



The Children's Hospital Research Institute of Manitoba

Research Theme Annual Report

v.October2022

PURPOSE:

The purpose of this report is to inform the Board of Directors of our research activity for this past year. The audience is diverse in their understanding of the scientific method, biology and medical terminology. It is critical to be concise, brief, and to use lay language. The Board uses this information to ensure that CHRIM's vision, mission and values are being fulfilled on an ongoing basis, and to report to the Foundation on productivity and responsibility to our donors.

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)

Allison Dart, MD, MSc, Department of Pediatrics and Child Health (co-lead)

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

Michel Aliani, PhD, Department of Food and Human Nutritional Sciences

Mandy Archibald, PhD, College of Nursing

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

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

Mission: Grounded in person-centeredness and equity, we are a translational research team, dedicated to improving the wellness of children and families living with diabetes across generations by making discoveries that impact clinical care and health policy.

Vision: Improving the world of families and children living with diabetes.

Who we are: The DREAM theme consists of 15 investigators, 20 trainees, and 6 Indigenous partners committed to improving the lives of children and their families living with diabetes. Over the last 10 years, our team has prioritized advancing knowledge about childhood onset type 2 diabetes, a growing chronic disease that disproportionately affects First Nation children in our province. This past year, our team has grown to include investigators specialized in type 1 diabetes research, all who played a key role in planning this year's DREAM symposium, which focused on type 1 diabetes research. Our transdisciplinary investigator team has prioritized patient-oriented research and meaningful engagement with community partners to ensure our efforts are focused on questions that are most important to individuals living with diabetes. Our strength is the interdisciplinary nature of our team, which includes a broad range of expertise. Members include pediatric specialists in endocrinology and nephrology, and basic scientists with expertise in islet biology, metabolism, extracellular vesicles, epigenetics, muscle physiology as well as cardiovascular and kidney disease.

What we do: Our team continues to focus on three primary pillars of research. With the core support of DREAM, all pillars have now been funded by large operating funds, 2 CIHR team grants and 2 CIHR SPOR Networks. 1. Novel interventions: Launch of a novel mental health skills intervention (iCARE 2.0: A Pilot Intervention of Dialectical Behavioural Therapy for Adolescents with Type 2 Diabetes) and funding of a peer-mentoring based lifestyle intervention for youth living with diabetes (Heart and Stroke Foundation Operating Grant: 2022-2023). Complications of diabetes: National iCARE Cohort to determine the biopsychosocial determinants of kidney disease in youth with type 2 diabetes— CIHR Project Grant (2021-2026) and CanSOLVE CKD SPOR Network: 2021-2026) 3. Developmental origins of type 2 diabetes and kidney disease in youth exposed to type 2 diabetes in utero (CIHR Team Grant: Diabetes Translational Solutions: 2022-2027).

Newer members of our team are also adding new areas of research, focused on understanding mechanisms of type 1 diabetes development, which may lead to new therapies. Specifically, Drs Peter Thompson and Jennifer Yamamoto have been awarded with over \$1M in CIHR grants for type 1 diabetes research. Since our inception, we have secured over \$52M in external funding to tackle these problems, created patient and community 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. 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 continues to be the fastest growing pediatric chronic disease in Canada. Manitoba is disproportionately affected by type 2 diabetes in youth, and First Nation children are 25 times more likely to be affected. Children are now diagnosed early, with high rates of complications including dialysis. We are dedicated to advancing knowledge that will address the Truth and Reconciliation Commission of Canada Call to Action #19 – that is to close healthcare gaps for First Nation children by working towards better, more relevant and culturally safe treatments for the next generation of children.

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 – 100 Years of Insulin: Featured Research awarded to Drs Brandy Wicklow, Allison Dart, Christine Doucette, 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 to better understand why children develop type 2 diabetes and kidney disease.
2. Dr. Elizabeth Sellers, BSc, MD, MSc is recognized as the Diabetes Canada 2022 Honoree of the 14th Annual Best Banting Gala. Dr. Sellers has been an integral part of the D-Camps program since 1993 at Camp Banting in Ontario and continues as Camp Medical Director for Manitoba's Camp Briardale. Dr. Sellers is also an active member of their National Medical Task Force for D-Camps.
3. Dr. Peter Thompson was awarded \$589,000 from the CIHR spring competition to focus on mechanisms and consequences of senescent beta cell accumulation.
4. Three DREAM trainees completed their PhDs in 2022: Taylor Morriseau from Dr. Vernon Dolinsky and Dr. Christine Doucette's labs, Stephanie Kereliuk from Dr. Vernon Dolinsky's lab, and Hanna Zegallai from Dr. Grant Hatch's lab.
5. A publication, led by Dr. Vernon Dolinsky, and co-authored by 11 DREAM members (including 3 trainees) was published in a leading scientific journal, identifying novel associations between DNA methylation and the serum metabolome of adolescents with type 2 diabetes. This study was an important output from the 1st CIHR team grant and reflects team collaboration within the theme.

In what way has CHRIM helped you to achieve one or more of the top 5 accomplishments from this past year?

CHRIM has helped the DREAM Theme achieve our top 5 accomplishments in several ways. CHRIM has provided the core funding that has opened the doors for the DREAM Theme to fund the annual DREAM Symposium, giving us opportunities to develop collaborations with researchers from other areas, and enhanced communication among DREAM researchers that has built the necessary collaborations for team grants. Previously DREAM funded the development of a unique mouse model to study mechanisms of early onset diabetes development in a genetic polymorphism that is common in the Anishinew people of northern Manitoba. This year, Dr. Taylor Morriseau completed her PhD work using this mouse which showed how a traditional First Nations diet may protect against type 2 diabetes development in mice carrying this genetic polymorphism. DREAM also supported bringing in a world expert in beta cell biology (Dr. Guy Rutter) for Dr. Morriseau's thesis defense and to establish new collaborations with researchers in Manitoba.

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

Our work as a team has led to a better understanding of the most important risk factors for complications in children living with diabetes. Mental health has emerged as an important challenge from patients which impacts their disease management. It is now the focus of the iCARE 2.0 pilot intervention: dialectical behavioral therapy for adolescents with type 2 diabetes. This intervention is a novel therapy for diabetes that focuses on mindfulness, and personal strengths. We are also working with Indigenous Knowledge Keepers to incorporate traditional medicine into the next phase of the study. If successful, this intervention will improve the quality of life of youth living with type 2 diabetes.

Research Funding

Total dollar value of your membership's research funding held in fiscal year 2020 (April 1, 2021 - March 31, 2022)

2021 – 2022 = \$4,830,280

Give a subtotal of ACTIVE research funding awarded (and held in Manitoba) in the past 12 months
2022 = \$3,782,219

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

DREAM Catalyst Grants 2022

1. "Molecular regulation of muscle" by Dr. Joseph Gordon for \$20,000.
2. "The Role of SIRT3 in gestational diabetes-induced heart disease" by Dr. Vernon Dolinsky for \$6,128.
3. "Biological action and proteomic cargo of chronic contractile activity-derived extracellular vesicles from skeletal muscle" by Dr. Ayesha Saleem for \$20,119.

Trainees

Identify the # of theme trainees

As of December 2022, DREAM currently has 20 trainees: 1 lab technician, 3 BSc students, 4 MSc students, 8 PhD students, 1 Post-Doc, and 3 pediatric residents. 3 trainees graduated with PhD's in 2022 and in January 2023 we will have 4 new trainees: 2 co-op students and 2 PhD students.

Identify the # of NEW theme trainees

There were 9 new DREAM theme trainees that joined the DREAM theme in 2022.

Identify any trainee led initiatives that received theme funding/personnel support

Due to pandemic related challenges in recruitment of new students and the number of trainees in DREAM declined, so unfortunately there were no new trainee led initiatives in 2022. We will reinstate the DREAM trainee group and trainee lectureship and other activities in 2023. DREAM previously contributed funding for the development of the Canadian Islet Research Network, which led to new CIHR funding in 2022 of a new national training platform (MyROAD). In 2022 MyROAD hosted the kickoff of a training and networking day at the Diabetes Canada meeting in Calgary, AB. This event was attended by four research trainees from DREAM at no cost for registration for the conference.

Justice, Equity, Diversity and Inclusion (JEDI)

In what way has the theme worked to advance EDI?

The DREAM Theme commissioned an audit on racism and are working to develop a 3-year action plan beginning in 2023 to implement changes for the future. This will be done using an Antiracism Pathway in three steps: 1) Truth and Self-Reflection, 2) Critical Consciousness & Antiracism, and 3) Advocacy and Partnership/Changing Policies. The action plan includes action items such as cultural sensitivity training (Manitoba Indigenous Cultural Safety Training – San'yas training and The First Nations principles of ownership, control, access, and possession (OCAP) training), conducting annual audits, and having a diverse hiring committee.

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.

iCARE and Next Generation Team

- A main priority of our team is to work collaboratively with Indigenous experts and community. We are committed to The First Nations principles of ownership, control, access, and possession (OCAP) principles. To more thoughtfully address these principles, we have worked over the last year to establish new partnerships with the Four Arrows Regional Health Authority and the First Nation Social Secretariat of Manitoba. This partnership will co-fund a First Nation Research Liaison to help us develop data sharing agreements, address data sovereignty and to facilitate knowledge exchange with community.
- Within the iCARE 2.0 pilot intervention: dialectical behavioral therapy for adolescents with type 2

diabetes, Linda Diffey, an Indigenous scholar is building an advisory circle to build the traditional Indigenous components of the intervention. This work has involved new relationships with Knowledge Keepers, and experts in Traditional Medicine.

Lucy Marzban:

In order to advance new research directions into the understanding of mechanisms that cause insulin producing cells to die in diabetes, collaborations were formed with an international leader in extracellular vesicle research, Dr. Elham Hosseini Beheshti, University of Sydney and an expert in beta cell apoptosis in diabetes, Dr. Dan Luciani, University of British Columbia and BC Children's Hospital Research Institute.

Peter Thompson:

A new collaboration with a leading expert in natural killer cell biology, Dr. Sam Kung, University of Manitoba Immunology to investigate the involvement of natural killer cells in the progression and development of type 1 diabetes, as well as how natural killer cells interact with stressed (senescent) beta cells. Further collaborations will also study whether these immune cells can be used for new therapies in type 1. This collaboration enabled funding of a Thorlakson Foundation grant (2022-2023).

Formed new collaborations with Drs. Audrey Parent (UC San Francisco Diabetes Center) and Dr. Janilyn Arsenio (University of Manitoba Immunology), who are leading experts in human islet biology, immunology and single-cell RNA-sequencing, to explore how immune cells interact with stressed human beta cells and define the gene expression patterns associated with small molecule-based targeting of stressed beta cells in type 1 diabetes with funding from CIHR Project Grant (2022-2027).

Established a collaboration with Dr. Alberto Pugliese (Director the Network for Pancreas Organ Donors with Diabetes (nPOD)) to examine the expression patterns of drug targets that were identified in the Thompson laboratory and translate these findings by examining tissue samples from pediatric donor type 1 diabetes samples. Through the George Eisenbarth nPOD award for team science, Helmsley Charitable Trust (2022-2023) candidate drug targets for mitigating beta cell stress (senescence) programs and slowing the progression of type 1 diabetes will be investigated.

Ayesha Saleem:

Formed an international team of collaborators through the Japanese Agency for Medical Research and Development (AMED) - Interstellar Alumni Funding Program, with the aim to rescue cellular alterations in aged pancreatic beta cells to restore insulin-secretion function. This team included Dr. Adrian Teo Kee Keong (A*STAR, Singapore), Dr. Shintaro Yamada (Kyoto University, Japan), Dr. Paola Vera-Licona (University of Connecticut, USA).

Identify any community partnerships the Theme has been involved with this year and include any details that highlight the partnership (events, meetings, workshops, etc.)

The iCARE 2.0 pilot intervention: dialectical behavioral therapy for adolescents with type 2 diabetes hosted a community gathering in spring 2022. The meeting was attended by Jackie McKee (iCARE PAG member), Lorraine McLeod (FNHSSM), Caroline Chartrand (KIM/MKO), Helen Settee (Can-Solve CKD), Vanessa Lillie (Knowledge Keeper), Ashley Hayward (NEIHR), Larissa Wodtke (NEIHR), Belinda Vandebroek (Knowledge Keeper), Byron Beardy (FARHA), Arlene Desjarlais (Can-Solve CKD), and iCARE PAG members Michelle, Gio, and Onalee. Results for a scoping review of prevention and management practices incorporating traditional Indigenous approaches with type 2 diabetes was presented. This review was led by 3 Indigenous students, and included the partnerships of several DREAM investigators, and Indigenous Knowledge Keepers.

Community project support: 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 funded 3 projects: The grants have been rolled out to the participants and they have resumed their projects and

hope to provide us with an update in 2023.

Identify how the Theme is working with patient partners if applicable.

The DREAM theme has patient engagement as a core value. We have continued to expand this in the past year. The iCARE and Next Generation studies continue to have Patient Advisory Group (PAG)'s. They continue to guide the overarching goals of the study, interpretation of results and development of knowledge translation materials. They have been instrumental in the planning of the iCARE 2.0 pilot intervention: dialectical behavioral therapy for adolescents with type 2 diabetes, and presented their stories at the Child Health Research Days in October. With the help of CHRIM, we were also able to fly in patient partners living with Type 1 diabetes to present at the annual DREAM Symposium. Team members are actively involved in the CanSOLVE CKD SPOR network, as well as the Diabetes Action Canada Network – both focused on Patient Oriented Research.

Supporting Documents (graphics, figures, impact reports, social media graphics, infographics, etc.)

antiracism pathway December 2022.pdf

DREAM Anti-racism plan V1.pptx

Email for Copy of Submission

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