

## **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

Lucy Marzban, [DMLS PhD, College of Pharmacy](#)

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

Jennifer Yamamoto, MD, MSc, FRCPC, Department of Medicine

## **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, 14 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 transdisciplinary investigator team consists of pediatric specialists in endocrinology and nephrology, basic scientists with expertise in islet biology, metabolism, 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, all of which are currently funded by large CIHR team grants and two CIHR SPOR Networks: (1) **Novel interventions** to prevent and treat type 2 diabetes (CIHR Pathways to Equity Team Grant and Diabetes Action Canada SPOR Network: 2019-2024); (2)

Biopsychosocial determinants of **complications of diabetes** (iCARE Cohort – CIHR Project Grant (2021-2026) and CanSOLVE CKD SPOR Network: 2021-2026) and (3) the **developmental origins** of type 2 diabetes in youth (CIHR Team Grant: Diabetes Translational Solutions: 2022-2027). 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 \$36.7M 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, the trainees within the theme 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 center 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 child 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)*

1. \$2M CIHR Team Grant: Diabetes Mechanisms and Translational Solutions – Awarded to Drs Brandy Wicklow, Christine Doucette, Allison Dart and Meaghan Jones, focused on The Developmental Origins of Pediatric Type 2 Diabetes and Early Renal Dysfunction. Grant includes several DREAM scientists as well as Indigenous scholars, patient partners and will provide 5 years of funding for translational research centred around the Next Generation and iCARE Cohort studies.
2. DREAM Theme completed an annual retreat on anti-racism and launched an audit into anti-racism-related metrics and policies within the Theme. As organizations engage in dismantling structural racism from within, DREAM worked with Drs Delia Douglas and Heather McRae to undertake the process of uncovering structural barriers to racialized individuals in our organization and develop a plan to address racism within our theme.
3. Two publications related to diabetes in leading scientific journals by Dr. Joe Gordon and others identifying novel signaling pathways that regulate glucose metabolism and heart function. These studies included multiple DREAM trainees and investigators demonstrating the importance of collaboration within the Theme.
4. Novel Insight into the lives of youth living with type 2 diabetes. A manuscript published in Canada's leading medical journal (CMAJ), led by Drs Wicklow and Dart in partnership with parent and youth co-researchers from the iCARE patient advisory group shed light on the complex social needs of youth living with type 2 diabetes.
5. Eight scientists secured seven national grants worth \$5.3M to mark the 100<sup>th</sup> anniversary of the Discovery of Insulin. Grants from CIHR and Diabetes Canada, including a prestigious CIHR New Investigator award to Dr. Mandy Archibald marked DREAM's best year of securing external funding since its inception in 2012. This represents an incredible 20:1 annual return on investment for the 2021 fiscal year.

## Translational team publications:

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. In 2021, our team published 101 papers, 22 presentations with 17 papers that included two or more members of DREAM. We believe that the publications below showcase this by highlighting the collaboration between multiple DREAM labs. (**DREAM PIs** are bolded, DREAM trainees/staff are underlined, *DREAM Indigenous partners* are italicized)

1. Cioana M, Deng J, Hou M, Nadarajah A, Qiu Y, Chen SSJ, Rivas A, Banfield L, Chanchlani R, **Dart A, Wicklow B**, Alfaraidi H, Alotaibi A, Thabane L, Samaan MC. Prevalence of Hypertension and Albuminuria in Pediatric Type 2 Diabetes: A Systematic Review and Meta-analysis. *JAMA Netw Open*. 2021 Apr 1;4(4):e216069.
2. Frejuk KL, Harasemiw O, Komenda P, *Lavallee B, McLeod L, Chartrand C*, Di Nella M, Ferguson TW, Martin H, **Wicklow B, Dart AB**. Impact of a screen, triage and treat program for identifying chronic disease risk in Indigenous children. *CMAJ*. 2021 Sep 13;193(36):E1415-E1422.
3. **Archibald, M., Dart, A., Wicklow, B.**, Pundyk, K., Marks, S., & **Sellers, E.** Youth Perceptions and Experiences of Type 2 Diabetes: Protocol for a Collaborative Knowledge Translation Approach and Qualitative Study. (2021) *Journal of Advanced Nursing*.
4. Martens, M.D., Seshadri, N., Nguyen, L., Chapman, D., Hensen, E.S., Xiang, B., Mendoza, A., Rattan, S., Gibson, S.B., Saleem, A., Hatch, G.M., Doucette, C.A, Karch, J.M., **Dolinsky, V.W.**, Dixon, I.M., West, A.R., Rampitsch, C., and **Gordon, J.W.** (2021) Misoprostol treatment prevents hypoxia-induced cardiac dysfunction through a 14-3-3 and PKA regulatory motif on Bnip3. *Cell Death and Disease* 12(12):1105.
5. Seshadri N and **Doucette CA**. (2021). Circadian Regulation of the Pancreatic Beta Cell. *Endocrinology*.162(9).
6. Cole, L.K., Agarwal, P., Doucette C., Fonseca, M., Xiang, B., Sparagna, G.C., Seshadri, N., Vandel, M., Dolinsky, V.W., Hatch, G.M. (2021) Tafazzin deficiency reduces basal insulin secretion and mitochondrial function in pancreatic islets from male mice. *Endocrinology* 162, 1-15. (Highlighted in Endocrine eNews, The Endocrine Society)
7. Slaght JL, Wicklow BA, Dart AB, Sellers EAC, Gabbs M, Carino M, McGavock JM. Physical Activity and Cardiometabolic Health in Adolescents with Type 2 diabetes: A cross sectional study. *BMJ Open Diabetes Research & Care* 2021; 9: e002134. PMID: 33990367.
8. Brunton N, Dufault B, **Dart A,** Azad MB, **McGavock J.** Maternal body mass index, offspring body mass index, and blood pressure at 18 years: a causal mediation analysis. *Int. J Obesity*. 2021 45; 2532-38
9. Hui A, *Phillips-Beck W, Campbell R, Sinclair S, Kuzdak C, Courchene E, Roulette M, Mousseau W, Beaulieu D, Wood e, Munroe G. Desjarlais F, Ludwig S, Wicklow B, McGavock J, Sellers EAC, Nickel N, Kiang D, Thiessen K, Pylypjuk C, Morris M, Shen XG.* Impact of Remote Prenatal Education on Program Participation and Breastfeeding in Rural and Remote Indigenous Communities. *Eclinical Medicine* 2021; 25: 35: 100851. PMID: 33997743.
10. Haifa A, **Wicklow BA, Dart A, Sellers EAC, McGavock J,** Lehana T, Samaan MC. The Tri-ponderal Mass Index as a measure of adiposity in youth onset type 2 diabetes: A cross-sectional analysis from Improving renal Complications in Adolescents with type 2 diabetes through REsearch (iCARE) study. *Scientific Reports* 2021; 27: 9111. PMID: 33907287
11. **Sellers EAC, Dart AB, McGavock J, Wicklow BA.** Cardiovascular comorbidity associated with albuminuria in youth onset type 2 diabetes: analyses from the iCARE study *Can J Diabetes* 2021: 45: 458-465 PMID: 34045147
12. Cole, L.K., Zhang, M., Chen, L., Sparagna, G.C., Vandel, M., Xiang, B., Dolinsky, V.W., Hatch, G.M. (2021) Supplemental berberine in a high fat diet reduces adiposity and cardiac dysfunction in offspring of mouse dams with gestational diabetes mellitus. *Journal of Nutrition* 151, 892-901. (Highlighted in Obesity and Energetics Offerings)
13. **Hatch, G.M., Cole, L.K., Vandel, M., Dolinsky, V.W.** (2021) Tissue specific knockout of the cardiolipin transacylase enzyme tafazzin in both liver and pancreatic beta cells protects mice from diet-induced obesity. *Expt. Biol. Virtual Meeting & e-Poster. FASEB J. Vol 35 Issue S1.*
14. Alfaraidi H, **Wicklow B, Dart AB, Sellers E, McGavock J,** Thabane L, Samaan MC. The Tri-ponderal Mass Index is associated with adiposity in adolescent type 2 diabetes mellitus: a cross-sectional analysis. *Sci Rep*. 2021 Apr 27;11(1):9111.

15. Carino M, Elia Y, **Sellers E**, Curtis J, **McGavock J**, Scholey J, Hamilton J, Clarson C, Pinto T, Hadjiyannakis S, Mertens L, Samaan MC, Ho J, Nour M, Panagiotopoulos C, Jetha M, Gabbs M, Mahmud FH, **Wicklow B**, **Dart A**. Comparison of Clinical and Social Characteristics of Canadian Youth Living With Type 1 and Type 2 Diabetes. *Can J Diabetes*. 2021 Jul;45(5):428-435.
16. Hrubeniuk TJ, Hay JL, MacIntosh AC, **Wicklow B**, Wittmeier K, **McGavock JM**, Sénéchal M. Interindividual variation in cardiometabolic health outcomes following 6 months of endurance training in youth at risk of type 2 diabetes mellitus. *Appl Physiol Nutr Metab*. 2021 Jul;46(7):727-734.
17. Sullivan KM, Scholey J, Moineddin R, Sochett E, **Wicklow B**, Elia Y, Xiao F, Mederios T, Sadi P, Burger D, Mahmud FH, **Dart AB**. Urinary podocyte-derived microparticles in youth with type 1 and type 2 diabetes. *Diabetologia*. 2021 Feb;64(2):469-475.

### 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 2021, which will be matched by KIM. These funds are being used to support wellness projects within the communities ranging from \$500-\$2000 each. The grants have been rolled out to the participants and they have resumed their projects and hope to provide us with an update in 2022.

### 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. The project is now funded to begin with the trial and will be impactful research towards child health.
- (2) Community Catalyst Grants: We provided \$10,000 in community catalyst grants by partnering with KIM and directly providing grants to 3 indigenous youths who will be creating projects directly impacting child and indigenous health.

### 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 = \$6,118,732**

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

**2021 = \$5,934,656**

### Catalyst Grants awarded in the past year (Title, PI, funding amount)

#### CHROM catalyst grants 2021

1. Bridge funding Joseph Gordon \$20,000

#### DREAM catalyst grants 2021

1. “The role of SIRT3 deficiency in the development of gestational diabetes” by Dr. Vern Dolinsky for \$4125.00
2. “Molecular regulation of cell death by Nix during diabetic heart disease” by Dr. Joe Gordon for \$12,500
3. “Dialectical behavioural therapy for youth at risk for type 2 diabetes”: by Jon McGavock \$12,500

## **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.

### Vern Dolinsky:

- Local:  
Amir Ravandi, St Boniface Research Centre, SIRT3 in cardiac metabolism project  
Saeid Ghavami, Dept of Anatomy and Cell Biology, cholesterol metabolism in tumours  
John Wilkins, Manitoba Centre for Proteomics, SIRT3 in cardiac metabolism project
- National:  
Luigi Bouchard, Sherbrooke University, miRNA project  
Dylan Burger, University of Ottawa, extracellular vesicles in GDM project
- International:  
Qiang Tong, Baylor University, SIRT3 in cardiac metabolism project

### Ayesha Saleem:

- Teo Kee Keong, Adrian – National University of Singapore
- Yamada, Shintaro – Kyoto University, Japan
- Vera-Licona, Paola - Center for Cell Analysis and Modeling, University of Connecticut Health

### Jon McGavock:

- Sean Dineen, Eimear Morrissey, Molly Byrne & D1NOW Young Adult Panel National University of Ireland, Galway
- Marie-France Hivert - Harvard University
- Phil Zeitler and Petter Adolfsson - University of Colorado

### Brandy Wicklow and Allison Dart

- Dr. Pedro Geraldes, Renal Scientist, Sherbrooke University. NextGen submission for CIHR Diabetes Team Grant
- Dr. Petter Bjornstad, University of Colorado, iCARE CIHR Team Grant 2021
- Dr. Phil Zeitler, Children's Hospital Colorado, iCARE CIHR Team Grant 2021
- Linda Diffey, University of Manitoba, Indigenous Collaboration, iCARE CIHR Team Grant 2021
- Dr. Ana Konvalinka, University of Toronto, iCARE CIHR Team Grant 2021
- Dr. Laurence Katz, University of Manitoba, iCARE CIHR Team Grant 2021

## **Trainees Events:**

- Spring lectureship and Trainee Career Development : Dr. Anna Gloyn, Stanford University: Virtual Event  
Mining Type 2 Diabetes GWAS for Gold : Drilling down on mechanisms for islet cell dysfunction
- Fall lectureship and Trainee Career Development : Dr. Deborah Lawlor, University of Bristol  
From Bradford to Bristol, via Mozambique and from socioeconomic position to genes and molecules
- Seminar series (multiple presentations throughout the year for trainees and PIs – including guest lecture by Dr. David Evans, Dr. Jim Johnson, article critiques, etc)
- Helped plan Diabetes Action Canada Trainee Day