

DREAM Annual Report 2020

### **Name of Theme**

DREAM - Diabetes Research Envisioned and Accomplished in Manitoba

### **Group Leader and Members**

*(Please list in alphabetical order by last name with primary departmental affiliation, if any, and indicate whether MD or PhD or both)*

Mandy Archibald, PhD, College of Nursing

Allison Dart, MD, MSc, Department of Pediatrics and Child Health

Vernon Dolinsky, PhD, Department of Pharmacology and Therapeutics (co-lead)

Christine Doucette, PhD, Department of Physiology and Pathophysiology

Joseph Gordon, PhD, Department of Human Anatomy and Cell Science/ Physiology and Pathophysiology

Grant Hatch, PhD, Department of Pharmacology and Therapeutics

Meaghan Jones, PhD, Department of Biochemistry and Medical Genetics

Jonathan McGavock, PhD, Department of Pediatrics and Child Health (co-lead)

Ayesha Saleem, PhD, Faculty of Kinesiology and Recreation Management

Elizabeth Sellers, MD, MSc, Department of Pediatrics and Child Health

Peter Thompson, PhD, Department of Physiology & Pathophysiology

Brandy Wicklow, MD, MSc, Department of Pediatrics and Child Health

### **Goals of the Program: Who We Are, What We Do and Why**

*Please give a narrative summary of your group's identity and purpose. This account should be written in lay language and should identify how the theme has added value to the research efforts of the individual investigators (MAX 1 page)*

**Mission:** The goal of the DREAM research theme is to improve the wellness of children and their families living with type 2 diabetes by making clinically relevant discoveries (that improve their lives). Using an integrated interdisciplinary approach we will translate discoveries into practice and policy.

**Vision:** We hope that discoveries we make in our clinical studies of children can be used to discover new mechanisms that lead to disease. The group of scientists that we have assembled will work closely on all aspects of research to make sure that our discoveries are meaningful to parents and children affected by diabetes. By working closely as a team, we are better able to make our discoveries meaningful and advance our knowledge faster than anything we could do on our own.

**Who we are:** The DREAM theme consists of 20 trainees, 13 investigators and 6 Indigenous stakeholders committed to improving the lives of children and their families living with, or at risk for type 2 diabetes. Within that commitment we recognize that type 2 diabetes disproportionately affects Indigenous youth in Manitoba, and in accordance with TRC Call to Action #18 acknowledge that this inequity is the direct result of trauma associated colonial policies and practices designed to marginalize Indigenous people in Canada. Our investigator team consists of pediatric specialists in endocrinology and nephrology, basic scientists with expertise in molecular biology, genetics, muscle physiology and cardiovascular disease and epidemiologists with expertise in maternal child health and community based participatory action research. Collectively we are all committed to solving the complex issues faced by young people living

with diabetes, ranging from the fundamental question “Why did I get diabetes at such a young age” to “What is the best way help children living with diabetes experience meaningful complication free lives?” We rely on translational, “team science” approaches, grounded in culturally safe practices, to address these questions.

**What we do:** Our team focuses on three primary pillars of research related to type 2 diabetes in youth: (1) **Novel interventions** to prevent and treat type 2 diabetes; (2) Biopsychosocial determinants of **complications of diabetes** and (3) the **developmental origins** of type 2 diabetes in youth. Within each of these pillars scientists design studies to unravel the complex factors that lead to type 2 diabetes and its complications using pre-clinical, clinical and population health approaches. Scientists from a range of backgrounds work collaboratively to design impactful research that could have the greatest impact on the children and families affected by type 2 diabetes. Since our inception, we have secured over \$22M in external funding to tackle these problems, created patient and stakeholder advisory committees to ensure that our work is relevant to families we serve, hosted symposia for members of the scientific and lay community and made numerous discoveries that have shaped the way doctors and families understand type 2 diabetes in youth. We are also deeply committed to fostering the next generation of scientists and clinicians in this area. To date, our trainees have secured over \$500,000 in funding to support their education, hosted numerous educational and interprofessional events to advance their careers and created national collaborations with other trainee groups to share knowledge and expand social networks. Collectively, this work has made the DREAM theme a nationally recognized centre of excellence in the area of pediatric diabetes research.

**Why do we do it?** Type 2 diabetes is the fastest growing pediatric chronic disease in Canada. Manitoba is disproportionately affected by type 2 diabetes in youth. For every children diagnosed with type 2 diabetes in other parts of Canada, there are 15 children diagnosed with type 2 diabetes in Manitoba. Type 2 diabetes in youth is associated with a large burden of complications and reduced life expectancy. Nearly 50% of children living with type 2 diabetes will be on dialysis by the time they are 35 years old. Type 2 diabetes affects youth that suffer from profound structural disadvantage. Most are poor, live in rural/remote areas and experience significant mental health comorbidities. Type 2 diabetes in youth is a major health challenge in Manitoba and requires Manitoba-made solutions.

### **Major Accomplishments (Milestones)**

*Please list up to 5 major accomplishments/milestones from the past year. (media, impact on child health, events, awards and recognitions)*

#### **DREAM trainees:**

Our trainees are the true highlight of the work we do. Despite this unusual year which has led to many changes and challenges, our trainees persevered and found ways to thrive. Below are some of their major accomplishments in 2020.

Publications: DREAM trainees successfully published 9 academic manuscripts this year, and 6 of those had a DREAM trainee as the first author.

#### Conference Awards:

Paul Dudley White International Scholar Award: Best abstract submitted from Canada at the American Heart Association Epidemiology | Lifestyle conference.

### Conference Awards:

Paul Dudley White International Scholar Award: Best abstract submitted from Canada at the American Heart Association Epidemiology | Lifestyle conference.

### *16th Annual Child Health Research Days:*

PhD Poster Competition:

1st place – Stephanie Kereliuk

3rd place – Matthew Martens

Honorable mentions – Mateusz Tomczyk & Taylor Morriseau

Dr. Goodbears Den (Oral Presentation Competition):

Gold Medal – Matthew Martens

Sex & Gender Awards (sponsored by Dr. Neeloffer Mookherjee):

Gold Award – Taylor Morriseau

Annual trainee lectureship: The lectureship was delivered virtually by Dr. Daniel Drucker from the University of Toronto titled “Glucagon-Like Peptides: Translational and Mechanistic Insights” on Nov. 12<sup>th</sup> 2020. The lectureship was followed by a career development discussion with Dr. Drucker and trainees. Attendance was good for this presentation, and the career development session afterwards was valuable and insightful.

San’yas cultural safety training: With most of the in person meetings cancelled this year, the trainees had to make a decision how best to utilize their budget. Cultural safety training is something that has come up with the group repeatedly, so they decided to allow trainees to use the funds to sign up for and complete the san’yas cultural safety training that is offered through the WRHA. This is a training that all DREAM PIs and many staff members have completed. 7 of the DREAM trainees are currently enrolled in this training.

### **Translational team publications:**

This year our team published 56 papers, with 10 that included two or more members of DREAM.

One main focus of the DREAM research team is to work collaboratively and translationally as is stated in our mission statement, we aim to use an integrated interdisciplinary approach to translate discoveries into practice and policy. We believe that the publications below showcase this by highlighting the collaboration between multiple DREAM labs. (**DREAM trainees** are bolded and *DREAM PIs* are italicized, and former DREAM members are underlined)

1. **da Silva Rosa SC, Martens MD, Field JT**, Nguyen L, **Kereliuk SM**, Hai Y, Chapman D, Diehl-Jones W, Aliani M, West AR, Thliveris J, Ghavami S, Rampitsch C, *Dolinsky VW, Gordon JW*. BNIP3L/Nix-induced mitochondrial fission, mitophagy, and impaired myocyte glucose uptake are abrogated by PRKA/PKA phosphorylation. 2020. Autophagy. ePub Ahead of Print. <https://doi.org/10.1080/15548627.2020.1821548>
2. Agarwal P, Brar N, **Morriseau T, Kereliuk SM**, Fonseca M, Cole L, Jha A, Xiang B, Hunt K, **Seshadri N, Hatch G, Doucette C, Dolinsky VW**. Gestational Diabetes Adversely Affects

- Pancreatic Islet Structure and Function in the Rat Offspring. 2019. *Endocrinology*. 160(8):1907-1925. <https://doi.org/10.1210/en.2019-00232>
- i. Chosen for Endocrine Society Thematic Issue on Diabetes 2019 based on high Altmetric Attention scores and Featured Article designations
  - ii. Selected as one of the Top 2019 Endocrine Studies by the Endocrine Society journals (featured in the December *Endocrine News Eureka!* 2019 article)
3. Meghan B. Azad, Alyssa Archibald, **Mateusz M. Tomczyk**, Alanna Head, Kyle G. Cheung, Russell J. de Souza, Allan B. Becker, Piushkumar J. Mandhane, Stuart E. Turvey, Theo J. Moraes, Malcolm R. Sears, Padmaja Subbarao, *Vernon W. Dolinsky*. (May 2020). Non-nutritive sweetener consumption during pregnancy affects adiposity in mouse and human offspring. Published in the *International Journal of Obesity*. <https://doi.org/10.1038/s41366-020-0575-x>
  4. **Martens, M.D., Field, J.T., Seshadri, N.**, Day, C., Chapman, D., Keijzer, R., *Doucette, C.R., Hatch, G.M., West, A.R., Ivanco, T.L., Gordon, J.W.* (2020). Misoprostol Attenuates Neonatal Cardiomyocyte Proliferation through Bnip3, Perinuclear Calcium Signaling, and Inhibition of Glycolysis. *Journal of Molecular and Cellular Cardiology* (IF: 5.055), 146, p 19-31. doi: <https://doi.org/10.1016/j.yjmcc.2020.06.010>.
  5. **Brunton N**, Dufault B, *Dart A*, Azad MB, *McGavock JM*. (2020). Maternal obesity before pregnancy predicts offspring blood pressure at 18 years of age – A causal mediation analysis. *JAMA Pediatrics*; Submitted.
  6. Guillemette L, *Wicklow B, Sellers EAC, Dart A, Shen G, Dolinsky V, Gordon J, Jassal D, Nickel N, Prior H, Duhamel T, Chateau D, McGavock J.* (2020) Intrauterine Exposure to Diabetes and cardiovascular Disease Risk in Adolescence and Early Adulthood: A Population – Based Birth Cohort Study. *CMAJ* 129; E1104-E1113

### **Awards and Funding:**

CFI funding (Ayesha), CFI funding (Meaghan), Ayesha nominated top 40 under 40 and a grant from US National Academy of Medicine

Many of our DREAM investigators have funding wrapping up this year, so a main focus was really on submission of grants for new funding next year. That being said DREAM researchers still secured 13 grants for a total of \$900,000 in new funding. Some of our newer members accomplished some great achievements this year, Drs. Saleem and Jones were both able to obtain CFI funding, Dr. Saleem also received a grant from the US National Academy of Medicine, and was chosen for the class of 2020 CBC Manitoba Future 40.

### **Diabetes Canada:**

We were very proud to have Dr. Christine Doucette elected as the Planning Committee Co-Chair for the Diabetes Canada Professional Conference, October 28-31, 2020, Virtual Conference. Dr. Doucette spent many years spearheading and coordinating the annual DREAM symposium and we are thrilled to see her utilize her skills, knowledge and networks to enhance the Diabetes Canada conference.

### **Community engagement:**

We worked closely with our stakeholders this year to partner with Keewatinohk Inniniw Minoayawin (KIM) Inc. to support community based wellness programming for Indigenous youth in Manitoba. In partnership with Dr. Barry Lavallee, CEO of KIM, the DREAM research theme will work collaboratively to facilitate awards to the communities within Manitoba to promote wellness. DREAM has contributed \$10,000 in 2020, which will be matched by KIM. These funds will be used to support wellness projects within the communities ranging from \$500-\$2000 each. We believe that this partnership and these projects are vital to hear the voices of the youth so that we can prioritize our research efforts accordingly.

We look forward to rolling these grants out in 2021 and hearing the voices from the youth in our communities!

### **In what ways has your work positively impacted child health? (1-2 examples)**

(1) Novel insight into treatment options for youth living with type 2 diabetes: iCARE patient advisory circle developed new curriculum and co-created infographics to help support other youth being seen for type 2 diabetes at the Children's hospital. Discoveries within the iCARE cohort study identified novel targets, particularly in the area of mental health that are associated with better health outcomes in youth.

(2) The IYMP team delivered culturally safe and community-tailored healthy living programming to over 1000 Indigenous children across Canada in late 2019, early 2020. This resilience-based healthy living curriculum supported cultural continuity and lifestyle behaviours that supported the prevention of type 2 diabetes.

### **Research Funding**

1. Total dollar value of your membership's research funding held in fiscal year 2020 (April 1, 2020 - March 31, 2021).

**2020-2021 = \$6,106,718**

**2015-2020 = \$23,691,866**

2. Give a subtotal of ACTIVE research funding awarded (and held in Manitoba) in the past 12 months.

**2020 = \$903,557**

3. Identify any Catalyst Grants awarded in the past year (Title, PI, funding amount)

#### CHROM catalyst grants 2020

1. Bridge funding Grant Hatch \$60,000

#### DREAM catalyst grants 2020

1. "In utero exposure to Type 2 Diabetes and long-term risk of renal disease in offspring: Analysis of prospective cohort data from the Manitoba Center for Health Policy Data Repository" Brandy Wicklow \$16,164

### **Collaborations**

Give a list of NEW collaborations in the last 12 months with other groups or organizations, and a brief description of your activity with each.

Brandy Wicklow:

- 1) Dr. Pedro Miguel Geralde; Sherbrooke University. NextGen submission for CIHR Diabetes Team Grant 2020.
- 2) Dr. Francis Lynn; University of British Columbia. NextGen submission for CIHR Diabetes Team Grant 2020.
- 3) Dr. Anthony Hanley; University of Toronto. CIHR Diabetes Team Grant 2020.
- 4) Dr. Baiju Shah; University of Toronto. CIHR Diabetes Team Grant 2020.
- 5) Dr. Tracey Galloway; University of Toronto. CIHR Diabetes Team Grant 2020.
- 6) Dr. Deborah Sloboda; McMaster University. CIHR Diabetes Team Grant 2020.
- 7) Michael Green?

Allison Dart and Brandy Wicklow:

- 1) Dr. Jim Scholey; University of Toronto. iCARE CIHR Diabetes Team Grant 2020.
- 2) Dr. Ana Konvalinka; University of Toronto. iCARE CIHR Diabetes Team Grant 2020.
- 3) Dr. Braden Manns; University of Alberta. iCARE CIHR Diabetes Team Grant 2020.
- 4) Dr. Hannes Rost; University of Toronto. iCARE CIHR Diabetes Team Grant 2020.
- 5) Dr. Joseph Penninger; University of British Columbia. iCARE CIHR Diabetes Team Grant 2020.

Joe Gordon:

- 1) Dr. Jason Karch; Baylor College of Medicine. We collaborate to characterize mitochondrial function and cell death in neonatal hearts exposed to hypoxic injury.
- 2) Dr. Luigi Bouchard; Université de Sherbrooke. Dr. Bouchard has invited me to join a CIHR Team Grant application evaluating the role of microRNAs in gestational diabetes. This application is in the LOI stage.

Jon McGavock:

- 1) Dr. Marie-France Hivert; Harvard University. CIHR Project Grant: Developmental origins of adolescent hypertension.
- 2) Dr. Rachel Freathy; University of Exeter. CIHR Project Grant: Developmental origins of adolescent hypertension.
- 3) Dr. Deborah Lawlor; University of Bristol. CIHR Project Grant: Developmental origins of adolescent hypertension.
- 4) Dr. Mary Jung; University of British Columbia. CIHR Project Grant: Dialectical Behavioural Therapy and Weight Management for Adolescent Obesity.
- 5) Dr. Katherine Morrison; McMaster University. CIHR Project Grant: Dialectical Behavioural Therapy and Weight Management for Adolescent Obesity.
- 6) Dr. Stasia Hadjiyannakis; CHEO. CIHR Project Grant: Dialectical Behavioural Therapy and Weight Management for Adolescent Obesity.
- 7) Dr. Jill Hamilton; SickKids. CIHR Project Grant: Dialectical Behavioural Therapy and Weight Management for Adolescent Obesity.

- 8) Dr. Ian Zenlea; Trillium Health Partners. CIHR Project Grant: Peer Mentoring and Self management for adolescents with type 1 diabetes.

Ayesha Saleem:

- 1) Dr. Shantanu Banerji; CancerCare Manitoba. CancerCare Manitoba Foundation Grant on a multi-disciplinary approach to measure the impact of commonly used local-modality lung cancer therapies on organ injury that may promote inflammation and contribute to lung cancer dissemination. My role: analysis of EVs in different lung cancer therapies and effect on tumour pathology/recurrence
- 2) Dr. Biniam Kidane; University of Manitoba - Surgery. CancerCare Manitoba Foundation Grant on a multi-disciplinary approach to measure the impact of commonly used local-modality lung cancer therapies on organ injury that may promote inflammation and contribute to lung cancer dissemination. My role: analysis of EVs in different lung cancer therapies and effect on tumour pathology/recurrence

Mentorship Opportunities for Trainees:

*Matthew Martens* (PI: Dr. Joe Gordon):

I was supposed to go to Asa Gustafsson's lab at the University of California San Diego in May, but that was cancelled due to COVID. It should be a 5 day immersion in her lab if/when things normalize. It was sponsored by the American Heart Associations Basic Science Early Career Committee.

*Stephanie Kereliuk* (PI: Dr. Vern Dolinsky):

The BCVS early career mentorship award is supported by the Early Career Committee of the Basic Cardiovascular Sciences Council (of the American Heart Association). The mentorship is with and funded (\$1500 USD) by Dr. Walter J Koch at Temple University in Philadelphia, PA. Dr. Koch is the William Wikoff Smith Endowed Chair in Cardiovascular Medicine, Professor and Chair Pharmacology and Professor and Director, Center for Translational Medicine. The mentorship was supposed to happen May 2020, but has been delayed due to COVID-19, with a tentative date set for the spring when the border reopens and institutional travel is allowed.

*Nicole Brunton* (PI: Dr. Jon McGavock):

My training was supposed to take place in Bristol at the University of Bristol MRC Integrative Epidemiology Unit under the supervision of Dr. Debbie Lawlor. I was originally scheduled to go last spring for four months (April – July) which was and still is delayed due to COVID. We haven't officially re-scheduled new dates yet.