

MICH MICROSCOPE

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Intervention Program Helping Youth



Left to right:
(Front) Heather Tiede, Billy Dubery, Heather Woodward
(Back) Curly Mousseau, Nathan Thomas, Jamie McKay

Photo: HSC Winnipeg



Message from the CEO and Scientific Director

**Terry Klassen, MD, MSc, FRCPC, Associate Dean, Academic Faculty of Medicine
University of Manitoba, Academic Director, The George & Fay Yee Centre for
Healthcare Innovation**

The New Year is always a time for reflection of what has happened in the previous year and looking to the future as to what we can improve and build upon. In so many ways, 2013 was a positive year. Our new recruits and members give added strength and once again remind us that the Manitoba Institute of Child Health is a place people want to come to.

New Members:

Dr. Michael Ellis, MD, FRCSC, Staff
Neurosurgeon, University of Manitoba,
Pan Am Clinic, Health Sciences Centre

Dr. Neeloffer Mookherjee, PhD, Assistant
Professor, Department of Internal Medicine,
University of Manitoba

Dr. Paul Fernyhough, PhD, Professor
- Departments of Pharmacology and
Therapeutics & Physiology, University of
Manitoba

Dr. Paul Masotti, PhD, Assistant Professor,
Department of Community Health Sciences,
University of Manitoba

Dr. Tiina Kauppinen, PhD, Assistant
Professor - Department of Pharmacology and
Therapeutics, University of Manitoba

Dr. Todd Duhamel, PhD, Assistant Professor,
Graduate Program Chair, Faculty of
Kinesiology and Recreation Management,
University of Manitoba

2014 Recruits:

Dr. Adrian West, PhD, Assistant Professor,
Physiology, University of Manitoba

Dr. Celia Rodd, MD, MSc, FRCPC(C),
Associate Professor, Pediatrics and Child
Health, University of Manitoba

Dr. Greg Hansen, MD, MSc, Assistant
Professor, Pediatrics and Child Health,
University of Manitoba

Dr. Elinor Simons, MD MSc FAAAAI FAAP,
Assistant Professor, Section of Allergy
and Clinical Immunology Department of
Pediatrics and Child Health, University of
Manitoba

Because of our growth and larger community, we have now also embarked on an update and expansion of our Policy and Procedure Manual, a guide book of sorts, that helps give us clarity as to how we function as a group. Just using someone's memory (I know mine is not what it used to be) was proving more and more challenging, so we now have a go-to place on the web and a hard copy binder in each research area that is very helpful.

Our research day helped us learn about resiliency and why so many children and youth do so well, in spite of challenging experiences. Because of the inspirational talk given by Michael Champagne, some of the MICH community showed support by going to the Bell Tower on a Friday evening in November.

There were large and small grants that our researchers received and some very key publications that show great promise on impacting on children and youth. This year promises to be an even stronger year, as our recruits find their place and have matured scientifically. We are starting to remodel our space to help make high quality space for our MICH researchers.

So I look forward to working with all of you in this New Year to help build even stronger research programs at MICH. Together we can make a difference in the lives of kids.

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The Manitoba Institute of Child Health was established in 2001. MICH is the research division of the Children's Hospital Foundation of Manitoba. It is the only research institute dedicated exclusively to pediatric research in the Prairie Provinces. At the Institute, over 270 world-class pediatric medical researchers, technical staff, students and support staff are involved in over \$8 million of research and clinical trial activity each year.

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Intervention program helping youth injured by violence



Violence in our community is having a lasting impact on youth, but a group of researchers, support workers and community members are working to make a difference.

In 2012 more than 1,000 youth came to the Health Sciences Centre Emergency Department to be treated for injuries due to violence. Dr. Carolyn Snider, MD, MPH, FRCPC, an emergency physician, Manitoba Institute of Child Health researcher and University of Manitoba professor found that a staggering 20% of the youth who are injured by violence will return with another injury due to violence within the next year.

Dr. Snider decided to develop a research program that looks at ways to help youth break this cycle. With the support of many community organizations, Dr. Snider developed the Emergency Department Violence Intervention Program (EDVIP). This program works by meeting youth in the emergency department at the time of their injury and pairs them with a support worker trained in providing wraparound care in order to minimize their future risk of violence-related injury. Her research team will study the effect of the EDVIP program on repeat injuries, housing, education and impact on the justice system.

“If that same number was quoted for stroke or heart attacks – or many of the other medical conditions that we treat in our Emergency Departments – people would be in an uproar,” Dr. Snider said.

Heather Woodward, a social worker working with youth in EDVIP, said the program is necessary to address some of the issues that youth face and help correct them so they don’t continually end up in the emergency room.

“There have been positive responses from the community, youth, the hospital and nursing staff. The goal is to reduce the amount of times a youth comes to the hospital because of violence, or eliminate it all together.” Woodward said.

“A lot of young people have been told what to do for so long, but the goal of the wraparound care is to work on what they want. Every youth will have their own goals, no two will be the same. I’m really excited to be part of the project and to see the difference it can make.”

Dr. Snider said the program is off to a positive start and she’s looking forward to reviewing the data in the fall.

“We have a fantastic team who are working with the youth and who are very engaged in the process,” she said.

“There’s too much of a cycle of violence, we need to come up with solutions. We have some anecdotal evidence that is quite positive, but we’ll have a better idea when we look at the preliminary data in the fall.”

EDVIP was started thanks to grants Dr. Snider received from MICH and the Canadian Institutes of Health Research.

For more information, visit <http://www.edvip.ca/>



Meet researcher Dr. Adrian West,

PhD, Assistant Professor, Physiology
University of Manitoba

Dr. Adrian West undertook his BSc, Honours and PhD at the University of Western Australia where he studied the mechanisms and physiology of intestinal haem iron absorption. Seeking new challenges, Adrian switched fields for his first postdoc to work in a respiratory physiology laboratory. During this time he studied the effects of dynamic mechanical strain on acute regulation of airway smooth muscle (ASM) force, and developed an interest in bridging the gap between whole-organ and cell-level mechanical properties.

In his new position at the University of Manitoba and MICH, Adrian plans to further develop these skills and establish a translational model of lung mechanobiology. This will allow him to determine how mechanical factors modulate signaling pathways in ASM and other lung cells, and how this may contribute to the pathogenesis of asthma.

In Their Own Words

What is developmental neuropathology?

By Dr. Marc Del Bigio, Professor, Department of Pathology, University of Manitoba, Canada Research Chair in Developmental Neuropathology

“Pathology” is the study of disease. “Neuro-” refers to the nervous system including the brain, spinal cord, nerves, and muscles. The term “Developmental” is added because the immature (i.e. developing) nervous system (in fetuses, infants, and children) is different than that of adults. Therefore, “Developmental neuropathology” is the study of diseases that affect the brain, spinal cord, and nerves of infants and children.

Dr. Del Bigio a neuropathologist, which is a medical specialist whose role is to diagnose diseases of the brain and nervous system mainly through microscopic examination of tissue samples. Through careful examination of autopsies, much has been learned about a wide range of brain diseases. However, research is still needed to form a deeper understanding that can lead to



Marc Del Bigio, MD, PhD, FRCPC

treatments. In 2001, Dr. Del Bigio established his research laboratory in MICH to study neurological diseases of childhood. In 2004 he was awarded the Canada Research Chair in Developmental Neuropathology, and that research chair was renewed in 2010.

Many disease processes can affect the developing nervous system, with serious consequences. Genetic abnormalities can prevent the brain from developing normally or can lead to a defective protein that allows the brain to gradually be destroyed. There are many rare diseases of this type. Abnormalities in the womb or premature birth can damage the brain through effects on the blood supply. Infections can damage the nervous system, particularly if they occur when a baby is growing in the mother’s womb. Chemical exposure can disturb normal brain development (for example drinking alcohol while pregnant can cause fetal alcohol spectrum disorder).

Dr. Del Bigio and members of his laboratory are working on several different projects:

1. The longest running project concerns brain damage that results from enlargement of fluid spaces (the ventricles) in the brain. This disease, which is called hydrocephalus, gradually destroys the axons, which are connections between nerve cells in the brain. Hydrocephalus can result in thinking and learning disabilities, impaired growth, and problems walking. Dr. Del Bigio has discovered several biochemical and mechanical pathways that lead to the brain damage. He and his group, which is currently made up of Alex Shulyakov (research associate), Dom DiCurzio (PhD student), and Emily Turner-Brannen (technologist), are now measuring

the effects of hydrocephalus on blood flow in the brain and testing drug therapies to reduce the brain damage caused by hydrocephalus.

2. The second long-term project is to understand the brain damage that follows premature birth-associated bleeding in the brain. Dr. Del Bigio and his previous students showed that blood could damage growing brain cells when it escapes from the blood vessels. This can result in cerebral palsy or severe mental retardation. He along with Xiaoyan Mao (research associate) and Dmitri Krassioukov-Enns (PhD student), are investigating precisely which components of blood are damaging and how they cause damage in order to develop effective drug therapies.
3. The most recent area of interest concerns the brain damage associated with fetal alcohol exposure. Dr. Del Bigio along with Jessica Jarmasz (MSc student) and Duaa Basalah (MSc student) are analyzing the cellular abnormalities in brain samples from autopsies and experimental studies. This work is being done in conjunction with a large group of MICH scientists and physicians who are interested in the epigenetic changes and neurologic disabilities caused by fetal alcohol exposure.
4. A fourth area of research concerns the mechanical properties of brain tissue. In collaborations with engineers, Dr. Del Bigio and group members including Alex Shulyakov (research associate) and Colin Kazina (PhD student), directly test the brain in order to understand how changes in the physical texture of brain during maturation can explain why brain injuries differ across the age spectrum.

In addition to these projects in his own lab, Dr. Del Bigio collaborates with other scientists to study the biology of brain tumors, brain development, and inflammation in the brain.



Doris Sawatzky-Dickson, RN, MN, IBCLC

Children's pain

By Doris Sawatzky-Dickson, Clinical Nurse Specialist, Health Sciences Centre NICU; Lecturer, Faculty of Nursing, University of Manitoba

The CIHR Team in Children's Pain started in 2007 with a group of researchers from across Canada who wanted to study and improve practices related to keeping children comfortable when they are ill or having painful procedures. Eight pediatric health centres got involved, including Winnipeg Children's Hospital.

I became the site investigator in Winnipeg in 2008 and was very fortunate to have a great study nurse, Sandy Taylor on board from the beginning. The project has involved reviewing thousands of patient charts to look at how pain assessment and management are documented. Four units at Children's Hospital were the initial focus. Two

of these units became the "study" units, and in them we formed a "Research Practice Council" of health care professionals from numerous disciplines to look at their own unit and determine what practices they would like to improve on related to pain assessment and management. Sandy worked with these councils and they did amazing work to make things better for the kids on their units.

The next phase of the study, which we are just completing, was to choose one of these two units to do "booster" sessions with, to see if they could keep moving forward in making improvements, without as much help from our team. In June we will have our last booster meeting with them. This large knowledge translation study has given a lot of Children's Hospital staff an opportunity to be a part of research, but also to learn how to translate research findings into real change that improves the lives of the kids they look after.

The research nurses across the country have put together a book called "Stories From The Floor" which you can access at this link: <http://ken.caphc.org/xwiki/bin/view/ChildrensPain/Stories+from+the+Floor>

The study will continue until March 2014 with collection of more information to show just how things have improved and to develop tools to help other pediatric units to do the same. I feel like I have just been along for the ride, as Sandy and the staff in the hospital have done most of the hard work, and I have just done my part to keep it moving along. The study team in Toronto works like a well-oiled machine and has been busy communicating and publishing the results all over the world. Thanks to MICH for supporting our team in Winnipeg!



Dr. Marni Brownell, PhD

Factors that predict out-of-home care during childhood: a comparison of three developed countries

By Dr. Marni Brownell, Associate Professor, Department of Community Health Sciences, University of Manitoba; Senior Research Scientist, Manitoba Centre for Health Policy

Countries around the world differ in the strategies they use to address child abuse and neglect. Nordic and some European countries employ a child and family welfare approach, providing supports to children and their families when there are concerns about a child's welfare. In contrast, in North America, a child safety approach is used – and this approach is based on statutory protection investigations conducted in order to determine risk of harm to the child, prior to any interventions being employed. Australian child welfare policy falls somewhere in the middle between the Nordic and North American strategies. Last year members of our research team published a paper in *The Lancet*

that showed that these different approaches yield vastly different rates of children in out-of-home care placements (Gilbert et al., 2012). One of the really surprising findings for me from this research was how much higher our rate of children in care is in Manitoba compared to other parts of the world. For example, Manitoba rates were 10 times higher than rates in Western Australia! Coming out of this research, we began wondering whether the risk factors for out-of-home placements also differ across jurisdictions.

In our current work we will be looking at child welfare data from three countries with similar data capabilities but different child welfare policies – in order to identify the factors related to entry into out-of-home care and whether these factors differ across countries. The three countries being examined are Canada (using data from Manitoba – held in the Manitoba Centre for Health Policy’s Population Health Research Data Repository), Australia (using data from Western Australia) and Denmark (using national data). We are hoping that this work will provide important new information to policy-makers about risks for out-of-home care and how these risks may or may not be mitigated by child welfare policies. The data Repository at MCHP provides a really important resource for studying child welfare issues at the population level – having information on out-of-home placements for all children in the province from the Child and Family Services Information System – that is linkable (using encrypted identifiers) to other data in the Repository – like area-level socioeconomic status from the Census, and maternal factors such as age, age at first birth, and mental health.

MICH Members Sharing Their Research

Harold Aukema, PhD, Professor, Department of Human Nutritional Sciences, University of Manitoba and lab members just had a paper published on eicosanoids in a model of adolescent nephronophthisis in the journal *Lipids*. Notably, this is work that stems largely from the work of two former Manitoba Institute of Child Health summer student awardees, Ashleigh Reid and Clara Lysecki. Additionally, it has helped strengthen his team’s collaboration with one of the world’s leading experts on animal models of cystic renal diseases, Shizuko Nagao.

Members of the team at the Manitoba FASD Centre, which includes Manitoba Institute of Child Health researchers Drs. Ana Hanlon-Dearman, Developmental Pediatrician at the Child Development Clinic, Children’s Hospital of Winnipeg and at the Manitoba FASD Centre; Assistant Professor, Department of Pediatrics and Child Health, University of Manitoba, Albert Chudley, Medical Director of the Genetics and Metabolism Program with the Winnipeg Regional Health Authority and is a Professor in the Departments of Pediatrics and Child Health, Biochemistry and Medical Genetics, University of Manitoba, Aziz Mhanni, Assistant Professor, Department of Biochemistry and Medical Genetics, University of Manitoba and Sally Longstaffe, Medical Director, Manitoba FASD Centre; Section Head, Child Development Clinic, Department of Paediatrics; Professor, Department of Pediatrics and Child Health, University of Manitoba travelled to Edinburgh, Inverness, and Dunblane Scotland. The FASD Diagnostic Team Training Presented by the Manitoba FASD Centre was done at the request of the Scottish Government.

Manitoba Institute of Child Health researcher Dr. Benedict Albeni, PhD, Associate Professor of Pharmacology & Therapeutics, University of Manitoba; Principal Investigator, St. Boniface Research Centre; Adjunct Professor of Electrical & Computer Engineering, University of Manitoba; Research Affiliate, Center on Aging and Chris Cadonic, BSc have had a book chapter approved for publication. The chapter “Memory Deficits and Transcription Factor Activity Following Traumatic Brain Injury” will be part of the book *Traumatic Brain Injury*. In this chapter they provided an introduction to the study of traumatic brain injury (TBI) and how it affects memory functioning. In addition, they surveyed some of the existing evidence that describes how TBI leads to memory impairment as measured in animal models and also the evidence for how TBI results in memory impairment as seen in human studies.

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Dr. Cheryl Rockman-Greenberg,
Professor and Head of the Department of Pediatrics and Child Health, University of Manitoba and Medical Director, Child Health Program, Winnipeg Regional Health Authority

News From the Lab

Dr. Mojgan Rastegar, PhD, DEA, MSc, BSc, Assistant Professor, Biochemistry & Medical Genetics, University of Manitoba Principle Investigator, Regenerative Medicine Program, Faculty of Medicine, University of Manitoba

1. The study towards the characterization of Decitabine (FDA approved drug) effect on brain cells was recently published in *Molecular Autism*. Decitabine is suggested to be used for autism, but its effect on brain cells was largely unknown prior to our study. This is a work done by Dr. Rastegar and two of her PhD students.

Paper title: Decitabine alters the expression of *Mecp2* isoforms via dynamic DNA methylation at the *Mecp2* regulatory elements in neural stem cells

Authors: Liyanage VR, Zachariah RM, and Rastegar M.

Reference: *Molecular Autism*. 2013 Nov 15;4(1):46 [PMID: 24238559].

Link: <http://www.molecularautism.com/content/pdf/2040-2392-4-46.pdf>

2. The collaborative research from my lab (Olson CO and Rastegar M) with UC Davis, United States, is recently published in the *Journal Human Molecular Genetics*. This work focuses on the generation and characterization of *Mecp2e1* null mice for modeling Rett Syndrome.

Paper title: Mice with an isoform-ablating *Mecp2* exon 1 mutation recapitulate the neurologic deficits of Rett syndrome

Authors: Yasui DH, Gonzales ML, Aflatooni JO, Crary FK, Hu DJ, Gavino BJ, Golub MS, Vincent JB, Carolyn Schanen N, Olson CO, Rastegar M, Lasalle JM. [PMID: 24352790]

Reference: *Human Molecular Genetics*. 2014 (in press)

3. Dr. Rastegar has been awarded a CIHR catalyst grant (together with Dr. James R. Davie, PhD) for their studies on the molecular mechanisms of Fetal Alcohol Spectrum Disorders (FASD).
4. CIHR Catalyst Grant on Environments, Genes and Chronic Disease (Rastegar M, and Davie JR)

Grant Title: Investigating the Cell Type-Specific Regulatory Role of Ethanol on *MeCP2* Expression

Dr. Soheila Karimi, PhD, Assistant Professor, Department of Physiology, University of Manitoba Principal Investigator, the Regenerative Medicine Program, University of Manitoba Principal Investigator, the Spinal Cord Research Center, University of Manitoba received a CIHR grant in the September 2013 competition and was ranked second in the panel.

Title: Neuroregenerative approaches to enhance white matter repair and functional recovery following traumatic spinal cord injury: reconditioning the injured microenvironment

Type: Open Operating Grant

Ranking: Second (3.08%) in Neuroscience A (NSA)

Term: 5 years



Dr. Rastegar



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