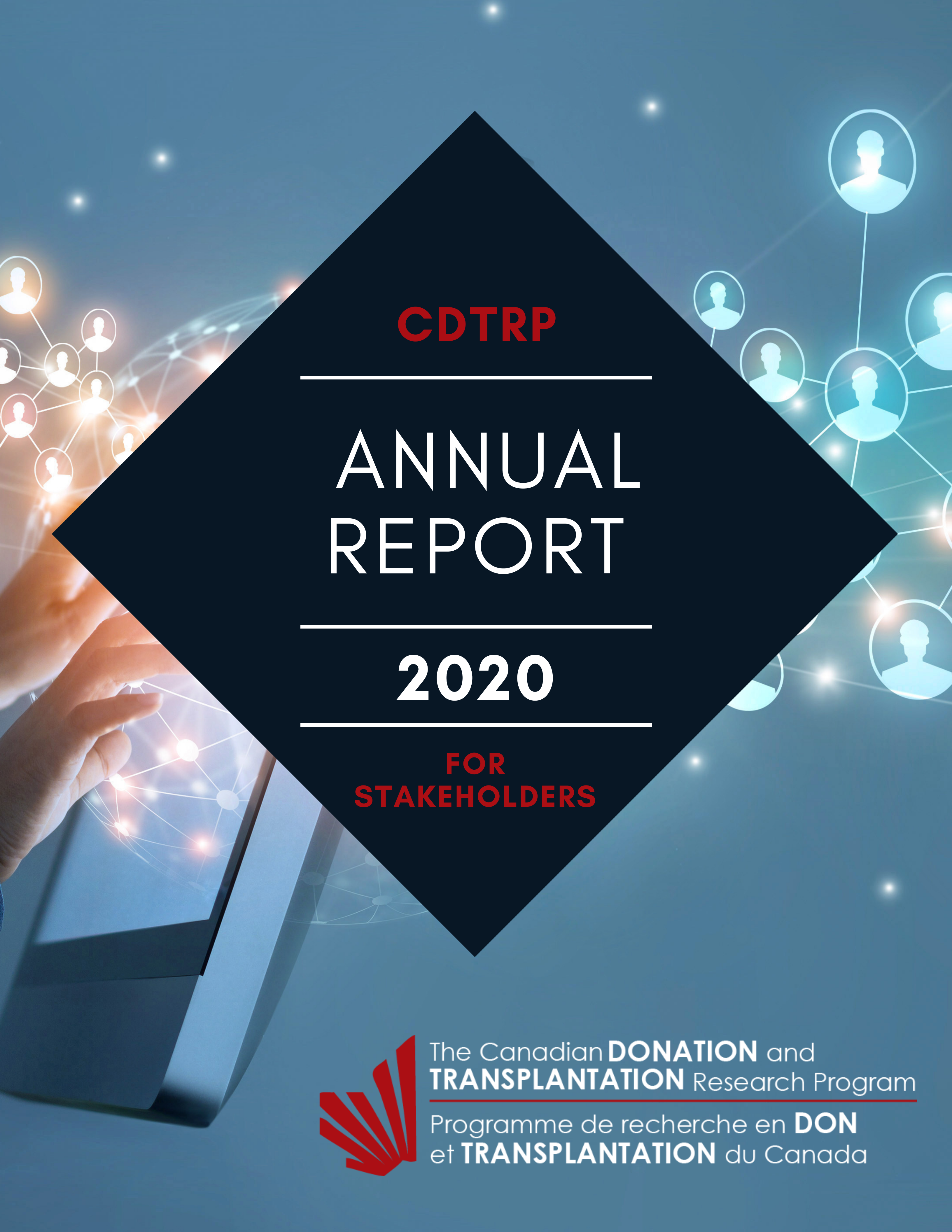

CDTRP

ANNUAL REPORT

2020

FOR STAKEHOLDERS

The Canadian **DONATION** and
TRANSPLANTATION Research Program

Programme de recherche en **DON**
et **TRANSPLANTATION** du Canada

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Executive Summary

The Canadian Donation and Transplantation Research Program (CDTRP) was founded with the goal of bringing together our country's diverse donation and transplantation research communities, integrating expertise in the health, natural, and social sciences. In 2018, we refreshed the network's vision – to fulfill every donation opportunity and turn transplantation into a cure, improving health outcomes and quality of life for Canadians – and updated its name to recognize Canada's greatly expanded capacity in donation research. We restructured the network within 5 inter-related Themes, a process shaped by a series of workshops with patients, donors, and families designed to identify their research priorities.

Over the past two years, the CDTRP has successfully transitioned from a national network that funds a selected group of research projects to one that offers research support, infrastructure, and collaboration opportunities to our growing community. We are leveraging the vast interdisciplinary expertise of the network, accelerating research and innovation projects towards impact, growing funding opportunities and success for our members, and positioning our trainees, early career researchers, and those taking non-traditional paths for productive careers in the field. We are fostering multidisciplinary collaborations across the four pillars of health research, as well as with engineering, chemistry, artificial intelligence, law, ethics, economics, among others, connecting to partner organizations, and integrating patients, families, and donors into research projects.

A maturing organization, the CDTRP now represents the 'go to' platform in Canada for donation and transplantation research, where investigators bring new ideas, find collaborators and partners, and receive individualized resources and infrastructure support to strengthen their research and increase their success. Our network has grown to include more than 300 researchers, trainees, collaborators, and knowledge users, including 28 patient, family and donor partners, at 37 sites across Canada. Our community's ability to independently produce, synthesize, and mobilize evidence, flexibly work together with our partners, and connect people and organizations to each other is forging the path to health, social, and economic impacts. Indeed, our connectivity is the most-valued aspect of the CDTRP: connecting researchers to each other, with our network of partner organizations and stakeholders, and with patient, family and donor partners. Together, the support to create these new linkages, along with specific research and education supports, underpins the innovative projects currently integrated into the network structure.

The CDTRP vision is for a Canadian donation and transplantation system that fulfills every donation opportunity and where transplant recipients feel that their chronic disease or refractory blood cancer is truly cured. Through research, innovation, and knowledge mobilization of the highest quality and rigour, and by collaborating with patients, family and donors and our partners every step of the way, our network – our community – can deliver this shared vision.

Research Highlights

The CDTRP currently supports over 120 individual research projects. Approximately three-quarters of these projects have external funding, to which the CDTRP network is adding value. Since Jan 2019, CDTRP has supported investigators in securing $8.9 million in new grant funding.

CDTRP-SUPPORTED PROJECTS INVOLVE A TOTAL OF:

695	160	28
COLLABORATORS	TRAINEES	PFD PARTNERS

Theme 1: Create a Culture of Donation

Nova Scotia was the first jurisdiction in North America to legislate opt-out consent. This consent model is frequently proposed as a solution to the chronic shortage of transplantable organs, but in some cases, has actually reduced donation opportunities. The "Legislative Evaluation: Assessment of Deceased Donation Reform" (LEADDR) project, led by Stephen Beed of the Nova Scotia Health Authority and Theme 1 Lead Matthew Weiss, is studying these system changes, including topics such as how to handle potential family override without losing the donation opportunity. This project will deliver high quality evidence on which provincial and federal policy makers can draw to ensure success of future donation and transplantation legislative reforms.

> **In just a few months, we built a national collaboration of 5 organizations and 2 PFD partners, developed the proposal, secured $1.2M in funding, and got the project off the ground. And it all started on a Theme 1 call.**
>
> -Chelsea Patriquin, CDTRP Research Manager

Theme 1 is also becoming a research leader in donation after MAID, after the 2018 change in laws that make this possible. At the time, there was no program developing a cohesive strategy to answer questions about this topic. Based on discussion on a Theme 1 call, CDTRP and CBS established an open working group for research in this area. Coordinated by CDTRP staff, 18 people joined the first meeting on October 19, 2020. This included a participant from the UK, and a researcher based in Nunavut, a geographic first for CDTRP.

Theme 2: Inform Universal Practices for Donation

The DePPaRT study made landmark advances in diagnosing circulatory death, with a seminal paper published in the *New England Journal of Medicine*. The study showed that cardiac activity often stops and re-starts several times during the dying process before it finally stops completely. The study provides evidence to support the current standard to wait for 5 minutes after the heart stops before determining death and proceeding to organ donation.

Several DePPaRT spin-off projects aim to provide clinical tools and improve critical care practices. These projects span the natural, health, and social sciences, including Indigenous perspectives. On March 2, 2020, the CDTRP hosted a workshop to discuss what it means to die as an Indigenous person versus what it means from a medical perspective. Participants included CDTRP members and Caroline Tait, lead for the Saskatchewan-based First Nations and Métis Organ Donation and Transplantation Think Tank.

> **DePPaRT is an outstanding example of the powerful impact that a national framework for collaborative team science can achieve. This diverse team has created new synergies and new knowledge that will help more Canadians become donors and more patients receive transplants.”**
>
> -Dr. Lori West, CDTRP Scientific Director and Officer of the Order of Canada (2020)

Project Highlight: NeuPaRT

As a spin-off project, Marat Slessarev and Teneille Gofton have added electroencephalogram and transcranial doppler data to the DePPaRT dataset to assess brain activity and blood flow during the process of dying. This will correlation of circulatory death, awareness, and brain death for evidence-based decisions. This study has funding from NSERC, the Academic Medical Organisation of Southwestern Ontario, and the New Frontiers in Research Fund (Exploration). The team will collaborate with Caroline Tait, a medical anthropologist and Indigenous health researcher, to integrate into the work an understanding of Indigenous beliefs regarding organ donation. Ethics and legal scholars are also studying the implications for Canadian organ donation policies and law.

Shapiro and colleagues were the first centre in North America to transplant a liver following normothermic preservation on the OrganOx Metra device. The latest work linked to this trial was published in April 2019 (Bral et al, 2019). The Organox system has approval in Europe (based on European multi-centre trials published in Nature in 2019) and is under review at Health Canada. Parallel work is underway in heart and lung ex vivo technology, as well as analyses of how best to accommodate such technology within the health care system.

Theme 3: Engineer and Allocate Better Grafts

A set of diverse Theme 3 investigators and topics representing fresh thinking has been funded through the CDTRP Innovation Grant competition. For example, Golnaz Karoubi and Siba Haykal brought work on vascularized composite allografts, a subject still in its infancy, into the CDTRP.

2019 Innovation Grant Awardee

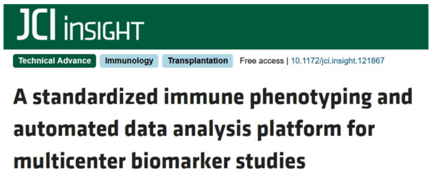
Golnaz Karoubi and **Siba Haykal**
University Health Network,
University of Toronto

Repopulation of Long Segment Tracheal Allografts for Transplantation

Although tracheal transplantation represents a possible solution for patients whose trauma or cancer has injured long segments of their airway, these patients still require long-term anti-rejection medication. A novel technique involves removing all the cells from a donor airway segment and repopulating it with patient-specific cells. Our study focuses on using a stem cell population that can be easily procured from recipients through simple techniques such as skin biopsies. The cells have the unlimited ability to grow and become airway-specific cells. Our goal is to evaluate these cells in a preclinical model. This is the first step in creating long segment airway scaffolds that can be transplanted without the need for anti-rejection medication.

Theme 4: Tailor an Optimal Immune System for Each Patient

The $1.5 million CARE trial on photopheresis-based cell therapy continues at six clinical (Montreal, Hamilton, Vancouver, Winnipeg, Ottawa, Toronto) and three manufacturing sites (Montreal, Vancouver, Winnipeg). The clinical outcome analysis is underway, as is the analysis of data collected from real-time immune monitoring. Other studies have now advanced to the point of seeking funding for new trials (e.g., the development of thymic Treg-therapy products, a collaboration between Megan Levings and Lori West).


JCI insight
Technical Advance Immunology Transplantation Free access | 10.1172/jci.insight.121867
A standardized immune phenotyping and automated data analysis platform for multicenter biomarker studies

Immune monitoring characterizes patients' immune status by analyzing a suite of biomarkers in clinical samples by flow cytometry. Historically, there was no standard methodology for doing so, limiting the community's ability to run multi-centre trials and compare results between studies. By bridging the gap between fundamental scientists and clinicians, landmark work has made this lack of a standard protocol a thing of the past. In collaboration with Beckman Coulter, a **platform that standardizes a set of flow cytometry panels**, designed to be used in multi-centre studies, allowing for maximal automation and inter-study comparisons, is now in use.

> **"In Ontario now, at least 20% of our donors now are increased-risk donors. Surgeons and physicians are now very accepting of organs from these donors, which is a major change from just a few years ago."**
> - Atul Humar

Originating from a joint CST-CDTRP consensus workshop in 2014, the use of increased risk donors is now incorporated into the standard of care. The workshop was published and disseminated, and CDTRP members (Atul Humar and others) gave presentations across the country to build awareness. Ontario was an early adopter of the new practices, and other provinces followed. Within 5 years, it has become a national standard.

Theme 5: Restore Long-Term Health

Key advances include the development of a national steering committee on Patient-reported Outcome Measures and the launch of two new functional groups: the Exercise Hub and the Mental Health Hub.

> **Everybody wants to improve outcomes for recipients, but these are the hardest challenges to tackle. That's why Theme 5 has the strongest singularity of purpose of all the themes.**
> **-** Tom Blydt-Hansen, Theme 5 lead

Project Highlight: Projet Laurent

Projet Laurent was initiated and co-created by PFD partners. After her son, Laurent, received a liver transplant but still wanted to keep his beloved pets in spite of warnings about disease transmission, Hélène Tessier took action. Through the PFD platform, she connected with CDTRP Executive Director and immunologist Mélanie Dieudé. To provide the evidence to enable transplant patients to live safely with their pets, they assembled a team of researchers in parasitology, veterinary science, immunology, mental health, clinical transplantion, anthropology, exercise science, and patient-reported outcomes. Hélène and Laurent, together with Mélanie, presented their project at the 2020 PFD Research Forum. This project is supported by key partners such as Canadian Transplant Association, Kidney Foundation of Canada, the Canadian Association for Mental Health, TRF British Columbia, Qualaxia, Cystic Fibrosis Canada and Health Canada.

RESEARCH OUTPUTS

PEER-REVIEWED PUBLICATIONS

99

In journals including Scientific Reports, American Journal of Transplantation, Blood, Transplantation, Science Advances, and Stem Cell Reports

NEW CLINICAL TRIALS

10

10 CDTRP-supported projects have led to new clinical trials launched or in development

CLINICAL GUIDELINES

3

CDTRP-supported projects have contributed to guidelines in routine fitness assessment, the Banff Classification for Allograft Pathology, and NDD donor management guidelines

PUBLIC OUTREACH & MEDIA

16

16 CDTRP-supported projects have participated in outreach events with schools or patients groups, or have been featured in the media, including on the front page of the National Post

NEW METHODOLOGIES

16

CDTRP-supported projects have developed 16 new methodologies for research and clinical use

NEW DATABASES

11

CDTRP-supported projects have created databases, for patients with GVHD, psychosocial data, and for pediatric deceased donor activity, among others.

Patient, Family, and Donor Partnership Platform

The CDTRP vision is that while scientists are experts on the diseases, patients and their families are experts on living with those diseases. The CDTRP Patient, Family and Donor (PFD) Partnership Platform is now recognized internationally as a model for effectively integrating patients, family members and/or living donors into research projects. Long-term relationship building with patients is now coming to fruition

In 2015, there were 3 patient researchers participating in 3 research projects. Now, 28 unique patient, family and donor partners are active as co-leads and co-researchers in 19 CDTRP projects, with 6 new projects starting up in 2020. The growth in numbers is in line with the cultural change around PFD engagement that has taken root among CDTRP researchers. Other organizations are now regularly seeking the CDTRP's advice on how to involve patients in research.

At a Theme 5 meeting, our 'patient partners' stated they prefer the term '**patient, family and donor (PFD) partner'** which is more inclusive of families and living donors.

The CDTRP now uses this new term in all themes and is beginning to see the change trickle through partner organizations

Growth has been on both sides of the researcher-PFD interaction. The Platform has seen not only more researchers that want to engage PFDs, but now has patients arriving with topics they want to muster the CDTRP's research expertise to tackle (e.g., Projet Laurent).

We are also connecting to patients on an international stage. In February 2020, the CDTRP sponsored the World Transplant Games, a biennial event organized by the World Transplant Games Federation (WTGF). At the Games, the CDTRP hosted an evening session entitled, "Educational Eats" on CDTRP methods of patient, family and donor engagement. Representatives from the WTGF then accepted our invitation to a panel for the CDTRP Patient, Family and Donor Research Forum. Now, the WTGF has struck an international research working group, inviting CDTRP researchers Drs. Dieudé, Mathur, Janaudis-Ferreira and Doré to join.

2020 World Transplant Winter Games
(photo courtesy Leanne Stalker)

Event Highlight: Patient, Family and Donor Research Forum

The CDTRP, in cooperation with the Organ Donation and Transplantation Collaborative, Canadian Society of Transplantation and fourteen national and international supporters, hosted a virtual Patient, Family and Donor Research Forum on October 15-16, 2020. The Forum was divided into four themes: Caregivers and Family; Transplant Recipients; Living Donors; and Future Avenues for Research. Each block was hosted by a PFD research partner who was also a member of the Planning Committee. The Planning Committee arranged for two pre-program presentations developed by CDTRP Trainees and **52 speakers** hailing from seven provinces, of which 21 were patients, family members, or donors. The conference had 50-70 attendees in each session, with registrations coming from 86 cities across Canada and around the world.

> “Numbers help identify problems, which is like identifying the what. But the why and the how...why something might be an issue or how we might be better able to fix it, those kinds of details come from patients. I think of it as the numbers are the black and white and the human piece is what provides the colour.”
>
> **Shilpa Raju, double lung transplant recipient, speaking at the 2020 PFD Research Forum**

CDTRP Research Innovation Grant Program

The CDTRP Innovation Grant program is a peer-reviewed, national competition that provides $30,000 in seed funding for new and innovative pilot projects, which are then integrated into and supported by the CDTRP national research structure. For the 2018 and 2019 competitions, the CDTRP and partners invested $1,080,000 to support new peer-reviewed research. The Innovation Grant program continues to be a highly valued component of the CDTRP: approximately half of Innovation Grant recipients report that this seed funding led to the procurement of larger external funding for scaled-up or spin-off projects.

Education and Career Development Platform

The Education and Career Development platform has grown from 25 participating trainees in 2018 to 32 in 2020. Since 2018, the CDTRP has hosted 20 training webinars, including a special series on our cross-cutting research priorities. In 2020, the CDTRP offered four seats per theme for the Ontario Indigenous Cultural Safety Program. The program is designed to develop understanding and promote positive partnerships between service providers and Indigenous people. Demand to participate in the course was so high that we already have a waitlist for 2021. Further, the platform is solidifying a partnership with the **Indigenous Cultural Safety Collaborative Learning Series** to help promote its webinars on our website and invite representatives for the 2020-21 CDTRP webinar series.

> **“I have been connected to people I would not otherwise have met. I’ve learned a lot about patient engagement and had the chance to meet patients, donors, and caregivers. Meeting these people had been invaluable in shaping my attitudes towards research.**
>
> CDTRP Trainee survey respondent”

Engagement to strengthen collaborations

The CDTRP now has connections with over 102 organizations across Canada and around the world. As the network matures, we are mobilizing our expertise in different ways and domains to bring the community together as a more equal partner. This has required clearer definition and communication of the boundaries of the CDTRP's mandate: we are focused on issues in donation and transplantation from an independent, evidence-based perspective and on bringing the national community together for research.

> **Partners see us as a resource now. It changes the dynamics of the conversation.**
>
> Mélanie Dieudé, CDTRP Executive Director

In 2020, pivoting to the virtual space due to the pandemic required a reorientation for which some of our partners had little experience. They turned to the CDTRP, which has years of experience—and success—operating as a virtual entity. Partners such as the Kidney Foundation of Canada and the Canadian Liver Foundation asked us to teach them how to use virtual communications platforms and host webinars as a new way of fundraising and sharing information with their members. In a similar vein, the CDTRP managed all 12 of the Canadian Critical Care Trials Group's webinars at the peak of the lockdown in Spring 2020, from issuing invitations, to hosting the platform, to running Q&A sessions. It demonstrated that the relationship with partners is not unidirectional but a symbiosis: the CDTRP is willing and available to support the ecosystem that in turn helps it thrive.

PROJECTS INVOLVING
NON-ACADEMIC PARTNERSHIPS

33%	10%
Theme projects	**Innovation grants**

PROJECTS INVOLVING
INTERNATIONAL COLLABORATIONS

35%	30%
Theme projects	**Innovation grants**

Increasingly, CDTRP is viewed by our partners as a source of research expertise. For example, a first working group has been launched with CBS on MAID (see Theme 1). The COVID-19 pandemic provided opportunities to strengthen the relationship and collaborations with all of our national and international partners, visible in outputs such as the Rapid Response Guidance for COVID-19 and organ donation and transplantation in Canada (see Project Highlights below). The CDTRP will capitalize on this growing reputation to offer our platforms as a support package that other networks can copy and learn from.

Partner Profile: TRFBC

The latest partner to sign on to the CDTRP Innovation Grant program is the Transplant Research Foundation of BC. TRFBC funds 2-3 peer-reviewed grants/year and manages the funding for the Addison Pediatric Transplant Research Project. They saw the value in merging these two programs with the CDTRP's Innovation Grant program, with gains in efficiencies and the use of a solid, trusted peer review system, knowing the best research will be selected for funding. An MOU to this effect is currently being executed.

Project Highlights

Patient Portal

Supported by Astellas Canada, the CDTRP launched the National Patient Portal in January 2021. This web portal will help patients across Canada navigate a complicated landscape to easily find the resources that are available to support them. The Portal will help transplant recipients obtain information related to their type of transplant, a resource map based on their geographical location, and a listing of research projects seeking patient participation. The purpose of this knowledge mobilization tool is to link patients with the wealth of resources and support that are currently available through a vast number of partners across Canada and to empower patients to improve self-management skills and self-efficacy.

Review of International Recommendations on COVID-19 and Organ and Tissue Donation and Transplantation

In March 2020, the CDTRP, CBS, and CST partnered to generate evidence-based, expert-informed rapid-response recommendations that are updated as evidence evolves. The bulk of the work in scoping recommendations from around the world was done by eight trainees who, by nature of their diverse backgrounds, were able to draw on the first guidelines, which were published in Asia, without translation. Recommendations were extracted, collated, grouped with summaries, and published on the CDTRP website (https://cdtrp.ca/en/covid-19-international-recommendations-for-odt/). We also published a repository of COVID-19 articles related to organ and tissue donation and transplantation, available here (https://cdtrp.ca/en/publications/open-access/). The repository now includes 1005 publications on donation, 1585 on transplantation, 2096 on immunosuppression and 268 on tissue.

Equity, diversity and inclusion

The CDTRP has long been proud to have a gender-balanced team across the leadership, investigators and trainees and is discussing how to make equally important progress considering other identity factors, including at their intersections. In terms of diversity among our PFD partners, the PFD Partnership Platform is aiming to grow the number of partners with different experiences. Presently, the demographics are heavily biased towards white women patients and caregivers, with few men and limited Indigenous or Black representation. The Platform is developing strategies to also increase its generational diversity (currently biased towards those in middle age). The CDTRP management team is also actively developing its own EDI policies, such as for recruitment.

For CDTRP events, we are exploring different approaches to accommodating accessibility requirements for those with disabilities, with the aim of developing standard procedures for all events. For the PFD Research Forum, for example, along with video recordings of the event, we published transcripts on the CDTRP website. For the 7th Annual Scientific Meeting in December 2020, we asked all attendees to indicate any requirements at the time of registration, in order to ensure the meeting was accessible to all of our members.

Event Highlight: Women in Transplantation Networking Session

In December 2020, CDTRP co-hosted Dr. Lara Danzinger-Isakov, who presented "Uneven Ground: Finding your feet during a pandemic" in conjunction with the Annual Scientific Meeting. 37 individuals attended the event.

The Canadian **DONATION** and **TRANSPLANTATION** Research Program
Programme de recherche en **DON** et **TRANSPLANTATION** du Canada

Women in Transplantation
an Initiative of The Transplantation Society

CDTRP ANNUAL SCIENTIFIC MEETING SPECIAL PRESENTATION

"Uneven Ground: Finding your feet during a pandemic"
Lara Danziger-Isakov

DECEMBER 2, 2020 • 6 PM EST

LIVE Q&A with **Lara Danziger-Isakov**
Hosted by: Lori West
Moderated by: Samantha Anthony

Looking Forward

The CDTRP has started on a journey of self-reflection to refine our positioning, both structurally and strategically, to ensure our long-term viability. We are currently undertaking two streams of evaluation: (1) internal and granular evaluation of the themes, platforms, and projects, and (2) engaging a third party for an arms-length, external evaluation. Through these two parallel activities, we are developing a clearer picture of where the greatest value of the network lies, which activities are most successful, which may need recalibration, and what community needs remain unmet. This process will provide CDTRP leadership with the information required to develop the CDTRP 2021-2031 Strategic Plan.

For an external evaluation, we contracted Juniper Consulting to review the CDTRP and its impact on the research community, and to assist with strategic planning for future steps. The 'diagnostic phase' was completed in September 2020, after over 60 interviews. We are now initiating Phase 2, a phase of strategic ideation and co-creation. At the ecosystem level, with key stakeholders (including patient, family and donor partners, clinicians, partner organizations and funders), through a series of facilitated discussions, we will develop a shared vision for enhancing the production and implementation of new knowledge in donation and transplantation to the benefit of Canadians. The outputs of this phase will be a final set of recommendations and a high-level, actionable implementation plan.

Appendix: 2019-2020 CDTRP Webinars

- Jan 28, 2019 - **Harold Atkins**: Lessons learned from moving clinical trials from idea into practice
- Feb 11, 2019–**Esmé Dijke and Lori West**: Moving the discovery of thymic T-regs from bench to clinical trial
- Mar 11, 2019 – **Jason Acke**r: Conducting research on cryopreservation
- Mar 25, 2019 – **Tania Janaudis-Ferreira**: Upcoming recommendations on exercise rehabilitation
- Apr 8, 2019 – **John Howell** (industry): What does a career in industry look like?
- Apr 23, 2019 – **Atul Humar**: Leading trials using infected organs in non-infected patients
- May 13, 2019 – **Ramesh Prasad**: Philosophy of transplantation
- May 27, 2019 – **Mamatha Bhat**: The role of the microbiome in donation and transplantation
- June 10, 2019 – **Ruth Sapir-Pichhadze**: Conducting research applying precision medicine technologies to prevent rejection
- Sep 3, 2019 – **Sapna Kuchadkar**: Professional social media, research and you
- Sep 16, 2019 – **Kate Headley**: Building a presence on social media
- Nov 18, 2019 – **Anette Melk** (Germany): How sex and gender affect transplantation
- Dec 2, 2019 – **Bethany J. Foster**: Sex and Gender in transplantation research
- Dec 16, 2019 – **Tom Blydt-Hansen**: Research in Pediatric Solid Organ Transplantation – the Canadian Context
- Jan 13, 2020 - **Donna Wall**: Clinical Trials in Pediatric BMT/CT – Trial design for small and heterogeneous cohorts
- Jan 27, 2020 - **Dorry Segev** (USA): Frailty and physiologic reserve
- Feb 24, 2020 - **Caroline Tait**: Saskatchewan First Nations and Métis Organ Donation and transplantation think tank: lessons learned
- Mar 9, 2020 - **Karen Yeates**: Setting Urgent Health Research priorities for Indigenous, rural and remote populations in Canada
- Apr 29, 2020 - **Istvan Mucsi, Vikas Sridhar and Deepali Kumar**: COVID-19 and Transplant Patients: Your Questions Answered
- May 13, 2020 – **Marie-Chantal Fortin and Isabelle Houde**: COVID-19 et les Patients Greffés – Réponse à vos Questions