000 to the program and, at their golf tournament this past July, they made a donation of \$25,000 to the b.r.a.i.n.child program. Now, they look forward to next year's event and continued support of such a great program.

**Thank you to everyone for each contribution. Your donations help us achieve our goals!**



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### 2008

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**Event photographers:**

Gord Cheong (Meagan's Walk)

Doug McMillan (Macri/Salon Collage Event)

Alex Rutka (Laughing with Ladybugs)

SickKids Graphic Centre





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To learn more about The Arthur and Sonia Labatt Brain Tumour Research Centre, visit [www.sickkids.ca/research/BTRC](http://www.sickkids.ca/research/BTRC).

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