







Diabetes Research Envisioned and Accomplished in Manitoba (DREAM) Theme

Manitoba Institute of Child Health

ANNUAL REPORT

October 31, 2014

Submitted by:

Dr. Grant M. Hatch & Dr. Jon McGavock Co-Directors of DREAM



### **History of DREAM**

The DREAM theme was established 2011, and began formal operations April 1<sup>st</sup>, 2012.

#### VISION

To improve the health of children with diabetes by making clinically relevant discoveries that will serve as the foundation for strategies to improve diagnosis, prevention and management of complications related to obesity and diabetes.

### LOCATION OF DREAM

DREAM is located on the 5<sup>th</sup> and 6<sup>th</sup> floors of the John Buhler Research Centre within the Manitoba Institute of Child Health.

### CHANGE IN STRUCTURE TO DREAM

As this was the end of the first 3 years of funding for the DREAM theme, our group held a 2-day strategic planning session at Hecla resort to reflect on the successes and barriers encountered over the past 3 years. A summary of the retreat is provided below. However some minor changes to the group structure emerged in response to these discussions. The largest change was the transfer of funds away from pilot grants to subthemes and towards core staff and collaborative opportunities. In an effort to align ourselves with CIHR's Strategy for Patient Oriented Research (SPOR), we are allocating funds towards the creation of a patient advisory committee and investing in inout from external experts into our program. We have also allocated funds for writing retreats for investigators to protect their time for writing grants. The small operating grants were reduced in size and will be provided on the basis of need, timeliness and novelty. We will continue to fund core clinical and basic science staff. Salaries for these individuals will be shared by members of DREAM. We plan to test this new model for 12 months before reevaluating.

### **PROGRESS IN 2014**

### CLINICAL EPIDEMIOLOGY CORE

To facilitate the productivity of our clinician scientists, one of the long-term goals for the DREAM Theme is to create a metabolic core within the Clinical Research Unit that consists of core staff trained in diabetes and metabolic assessments. This year we hired our first part-time clinical research nurse and moved key employees into the CRU to strengthen the relationship between research assistants involved in the program. Currently we pay 0.5 FTE for a clinical research nurse that works for all DREAM-related clinical and epidemiological studies. Our vision is for the use DREAM core funding to support 20-50% salaries for these positions with the remainder provided through individual researcher grants. On behalf of DREAM, Dr. Hatch submitted a CFI for support of infrastructure to support this core



### **ADVISORY GROUP**

The majority of the youth treated for type 2 diabetes in the Children's Hospital are First Nations, Metis or Inuit. In an effort to comply with guidelines for participatory action research and ensure that the research we are doing is tailored to the needs of Aboriginal families, Dr. Heather Dean assembled a group of Aboriginal stakeholders, health care providers and scientists to advise the Developmental Origins sub-theme. In 2013, we approached Dr. Dean to ask if the advisory group would consider advising the entire DREAM team. This group will advise on research questions, knowledge translation activities and provide approval for research related to diabetes in Aboriginal youth. We plan to expand on the advisory committee, which consists largely of high ranking stakeholders in maternal and child health within the Indigenous community, and develop a patient advisory committee, that will serve as the voice of children and mothers affected by diabetes.

### **HECLA RETREAT**

In 2014 DREAM held a retreat at Hecla Resort from May 30-31, 2014. Dr. Judy Anderson, Professor/Head of the Department of Biological sciences facilitated the retreat. The attendees included 10 members from DREAM, 2 members from Biology of Breathing group (Richard Keijzer and Andrew Halayko) and 2 community members involved in the Advisory committee: Frances Desjarlais from Manitoba First Nations Diabetes Committee and Wanda Philips-Beck with Assembly of Manitoba Chiefs. The retreat focussed on strengthening our relationships with Indigenous communities/stakeholders over the next three years. Recruitment of potential members to DREAM was discussed in the context of establishing DREAM as a leader in Developmental Origins of Disease. Collaboration between DREAM members within and outside of Winnipeg was addressed and discussion was focussed on enhancing communication between all members. Finally, the development of a new model of DREAM which focussed on recruitment and how to make best use of our existing infrastructure and resources was discussed. The rollout of the discussions outlined strategies to achieve these goals.

### **RECRUITMENT OF NEW SCIENTISTS**

One of our long-term goals is to expand our research team to increase expertise in specific areas. This year we recruited Dr. Megan Azad to the core DREAM group. This past year Dr. Meghan Azad joined DREAM as a full member. Dr. Azad is an Assistant Professor at the University of Manitoba (Department of Pediatrics & Child Health) and a Review Manager at the George & Fay Yee Centre for Healthcare Innovation. She joined the Manitoba Institute of Child Health in 2014. Her research focuses on the gut microbiome and the early-life origins of chronic disease. With training and experience in molecular biology, epidemiology, and knowledge synthesis, Dr. Azad has a broad range of expertise in both basic and clinical health sciences. Prior to joining MICH, Dr. Azad received her PhD from the University of Manitoba (Biochemistry & Medical Genetics) and completed postdoctoral training at the University of Alberta (Pediatrics), receiving over \$1.2M in fellowship funding and research awards, including the prestigious Banting Fellowship, the international Parker B. Francis Fellowship and the CIHR Lindau Prize.



### TRAINING OF HIGHLY QUALIFIED PERSONNEL

Recently, DREAM successfully formed a journal club (DREAM Catchers) which provides students and trainees the opportunity to not only share and discuss relevant hot research papers, but to share work in progress, obtain critical feedback on research projects and hone oral communication skills. We also use journal club as an opportunity to invite world-renowned researchers to meet with trainees and discuss exciting new avenues of research, career paths and advice on balancing work and home life. This year DREAM catchers selected a governing council and invited an array of speakers from within and outside the DREAM group. Graduate students across various pillars attended sessions with DREAM members, that included both clinicians and basic scientists. The translational nature of this environment cultivated a greater appreciation for the clinical and fundamental aspects of research related to type 2 diabetes in youth. With the leadership of Dr. Christine Doucette, the lead for the DREAM catchers group, we have increased the number of trainees in the program by 25% from 45 to 57. Trainees played a major role in Child Health Research Day, taking home ~30% of awards and nominations to the Goodbears Den. Trainees will be highlighted at this years DREAM symposium, where 23 will be presenting their work in poster and oral presentations.

### **CURRENT MEMBERSHIP**

Dr. Grant Hatch	Co-Director, DREAM, Professor Pharmacology and Therapeutics, Biochemistry and Medical Genetics
Dr. Jon McGavock	Co-Director, DREAM, Assistant Professor, Department of Pediatrics and Child Health

Dr. Megan Azad	Associate Professor, Pediatrics and Child Health		
Dr. Tom Blydt-Hansen	Associate Professor (left Manitoba September 2014)		
Dr. Alison Dart	Assistant Professor, Pediatric Nephrologist		
Dr. Jim Davie	Professor, Scientific Director, MICB		
Dr. Heather Dean	Professor, Pediatric Endocrinologist		
Dr. Vern Dolinsky	Assistant Professor, Department of Pharmacology and		
	Therapeutics		
Dr. Christine Doucette	Assistant Professor, Department of Physiology		
Dr. Paul Fernyhough	Professor, Pharmacology / Neurodegenerative Diseases		
Dr. Joe Gordon	Assistant Professor, Faculty of Nursing		
Dr. Elizabeth Sellers	Associate Professor, Pediatric Endocrinologist		
Dr. Geert tJong	Clinical Pharmacologist, Medical Leader, CRU		
Dr. Brandy Wicklow	Assistant Professor, Pediatric Endocrinologist		
Dr. Kristy Wittmeier	Physiotherapist,		
Non Faculty Members			
Erika Bloomfield	Research Coordinator		
Taralyn Stierman	Research Nurse		



### **INFRASTRUCTURE**

Each member of DREAM has his/her independent research program and is expected to secure extramural funding and other infrastructural support to conduct his/her research studies. DREAM is designed to support core staff, facilities and equipment for research related to type 2 diabetes carried out by core members. DREAM also serves as a communal resource to support the research activities of ancillary members, the University of Manitoba and other institutions. The various scientific programs of DREAM also serve as catalysts to facilitate research collaboration and exchange of expertise between members internal and external to the University.

### MANAGEMENT OF DREAM AND BUSINESS MEETINGS

The DREAM Theme conducts monthly scientific and business meetings with all core members. The Management Committee of the DREAM, consisting of Drs. Hatch and McGavock, and sub theme leaders are responsible for the general operation of DREAM. The day-to-day operation of DREAM is currently carried out by the theme codirectors and the DREAM coordinator, Erika Bloomfield.

### TRAINING ENVIRONMENT FOR DREAM TRAINEES

Trainees of DREAM are provided access to a top-notch training environment at MICH. MICH fosters multi-disciplinary research interactions that facilitate translational research between the pre-clinical, clinical and population health-based sciences. Additionally, MICH provides an open and collaborative environment, which houses many eminent researchers with whom our trainees forge strong research collaborations and receive mentoring and guidance. Another excellent training opportunity for our trainees is participation in our Annual Diabetes Symposium, which is organized and hosted by DREAM. Over the past three years, this symposium has grown significantly and now includes attendees and presentations from international researchers, local researchers, trainees and a poster session, in which trainees are strongly encouraged to present their work (either in poster or oral form). This year, we received 23 abstracts for poster presentations (83% of which are DREAM trainees). This symposium provides a excellent opportunity for trainees to showcase their work and allow them to network with both local and international leaders in the diabetes field.





## Highlights of trainee activities and investment in DREAM-specific trainees in 2014

### **Doucette Lab Training:**

As pre-clinical research scientist on the DREAM team, I have had the opportunity to train and mentor three summer students over the past two summers. Trainees in my lab gain significant experience in various fundamental laboratory skills and techniques, which include planning/designing experiments, data analysis, interpretation of data, oral presentations, manuscript writing, mammalian cell culture, gene expression analyses, protein assays, insulin secretion assays, transfection of cells with genes of interest and many other cellular and molecular analyses. The trainees in my lab are encouraged to participate in the DREAM Catchers journal club and present both research articles and work-in-progress seminars during the summer term. Additionally, Doucette lab trainees are encouraged to present their work at both local and national conferences. For specific projects and their successes, please see below:

### 1) **Steven Cooper** (Summer 2013, 2014):

Project title: Investigating the physiological role of uncoupling protein 2 in the regulation of daily rhythms of insulin secretion

Funding: MICH undergraduate Summer Studentship recipient (2014) Successes:

Findings from Steven's two summers of research has contributed to the generation of 3 publication-quality figures which we hope to publish in the near future

Steven presented his research at MICH rounds (August 2013) Steven's work was presented at Child Health Research Day (2014), 3rd Annual DREAM Symposium (2014) and the Canadian Diabetes Association Clinical and Scientific Annual Meeting (2014)

 Michael Jonasson (Summer 2014): Project title: Determining the impact of high-fat exposure on UCP2-regulated rhythmic insulin secretion: implications for beta cell failure in type 2 diabetes



Funding: MICH undergraduate Summer Studentship recipient (2014) Successes:

-Michael's work has led to the generation of novel, high-impact data that discerns for the first time a pathophysiological role of UCP2 in the mediating high-fat-diet-induced beta cell failure, which we hope to have submitted for publication within the next 12 months

-Michael has presented his research at MICH Rounds (Aug 2014), DREAM Journal club (July 2014), Child Health Research Day (2014), 3rd Annual DREAM Symposium (2014) and the Canadian Diabetes Association Clinical and Scientific Annual Meeting (2014)

### 3) **Tianna Flett** (Summer 2014):

Project title: Mechanisms of HNF1aG319S-induced beta cell failure: Implications for the development of youth-onset type 2 diabetes

Funding: DREAM undergraduate Summer Studentship recipient (2014) Successes:

-Tianna`s work demonstrates for the first time that the HNF1aG319S polymorphism impairs insulin secretion, which is exacerbated by the presence of high fat, providing significant insight into the development of early-onset type 2 diabetes in aboriginal youth that are carriers of this polymorphism.

-Tianna's work has provided rationale for the creation of a mouse model of the HNF1aG319S so that we can better understand how this polymorphism specifically leads to a more rapid onset of type 2 diabetes, which is currently underway.

-Tianna has presented his research at, DREAM Journal club (August 2014), Child Health Research Day (2014) and the 3rd Annual DREAM Symposium (2014).

# Dolinsky Lab

### 1) Troy Pereira (2012-2014):

• *Thesis title:* Influence of gestational diabetes on the programming of metabolic health outcomes in offspring.

• *Funding*: Stipend was funded by the University of Manitoba start-up funds to Dr. Dolinsky and later an MHRC/MICH Studentship. The project was funded by University of Manitoba and MICH start-up funds to Dr. Dolinsky. In addition, DREAM contributed funds to support metabolomics analyses of liver and muscle tissues of rodent offspring from Troy's rodents. A grant from MMSF to Dr. Dolinsky also funded this project.

### • Successes:

• Troy completed and defended his MSc thesis (August 2014)

• Findings from Troy's work has contributed to co-authorship of two publications on projects with collaborators (Biochimica Biophysica Acta and Am. J. Physiology). In addition, in the fall of 2014 Troy's primary thesis project has been submitted to the Journal of Physiology as first author. He has also completed a literature review as co-first author, which was submitted to Biochemistry and Cell Biology.

• Troy's unpublished work has also contributed to the pilot for several



projects being conducted by current trainees (Brar, Moyce and Kereliuk) so it is anticipated that he will have additional publications.

• Troy's has presented his research in several conferences and symposia including Child Health Research Day (2012 and 2013), the Institute of Cardiovascular Sciences Poster Day (2013), the Canadian Society of Pharmacology and Therapeutics Meeting (2014), the Canadian Student Health Research Forum (2013 and 2014) and the joint meeting of the Canadian Diabetes Association and Canadian Cardiovascular Congress in Montreal (October 2013).

oTroy has received several awards during the course of his training:

- Manitoba Health Research Council Studentship, 2013
- Dean of Graduate Studies Award for poster presentation at the Canadian Student Health Research Forum, 2013
- Clive Greenway Award, Best Graduate Student Presentation in Dept of Pharmacology, 2013
- First place, graduate student poster award at the MICH Child Health Research Day, 2013
- MICH Travel Award to attend CCC/CDA Scientific Meeting in Montreal, 2013

• Dr. Dolinsky has presented Troy's research in several venues including the 1<sup>st</sup>, and 2<sup>nd</sup> annual DREAM Symposia (2012 and 2013), MICH Research rounds (April 2013 and 2014), the Cardiovascular Forum for Promoting Centers of Excellence (2014), the Canadian Lipid and Lipoprotein Conference (2014) and the Canadian Diabetes Association Clinical and Scientific Annual Meeting (2014).

### 2) Brittany Moyce (Summer 2013 and May 2014-present):

- Project title: The role of adiponectin in gestational diabetes,
- *Funding:* Stipend is funded by MHRC and beginning October 2014 by CIHR. The project is funded by MHRC and beginning October 2014 by CIHR.

### • Successes:

• Brittany started her graduate program in my lab in May 2014

• Brittany's work during the summer of 2013 provided preliminary data from the adiponectin knock-out mouse model that supported our hypothesis that adiponectin deficiency contributes to gestational diabetes. This data was critical in supporting the application for funding from CIHR (which ranked #2 within the Diabetes/Obesity/Lipids committee). We anticipate that based on progress with this project we hope to submit for publication within the next 12 months.

• Brittany also contributed some data that was included in a publication submitted to the Journal of Physiology (2014) with Brittany as fourth author. She has also completed a literature review as co-first author, which was submitted to Biochemistry and Cell Biology (2014).

• Brittany has presented her research in several conferences and symposia including Child Health Research Day (2013 and 2014), the Canadian Society of Pharmacology and Therapeutics Meeting (2014), and the Canadian Diabetes Association Clinical and Scientific Annual Meeting (2014).



- Brittany has received several awards at this early stage of her training:
  - Peter Dresel Award for the best graduate student oral presentation at the Canadian Society of Pharmacology and Therapeutics Meeting, 2014
  - Third place, graduate student poster award at the MICH Child Health Research Day, 2014

### 3) Stephanie Kereliuk (Summer 2014-present):

• **Project title:** Gestational diabetes and the developmental origins of diabetic cardiomyopathy.

• *Funding:* Stipend and project are funded by a Heart and Stroke Foundation grant to Drs. McGavock and Dolinsky

### • Successes:

 Working through the summer of 2014 with the echocardiography technician, Bo Xiang, Stephanie has already demonstrated that the young rat offspring of gestational diabetic mothers develop cardiac hypertrophy. She is making good progress as has now begun graduate studies in my laboratory in September.

 Stephanie also contributed some sections to a literature review and is third author on the manuscript that was submitted to Biochemistry and Cell Biology (2014).

 Stephanie has already presented her data at Child Health Research Day (2014).

• Stephanie has received several awards at this early stage of her training:

- Third place, "Dr. Good Bear's Den" trainee oral presentations at MICH Child Health Research Day, 2014
- Second place, graduate student poster award at the MICH Child Health Research Day, 2014

### 4) Kristyn Campbell (Summers 2012 and 2013):

• **Project title:** Determining the role of the Hepatic Nuclear Factor 1-alpha G319S polymorphism in liver lipid metabolism.

• *Funding:* University of Manitoba undergraduate Summer Studentship recipient (2012) and NEAHR/MICH joint studentship funding in 2013. Project was funded by University of Manitoba start-up funds to Dr. Dolinsky in 2012 and a MICH grant to Dr. Doucette/Dolinsky in 2013.

### • Successes:

• Kristyn's preliminary work generating stably transfected cell lines and performing gene expression analysis provided the foundation for obtaining funding for the project from MICH and the rationale for generating an animal model (currently underway).

 Kristyn also contributed some gene expression data and insulin analysis data that was included in a publication submitted to the Journal of Physiology (2014) with Kristyn as third author.

 Kristyn presented her research at Child Health Research Day (2013), the Network Environments for Aboriginal Health Research Student Colloquium (2013), and the Undergraduate Research Poster Competition at the University of Manitoba (2013).



- Kristyn received several awards at this early stage of her training:
  - Second place, graduate student poster award at the MICH Child Health Research Day, 2013
  - MHRC Studentship, 2014, currently doing her graduate training at the National Microbiology Lab in Winnipeg

### 5) Kyle Cheung (Summers 2012, 2013, 2014):

- Project title: SIRT3 attenuates doxorubicin-induced cardiotoxicity
- Funding: MICH undergraduate Summer Studentship recipient (2014)

### • Successes:

• Kyle's work over three summers has contributed to a first-author manuscript that was submitted to the Journal of Biological Chemistry and is currently being revised for resubmission to address reviewer questions.

 $_{\odot}$  Kyle presented his research at Child Health Research Day (2013 and 2014) and the Undergraduate Research Poster Competition at the University of Manitoba (2013).

### 6) Navdeep Brar (Summer 2014):

• **Project title:** Maternal gestational diabetes increases the susceptibility of young rat offspring to maladaptive pancreatic islet development.

• *Funding:* Stipend was funded by MHRC Establishment funding to Dr. Dolinsky. The project was funded by a MHRC grant to Dr. Dolinsky.

### • Successes:

• Working through the summer of 2014 with my technician, Mario Fonseca, Nav already demonstrated that the young rat offspring of gestational diabetic mothers fail to increase the beta cell mass in response to a high fat diet. As a result these rats are predisposed to develop impaired glucose tolerance. She made excellent progress mastering immunofluorescence, confocal microscopy and islet morphometric analyses and we anticipate to have submitted for publication within the next 12 months.

 Nav presented her research at Child Health Research Day (2014) and the Undergraduate Research Poster Competition at the University of Manitoba (2014).

### Gordon Lab

### 1) Wajihah Mughal (PhD student):

*Project title:* Myocardin regulates mitochondrial function to prevent programmed cell death during cardiac development

• **Funding**: MICH/MHRC Studentship recipient (2014)

### - Successes:

o Wajihah's data has generated several figures examining the role of microRNA-133a in mitochondrial regulation. This data has contributed substantially to a manuscript that has been submitted to EMBO J as a presubmission enquiry. We anticipate that this paper will be published in the next



year. In addition, Wajihah has several figures completed on a follow-up project examining the role of myocardin in microRNA-133a expression.

Wajihah presented her research at DREAM Journal Club (May 2014)
Wajihah's work was presented at Child Health Research Day (2013 and 2014), the Canadian Student Health Research Forum, Winnipeg 2014, the Canadian Diabetes Association Clinical and Scientific Annual Meeting (2014), and is currently submitted as an abstract to the Keystone Symposia on Diabetes and Metabolic Dysfunction

# 2) Lucas Nguyen (Summer 2013 and 2014):

**Project title:** Determining the role of skeletal muscle microRNA-133a in early-onset insulin resistance.

*Funding:* MICH undergraduate Summer Studentship recipient (2014)

### · Successes:

o Lucas's data has contributed to figures examining how microRNA-133a regulates Nix expression. This data is included in our manuscript submitted to EMBO J as a presubmission enquiry. In addition, has identified novel post-translational modifications in Nix that regulate its function.

o Lucas presented his research at the MICH Student Day (August 2014)

o Lucas's work was presented at Child Health Research Day (2013 and 2014), the Canadian Diabetes Association Clinical and Scientific Annual Meeting (2014), and is currently submitted as an abstract to the Keystone Symposia on Diabetes and Metabolic Dysfunction.

# 3) Steven Piotrowski (Summer 2014):

**Project title:** Regulation of MEF2 and SRF by PKCdelta.

• **Funding:** DREAM Summer Studentship recipient (2014)

### - Successes:

o Steven's data has contributed to figures examining how PKCdelta regulates the transcriptional activity of MEF2 and SRF. This data is included in our manuscript submitted to EMBO J as a presubmission enquiry.

o Steven's work was presented at Child Health Research Day (2014)

o Steven is currently a 1<sup>st</sup> year student in the Physician Assistant Program at UofM.



### SCIENTIFIC MEETINGS

For the past three years, DREAM has used DREAM funds to host an annual research symposium focused on cutting-edge research in the field of youth-onset Type 2 Diabetes. Typically, this symposium has been composed of keynote talks from local, national and international speakers, short-talks from local speakers to highlight DREAM research and a symposium dinner, which allows DREAM team members and invited speakers to have the opportunity to build relationships, network and collaborate. This year, we have added new elements to the symposium and as a result, not only has attendance significantly increased, but we have attracted preeminent world-leaders in the diabetes research filed deliver highly-relevant and impactful keynote talks. This year we significantly changed the format of the symposium to allow for greater networking opportunities and participation by our trainees.

A major change to the scientific program this year, was the addition of a poster session and a networking reception that affords trainees the opportunity to share their work with both the local diabetes research community as well as with the invited speakers and attendees. This creates opportunities for the trainees to network, build collaborative relationships as well as the opportunity to receive relevant feedback on their research projects. We are excited to announce that we received a total of 23 poster abstracts for this year's symposium, which far exceeded our expectations. Importantly, 83% of these abstracts were from DREAM-related trainees, demonstrating the excellent opportunity that this symposium creates to highlight DREAM-based research within our scientific community. Of the 23 abstracts that were received, the top three abstract submissions were invited to present a short oral presentation during the symposium. Not only are we proud to highlight the top-notch trainees and their research that is being performed by DREAM and the University of Manitoba, but we are also excited to give the students/trainees an opportunity to hone their oral presentation skills and share their research in a well-attended public forum. With the addition of the poster session, trainee oral presentations and networking reception, we have significantly increased attendance at our symposium, which has gone from ~30-40 in years 1 and 2 to over 80 this year. This year we attracted participants from several different departments within U of M as well as attendees from other universities. We are thrilled with the changes to the symposium that we have made this year and look forward to seeing its growth in the years to come.

The 3<sup>rd</sup> Annual Symposium is scheduled for November 13, 2014. The focus this year is Developmental Origins of Diabetes. The keynote speakers include:

- Dr. Susan Ozanne, University of Cambridge
- Dr. Dana Dabelea, University of Colorado Denver
- Dr. Sandra Davidge, University of Alberta

Local speakers include:

- Dr. Heather Dean
- Dr. Meghan Azad
- Dr. Brandy Wicklow



# 2014 Symposium Agenda:

Time	Speaker	Title
		You are what your mother ate: how 9 months
8:00 - 9:00	Dr. Susan Ozanne	in the womb shapes your diabetes risk
Pediatric Grand Rounds	University of Cambridge	Heather Dean Annual Lecture in
		Excellence in Diabetes
9:00-9:20	Light breakfast, registration	Poster set-up
	DREAM	
9:20 - 9:30	Directors' Opening Remarks	Dr. Jon McGavock & Dr. Grant Hatch
		Historical Perspectives on
9:30-10:30	Dr. Heather Dean	type 2 diabetes in children in Manitoba:
		How we came to study the developmental origins of this
		disease
10:30-10:50	Selected Abstract Talk	ТВА
10:50-11:10	Selected Abstract Talk	ТВА
11:10-11:30	Selected Abstract Talk	ТВА
11:30-12:00	Lunch	Posters open
12:00-13:00	Dr. Dana Dabelea	Developmental Origins of Pediatric
MICH Research Rounds	University of Colorado Denver	Obesity and Type 2 Diabetes
		Is a child's risk of diabetes determined at birth?
1:00-1:45	Panel Discussion/Debate	Or can it be modified?
1:45-2:00	Coffee Break	Posters Open
2:00-2:30	Dr. Meghan Azad	Discoveries from Dirty Diapers:
		Developmental Origins of Gut Microbiota
2:30-3:00	Dr. Brandy Wicklow	Next Gen
2:00 4:00	Dr. Sandra Davidga	Upposite induced introutering growth restriction. Effects are
3:00-4:00	Dr. Sanara Daviage	nypoxia-induced intrauterine growth restriction: Effects on
	University of Alberta	intervention strategies
4:00 5:00	Dector Specien/	Abstract Awards
4:00-5:00	Poster Session/	ADSTRACT AWARDS
	wine & Cheese	

# **COLLABORATIONS AND NETWORKING**

DREAM has begun to develop active collaborations with other research groups within the Faculty of Medicine and colleagues elsewhere. Current collaborations with other institutions include: Harvard University University of Alberta Ontario Public Health SickKids McMaster University University of Toronto University of Colorado Medical School University of Calgary Children's Hospital of Eastern Ontario



### MHRC CLUSTER

In the spring of 2014, the DREAM executive met with the executive from the Biology of Breathing (BoB) to discuss the potential for a collaboration on the recently launched Research Manitoba initiative to fund new clusters (or teams) of researchers focused on areas that were of interest to Manitobans. As the DREAM research group had previously demonstrated an interest in focusing our team on the study of the developmental origins of diabetes. The rationale for the shift in our mission was related in large part to clinical observations and seminal discoveries by the pediatric endocrinologosists on the team, that children born to mothers with pre-gestational diabetes displayed a dramatically higher risk for type 2 diabetes, than children not exposed to diabetes in the womb.

At a group retreat in Hecla, we decided that the developmental origins of diabetes would be our primary theme over the next three years and that collaborating with BoB would enhance our capacity to study more extensively the developmental origins of the most common chronic diseases facing children in Manitoba: type 2 diabetes, obesity, asthma and allergies. In collaboration with members of BoB we submitted a letter of intent to Research Manitoba at the end of June 2014. The outline of the proposed Cluster is provided below. We will cover all four pillars of research described by CIHR and are aligned with the signature initiative of the Institute for Human Development, Child and Youth Health. The reviews from our letter of intent were very positive and our team was asked to submit a full proposal in January 2015. A successful application will bring an additional \$2.5 million to MICH.



### **DREAM PRODUCTIVITY 2014**

Support for development of DREAM was based initially on a \$675,000 investment (2012-2014) provided by the Manitoba Institute of Child Health (MICH).

\$175,000 in 2012 \$250,000 in 2013 \$250,000 in 2014

Each member of DREAM has his/her own departmental affiliation, research laboratory, research grants and research personnel to support his/her research program. Research support currently held by members of DREAM includes grants from:

- Canadian Institutes of Health Research (CIHR)
- Canadian Cancer Society
- Heart and Stroke Foundation of Canada
- Canadian Foundation for Innovation (CFI)
- Canadian Diabetes Association (CDA)
- MHRC
- The Lawson Foundation
- NSERC

Collectively, theme members secured 36 operating, equipment and salary wards totalling over \$6.6 million in research funding in 2014 (see attached table below). Highlights for this year included new large competitive grants for young investigators: Drs Vern Dolinsky (\$503,000/5yrs) and Joe Gordon (\$75,000/2yrs) each secured operating grants from CIHR and the MHRC respectively. Support for DREAM Theme funding was also integral in securing Dr. McGavock's CIHR Applied Health Chair (\$1,000,000 over five years, 2014-2019). Finally, Dr. Hatch was able to secure 3 operating grants from national agencies to continue to pursue his interest in mitochondrial biology. Our group has also submitted a CFI application and was shortlisted to submit an application to the MHRC Team grant program. The infrastructure will be housed within the MICH laboratories on the 6<sup>th</sup> floor of the John Buhler Research Centre.

Since 2012, the number of publications by the team has increased significantly from just under 80 for the team to just over 115 (an increase of ~40%). The total number of grants increased from 15 to 36 over the past 3 years. We have secured our first national chair, renewed two CRC chairs and secured 2 new investigator awards for DREAM members.







# **DREAM PRODUCTIVITY 2014**





# Grants Awarded in 2014 to DREAM members

Member	Agency	Amount	Duration	Funding/yr	Туре
Azad, Co-I	CIHR	\$100,000	2014-2015	\$100,000	Operational
Azad, Co-I	WCHRI	\$50,000	2014-2015	\$50,000	Innovation
Dart, Co-I	CHILDNEPH	\$100,000	2014-2015	\$100,000	Start-Up
Davie, Pl	CCSRI	\$196,000	2014-2016	\$98,000	Operational
Davie, Pl	Cancer Care MB Fdn.	\$120,000	2014-2016	\$60,000	Operational
Davie/Doucette	MICH	\$40,000	2014-2015	\$40,000	Operational
Davie, Pl	CIIFAC	\$10,000	2014-2016	\$20,000	Operational
Dolinsky, Pl	CIHR	\$503,000	2014-2019	\$100,600	Operational
Dolinsky, Pl	Diabetes Foundation of	\$75,000	2014-2017	\$25,000	Operational
	Manitoba				
Dolinsky, Pl	Stewart Whitman	\$20,000	2014	\$20,000	Salary
•	Young Inv. Award				
Dolinsky, Pl	MHRC/MICH bridge	\$40,000	2014-2015	\$40,000	Operational
Dolinsky, Co-I	MICH/CHF	\$40,000	2014-2015	\$40,000	Operational
Doucette, PI	MICH	\$40,000	2014-2015	\$40,000	Operational
Doucette, PI	MICH/MMSF	\$25,000	2014-2015	\$25,000	Operational
Gordon, PI	MHRC	\$75,000	2014-2016	\$37,500	Operational
Hatch	NSERC	\$165,000	2014-2019	\$33,000	Discovery
Hatch	HSFC	\$266,975	2014-2017	\$88,991	Operating
Hatch	Barth Syndrome	\$54,340	2014-2015	\$26,000	Development
Hatch	NIH	\$26,000	2014-2015	\$26,000	Conference Support
McGavock, Pl	CIHR	\$1,000,000	2014-2019	\$200,000	Research Chair
McGavock, PI	Alberta Innovates/CRIO	\$3,200,000	2014-2019	\$640,000	Operating
	Team				
McGavock, PI	CIHR	\$455,000	2014-2017	\$151,667	Operating
McGavock, PI	Lawson Foundation	\$20,000	2014	\$20,000	Operating
McGavock, PI	Health Canada	\$10,000	2014	\$10,000	Operating
McGavock, PI	MHRC	\$7,500	2014	\$7,500	Operating
McGavock, PI	CIHR	\$25,000	2014	\$25,000	Operating
McGavock, Co-I	CIHR	\$10,000	2014	\$9,500	Operating
McGavock, PI	MHRC	\$65,000	2014	\$65,000	Operating
McGavock, Pl	U of M	\$7,000	2014	\$7,000	Operating
Sellers, Co-I	MMSF	\$15,000	2014-2015	\$15,000	Operating
T 'Jong,PI	MICH	\$37,910	2014-2015	\$37,910	Operating
Wicklow	MICH	\$50,000	2014	\$50,000	Operating
Wittmeier, PI	CIHR	\$10,000	2014-2015	\$10,000	Operating
Wittmeier, Co-I	Child Health Advisory	\$4,262	2014	\$4,262	Operating
	Council				
TOTAL	36	\$6,877,987		\$2,043,930	
TOTALS	GRANTS	AMOUNT		AMOUNT/YR	
2012	17	\$4,007,320		\$1,117,000	
2013	24	\$9,138,770		\$3,046,257	
2014	36	\$6,683,487		\$2,043,930	



# PUBLICATIONS







#### Megan Azad

#### Publications 2014 (6)

1. Bridgman SL, Azad MB, Field CJ, Letourneau N, Johnston DW, Kaplan BJ, Kozyrskyj AL. Maternal perspectives on the use of probiotics in infants. *BMC Complementary and Alternative Medicine* 2014. (In Press)

2. Persaud RP, Azad MB, Chari RS, Becker AB, Sears MR, Kozyrskyj AL. Perinatal antibiotic exposure of neonates in Canada and associated risk factors: a population-based study. *The Journal of Maternal-Fetal & Neonatal Medicine* 2014. (In Press)

3. Azad MB, Bridgman SL, Becker AB, Kozyrskyj AL. Infant antibiotic exposure and the development of childhood overweight and central adiposity. *International Journal of Obesity* 2014. (In Press)

4. Konya T, Koster B, Maughan H, Escobar M, Azad MB, Guttman D, Sears MR, Becker AB, Brook JR, Takaro TK, Kozyrskyj AL, Scott JA, and the CHILD Study Investigators. Associations between bacterial communities of house dust and infant gut. *Environmental Research* 2014. 131:25-30.

5. Azad MB, Coneys JG, Kozyrskyj AL, Field CJ, Ramsey CD, Becker AB, Friesen C, Abou-Setta AM, Zarychanski . Probiotic supplementation during pregnancy or infancy for the prevention of asthma and wheeze: A systematic review and meta-analysis. *British Medical Journal* 2013. 347:f6471.

6. Salman MS, Masood S, Azad MB, Chordirker BN. Ethnicity and Geographic Distribution of Pediatric Chronic Ataxia in Manitoba, Canada. *Canadian Journal of Neurological Sciences* 2014. 41:29-36.

#### Tom Blydt-Hansen

#### Publications 2014 (4)

1. Arias M, Rush D, Wiebe C, Gibson I, Blydt-Hansen T, Nickerson P, Sellarés J, López-Hoyos M, San Segundo D, Crespo-Leiro M, Marzoa-Rivas R, Barge-Caballero E, Paniagua-Martín M, Román A, Serón D, Böhmig G, Schwaiger E.. (2014). Antibody-Mediated Rejection: Analyzing the Risk, Proposing Solutions.. Transplantation. 98(3): 3-21.

2. Mathur S, Janaudis-Ferreira T, Wickerson L, Singer LG, Patcai J, Rozenberg D, Blydt-Hansen T, Hartmann EL, Haykowsky M, Helm D, High K, Howes N, Kamath BM, Lands L, Marzolini S, Sonnenday C.. (2014). Consensus Recommendations for a Research Agenda in Exercise in Solid Organ Transplantation.. American Journal of Transplantation.

3. Blydt-Hansen TD, Pierce CB, Cai Y, Samsonov D, Massengill S, Moxey-Mims M, Warady BA, Furth SL. (2014). Medication Treatment Complexity and Adherence in Children with CKD.. Clinical journal of the American Society of Nephrology. 9(2): 247-54.

4. Humar, Atul; Kucirka, Lauren; Wright, Linda; Gill, John; Renner, Eberhard; Kiberd, Bryce; Segev, Dorry; Kim, Joseph; Knoll Greg; Blydt-Hansen, Tom et al. (2014). Guidance on the use of increased infectious risk donors for organ transplantation. Transplantation.

#### Dr. Allison Dart

#### Journal Articles 2014 (9)

1. Blydt-Hansen, TD; Dart, AB. (2014). How should we identify early chronic kidney disease risk in nonkidney transplant recipients?. Pediatric Transplant. 18(7): 661-2.

2. Sood MM, Manns B, Dart A, Hiebert B, Kappel J, Komenda P, Molzahn A, Naimark D, Nessim S, Rigatto C, Soroka S, Zappitelli M, Tangri N. (2014). Variation in the Level of eGFR at Dialysis Initiation across Dialysis Facilities and Geographic Regions. Clin J Am Soc Nephrol. 9(10): 1747-56.

3. Dart A, Wicklow B, Sellers E, Dean H, Malik S, Walker J, Chateau D, Blydt-Hansen T, McGavock J.



(2014). The Improving renal Complications in Adolescents with type 2 diabetes through Research (iCARE) cohort study: rationale and protocol. Canadian Journal of Diabetes. 38(5): 349-55.

4. Samuel, S.; Scott, S.; Morgan, C.; Dart, A.; Mammen, C.; Parekh, R.; Nettel-Aguirre, A.; Eddy, A. et al.(2014). The Canadian Childhood Nephrotic Syndrome (CHILDNEPH) Project: overview of design and methods. Canadian Journal of Kidney Health and Disease. 1(17) 5. AB Dart, CA Ruth, EA Sellers, Wendy Au, HJ Dean. (2014). Pre-gestational and Gestational Diabetes are Associated with Congenital Anomalies of the Kidney and Urinary Tract. American Journal of Kidney Diseases.

6. Bikaramjit, SM; Manns, BJ; Dart, AB Kappel, J; Molzahn, A; Naimark, D; Nessim, S; Soroka, S; Zappitelli, M; Sood, M. (2014). An assessment of dialysis provider's attitudes towards timing of dialysis initiation in Canada. Canadian Journal of Kidney Health and Disease. 3(1)

7. Sood MM, Tangri N, Hiebert B, Kappel J, Dart A, Levin A, Manns B, Molzahn A, Naimark D, Nessim SJ, Rigatto C, Soroka SD, Zappitelli M, Komenda P. (2014). Geographical and regional variation in the use of peritoneal dialysis in Canada: A cohort study.. Open Canadian Medical Association Journal. 2(1):E36-44.

 Samuel S, Bitzan M, Zappitelli M, Dart A, Mammen C, Pinsk M, Cybulsky AV, Walsh M, Knoll G, Hladunewich M, Bargman J, Reich H, Humar A, Muirhead N. (2014). Canadian Society of Nephrology Commentary on the 2012 KDIGO Clinical Practice Guideline for Glomerulonephritis: Management of Nephrotic Syndrome in Children. American journal of kidney diseases : the official journal of the National Kidney Foundation. 63:(3): 354-62.
Cybulsky AV, Walsh M, Knoll G, Hladunewich M, Bargman J, Reich H, Humar A, Samuel S, Bitzan M, Zapitelli M, Dart A, Mammen C, Pinsk M, Muirhead N. (2014). Canadian Society of Nephrology Commentary on the 2012 KDIGO Clinical Practice Guideline for Glomerulonephritis: Management of Glomerulonephritis in Adults. American journal of kidney diseases: the official journal of the National Kidney Foundation. 63(3): 363-77.

### Jim Davie

### Publications 2014 (7):

1. Khan, D.H., Gonzalez, C., Cooper, C., Sun, J.M., Chen, H.Y., Healy, S., Xu, W., Smith, K.T., Workman, J.L., Leygue, E., and Davie, J.R. (2014) RNA-dependent dynamic histone acetylation regulates MCL1 alternative splicing. **Nucleic Acids Res**., <u>42</u>, 1656-1670.

2. Khan, D.H. and Davie, J.R. (2014) Dual cross-linking ribonucleoprotein immunoprecipitation assay. **Biochem Cell Biol.** <u>92</u>, 317-319.

3. Jahan, S. and Davie, J.R. (2014) Protein arginine methyltransferases (PRMTs): role in chromatin organization. **Adv. Biol. Regul.** in press.

4. Gang, H., Hai, Y., Aviv, Y., Margulets, V., Leygue, L., Davie, J.R., and Kirshenbaum, L.A. (2014) Alternative splicing of Bnip3 switches cell life and death in cancer cells. **Cell Death and Differentiation**, in preparation.

5. Liyanage, V.R.B., Zachariah, R.M., Davie, J.R. and Rastegar, M. (2014) Ethanol deregulates MeCP2 *via* interplay between 5-methylcytosine and 5-hydroxymethylcytosine at its regulatory elements during neural stem cell differentiation. <u>in review.</u>

### **Book Chapters**

1. Drobic, B., Pérez-Cadahía, B., Khan, P., Healy, S. and Davie, J.R. (2014) Role of mitogen and stress activated kinases in histone phosphorylation. **Landes Bioscience. Editor:** J. Simon C. Arthur. **ISBN:** 978-1-58706-661-0. Chapter 2, pp. 29-47.

2. Liyanage, V., Jarmasz, J.S., Murugeshan, N., Del Bigio, M.R., Rastegar, M. and Davie, J.R. (2014) DNA modifications: Function and applications in normal and disease states. In: DNA Methylation. *Biology.* Guest Editor: Proof. Dr. Melanie Ehrlich. MDPI AG, Postfach, CH-4005 Basel, Switzerland.

### Heather Dean

#### Publications (15)

1. Grymonpre R., Ateah C., Dean H., Heinonen T., Holmqvist M, MacDonald L., Ready E., Wener P.. Using an Interprofessional Education for Collaborative Person Centred Practice (IECPCP) Framework for Sustainable Program Implementation: The University of Manitoba Experience. Journal Interprofessional Care.

2. Dart A, Ruth C, Sellers E, Dean H. Pre-gestational and Gestation Diabetes are Associated with Congenital Anomalies of the Kidney and Urinary Tract. Am J Kidney Disease. In Press

3. Grymonpre R., Dean H., MacDonald L., Fricke M., Ateah C., Holmqvist M., Kural B., James M., Wener P. An Inventory of Interprofessional Learning Opportunities at the University of Manitoba: A 'Real Time' Quality Improvement Strategy (in press). Journal of Research in Interprofessional Education. Submitted

4. Dean H, Sellers E. Why Children with Diabetes Matter to all of Us: The Seven Generations. Can Journal of Diabetes. 38: 219-218.

5. Dart A., Wicklow B., Sellers E., Dean H., Malik S., Walker J., Chateau D., Blydt-Hansen T., McGavock J.. The Improving renal Complications in Adolescents with type 2 diabetes through Research (iCARE) cohort study: rationale and protocol.. Canadian Journal of Diabetes. In Press

 Singer J., Putulik C., Martin B., Dean H., Trepman E., Embil J.. Food Consumption, Obesity, and Abnormal Glycemic Control in a Canadian Inuit Community. Clinical Obesity. In Press
Reid A., Hui A., Beck L., Ludwig S., McGavock J., Phillips-Beck W., Dean H., Shen G. (2014). Reducing Barriers for Pregnant Women in Rural/Remote First Nations Communities to Participate in Prenatal Program Through Community-Oriented Approaches. Am J Public Healht. In Press

8. Dean HJ, MacDonald L, Alessi-Severini S, Halipchuk JA, Sellers EA, Grymonpre RE. (2014). Elements and enablers for interprofessional education clinical placements in diabetes teams. Can J Diabetes. 38(4): 273-8.

9. Sellers E, Marks S, Rodd C, Wicklow B, Dean H. (2014). Atypical diabetes: clarifying the muddy waters. CMAJ - Letter to the editor.

10. Joyal K, Katz C, Dean HJ, Harder N.. (2014). Interprofessional Education using Simulation of an Overnight Inpatient Ward Shift.. Journal of Interprofessional Care.

11. Knip M, Åkerblom HK, Becker D, Dosch HM, Dupre J, Fraser W, Howard N, Ilonen J, Krischer JP, Kordonouri O, Lawson ML, Palmer JP, Savilahti E, Vaarala O, Virtanen SM; TRIGR Study Group. (2014). Hydrolyzed infant formula and early β-cell autoimmunity: a randomized clinical trial. JAMA. 311(22): 2279-87.

12. Eskicioglu P, Halas J, Śénéchal M, Wood L, McKay E, Villeneuve S, Shen GX, Dean H, McGavock JM.. (2014). Peer mentoring for type 2 diabetes prevention in first nations children. Pediatrics. 133(6): 1624-31.

13. Mollard R., Senechal M., MacIntosh A., Hay J., Wicklow B., Wittmeier K., Sellers E., Dean H., Ryner L., Berard L., McGavock J. (2014). Dietary determinants of hepatic steatosis and visceral adiposity in overweight and obese youth at risk of type 2 diabetes. J Clinical Nutrition. 99(4): 801-12.

14. Eskiciouglu P., Halas J., Senechal M., Wood L., McKay E., Villeneuve S., Shen G., Dean H., McGavock J. (2014). The Aboriginal Youth Mentorship Program (AYMP): Peer mentoring for Type 2 Diabetes Prevention in First Nations children living in a northern isolated setting. Pediatrics. 133: 1624-31.

15. Israels SJ, McNicol HJ, Dean HJ, Cognasse F, Sellers EAC. (2014). Markers of Platelet Activation in Adolescents with Diabetes Mellitus. Diabetes Care.



### <u>Vern Dolinsky</u>

Publications (10)

1. DOLINSKY V.W. and Dyck, J.R.B. Experimental studies of the molecular pathways regulated by exercise and resveratrol in heart, skeletal muscle and the vasculature. *Molecules* **19**: 14919-14947 (2014).

Baczko, I., Liknes, D., Yang, W., Hamming, K., Searle, G., Jaeger, K., Husti, Z., Klausz, G., Pap, R., Saghy, L., Varro, A., **DOLINSKY V.W.**, Shaohua, W., Rauniyar, V., Hall, D., Dyck, J.R.B. and Light, P.E. Characterization of a novel multi-functional resveratrol derivative for the treatment of atrial fibrillation. *Br. J. Pharmacol.* **171**: 92-106 (2014)
Guo, J., Breen, D.M., Pereira, T.J., Zhang, H., Ghanim, H., Mroziewicz, M., Fantus, I.G., Bendeck, M.P., Dandona, P., **DOLINSKY V.W.**, Heximer, S.P., and Giacca, A. The Vasculo-protective effects of insulin are endothelial nitric oxide synthase-dependent. *Atherosclerosis* (2014) Revision requested.

4. Guo, J., Pereira, T.J., Breen, D.M., **DOLINSKY V.W.** and Giacca, A. Metformin does not decrease neointimal formation in a rat model of restenosis. *Am. J. Physiol. Endo. Metab.* (2014) Revision requested.

5. Pereira, T.J., Fonseca, M.A., Campbell, K.E., Moyce, B.L. Cole, L.K., Hatch, G.M., Klein, J., Aliani, M. and **DOLINSKY V.W.** Gestational diabetes alters the hepatic metabolite profile and contributes to steatosis in young rat offspring. *J. Physiol.* (2014)

 Cheung, K., Cole, L.K., Ma, X., Xiang, B., Chen, K., Myal, Y. Hatch, G.M., Tong, Q. and DOLINSKY V.W. SIRT3 attenuates doxorubicin-induced oxidative stress and improves mitochondrial respiration in cardiac myocytes. J. Biol. Chem. (2014) Revision requested.
Wicklow, B., Wittmeier, K., 't Jong, G.W., McGavock, J., Robert, M., Duhamel, T. and DOLINSKY V.W. Safety and efficacy of resveratrol for the treatment of non-alcoholic fatty liver disease and associated insulin resistance in overweight and obese adolescents: rationale and protocol. *Biochemistry and Cell Biology* (2014).
Pereira, T.J., Moyce, B.L. Kereliuk, S., and DOLINSKY V.W. Influence of Maternal

8. Pereira, T.J., Moyce, B.L. Kereliuk, S., and **DOLINSKY V.W.** Influence of Maternal Overnutrition and Gestational Diabetes on the Programming of Metabolic Health Outcomes in the Offspring: Experimental Evidence. *Biochemistry and Cell Biology* (2014).

9. **DOLINSKY, V. W.,** Soltys, C.L., Rogan, K.J., Zordoky, B.N., Haykowsky, M.J., Young, M.E., Jones, L.W. and Dyck, J.R.B. Resveratrol prevents pathological but not physiological cardiac hypertrophy via differential regulation of pro-hypertrophic signaling pathways. *J. Mol. Med.* (2014)

### **BOOK CHAPTERS**

1. Meija, E., **DOLINSKY V.W.** and Hatch, G.M. Role of phospholipases in regulation of cardiolipin biosynthesis and remodeling in the heart and mammalian cells. In: *Phospholipases in Health and Disease*, edited by P.S. Tappia and N.S. Dhalla (2014). New York: Springer Science. p. 39-53

### **Christine Doucette**

#### Journal Articles 2014 (1)

1. Troy J Pereira, Mario A Fonseca, Kristyn E Campbell, Brittany L Moyce, Laura K Cole, Grant M Hatch, Christine A Doucette, Julianne Klein, Michel Aliani, Vernon W Dolinsky. (2014). Maternal gestational diabetes mellitus increases the susceptibility of rat offspring to obesity and hepatic steatosis via disrupted liver metabolome. The Journal of Physiology.

### Paul Fernyhough

### Publications (4)

1. Roy Chowdhury, S.K., Saleh, A., Akude, E., Smith, D.R., Tessler, L., Calcutt, N.A. and P. Fernyhough (2014). Ciliary neurotrophic factor signals via STAT3 to enhance mitochondrial



bioenergetics in neurons from streptozotocin-diabetic rodents. Cellular and Molecular Neurobiology. 34, 643-649.

2. Verkhratsky, A. and P. Fernyhough (2014). Calcium signalling in sensory neurones and peripheral glia in the context of diabetic neuropathies. Cell Calcium. In Press.

3. Menard, C.E., Durston, M., Zherebitskaya, E., Smith, D.R., Glazner, G.W., Fernyhough, P., Freed, D.H., Tian, G., and R.C. Arora (2014). Temporal dystrophic remodeling within the intrinsic cardiac nervous system of the streptozotocin-induced diabetic rat model. Acta Neuropathologica Communications. 2, 60.

4. Biessels, G.-J., Calcutt, N.A., Cotter, M., Feldman, E.L., Fernyhough, P., Mizisin, A.J., and A.A. Sima et al. (2014). Advances in phenotyping animal models of diabetic neuropathy: a consensus statement. Journal of Peripheral Nervous System. 19, 77-87.

#### Joe Gordon

#### Publications 2014 (2)

1. Mughal W, Nguyen L, Pustylnik S, Piotrowski S, Chapman C, Du M, Ali N, Grigull J, Halayko AJ, Aliani M, Pereira T, Dolinsky VW, Rampitsch C, McDermott JC, **Gordon JW.** A conserved MADS-box phosphorylation motif regulates mitochondrial function and skeletal, cardiac, and smooth muscle cell differentiation. (EMBO J, presubmission inquiry).

2. Archibald, A., Hossain, Z., Mughal, W., Friel, J., **Gordon, J.W.,** & Diehl-Jones, W. (2014). Regulation of enterocyte necrosis by Bnip3 following exposure to human milk fortifiers. American Journal of Physiology: Gastrointestinal and Liver Physiology. (in preparation).

#### Jon McGavock

Publications (22)

1. Hay J, Wittmeier K, Wicklow B, MacIntosh A, Dean H, Sellers E, Duhamel T, Ready E, Gardiner P, McGavock J. (2014). Physical activity intensity and diabetes risk factors in overweight youth. The POWER Trial. Diabetes Care. Submitted

2. Wicklow B, Griffith A, Dumontet J, Venopaul N, McGavock J. (2014). Pancreatic triglyceride content is not associated with beta cell dysfunction in youth-onset type 2 diabetes. Pediatric Obesity. Submitted

3. Shen GX, Shafer L, Martens P, Sellers E, Torshizi A, Ludwig S, Phillips-Beck W, Heaman M, Prior H, McGavock J, Morris M, Dart A, Head HJ.. (2014). Impact of Breastfeeding Initiation on the Incidence of Type 2 Diabetes in Mothers and their Offspring: A Population-based Study in Manitoba.. NEJM. Submitted

4. Senechal M, Rempel M, MacIntosh A, Hay J, Wicklow B, Wittmeier K, Shen G, Duhamel T, McGavock J. (2014). Cardiorespiratory fitness is a determinant of the metabolic response to training in overweight adolescents. Diabetologia. Submitted

5. MacIntosh A, Mollard R, Rinaldi R, Torrance B, Ball GD, Majumdar S, Plotnikoff R, Veugelers P, Boule N, Wozny P, McCargar L, Downs S, Lewanczuk R, McGavock JM. (2014). Is physical activity associated with remission to healthy weight status in obese youth? Pediatric Obesity. Submitted

6. Dart A, Wicklow B, Sellers E, Dean H, Malik S, Walker J, Chateau D, Blydt-Hansen T, McGavock J. (2014). The Improving renal Complications in Adolescents with type 2 diabetes through Research (iCARE) cohort study: rationale and protocol.. Can. J Diabetes. Revision Requested

7. Comte M, Hobin E, Manske S, Casey C, Griffith J, Leggett C, Veugelers P, Murnaghan D, McGavock J. (2014). Is the Provision of Physical Education to Senior Years Students Associated With Greater Physical Activity Levels? Insight into a Province-Wide Policy. Journal of Physical Activity and Health. Published



8. Protudjer J, Dumontet J, McGavock J. (2014). My Voice: A qualitative study of the lived experience of managing type 2 diabetes with lifestyle choices in adolescents. Canadian Journal of Diabetes. Accepted

9. MacMillan F, Yardley J, Hay J, MacIntosh A, Wicklow B, Wittmeir K, McGavock J. (2014). The blood pressure response to exercise is not exaggerated in youth with type 2 diabetes. Pediatric Diabetes. In Press

10. Senechal M, McGavock J, Church T, Lee D, Earnest CP, Sui X, Blair S. (2014). Cut-Points of Muscle Strength Associated with Metabolic Syndrome in Men in the Aerobics Center Longitudinal Study. Medicine and Science in Sports and Exercise. 46(8): 1475-81.

Saad V, Wicklow B, Wittmeier K, Hay J, MacIntosh A, Ryner L, Berard L, McGavock J.. (2014). A practical algorithm to predict hepatic steatosis in obese youth. Pediatric Obesity.
Vander Ploeg KA, Maximova K, McGavock J, Davis W, Veugelers P. (2014). Do school-based physical activity interventions increase or reduce inequalities in health?. Soc Sci Med.. 112: 80-87.

13. Schaefer L, Plotnikoff RC, Majumdar SR, Mollard R, Woo M, Sadman R, Rinaldi RL, Boulé N, Torrance B, Ball GD, Veugelers P, Wozny P, McCargar L, Downs S, Lewanczuk R, Gleddie D, McGavock J. (2014). Outdoor Time Is Associated with Physical Activity, Sedentary Time, and Cardiorespiratory Fitness in Youth.. J. Pediatrics.

14. Sénéchal M, Ayers CR, Gore MO, See R, Abdullah SR, Berry JD, McGuire DK, McGavock J. (2014) Is Cardiorespiratory Fitness a Determinant of Cardiomyopathy in the Setting of Type 2 Diabetes? Diabetes and Vascular Disease Research.Published

15. McLean L, Russell K, Tenenbein M, Warda L, McGavock J.. (2014). Age and the risk of All-Terrain Vehicle (ATV)-related injuries in children and adolescents: Injury patterns and legislative impact assessment through the Canadian Hospitals Injury Reporting and Prevention Program CHIRPP database. CMAJ. Submitted

16. Schaffer L, Dean H, Martens P, Heaman M, Phillips-Beck W, Dart A, McGavock J, Shen GX. (2014) Long Term Impact of Gestational Diabetes on Subsequent Development of Type 2 Diabetes in Mothers and Offspring in Manitoba.. NEJM.

17. Eskicioglu P, Halas J, Sénéchal M, Wood L, McKay E, Villeneuve S, Shen GX, Dean H, McGavock JM. (2014). Peer mentoring for type 2 diabetes prevention in first nations children.. Pediatrics. 133(6):e1624-31.

18. Durksen A, Downs S, Mollard R, Forbes L, Ball G DC, McGavock J. (2014). The Association Between Time Spent in Vigorous Physical Activity and Dietary Patterns in Adolescents: Cross-Sectional Study. J Phys Act Health. In Press

19. Mollard RC, Sénéchal M, Macintosh AC, Hay J, Wicklow BA, Wittmeier KD, Sellers EA, Dean HJ, Ryner L, Berard L, McGavock JM. (2014). Dietary determinants of hepatic steatosis and visceral adiposity in overweight and obese youth at risk of type 2 diabetes.. The American journal of clinical nutrition. Published

20. Santos RG, Durksen A, Rabbanni R, Chanoine JP, Lamboo Miln A, Mayer T, McGavock JM. (2014). Effectiveness of Peer-Based Healthy Living Lesson Plans on Anthropometric Measures and Physical Activity in Elementary School Students: A Cluster Randomized Trial. JAMA pediatrics.

21. Hobin E, So J, Rosella L, Comte M, Manske S, McGavock J. (2014). Trajectories of Objectively Measured Physical Activity among Secondary Students in Canada in the Context of a Province-Wide Physical Education Policy: A Longitudinal Analysis.. Journal of obesity. 2014 Published

22. Vander Ploeg KA , McGavock J , Maximova K , Veugelers PJ. (2014). School-Based Health Promotion and Physical Activity During and After School Hours.. Pediatrics.Published



### Grant Hatch

#### Publications 2014 (11):

1.Zhaojie, M., Ming, Z., Shengnan, W., Xiaojia, B., HATCH, G.M., Jingkai G., and Li, C. (2014) Amorphous solid dispersion of berberine with absorption enhancer demonstrates a remarkable hypoglycemic effect via improving its bioavailability. Intl. J. Pharmaceutics 467, 50-59.

2.Guan, F.Y., Gu, J., Li, W., Zhang, M., Ji, Y., Li, J. Li, C. and HATCH, G.M. (2014) Compound K protects pancreatic B-cells against apoptosis through inhibition of the AMPK/JNK pathway in type 2 diabetic mice and in MIN6 B-cell. Life Sciences 107, 42-49.

3. Poirier, S., Mamarbachi, M., Samami, S., Demers, A., Chang, T.Y., Vance, D.E., HATCH, G.M. and Mayer, G. (2014) The epigenetic drug 5-Azacytidine interferes with cholesterol and lipid metabolism. J. Biol. Chem. 289, 18736-18751.

4. Dalvi, D., Nguyen, H., Mitchel, R.W., On, N., Aukema, H.M, Miller, D.W. and HATCH, G.M. (2014) Exogenous arachidonic acid mediates permeability of human brain microvessel endothelial cells. J. Neurochem. (*submitted*).

5. Cheung, K., Cole, L.C., Xiang, B., Chen, K., Ma, X., Myal, Y., HATCH, G.M., Tong, Q. and Dolinsky, V.W. (2014) SIRT3 attenuates doxorubicin-induced oxidative stress and improves mitochondrial respiration in H9c2 cardiomyocytes. J. Biol. Chem. (*in revision*).

6. Pereira, T.J., Fonseca, M.A., Campbell, K.E., Moyce, B.L., Cole, L.K., HATCH, G.M., Doucette, C.A., Klein, J., Aliani, M. and Dolinsky, V.W. (2014) Maternal gestational diabetes mellitus increases the susceptibility of young rat offspring to diet-induced metabolic syndrome. J. Physiol. (London) (*submitted*)

7. Dalvi, S., On, N., Nguyen, H., Pogorzelec, M., Miller, D.W. and HATCH, G.M. (2014) The blood brain barrier: Regulation of fatty acid and drug transport. In: *Neurochemistry* (Heinbockel, T., ed.), ISBN: 978-953-51-1237-2, InTech:

http://www.intechopen.com/books/neurochemistry/the-blood-brain-barrier-regulation-of-fattyacid-and-drug-transport. Rijeka, Croatia, pp. 1-58.

8. Mejia, E.M, Nguyen, H. and HATCH, G.M. (2014) Mammalian cardiolipin biosynthesis. Chem. Phys. Lipids. 179, 11-16.

9. Mejia, E.M., Cole, L. and HATCH, G.M. (2014) Cardiolipin metabolism and the role it plays in heart failure and mitochondrial supercomplex formation. Cardiovasc. Hematol. Disord. Drug Targets. 14, 98-106.

10. Mejia, E.M. and HATCH, G.M. (2014) Mitochondrial Phospholipids: Role in Mitochondrial Function. J. Bioenerg. Biomembr. (*accepted*)

11. Chang, W., Chen, L. and HATCH, G.M. (2014) Berberine as a therapy for type 2 diabetes and its complications: From mechanism of action to clinical studies. Biochem. Cell Biol. (submitted).

### Elizabeth Sellers

#### Publications 2014 (9)

1. Hui AL, Ludwig S, Gardiner P, Sevenguysen G, Dean HJ, Sellers EA, McGavock J, Morris M, Sen GX, Jiang D. (2014). Effects of lifestyle intervention on dietary intake, physical activity level, and gestational weight gain in pregnant women with different pre-pregnancy Body Mass Index in a randomized control trial. BMC Pregnancy Childbirth. 14(1): 331.

2. Dean HJ, Sellers EA. (2014). Why children with diabetes matter to all of us: the seven generations. Can J Diabetes. 38(4): 217-8.

3. Aylward NM, Shah N, Sellers EAC. (2014). The ketogenic diet for the treatment of myoclonic astatic epilepsy in a child with type 1 diabetes mellitus. Can J Diabetes. 38(4): 223-4.

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9. Dart AB , Martens PJ , Rigatto C , Brownell MD , Dean HJ , Sellers EA. (2014). Earlier onset of complications in youth with type 2 diabetes. Diabetes care

### Geert 't Jong

#### Publications 2014 (1)

Koffeman AR, Valkhoff VE, Jong GW, Warlé-van Herwaarden MF, Bindels PJ, Sturkenboom MC, Luijsterburg PA, Bierma-Zeinstra SM. Ischaemic cardiovascular risk and prescription of non-steroidal anti-inflammatory drugs for musculoskeletal complaints. Scand J Prim Health Care. 2014 Jun;32(2):90-8

#### **Brandy Wicklow**

### **Journal Articles (5)**

1. Dart A., Wicklow B., Sellers E., Dean H., Malik S., Walker J., Chateau D., Blydt-Hansen T., McGavock J.. The Improving renal Complications in Adolescents with type 2 diabetes through Research (iCARE) cohort study: rationale and protocol. Canadian Journal of Diabetes. In Press

2.Sellers E, Dean H, Wicklow B, Marks S, Rodd C. (2014). Atypical diabetes: clarifying the muddy waters. CMAJ.Published

3. (2014). Pancreatic triglyceride content is not associated with youth onset type 2 diabetes. Journal of Clinical Endocrinology and Metabolism.

#### **Revision Requested**

4. Wicklow B., Sellers E. (2014). Maternal health issues and cardio-metabolic outcomes in the offspring: a focus on Indigenous populations. Best Practice & Research clinical Obstetrics & Gynecology. (29.2)

5. Mollard RC, Sénéchal M, MacIntosh AC, Hay J, Wicklow BA, Wittmeier KD, Sellers EA, Dean HJ, Ryner L, Berard L, McGavock JM. (2014). Dietary determinants of hepatic steatosis and visceral adiposity in overweight and obese youth at risk of type 2 diabetes.. American Journal of Clinical Nutrition. 99(4): 804-812.

### Kristi Wittmeier

### Publications 2014 (5)

 McGavock J, Hay J<sup>\*</sup>, Wittmeier K<sup>\*</sup>, MacIntosh A, Duhamel T, Sellers E, Dean H, Ready E, Berard L, Kriellaars D, Gardiner P, Wicklow B. *Physical Activity Intensity and Type 2 Diabetes Risk in Overweight Youth: The POWER Trial a Randomized Controlled Trial. Submitted to Obesity October 2014.* \*denotes equal contribution to the work.
Wittmeier K, Holland C, Hobbs K, Crawford L, Milne B, Beauchamp C, Morris M, Keijzer R. *Analysis of a parent initiated social media campaign for Hirschsprung's Disease.* Journal of

Internet Medical Research 2014 (In Press)



Lomotey R, Mulder K, Nilson JA, Schachter C, Wittmeier K, Deters R. *Mobile self-management guide for young men with mild hemophilia in cases of minor injuries.* Network Modeling Analysis in Health Informatics and Bioinformatics 2014 3 (1), 1-10.
Daymont C, McDonald P, Wittmeier K, Reed M, Moffatt M. *Variability of physicians' thresholds for neuroimaging in children with recurrent headache.* 2014 BMC Pediatrics 14:162.
Mollard R, Sénéchal M, MacIntosh AC, Hay J, Wicklow BA, Wittmeier K, Sellers E, Dean H, Ryner L, Berard L, McGavock J. Dietary determinants of hepatic steatosis and visceral adiposity in overweight and obese youth at risk of type 2 diabetes. American Journal of Clinical Nutrition. Published online ahead of print Feb 2014.

# FINANCIAL PROGRESS REPORT

The \$250,000 allocation for 2014 provided grant funding for each of the three themes as well as support for the Research Coordinator, Erika Bloomfield. In addition, support of the November 13, 2014 Scientific Meeting was provided through the allocation.

Budget Proposal for DREAM	for 2015		
Expenditure	Unit Cost	#/year	Total
1. OPERATING			
SHARED			
Coordinator	\$60,000.00	1	\$60,000.00
Writing Retreats	\$1,000.00	3	\$3,000.00
Advisory Group	\$625.00	4	\$2,500.00
Patient Advisory Group	\$2,500.00	1	\$2,500.00
Guest Speakers	\$1,500.00	2	\$3,000.00
Grant Reviews	\$250.00	8	\$2,000.00
CLINICAL Clinical Bacaarch Nursa Coordina	470 000 00	0.2	¢21 000 00
iCAPE Support	\$70,000.00	0.3	\$21,000.00
Next Con Support	\$55,000.00	0.4	\$22,000.00
Small Grant Support	\$33,000.00	0.4	\$22,000.00
	\$20,000.00	<b>T</b>	φ20,000.00
BASIC			
Seahorse Support	\$65,000.00	0.4	\$26,000.00
Small Grants	\$20,000.00	2	\$40,000.00
Sub-Total			\$224,000.00
2. TRAINEE RECRUITMENT			
Recruitment visits	\$1,000.00	4	\$4,000.00
Sub-Total			\$4,000.00
3. MEETINGS			
Annual symposium	\$10,000.00	1	\$10,000,00
Monthly meetings	\$200.00	10	\$2,000.00
Cub Tatal	•		
Sub-Total			\$12,000.00
4. ADMINISTRATION			
Group leader stipends	\$5,000.00	2	\$10,000.00
Sub-Total			\$10,000.00
			\$224 000 00
TRAINEES			\$4 000 00
MEETINGS			\$12,000.00
ADMINISTRATION			\$10,000.00
TOTAL ANNUAL REQUEST			\$250,000.00