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Opening letter

28 May 2019

Dear reader,

It is our pleasure to present the 2018–2019 Canadian Blood Services Centre for Innovation annual progress report. This past year we celebrated the 20-year anniversary of Canadian Blood Services and the launch of a new chapter with a renewed purpose, mission and brand. The organization’s commitment to Canadians remains unchanged — as Canada’s biological lifeline, Canadian Blood Services makes a promise for life. The Centre for Innovation is honoured to continue to support Canadian Blood Services in keeping its promise.

The work of the Centre for Innovation helps safeguard the quality and safety of Canadian Blood Services’ products and services, engage and create strong connections with partners and stakeholders, and continuously improve and innovatively transform systems and processes. This report details achievements that have been made over the past year by our network of scientists, medical experts, research partners, and collaborators.

Program highlights for the year include:

- We supported 124 investigators through our funding and our products for research programs.
- Our research network published 163 peer-reviewed publications and delivered over 300 presentations at local, national, and international conferences.
- We wrote 26 technical reports to share with Canadian Blood Services and partners to support decision-making.
- We attracted over 3,700 attendees to Centre for Innovation led or supported knowledge exchange and educational events.

In particular, our accomplishments include:

- Data from post-implementation changes to a donation criterion demonstrated that moving from a permanent to a five-year deferral for donors with cured cancers led to a substantial decrease in donor deferrals, with deferrals for first-time donor reduced from 9.4 to 3.2/1,000.
- Research funded by our newly established Blood Accelerator Efficiency Program demonstrated the feasibility of a non-invasive prenatal RhD test that will reduce unnecessary antenatal anti-D injections. Results informed business development activities.
- Research-informed improvements in the monocyte monolayer assay, a test that can help choose the safest blood for hard-to-match patients, have supported its migration from the research laboratory to the clinical laboratory. This assay will soon “go live” in the Edmonton diagnostics laboratory.
• Product and process development supported the introduction of a new platelet pooling set, which received Health Canada approval in 2018–2019. The new platelet pooling set improves consistency in platelet yields.

• The National Advisory Committee on Blood and Blood Products in Canada endorsed the International Collaboration for Transfusion Medicine Guideline (ICTMG)’s platelet guidelines. ICTMG also published three systematic reviews, a guidance document and resources on the evidence-based management of fetal and neonatal alloimmune thrombocytopenia.

• The Centre for Innovation contributed to a Consensus Conference on Patient Blood Management which established 10 clinical recommendations and 12 research recommendations for red blood cell transfusion in adult patients.

• The Centre for Innovation published discovery research linking a plasma protein with platelet clotting and suggesting a new link between diet and heart health. Lead scientist, Dr. Heyu Ni, received a prestigious Canadian Institutes of Health Research Foundation Grant.

We remain deeply grateful for the ongoing support we receive from our funders, Health Canada and the provincial and territorial ministries of health, and our partners and colleagues across the transfusion and transplantation medicine communities. We look forward to continuing to innovate and educate to support Canada’s Lifeline in its vigilant stewardship of the Canadian system of life essentials for transfusion and transplantation.

Sincerely,

Dr. Isra Levy  
Vice President, Medical Affairs and Innovation  
Canadian Blood Services

Dr. Chantale Pambrun  
Director, Centre for Innovation  
Canadian Blood Services
Executive summary

The 2018–2019 Canadian Blood Services Centre for Innovation annual progress report provides an update on the activities and achievements of the Centre for Innovation over the past fiscal year (1 April 2018–31 March 2019). We begin by providing an overview of the Centre for Innovation, with a focus on how we prepare Canadians for tomorrow by keeping abreast of key trends and developments that may impact the transfusion and transplantation industries. Aligning with Canadian Blood Services’ pillars, we present our accomplishments in 2018–2019 under the themes of Safeguard – Engage – Improve. In “Safeguard”, we describe our work to maintain a balance between donor and recipient health and sufficiency of supply. In “Engage”, we highlight the Centre for Innovation’s Canada-wide network and international connections and describe how the Centre for Innovation leverages these connections to support research, guideline development, training, education and professional development. Under the theme “Improve”, we describe the advances made to bring about improvements to the Canadian system of life essentials, which includes blood, plasma, stem cells, and organs and tissues. Throughout the report, the interdisciplinary and collaborative nature of the Centre for Innovation is evident. The report includes contributions from the Centre for Innovation’s scientists, development staff, medical directors and consultants, project managers, as well as funding recipients, collaborators, and partners. The report concludes with a governance section outlining the Centre for Innovation’s outputs and outcomes for this funding cycle and with appendices detailing the projects funded through our programs, and the diverse publications resulting from our activities.

1 The names of the Canadian Blood Services staff, including Centre for Innovation investigators, medical experts and epidemiologists, and the names of organizations and investigators receiving funding from the Centre, are bolded throughout the report.
The Centre for Innovation

When Canadian Blood Services was formed, it was with the knowledge that a new approach to research and development was an essential component of a safe and effective blood system. In its first report to Canadians in 1998-99, Canadian Blood Services acknowledged that its firm commitment to research and development represented “no less than a commitment to embracing constant change for the future.” Twenty years later, the Canadian Blood Services’ Centre for Innovation — the heart of the organization’s research and development activities — continues to embrace and lead change.

We’re clear about our purpose

The Centre for Innovation aligns with Canadian Blood Services’ pillars: Safeguard – Engage – Improve. Working along the entire “life-to-life” continuum, the Centre for Innovation serves Canada’s Lifeline to ensure its continued safety, quality, and sufficiency.

The Centre for Innovation is primarily funded by a contribution agreement with Health Canada, matched by funds from provincial and territorial ministries of health. In 2017-18, Health Canada renewed our funding for another 5-year cycle. This renewal allowed us to refresh our key priority activities and performance metrics (Figure 1).

“…we must be innovative, reinventing today so we can find better answers for tomorrow.”

— from Canadian Blood Services’ mission

We know where we add value

Housed within Canadian Blood Services’ Medical Affairs and Innovation division, the Centre for Innovation establishes strategic alliances to conduct research, development, and knowledge mobilization in support of a safe, effective, and responsive blood system.

The Centre for Innovation comprises an interdisciplinary and collaborative Canada-wide network of experts. The knowledge it generates increases our collective understanding of the blood system, it informs best practices and influences policies.

Research, led by associate director of research William Sheffield, provides new insight through investigator-driven discovery research on blood and blood products, plasma, stem cells, and related topics.

Priorities include: promoting appropriate blood product utilization; ensuring adequate blood product supply; minimizing adverse effects of blood product transfusion; optimizing blood product quality; and
replacing or improving blood products through new therapies or technologies.

Product and Process Development, led by associate director Ken McTaggart, conducts applied development work to support Canadian Blood Services operations and transformational change through innovation.

Priorities include: deepening the understanding of our products and the processes used to manufacture them; developing new or next generation products and the processes used to manufacture them; improving current generation products and the processes used to manufacture them; and problem solving.

Knowledge Mobilization and Strategic Alliances, led by associate director Sophie Chargé, supports the health care system by bridging the Canadian network of people, resources and knowledge.

Priorities include: supporting research and training; influencing clinical practice; knowledge management; and establishing strategic alliances.

We’re constantly focused on quality

We work along the entire “life-to-life” continuum to safeguard and improve Canada’s Lifeline. In everything we do, the safety of blood and blood products for patients is at the forefront of our minds. We support Canadian Blood Services’ efforts to continuously improve products and processes and to help every patient, match every need, and serve every Canadian.

We look to the future

We engage with colleagues, scientific and medical experts, nationally and internationally, to keep abreast of developments that may impact Canada’s Lifeline.

In 2018–2019, a Canadian Blood Services’ horizon scan identified key trends that the blood industry should monitor and be prepared for. These trends may impact every facet of the blood industry, with the potential to bring innovative change to many areas, from production and supply chain management, to how we engage with donors.

For example, precision medicine is a trend that may impact the blood industry, although how is unclear. On one hand, transfusion and transplantation medicine have always been, by necessity, personalized to the individual — each unit must be matched to its recipient. Emerging evidence, much of which has been generated in Canada with support from the Centre for Innovation, suggests that donor and recipient factors may impact product quality, efficacy and transfusion outcomes — findings that potentially put the blood industry on a path towards a greater level of “precision”.

Evidence of this growing trend in precision medicine is reflected in the increasing research using Canadian Blood Services’ data; generating the evidence-base for
individually-tailored products requires a link between donor and product characteristics, and recipient outcome data. In the future, donors could be directed towards giving the type of product they are best suited to, and the matching of donors with recipients could go beyond tissue typing requirements.

Climate change also contributes to a rapidly changing landscape with impacts likely to be felt on many levels by the blood industry. Horizon-scanning for emerging infectious diseases must consider the growing geographical range of insect-borne diseases. Adoption of pathogen inactivation technologies to protect against transfusion-transmitted diseases may play an increasing role in blood safety in Canada.

The evolution of technologies and risks crystallizes the importance of building capacity for a sustainable and progressive blood system. Preparing Canadians for tomorrow, the Centre for Innovation is evolving its programs to address changing needs. It is enhancing research and training programs and development infrastructure to ensure future system capabilities. It is strengthening connections with national and international colleagues to ensure we stay at the forefront of developments in the field for the benefit of all Canadians.
We are proud to be part of “the connection between the profound discoveries of science and the joyful restoration of health.”

Learn more about Canadian Blood Services' mission.
Safeguard

At Canadian Blood Services, blood safety for every patient is paramount. We are also committed to protecting the health of the donors who give so generously of themselves to contribute to Canada’s Lifeline. The Centre for Innovation supports research to ensure a balance between sufficiency of supply and the health and safety of donors and recipients.

Safeguarding donors

Donor health is safeguarded by multiple elements, including donor health questions, inter-donation interval, and hemoglobin testing during the collection process.

Research from the Centre for Innovation and other organizations shows that iron deficiency is common in whole blood donors.1-4 This is particularly true for female donors and frequent donors. Iron is important for our health.5, 6 If iron-deficient donors continue to be in negative iron balance, they may develop iron deficiency anemia, which can lead to tiredness, diminished exercise or work capacity, and other symptoms. Iron is also important in pregnancy to ensure normal fetal development.

In 2017, informed in part by a large study of ferritin levels in Canadian blood donors1, Canadian Blood Services changed donor eligibility criteria to reduce the risk of iron deficiency. This year, Canadian Blood Services medical director Mindy Goldman and associate director of epidemiology and surveillance Sheila O’Brien looked at the impact of these changes.7

In female donors who were asked to donate less frequently (i.e. minimum inter-donation interval for female whole blood donors was increased from 56 days to 84 days), hemoglobin deferral rates decreased from 13.0 per cent to 9.5 per cent and mean hemoglobin levels increased from 135.0 g/L to 136.2 g/L. In males whose deferral criteria became more stringent (i.e. minimum hemoglobin cut-off for male donors was increased from 125 g/L to 130 g/L), both hemoglobin deferral rates and hemoglobin levels increased slightly. As expected, the number of donations per year decreased by 12 per cent in females and 4 per cent in males. To make up for this
decrease, additional new and lapsed donors were recruited, so that overall the donor base expanded by 5.8 per cent. In this way, safeguarding donor health and maintaining the blood supply can be balanced for the benefit of all Canadians.

**Goldman** and **O’Brien** also assessed donor return rates, donation frequency, and re-tested donor ferritin levels. In the 2017 study, ferritin levels in over 12,500 donors were tested and those with low ferritin levels were informed and not called for donation for six months. While most donors followed the advice to stop donating for six months, re-testing ferritin showed that increasing the inter-donation interval led to some recovery of ferritin levels, but most low-ferritin donors continued to have low or borderline levels on retesting. This suggests that safeguarding donors in the long-term requires sustained efforts to encourage donors to improve their iron intake. We will continue to investigate improving donors’ iron stores to safeguard their health.

**Finding harmony in blood donation complications**

Blood donors may experience complications during or after donation, the majority of which are pre-faint or faint (vasovagal) reactions. Several years ago, **Goldman** led a multinational collaboration that published “harmonized” definitions of blood donation complications, giving the field much-needed standardized terms.

In 2018, **Goldman** and colleagues validated these harmonized definitions. Results from 54 respondents across 25 countries showed that their use led to greater consistency in diagnoses of complications related to blood donation. Finding harmony helps increase focus on donor safety and enables valuable information exchange among countries.

**Safeguarding recipients**

The health of recipients is safeguarded in part by donor deferral questions and the testing of collected blood that are informed by a surveillance system. These elements are important aspects of a multi-layered approach to blood safety.

The latest Surveillance Report (published in August 2018) indicates that transmissible blood-borne infections continue to be very rare in Canadian Blood Services donors. The data support very low transmissible infection rates and very low residual risk estimates of a potentially infectious donation from a unit of blood.
Threats from emerging pathogens continue to be monitored. The tick-borne parasite, *Babesia microti*, which causes babesiosis, is a concern in Canada and the US and appears to be in the early stages of becoming established in some parts of Canada. This year, O’Brien participated in an international survey to understand the impact of parasitic infections such as babesiosis and malaria on blood safety. This study highlighted that, in contrast to mitigation efforts against bacterial and viral risks, mitigation efforts against parasitic risks varied widely and depended on several factors, including the availability of tests, public health priorities, and socioeconomic constraints.

Malaria is a parasite of concern worldwide, even in non-endemic countries such as Canada. O’Brien led a study analyzing malaria policy decisions in non-endemic countries, which demonstrated that risk assessments in the countries studied were consistent with those recommended by the Alliance of Blood Operators Risk Based Decision-Making Framework. In Canada, malaria risk is managed by deferring donors at risk of malaria.

In 2018, O’Brien and Goldman and colleagues Yves Grégoire and Gilles Delage from Héma-Québec investigated how the risk of transfusion-transmission of Human T-cell lymphotropic viruses (HTLV) would change if the donor screening approach was changed. Since 1990, all blood donations in Canada have been tested for HTLV and since then, there have been no identified cases of HTLV transmission by transfusion, the rate of HTLV in Canadian blood donors is unchanged, and almost all donations that test positive for HTLV are from first-time donors. Modern blood manufacturing processes, particularly the use of universal leukoreduction, means there may be limited benefit to testing all donations for HTLV. Their study suggested that moving from testing all donations for the virus HTLV to testing only first-time donors would have a negligible impact on risk to recipients. These data will inform future decisions on changes to HTLV testing.

Read the Research Unit describing this work here.

The work of Goldman and O’Brien assists Canadian Blood Services in re-evaluating donor testing and/or donor eligibility criteria that have been in place for several years, to ensure they remain useful and align with current evidence on infectious risks.

Safeguarding sufficiency

Evolving eligibility criteria

While maintaining the safety of the blood supply, Canadian Blood Services strives to restrict donor eligibility as little as possible. Research-informed changes can help improve donor inclusivity without compromising safety of the blood supply.

Following a large Scandinavian study that provided convincing evidence that cancer cannot be transfusion-transmitted, Canadian Blood Services changed from a
permanent deferral to a 5-year deferral for donors with some forms of non-cutaneous cancer. Goldman and O’Brien investigated this change’s impact and found a substantial reduction in deferrals for first-time donors, from 9.4 to 3.2 deferrals/1,000 donations. Overall, deferrals reduced from 3.1 to 1.1 per 1,000 donations. As well as increasing the number of eligible donors, this study shows the importance of re-evaluating criteria as new data becomes available.

Older age is another factor which historically limited blood donor eligibility despite a lack of supporting evidence. Canadian Blood Services made changes several years ago to allow healthy older individuals to safely donate and make a significant contribution to the blood supply past arbitrary age limits. In the last year, Goldman participated in a project with the international Biomedical Excellence for Safer Transfusion collaborative, which concluded that excluding donors based solely on older age appears to be unwarranted.

Canadian Blood Services has been progressively evolving the deferral policy for men who have sex with men (MSM) from a permanent deferral, to five years, to one year, to (in June 2019) a 3-month deferral. Studying donor compliance with the 5- and 1-year deferrals, O’Brien and Goldman showed no impact on noncompliance rates; and in contrast to what had been predicted by earlier modelling studies, the shorter time deferrals did not impact HIV rates or incidence in donated blood. Shorter time deferrals did lead to a small increase in eligible MSM donors. The MSM Research Program continues to support research to develop adequate evidence for alternative screening approaches for blood or plasma donors, which could evolve the current eligibility criteria for MSM while maintaining safety of the blood supply. Results from this program are expected later in 2019–2020.

Designing the blood supply

John Blake developed a mathematical model of the blood supply to support strategic decision-making and ensure demand for blood products can be met efficiently. Applying this to a case study of the blood supply in Colombia, Blake demonstrated how the model can take into account local circumstances.

Ensuring appropriate utilization of blood products

An appropriate donor base is critical to maintaining sufficiency of supply, but equally important is the appropriate utilization of blood products. Blood transfusion is one of the most frequently used medical interventions, and like any intervention, it comes with benefits, risks and costs.

Patient blood management, or PBM, aims to improve patient outcomes by limiting transfusions and focusing on conserving the patient’s own blood. In 2019, an international committee including Canadian
Blood Services chief scientist Dana Devine published evidence-based PBM guidelines developed at a consensus conference in Frankfurt. The committee established 10 clinical recommendations and 12 research recommendations for red blood cell transfusion in adult patients in three areas: preoperative anemia, red blood cell transfusion thresholds, and the implementation of PBM programs. The committee took a rigorous approach, conducting a meta-analysis on the more than 17,000 literature citations associated with the questions asked. The resulting recommendations provide a foundation to support clinical practice; however, the committee noted a lack of strong evidence to answer several of the questions posed, highlighting the need for additional research and guideline development in this area.

Modelling rare blood flow
Blood type is determined by whether specific molecules called antigens are present or absent on red blood cells. There are more than 300 red blood cell antigens and more than 30 blood group systems, including the ABO and Rh groups. Some combinations of antigens are far less common than others, making some blood types rarer than others. Blood is considered rare if the combination of antigens is only found in one person in 500 and very rare if only found in one person in 1,000.

To help meet the needs of Canadians with rare blood, Canadian Blood Services engineer John Blake and associate medical director Gwen Clarke used simulation modelling to understand how to optimize the blood operator’s inventory of rare blood types to meet demand.

They found that keeping a modest inventory of frozen rare blood types, combined with increased screening of donors for rare blood types, provides the greatest chance of ensuring that Canadian patients with rare blood have access to red blood cell transfusions when they need them.

Based in part on these results, the Canadian Blood Services rare blood program is re-sizing its cryopreserved inventory to help the program operate more efficiently. This could lead to cost savings in the long term. Any discarded units will be used as rare blood reagents for serological testing, or for research on cryopreservation of red blood cells.

Read the Research Unit describing this work here.

Canadian Blood Services is currently exploring new technologies such as next-generation sequencing to allow extended testing of many more donors to identify those with rare blood.

Hear Gwen Clarke describe the Canadian Blood Services Rare Blood Program and its partnership with the International Rare Donor Panel to help save lives around the world here.
To help every patient, match every need, and serve every Canadian

Learn more about Canadian Blood Services’ vision
At Canadian Blood Services we are committed to informing donors and the public about the research we do and how it may inform decisions to improve the blood system. The Centre for Innovation builds strong connections with diverse stakeholders to facilitate research, guideline development, training, education and professional development.

Engaging current and future donors

Engaging with the public on research and education

Part of the Centre for Innovation’s science communication strategy, developed in collaboration with the public affairs division, is a weekly R.E.D. (Research, Education, Discovery) blog which attracted more than 40,000 views last year. The 2017 blogs about blood donation and iron wellness remained among the most viewed, while blogs about our research on MSM eligibility and donor deferral policies topped the 2018 list.

Read the R.E.D. blog announcing the five most read stories of 2018 here.

Over the last year, we teamed-up with Science Borealis and the Centre for Blood Research to launch our first-ever Lay Science Writing Competition. This competition engaged our research trainees and gave them an opportunity to showcase their research on R.E.D. Within the theme “research that matters,” trainees were to describe their research’s impact on the transfusion and transplantation system and/or on our society.

The competition winner was Jennie Haw, a Canadian Institutes of Health Research (CIHR) Health System Impact Postdoctoral Fellow supported by our training programs and working under the supervision of Dana Devine. Her prize-winning entry, now published on R.E.D., provides the public with a glimpse into the research conducted...
at Canadian Blood Services to optimize cord blood donor recruitment for the national public cord blood bank.

As a sociologist, I take the view that nothing in the social world happens in a vacuum. People (and organizations) don’t make decisions or act independently of the broader context within which they live and act.”

— Jennie Haw, Lay Science Writing Competition winner. Read more here.

Research & Education Round Up

The Centre for Innovation distributes a monthly e-newsletter. In 2018—2019, the number of subscribers rose to more than 1,300, a jump of 53 per cent. The open rate — a measure of the percentage of subscribers who open the e-newsletter and an important indicator of engagement — remained high at 39 per cent. The newsletter keeps our community engaged by providing information about our latest publications, funding competitions and upcoming events.

Engaging with stakeholders to evolve the MSM criteria

In 2017, Canadian Blood Services in partnership with Héma-Québec launched the MSM (men who have sex with men) Research Program to ensure the generation of adequate evidence-based research for alternative screening approaches for blood or plasma donors.

With a second funding competition completed in the last year, this unique MSM Research Program now comprises 15 research teams. A strong emphasis was placed on engaging appropriate stakeholders in these projects, facilitated in part through the Canadian Blood Services’ stakeholder relations group. Several projects use a community-based research approach, engaging patient groups,
LGBTQ+ community members, blood donors and the public. For example, “Sex Now 2018: A national survey on blood donation and undiagnosed blood-borne infections”, led by Nathan Lachowsky from the University of Victoria, engages an impressive number of researchers and organizations from across Canada.

**Organizations engaged in Lachowsky’s project supported by the MSM Research Program:**

- AIDS Coalition of Nova Scotia
- AIDS Committee of Toronto
- BC Centre for Disease Control
- Canadian Blood Services
- Centre for Sexuality Calgary
- CruiseLab Toronto
- Edmonton Men’s Health Collective
- Gilead Sciences Canada
- Health Initiative for Men Vancouver
- Héma-Québec
- HIV Community Link Calgary
- Living Positive Resource Centre
- Kelowna (Men’s Health Initiative)
- London InterCommunity Health Centre
- MAX Ottawa
- Ontario HIV Treatment Network
- Our Own Health Centre Winnipeg
- prideHealth Nova Scotia Health Authority
- Public Health Agency of Canada
- RÉZO Montréal
- Safeworks Harm Reduction Calgary
- SHARP Foundation
- Sunshine House Winnipeg
- Winnipeg Pride Society

The impact of the MSM Research Program is likely to be seen over the next couple of years, once the projects are completed. Results from a modeling project led by **O’Brien**, however, have already informed recent work completed by Canadian Blood Services and Héma-Québec to reduce the MSM waiting period from one year to three months which will be implemented on June 3, 2019.

Read the R.E.D. blog about **Sheila O’Brien’s modelling project** [here](#).

**Engaging a Canada-wide network of research experts**

**Dedicated funding brings teams together for discovery research and development activities**

A unique element of the Centre for Innovation’s strategy is its nine competitive research funding programs. These programs are designed to address key strategic research priorities while engaging the right individuals so that their expertise is brought to bear on important issues. In 2018–2019, 55 research projects received funding through these research programs, including 14 new projects (Appendix I).

Of note is the Blood Efficiency Accelerator Award Program, launched late last year, which now funds eight teams conducting innovative research to improve the efficient and appropriate utilization of blood products. While any Canadian academic can submit their project ideas to the program, the project team must include at
least one Canadian Blood Services employee to ensure alignment with and applicability to our organizational needs.

Ongoing engagement with our research network

To engage our core group of researchers, the Centre for Innovation hosts monthly scientists’ meeting webinars to discuss “work-in-progress” and foster collaboration. We also bring our research network together for our annual Research Day. In June 2018, Research Day brought together 68 professionals, including scientists, physicians, research trainees, and laboratory staff and technicians, to discuss various research projects supported by the Centre for Innovation.

Research Day took place just prior to the 35th Congress of the International Society for Blood Transfusion, which was held in Toronto. Our research network took advantage of this opportunity to connect with the Canadian and international transfusion community. Our medical and scientific experts led or participated in more than 30 talks and presented almost 100 presentations as part of the scientific programme.

The Centre for Innovation also hosted an exhibit to showcase our research and education initiatives. The exhibit booth was hub for our immediate and broader transfusion medicine and science community during the four days of congress events. By creating an inviting space for engagement, we truly welcomed the world to learn more about Canadian Blood Services and the Centre for Innovation. We engaged with delegates from almost 40 different countries and met hundreds of representatives from blood operators and transfusion services from every corner of the world.

knowledge creation

189 grants and awards

- research programs 55
- development research programs 68
- research laboratory support programs 11
- external research funding programs 20
- clinical guideline development programs 5
- national training programs 20
- education programs 10
Members of the Canadian Blood Services research network at the 2018 ISBT Congress in Toronto
The McMaster Centre for Transfusion Research

The McMaster Centre for Transfusion Research (MCTR), with funding from the Centre for Innovation, brings together world-class researchers in transfusion medicine and hematology along with highly skilled biostatisticians, coordinators, research assistants and students. MCTR is breaking new ground in big data research, clinical trials, meta-analytic methods and guideline development and dissemination. Their mission is to advance transfusion science through innovative methodology and collaborative research. Here we highlight some of the MCTR key activities over the last year.

Through the competitive Transfusion Medicine Program Support Award, the Centre for Innovation supports clinical research at two institutions: the MCTR, led by Donald M. Arnold (pictured), and the Quality in Utilization, Education and Safety in Transfusion (QUEST) at the University of Toronto, led by Jeannie Callum. On February 1 2019, Dr. Arnold was renewed as the John G. Kelton Chair in Translational Research at McMaster University.

Blood utilization and supply

TRUST (Transfusion Research, Utilization, Surveillance and Tracking), the MCTR’s database of transfused and non-transfused patients in Hamilton hospitals, is central to the MCTR research on blood utilization and supply. In collaboration with Canadian Blood Services and investigators from McMaster University, MCTR is designing a robust demand-forecasting model for blood products and plasma derivatives. Incorporating clinical transfusion data from TRUST, this tool will use data visualization techniques, statistical methods and machine learning algorithms to improve the accuracy of forecasting demand. Also using the TRUST database, MCTR is currently studying platelet transfusions in critically ill patients to determine optimal role for platelet transfusions in this population.
Hemostasis & bleeding disorders

MCTR is working to improve treatments for patients with bleeding disorders, who often require blood products. MCTR is addressing the escalating use and limited supply of IVlg by exploring alternative treatments. Last year, MCTR published a systematic review on rituximab as an alternative to IVlg for autoimmune diseases.\(^2\)\(^8\) This student-led project was funded by a Canadian Blood Services studentship award, and was a collaboration between MCTR, Canadian Blood Services’ Kathryn Webert, and others. Donald M. Arnold recently completed a randomized trial of IVlg vs. oral eltrombopag for patients with immune thrombocytopenia requiring surgery, with the methods paper for this trial published in 2019.\(^2\)\(^9\)

MCTR is also in the process of completing two impactful hemophilia related studies. One study is a user experience assessment of a new clinical management system, the Canadian Bleeding Disorders Registry; and the second study is a mixed methods study to understand the psychosocial impact of hemophilia on caregivers.

Health outcomes of recipients and donors

A soon-to-be published systematic review (Zeller et al, Vox Sang, in press) and a database project exploring the effect of sex-matched red blood cell transfusion on recipient outcomes suggest that sex may need to be considered in the ideal ‘crossmatch’ when selecting red blood cells for transfusion.\(^3\)\(^0\) Further studies and trials in collaboration with the CIHR and the National Institutes of Health (NIH) are underway. MCTR are also using a new software platform to examine the clinical impact of 7-day platelets on transfusion recipient outcomes.

Dr. Shuoyan Ning, an MCTR medical staff and former transfusion medicine residency fellow supported by Canadian Blood Services, was awarded the Hamilton Health Sciences New Investigator Award for her project to evaluate the clinical impact of the Canadian Blood Services’ policy change to 7-day platelet storage.
International Collaboration for Transfusion Medicine Guidelines

The International Collaboration for Transfusion Medicine Guidelines (ICTMG) creates and promotes evidence-based clinical guidelines to optimize transfusion care in Canada and worldwide. The ICTMG currently comprises 28 members from 10 countries and engages an additional 51 experts from another eight countries. The Centre for Innovation supports the ICTMG chair, Nadine Shehata, and hosts the ICTMG secretariat. Here we highlight some of the ICTMG key activities over the last year.

Optimizing the management of FNAIT and HDN

Fetal and neonatal alloimmune thrombocytopenia (FNAIT) occurs when maternal IgG alloantibodies to human platelet antigens cross the placenta and cause fetal platelet destruction. While incidence is low, the consequences of FNAIT to the fetus or newborn can be devastating. ICTMG completed three systematic reviews\(^3\) and recently published a guidance document for evidence-based management of FNAIT.\(^3\) To help with implementation of the recommendations, ICTMG developed resources for physicians, including an algorithm for management, a podcast and a slide set.

It also developed patient resources. Two patients who experienced FNAIT participated in a podcast and a FNAIT patient pamphlet was developed and translated into several languages. The guidelines and accompanying resources have been disseminated widely through presentations at international conferences, through various specialized publications, and are available at the ICTMG website (ictmg.org). ICTMG is also developing guidelines for hemolytic disease of the newborn (HDN), the red blood cell equivalent of FNAIT. An international panel of experts has been convened to develop these guidelines.

Optimizing platelet transfusion

Last year, the National Advisory Committee on Blood and Blood Products in Canada endorsed the 2015 ICTMG guidelines on platelet transfusion for patients with hypoproliferative thrombocytopenia. The ICTMG also re-convened a platelet development guideline group to update these guidelines and expand their scope. The group includes hematologists, anesthesiologists, transfusion medicine specialists and methodologists, as well as representatives from the World Federation of Societies of Anesthesiologists, the European Society of Anesthesiology, and the AABB.

Optimizing transfusions for patients with hemoglobinopathies

Patients with sickle cell disease and ß-thalassemia are dependent upon red blood cell transfusions. For this patient group, alloimmunization is a well-recognized risk of
transfusion and can lead to delayed hemolytic transfusion reactions and delays in providing transfusions. ICTMG convened an international panel to provide guidance on optimizing the red blood cell product administered to these patients.\textsuperscript{35} Resources for physicians including a slide set, algorithm and podcast are available at the ICTMG website.

Addressing the gaps

As documented by the ICTMG, there is limited rigor in guideline development for transfusion of red blood cells and plasma, as well as duplication and inconsistencies in recommendations.\textsuperscript{36} The ICTMG continues to address this gap and the collaborative’s efforts over the last year highlight the success of multidisciplinary international teams to reach consensus on transfusion-related clinical guidelines. The dialogues allow members to recognize the diversity in treatment internationally and enable the development of recommendations that can be applied locally and internationally while avoiding duplication of efforts.
Training, education and professional development

The Centre for Innovation builds capacity in transfusion and transplantation science and medicine by facilitating formal training and education opportunities for trainees and professionals at various stages in their careers. We also develop and disseminate resources for health care professionals in the field of transfusion and transplantation science and medicine, and work with partners to amplify their reach.

Training the next generation of transfusion scientists

The unique positioning of the Centre for Innovation, at the interface of academia and Canadian Blood Services, provides an exceptional environment for trainees within our research network to develop critical thinking skills while experiencing first-hand the application of research for the benefit of the blood system and Canadian patients.

Over the last year, the Centre for Innovation’s Graduate and Postdoctoral Fellowship Programs provided salary support to 18 junior researchers conducting projects aligned with our research priorities across Canada. In addition, the Centre for Innovation’s 11 discovery and development scientists supervised more than 41 graduate trainees and postdoctoral fellows with funding from research grants or external sources. In 2018–2019, 12 trainees completed their training: seven masters students (MSc), three doctoral students (PhD) and two post-doctoral fellows.

In the last year, the Centre for Innovation has leveraged its unique position to provide opportunities for trainees to engage with Canadian Blood Services and better understand the research needs of the blood supplier. In May 2018, an inaugural Trainee Workshop saw 13 trainees and 12 staff participate in a tour of our manufacturing facility in Brampton. Trainees learned from staff about Canadian Blood Services’ fresh blood products manufacturing processes, and the measures in place to ensure products safety and supply. It was also a chance for these budding transfusion scientists from across Canada to connect and expand their network.

We have also increased opportunities for our research trainees to engage with members of the Canadian Blood Services research networks. We awarded 14 travel bursaries to our trainees to attend our
Research Day in Toronto. Post-doctoral fellows Jennie Haw, Yoelys Cruz-Leal and Syed Qadri were also given the opportunity to present their research to the group.

Through its continuing collaboration with the Centre for Blood Research, the Centre for Innovation supported seven summer and four graduate students at the University of British Columbia. The Centre for Innovation also supports the Centre for Blood Research annual Norman Bethune and Earl W. Davie symposia. These highly regarded symposia feature expert presentations from Canadian and international experts, as well as from patients, and are broadcasted to facilitate remote attendance. They are excellent learning and networking experiences for trainees, patients, and established researchers alike.

“At the symposium, you can meet patients, scientists and doctors. I had the opportunity to talk to a trauma surgeon today, which gave me a new perspective on my research. It’s a great event that provides wonderful opportunities for students!”

Wayne Zhao (Devine Laboratory) describing the 2018 Earl W. Davie Symposium.

Education for medical professionals

Transfusion medicine residency program

In partnership with Canadian Blood Services associate medical director Robert Skeate, the Centre for Innovation continues to provide support to the training of transfusion medicine specialists via the Royal College of Physicians and Surgeons’ Transfusion Medicine Areas of Focused Competency diploma program. Through their affiliation with Canadian Blood Services, these specialists gain a unique exposure to the Canadian blood system that prepares them to contribute to new advances in this field and engages them in a national network. In 2018–2019, two fellows graduated from this program: Shouyan Ning from the MCTR and Matthew Yan, who has now been appointed to a Canadian Blood Services medical officer position.

Transfusion medicine camp

The Centre for Innovation continues to provide administrative and technological support to facilitate Transfusion Camp, a novel and scalable approach to delivering transfusion education to medical trainees across Canada.

This unique program, now in its fourth year of national expansion, is led by QUEST at the University of Toronto, and consists of five one-day events including lectures and team-based learning sessions. In 2018–2019, McGill University and Northern
Ontario School of Medicine joined eight other Canadian universities and Oxford University, bringing the number of fellows registered for this program to more than 250 representing more than 10 specialties. An evaluation conducted during the year demonstrated that Transfusion Camp increased transfusion medicine knowledge, fostered a positive attitude toward transfusion medicine, and enabled a self-reported positive impact on transfusion practice in postgraduate trainees (publication forthcoming).

The camp continues to expand. Plans to include an additional five universities for 2019–20 are currently underway, including four programs in Québec, in collaboration with Héma-Québec.

Professional development for health care professionals
Since 2007, Canadian Blood Services, under the leadership of medical director Peter Lesley, and the Ontario Regional Blood Coordinating Network co-chair an annual transfusion medicine symposium in partnership with a community hospital. In April 2018, the education program developed with Halton Healthcare-Oakville Trafalgar Memorial Hospital focused on managing patients with iron deficiencies. In recent years, with videoconferencing and webcasting technology provided by the Ontario Telemedicine Network, the reach of this symposium has been extended to include more hospitals across Ontario and Canada. In 2018, 125 health care facilities participated, including nine Canadian Blood Services sites, and five non-Canadian sites, making this event international in scope, engaging 1,250 professionals.

In a similar vein, the Centre for Innovation provided financial support for the 2018 Saskatchewan Transfusion Medicine Symposium, which attracted 114 professionals, and Canadian Blood Services partnered with the BC Provincial Coordinating Office to co-chair an Annual Education Session on Blood Transfusion Issues.

Online resources for health care professionals
In collaboration with the Canadian transfusion medicine community, the Centre for Innovation develops educational resources for health care professionals that are made available free of charge via the Canadian Blood Services Professional Education website, profedu.blood.ca. This website provides original articles, best and leading practices, course resources, educational event information, and more.
2018–2019, the website recorded 251,000 sessions engaging 214,000 users (a 60 per cent increase from last year), with 375,000 page views. Users are primarily from Canada (35 per cent).

The 18 chapters of the Clinical Guide to Transfusion continue to be the most sought-after resources, with more than 137,000 page views. In 2018–2019, the Centre for Innovation completed the latest cycle of revisions to the guide, and each chapter is now updated in both French and English. User satisfaction rates with the guide remain high at 95 per cent.

Many other resources were added to the Professional Education site in 2018–2019, including:

- several resources on serological best practices. 37-42
- a popular article on TRALI, which has almost 50,000 page views, and is the most-visited content after the Clinical Guide to Transfusion. 43,44

User satisfaction rates with the Professional Education site amongst Canadian hospitals are also high at 94 per cent. These educational resources are further disseminated via the Centre for Innovation’s monthly e-newsletter, the R.E.D. blog, partners’ newsletters including Canadian Blood Services’ BloodNotes, Canadian Blood Services customer letters, and in presentations delivered by Canadian Blood Services to hospital stakeholders.

Through its BloodTechNet competitive program, the Centre for Innovation continues to fund projects aimed at delivering educational tools and resources that support the development of skills, knowledge, and expertise of health professionals in the transfusion, cellular therapy, and transplantation communities in Canada. For example, in 2018–2019, Andrew Shih’s BloodTechNet-funded Blood & Clots project continued to develop educational resources for practitioners on how to manage patients who are bleeding, clotting, or both, which can be found on CanadiEM, an online portal for emergency medicine specialists. 45
Dr. Andrew Shih promoting his Blood & Clots Series of educational resources at the ISBT Congress.
Improve

Half of all Canadians will either need blood or know someone who needs it. Through discovery research and applied development work, the Centre for Innovation helps Canadian Blood Services continuously improve its blood products and the processes used to manufacture them. We provide innovative, effective, sustainable solutions to optimize Canada’s Lifeline and to ensure Canadians continue to be supplied with the highest quality blood products.

Blood
Expanding Canadian Blood Services’ formulary of products

Canadian Blood Services collects more than 700,000 whole blood donations every year. These are separated into red blood cell, platelet, and plasma components. Component therapy has been the gold standard for decades. It is beneficial to patients in many settings, allowing for the transfusion of only the blood product(s) the patient needs, while maximizing the number of patients who can be treated with each whole blood donation.

There is, however, a re-emergence of interest in using whole blood in certain settings — particularly massive trauma. While civilian care shifted exclusively to component therapy over the past 50 years, in some military trauma settings, “walking donor” programs in the field meant whole blood continued to be used for resuscitation. Lessons from military settings, as well as emerging evidence supporting the benefits of “balanced” massive transfusion protocols (where components are transfused in the correct ratio to recapitulate whole blood), suggest that whole blood may be the optimal fluid to replace blood loss in massive trauma.
Canadian Blood Services is actively investigating the (re)-introduction of whole blood as a “new” specialized product to its formulary to meet both military and civilian needs. With support from the Centre for Innovation’s product and process development group, Canadian Blood Services is investigating optimal processes to manufacture, characterize, label, store, distribute, and quality control test leukoreduced cold-stored whole blood.

Platelets

Platelets are essential for blood to clot effectively and prevent bleeding. Patients with low platelet counts (thrombocytopenia) due to disease or injury may need a platelet transfusion to reduce their risk of bleeding.

Due to their storage temperature, platelet components are at particular risk of bacterial contamination, presenting a rare but potentially serious risk to recipients. Testing of platelets for bacteria and other mitigation strategies can reduce the risk of bacterial contamination and improve the safety of platelets. Informed by evidence from the Centre for Innovation’s microbiologist, Sandra Ramirez-Arcos, Canadian Blood Services introduced a new platelet testing algorithm and extended the shelf life of platelet products from 5 to 7 days in 2017. This improved the safety profile of platelets and led to a system-wide reduction in the number of platelet units discarded due to outdate.

How well bacteria grow and survive in the environment of a platelet bag determines how potentially serious a transfusion-transmitted infection might be if a contaminated unit were transfused. The Centre for Innovation’s Ramirez-Arcos has found that Staphylococcus epidermidis, the predominant bacterium found in contaminated platelets, forms aggregates called “biofilms” in platelet products. When clumped together in biofilms, bacteria may be missed by current screening tests. Being in a biofilm may also help bacteria survive in a platelet product, as they are better protected from immune factors. Ramirez-
Arcos and her team are investigating the complex interactions between platelets and bacteria within a platelet bag. They have also demonstrated that combinations of three synthetic antimicrobial peptides can inhibit biofilm formation in platelets, but further research is needed to improve their activity against established biofilms.

Pathogen inactivation for platelets
Pathogen inactivation technologies offer broad-spectrum treatment against potential pathogens (bacteria, viruses, and parasites) within blood and blood products, and may potentially fill in the gaps in current blood safety approaches. These technologies target and damage nucleic acids (DNA and RNA) in pathogens using ultraviolet (UV) light, preventing the pathogen from reproducing, and effectively destroying its ability to cause illness. Products treated with pathogen inactivation technologies are called “pathogen-reduced” products.

Read our R.E.D. blog on Pathogen Inactivation.

In 2018, the INTERCEPT pathogen inactivation technology by Cerus Corporation was licensed in Canada to treat platelet components. This is the first, and currently only, platelet pathogen inactivation system licensed for use in Canada. With support from Medical Affairs and Innovation, including the Centre for Innovation, Canadian Blood Services is actively investigating the best approach to make pathogen-reduced products available to Canadian patients.

“Our blood products are currently deemed safe from known infectious diseases. However, they could face risks from emerging pathogens, as well as from the bacterial contamination of platelets. We will therefore begin offering Canadian patients access to pathogen-inactivated fresh blood products, phasing in new technologies (as they are licensed) to create an additional layer of safety assurance across the blood system.”

From Canadian Blood Services’ Strategic Plan 2019–2024

While the use of pathogen inactivation technologies by blood operators continues to expand, several interesting research questions remain. For example, studies, including several conducted by the Centre for Innovation, show that in terms of laboratory-measured (in vitro) quality and function, pathogen-reduced platelets are different to untreated platelets. This year, Dana Devine, in collaboration with the Australian Red Cross Blood Service, surveyed available publications to understand these changes. Despite many studies in this area, few conclusions can be drawn. Devine’s review, however, highlighted that the signalling protein kinase p38 is potentially important in regulating the impact of pathogen inactivation treatment on platelets.

Do these changes in laboratory-measured tests of platelet quality and function matter clinically? Canadian Blood Services medical
consultant Alan Tinmouth and several researchers based at Canadian Blood Services-supported QUEST and MCTR, participated in the PREPAReS (Pathogen Reduction Evaluation and Predictive Analytical Rating Score) noninferiority trial, which sought to answer this question.

“Pathogen inactivation remains an important tool to improve the safety of platelet transfusions, particularly with respect to bacterial contamination. We may just have to strike a risk balance while the technologies of pathogen inactivation and platelet storage solutions continue to evolve.”

Dr. Dana Devine Canadian Blood Services’ chief scientist

PREPAReS was conducted in 10 sites in three countries, including five sites in Canada. It compared the efficacy of pathogen-reduced platelets with standard plasma-stored platelets for the prevention of bleeding in patients with hematologic malignancies and thrombocytopenia,55 and found that pathogen-reduced platelets were noninferior to untreated platelets in preventing World Health Organization grade 2 or higher bleeding. These data, in particular the Canadian data, will help inform Canadian Blood Services’ decision-making process as it pursues introducing pathogen inactivation technologies.

Although the PREPAReS trial showed no impact on efficacy, other clinical studies have indicated that there does appear to be a trade-off. The increased safety profile of pathogen-reduced platelets may go hand-in-hand with small decreases in transfusion effectiveness, which may lead to an increase in transfusion frequency.56-58 These differences in findings from clinical trials highlight outstanding research questions about the optimal combinations of pathogen inactivation technologies, platelet production methods, and platelet additive solutions.

Dana Devine reviewed this topic in JAMA Oncology59 and noted that platelet additive solutions, and indeed pathogen inactivation, are relatively new technologies, and we need to learn more.

A new platelet pooling set

Over the past year, Canadian Blood Services rolled out new blood component processing equipment across the organization. Included in this roll-out were new platelet pooling sets. The product and process development group worked on the Request for Proposals for the new Platelet Pooling Set, qualifying the bag set and ensuring that its introduction would lead to additional benefits, in particular an improvement in the consistency of platelet yields.60,61
Improving quality control processes
Blood products are quality control tested to ensure ongoing safety and quality. Current quality control processes require that the entire blood product destined for quality control testing be removed from the inventory, precluding their transfusion to patients. This is the fate of a small percentage of all blood that is donated. The Centre for Innovation has been exploring an alternative approach — using small aliquots drawn from units at production for quality control testing.\(^{62-64}\) Called non-destructive quality control testing, this could improve product availability and reduce production costs while maintaining product quality.

After several years of development work, in 2018–2019, the Centre for Innovation’s product and process development group, together with Canadian Blood Services’ supply chain supported studies led by the Quality & Regulatory Affairs division to test non-destructive quality control testing of platelets in the manufacturing environment. The results were promising. Non-destructive quality control testing of apheresis and pooled platelet products can be consistently achieved in the Canadian Blood Services manufacturing environment and gives results similar to existing testing.

The development work is now coming to an end, and the evidence generated is being used by Canadian Blood Services to prepare a business case to operationalize non-destructive quality control testing for platelets.

Bringing the board to the bench
The Centre for Innovation was delighted to engage with members of the Canadian Blood Services’ Board of Directors and Executive Management Team and demonstrate non-destructive quality control testing during a tour of the development laboratories in Ottawa in March 2019.

At the same time, Ken McTaggart continues to lead development studies to apply a similar non-destructive quality control testing approach to red blood cell products. These studies also involve Janet McManus and Peter Schubert, who assessed the feasibility of non-destructive quality control testing of red blood cells, Sandra Ramirez-Arcos who is exploring the feasibility of using these aliquots in an alternative sterility testing algorithm for red blood cells, and John Blake who conducted modeling studies to understand the impact.
of volume depletion on the dose of red blood cells remaining in the unit.

Two other novel non-destructive quality control approaches for red blood cells were explored this year. A collaboration between Jason Acker and Canadian Blood Services adjunct scientist and chief technology officer at LightIntegra Technology Inc. Elisabeth Maurer explored a different way to look at red blood cell quality. They used the non-destructive sampling of red blood cell products pioneered by the product and process development group and examined the usefulness of extracellular vesicle content in the aliquot as an alternative indicator of red blood cell quality.65-67

Read the Research Unit describing this work here.

Dana Devine has been collaborating with Robin Turner and Michael Blades at the University of British Columbia, to explore a technology called Raman spectroscopy as an alternative approach to measure red blood cell quality.68 With Raman, measurements of blood products can be made without breaching the sterility of the blood bag. This technology could represent a new way to check the quality of blood without opening the bag and make it possible to assess quality just before it is transfused to the patient.

Read the R.E.D. blog about this work here.

Red blood cells

Red blood cells are the most common blood product distributed by Canadian Blood Services. Stored for up to 42 days in the refrigerator, red blood cells are used to treat anemia and blood loss to improve oxygen delivery to tissues. During storage red blood cell units undergo changes, which are collectively termed the storage lesion.

Understanding and improving red blood cell products

The presence of extracellular vesicles in red blood cell units, and their potential value as a marker of red blood cell quality was a focus in 2018–2019. Extracellular vesicles are very small membrane-bound blebs shed by cells. They are indicative of cellular activation or degradation and may provide information on product quality. Their relationship to manufacturing methods and donor factors, and whether they impact patient outcomes, however, remains unclear. Jason Acker, in collaboration with colleagues from Vitalant Research Institute and Blood Centers of the Pacific in San Francisco, as well as other international collaborators, found that manufacturing methods significantly affect red blood cell unit extracellular vesicle characteristics and may impact how they interact with the immune system.69

Another study by the Acker laboratory demonstrated that donor age and sex impact red blood cell unit extracellular vesicle levels and influence how red blood cell supernatants modulate immune cells in an in vitro system.70
The Acker laboratory also continued its exploration of liposome treatment to limit red blood cell storage lesion, showing that treatment improved the blood flow (hemorheological) properties of stored human red blood cells, with no significant impact on their metabolic function.71

**Advance knowledge**

246 knowledge products
163 peer-reviewed publications
56 website publications
26 technical reports
1 newspaper or magazine article

**Improving a vital prenatal test**

To prevent hemolytic disease of the fetus and newborn (HDFN) associated with RhD sensitization, Canadian guidelines recommend that RhD-negative women who may be carrying a RhD-positive infant receive an antepartum dose of Rh immunoglobulin at 28 weeks’ gestation, as well as a postpartum dose. Up to 40 per cent of antepartum injections, however, are unnecessary because the fetus is also RhD-negative.

Cell-free fetal DNA found in the mother’s plasma provides an opportunity for more accurate and non-invasive prenatal diagnosis. Supported by a Blood Efficiency Accelerator Program award, Jason Acker and Gwen Clarke explored the feasibility of using a single-exon real time PCR test to test for the presence of the RHD gene in a D-negative pregnant woman to determine which women are carrying a RhD-positive fetus.

This approach, which is already in use in Sweden, was shown to be a clinically feasible way to determine fetal RhD status when used to test maternal plasma samples after 12 weeks’ gestation.72 With an estimated cost per test of less than $30, introducing this test could lead to significant cost savings by reducing the need for Rh immunoglobulin.

Based on these promising results, the project team visited Sweden to evaluate the infrastructure and logistics for how this test could be implemented by Canadian Blood Services. These results are helping to inform decisions around the development of a national program for non-invasive prenatal testing.
From the research lab to the clinical lab – Improving an assay to help find the best match for patients

For patients with rare blood types or other difficult-to-crossmatch patients, Canadian Blood Services performs cross-matching tests to match patients with donors and avoid potentially serious transfusion reactions.

One such test is the monocyte monolayer assay (MMA) pioneered by Canadian Blood Services scientist Donald R. Branch. The MMA has long been used in research and academic laboratories and has been proven effective as a test to predict the clinical significance of antibodies and aid in the selection of donor blood for transfusion. Its usefulness as a test in clinical laboratories, however, has been limited by practical restrictions — for example, the need to obtain a fresh blood sample.

In a collaborative effort published this year, Jelena Holovati, a Centre for Innovation adjunct scientist, together with Donald R. Branch and Jason Acker addressed this issue. The researchers developed a freezing technique to store cells isolated from blood components left over from Canadian Blood Services manufacturing processes. In the assay, these cells performed as well as cells isolated from fresh blood. Using cells sourced from a product usually discarded during blood component manufacturing increases the usefulness of the MMA, making it easier to provide the safest blood product to the right patient.

This work has supported the migration of this test from the research lab to the clinical lab.

Canadian Blood Services are currently working to implement this MMA test in Canadian Blood Services' Edmonton diagnostics laboratory. It will “go live” as an orderable test in 2019 and will help determine the most appropriate blood for transfusion in patients with complex antibodies or rare phenotypes where there might not be a perfect match.

Improving cryopreservation

The key to successfully cryopreserving cells lies in limiting any damage to the cells by manipulating the formation of ice inside and outside of the cells through careful control of cooling and warming conditions. Jason Acker and colleague Robert Ben are investigating small molecule ice recrystallization inhibitors as “cryoprotectants” – agents that help limit the damage to cells during freezing or thawing. In 2018, Acker and Ben showed that small molecule ice recrystallization inhibitors can enter red blood cells and control intracellular ice recrystallization during freezing, showing that these inhibitors have potential to improve cryopreservation of cells and tissues.
Training international students to perform the monocyte monolayer assay. Charlotte Paquet (France), Mairead Holton (Ireland), and Elodie Dupeuble (France) watch Selena Cen (Branch laboratory, Canadian Blood Services) perform the monocyte monolayer assay.
Dr. Heyu Ni: achieving research excellence

Canadian Blood Services scientist Heyu Ni is a researcher at the top of his game. An immunologist and hematologist, Ni has led many paradigm-altering studies. His work has advanced fundamental understanding of how blood clots, helped identify new targets for anti-thrombotic therapies, and shed light on the mechanisms of devastating bleeding disorders such as fetal and neonatal alloimmune thrombocytopenia (FNAIT) and immune thrombocytopenia (ITP).78-83 His goal is to identify better treatments for patients with bleeding disorders and immunological diseases.

In 2018–2019, Ni’s team, based at the Keenan Research Centre for Biomedical Science at St. Michael’s Hospital, Unity Health Toronto, published 11 peer-reviewed scientific papers and two book chapters. Notable among them was a study published in *Nature Communications* which linked a plasma protein called Apolipoprotein (Apo)A-IV with platelet clotting for the first time.84 Ni’s team showed that ApoA-IV blocks platelet aggregation, suggesting it could have protective effects against thrombotic disorders such as heart attack and stroke.
This discovery received worldwide media attention. It suggests an interesting new link between diet and heart health. After digestion of a meal, platelets in the blood become activated, meaning a higher chance they may clot. Levels of ApoA-IV also increase in blood following digestion of food, particularly foods high in unsaturated fats, such as olive oil. Ni is continuing to study ApoA-IV and platelets to design novel therapies for disorders associated with platelet clotting and inflammation.

An engaged collaborator
A great team and key collaborators contribute to Ni’s research excellence. Ni has worked with high profile researchers in Canada and across the globe. If Ni is not in the laboratory, it’s likely because he is travelling for scientific meetings. Ni or members of his team have given more than 220 presentations to scientific and medical colleagues over the past five years. In 2018–2019, Ni published a high impact study in collaboration with his Canadian Blood Services colleagues Alan Lazarus and Donald R. Branch. This trio of Toronto-based experts often work closely together. The study, published in Blood, showed that platelets, through a protein called GPIbα, contribute to the steady-state production of thrombopoietin by the liver.85-87

Thrombopoietin stimulates platelet production from platelet precursor cells in the bone marrow.

“I am most proud of the many excellent students I have trained, who are also using their skills to contribute to medical sciences and patient care.”

Dr. Heyu Ni

The link between platelet GPIbα and thrombopoietin was not previously known, and this study has important implications in bleeding diseases. Ni is also working with Canadian Blood Services scientist William Sheffield, to compare plasma and plasma protein concentrate transfusion for the control of bleeding.

Training the next generation
Ni demonstrates a real commitment to training the next generation of scientists and physicians. Throughout his career, he has supervised or co-supervised more than 120 undergraduate, graduate or post-graduate trainees. In fact, among his many original discoveries that have contributed to medical science and transfusion medicine, including those that may lead to new therapies, he considers his training of the next generation to be the work of which he is most proud.

Ni is supported by two Canadian Blood Services-CIHR Partnership Operating Grants and is a co-investigator with Canadian Blood Services colleagues on three Intramural Research Grants. In 2018, Ni was awarded a highly competitive and prestigious CIHR Foundation Grant which provides long-term support for the pursuit of innovative, high-impact research programs.
Plasma

Plasma is the protein-rich liquid component of blood that supports the immune system and controls excessive bleeding. Plasma is transfused to prevent or treat bleeding; however, much of the plasma collected by Canadian Blood Services is sent to international companies to be fractionated into plasma-derived products such as intravenous immune globulin (IVIg). In Canada and around the world, demand for IVIg is growing, increasing pressure on supply. In response, in 2018, Canadian Blood Services committed to increasing plasma sufficiency in Canada. In 2018–2019, the Centre for Innovation continued efforts to understand IVIg and other plasma products and the diseases they treat to improve treatments and find alternative therapies that may help reduce the demand for these valuable resources.

What’s in a bag of plasma?

Plasma can be separated from a whole blood donation (recovered plasma) or obtained by apheresis donation (source plasma).

In 2018–2019, researchers from the Centre for Innovation sought to better understand the quality of recovered plasma. William Sheffield and Craig Jenkins tested levels and activities of important plasma factors for coagulation in recovered plasma, and measured levels of immunoglobulin, from which IVIg is made. This study found that the way in which plasma is manufactured from whole blood impacts the composition of recovered plasma; recovered plasma contains more immunoglobulin when the time between blood donation and manufacturing into plasma is shorter.

Read the Research Unit describing this work here.

Many plasma-derived drugs, including IVIg and coagulation factors, are essential, life-saving treatments. Since Canadian Blood Services currently relies heavily on recovered plasma for fractionation, and with pressure on plasma supply increasing, having detailed information about how manufacturing methods may impact yields of plasma-derived drugs is valuable.

Bleeding and clotting – a delicate balance

A delicate balance exists between clotting and bleeding. If blood cannot clot effectively, there is a risk of bleeding. If blood clots too easily, there is a risk of thrombosis, including heart attack, stroke and other serious conditions. Anticoagulants, or blood thinners, are medicines used to treat patients who experience unwanted or excess blood clotting.
Ed Pryzdial has been studying some newer anticoagulant drugs. These newer drugs specifically target and inhibit a clotting factor called factor Xa. They work by decreasing the formation of clots. Recent research from the Pryzdial laboratory, however, has found an additional way in which these drugs may help patients with too much clotting — by enhancing “clot-busting”. The process of clot busting, dissolving a clot once bleeding has been stopped, is an important way of managing clotting.94

Factor Xa’s role in forming clots is well-known, but its role in busting clots is less well-established. This study also sheds light on how factor Xa enhances clot busting — knowledge which could be used to design more effective anticoagulant drugs in the future.

William Sheffield has been studying hirudin, a small protein found in medicinal leech secretions. It is a potent antithrombotic agent, but its use is limited by bleeding side effects. He engineered an activated coagulation factor XI (FXIa)-activatable hirudin-albumin fusion protein that should reduce thrombosis without promoting bleeding. The results showed that the engineered fusion protein had a superior benefit/risk profile to constitutively active hirudin-albumin but was less effective than another protein engineered previously by this laboratory.95 The previously engineered protein was activated by plasmin, a clot-busting enzyme.

Improving IVIg therapy

Intravenous immune globulin (IVIg) is a fractionated human plasma product made of pooled donations from thousands of individuals. It is used to treat immunodeficiency, as well as many autoimmune and inflammatory conditions. IVIg is an expensive treatment and a limited resource. In Canada a 10-year retrospective cohort study of all patient encounters involving an IVIg transfusion from 2007 to 2016 at a four-site tertiary care hospital in Ontario revealed that a total of 1,658,159 g of IVIg was administered in that period.96 Authors on the study included Canadian Blood Services’ Goldman, Shehata and Tinmouth. Trends showed ongoing increases in the number of patients treated with IVIg, despite some short-term changes when provincial initiatives to optimize IVIg use were introduced. These findings suggest novel initiatives aimed at reducing the dose of IVIg prescribed and rationalizing its use are needed.

IVIg’s mechanism of action in many of the diseases it is used to treat remains unclear. The Centre for Innovation supports research to understand how IVIg works and to develop alternatives treatments. Canadian Blood Services CIHR-funded researcher Laura Sly hopes her work will help identify novel targets to replace or improve IVIg therapy and define who can or cannot be effectively treated with IVIg. Her overall goal is to optimize its use in the health care system. This year, her team uncovered a potential mechanism by which IVIg may reduce inflammation — it causes human
white blood cells to produce large amounts of an anti-inflammatory cytokine called interleukin 10.97 Interestingly, this research also showed that a certain gene that codes for a receptor for IVIg comes in two forms in people. The form a person has influences how well IVIg works and how much interleukin 10 is produced. This intriguing finding suggests that sequencing this gene in patients may help predict who will be the best responders to IVIg therapy.

Although relatively rare, adverse events such as hemolytic anemia and thrombosis, can complicate the administration of IVIg.98,99 More frequently, serological problems can be associated with the administration of IVIg. Last year, Donald R. Branch published a review of these potential transfusion service challenges associated with IVIg administration, which can include ABO discrepancies, positive direct antiglobulin tests, positive antibody detection tests, and incompatible crossmatches.100

Canadian Blood Services scientists Alan Lazarus and Donald R. Branch continued their work to understand bleeding disorders that are often treated by IVIg, particularly immune thrombocytopenia (ITP). ITP is characterized by destruction of platelets leading to an increased risk of bleeding. Work by Lazarus and colleagues Heyu Ni and John Semple sought to understand the origin in abnormalities in megakaryocytes (cells in the bone marrow that produce platelets) associated with ITP.101 Branch showed that an immune modulator, the cytokine interleukin (IL)-11, may play an important role in the amelioration of ITP by IVIg.102

**Experimental immunotherapeutic shows promise**

Canadian Blood Services scientist Mark Scott has been investigating the immune system. Recognizing that the delicate balance between pro-inflammatory and anti-inflammatory responses in the body can play a central role in cancer, Scott sought ways to modify the immune system and tip the balance towards an anti-cancer response. He is researching a “biomanufactured immunotherapeutics” approach – manufacturing biological drugs in laboratory “bioreactors” that can modulate the immune system. Using this approach, Scott and his team have developed an experimental therapeutic named IA1. This acellular product is generated from the secretions of immune cells following exposure to alloantigens (i.e. antigens the immune cells do not recognize). When immune cells isolated from blood were treated with IA1, they successfully inhibited the growth of cancer cells.103 A second biomanufactured therapeutic, TA1, has also been produced that calms the immune system and could potentially be used to treat autoimmune diseases.104 This TA1 biotherapeutic is experimental, but is inexpensive to produce, and if developed further, may help to calm the immune response in autoimmune diseases many of which are treated with IVIg today.
Stem cells

Blood stem cells are immature cells that can develop into any cell present in the bloodstream (i.e. red blood cells, white blood cells, or platelets). Blood stem cells can be isolated from bone marrow, circulating blood, or umbilical cord blood. Blood stem cells can be used to treat more than 80 diseases and disorders, including certain types of cancer such as leukemia, lymphoma and myeloma.

Canadian Blood Services runs a registry of healthy people willing to be stem cell donors should they be a match for a patient in need. It also runs a national public Cord Blood Bank that collects and stores umbilical cord blood samples for patients in need.

The Centre for Innovation supports research to help improve the processes of collecting, storing, and using stem cells. Nicolas Pineault, a member of the Centre for Innovation’s product and process development team, heads up a laboratory focused on developing procedures and improving standards for cord blood collection by the national public Cord Blood Bank. In 2018–2019, his group helped the bank troubleshoot an important assay. The measurement of viable CD45+ cells in thawed cord blood unit segments is an important indicator of a unit’s quality before it’s released for transplantation.

Development research prompted by discrepancies in measurements across cord blood banks identified factors that may affect the viability of CD45+ cells in the samples, impacting the accuracy of the measurement. To improve the accuracy of this assay, Pineault’s group recommended that a red blood cell lysis step be removed during sample preparation.

Pineault’s laboratory also researches new ways to improve blood stem cell transplants in patients. His team is working on ex vivo expansion of stem cells and progenitor cells. The hope is that growing larger numbers of cells in the laboratory before transplantation into a patient may help overcome the slow engraftment of platelets associated with transplants from cord blood units. Using a cellular engineering approach, Pineault and his team have developed growth conditions that improve the expansion of these cells, and in 2018–2019, they published a report detailing the factors thought to be responsible for these effects.
Organs and tissues
The Centre for Innovation, in consultation with Canadian Blood Services’ Organ and Tissue Donation and Transplantation (OTDT) group, supports research in organ and tissue donation and transplantation primarily through the James Kreppner Award and the Kenneth J. Fyke Award Programs.

Ethics and medical assistance in dying
This year, the James Kreppner Award Program continued to support projects led by Jennifer Chandler and Vanessa Gruben, who are working to identify the legal and ethical challenges around organ donation in Canada. The studies focus on understanding public and professional stakeholder attitudes towards organ and tissue donation in the contexts of ante-mortem interventions.

Their aims are to increase access to organ donation or improve donation outcomes after cardiocirculatory death within the context of medical assistance in dying legislation. These studies will tackle the challenging issue of whether those accessing medical assistance in dying would be eligible to donate organs, and the associated ethical and legal questions that arise.

Additional work is underway to better understand the experiences of health care professionals who have participated in, or may be called upon to participate in, medical assistance in death and organ donation — a topic that has not been addressed in any detail.

Collectively, their work will contribute to a better understanding of ethical and legal challenges facing the Canadian organ and tissue donation system and will inform policy and legislative reform to address these challenges.

Commercialization of blood and tissue in Canada
In 2018–2019, the James Kreppner award was awarded to the University of Saskatchewan’s Alana Cattapan. Human tissue legislation in Canada varies from province to province. Cattapan’s research aims to identify how blood and tissues are governed across Canada, and how these policies have evolved. Her research will investigate legal, ethical and social issues related to the commercialization of human tissues and will provide comparative data upon which recommendations to reform and harmonize legislation across Canada can be built.

Read our R.E.D. blog announcing this award here.
Governance

The Centre for Innovation continues to benefit from sound governance by Canadian Blood Services, with oversight provided by the external Scientific and Research Advisory Committee (SRAC) and by the Canadian Blood Services board of directors’ Safety, Research and Ethics Committee (SREC). In 2018, Anne McFarlane was appointed chair of the SREC, replacing interim chair Kevin Glasgow. Program administration is strongly supported by Canadian Blood Services’ enabling functions: talent management, finance, legal, information technology, and others.

The Research Ethics Board

The Centre for Innovation hosts the Canadian Blood Services Research Ethics Board (REB) secretariat. The REB reviews all research involving human participants conducted by or on behalf of Canadian Blood Services. This includes all research involving either personal information or biologic materials (e.g. blood, stem cells) collected by Canadian Blood Services. Without approval from the REB, a research project involving human participants cannot go ahead. The REB also advises Canadian Blood Services on bioethical issues in research.

Several improvements to the Research Ethics Program were implemented in 2018–2019. The program facilitated access to Canadian Blood Services’ data for research purposes by establishing a new process and implementing a new operating procedure. The program also brought about improvements with new technology to more efficiently manage and track study proposals. REBIT (or the Research Ethics Board Information Technology system) was designed in-house in collaboration with the Information Technology division and launched in 2018.

174 files handled by our Research Ethics Board
new study proposals 52
study renewals/amendments 84
studies closed 38

5,158 blood products distributed
3,515 to 68 production improvement projects
1,643 to 41 Canadian researchers

155 cord blood products
distributed to 6 Canadian researchers
A new performance metric framework

The Centre for Innovation reports on its performance and progress towards meeting strategic objectives to Canadian Blood Services’ executive management team and board of directors, and Health Canada. During the year, the Centre for Innovation’s performance measurement framework was reviewed and updated in collaboration with Health Canada, with revisions to the existing outputs and outcomes. This significantly changed our program indicators, including the introduction of one new output and five new outcomes, and the substantial revision of two outputs and five outcomes (see Figure 2 showing select program indicators).

This improved performance measurement framework ensures that the Centre for Innovation can demonstrates its contribution to the Canadian health system and the health of Canadians. Reporting on the performance measurement framework meets the reporting requirements of Health Canada’s contribution funding agreement for the Centre for Innovation and will support future evaluations assessing the relevance and performance of the program.
<table>
<thead>
<tr>
<th>Intended Outputs &amp; Outcomes</th>
<th>Indicators</th>
<th>2017–2018</th>
<th>2018–2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outputs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grants and awards</td>
<td>Number of grants and awards provided (Appendix I)</td>
<td>152</td>
<td>189</td>
</tr>
<tr>
<td>Learning opportunities</td>
<td>Number of presentations and events</td>
<td>410</td>
<td>434</td>
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<tr>
<td>Supported network</td>
<td>Number of distinct Canadian investigators supported</td>
<td>N/A</td>
<td>124</td>
</tr>
<tr>
<td>Immediate Outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canadian researchers advance knowledge on blood safety</td>
<td>Number of knowledge products published (Appendix II)</td>
<td>416</td>
<td>246</td>
</tr>
<tr>
<td>Stakeholders access information on blood safety</td>
<td>Number of stakeholders attending events</td>
<td>N/A</td>
<td>3,763</td>
</tr>
<tr>
<td></td>
<td>Page views of significant program websites</td>
<td>N/A</td>
<td>346,555</td>
</tr>
<tr>
<td>Stakeholders are equipped with the knowledge, skills, and supports required to enhance blood safety</td>
<td>Percentage of event attendees reporting knowledge gain</td>
<td>N/A</td>
<td>89%</td>
</tr>
<tr>
<td></td>
<td>Number of Highly Qualified Personnel completing training</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>Intermediate Outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Key research stakeholders in the transfusion and transplantation community use program research findings to inform blood safety</td>
<td>Percentage of staff researchers with H-index ≥ Canadian science standard of 10.6 (Appendix II)</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Key stakeholders make improvements in blood safety</td>
<td>Number of new or updated blood safety measures informed by the program</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>Ultimate Outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canadians have access to appropriate and effective health services</td>
<td>Number of stakeholders reporting that Canadian Blood Services plays an essential role in achieving patient outcomes</td>
<td>N/A</td>
<td>99%</td>
</tr>
</tbody>
</table>

Figure 2. Select program outputs and outcomes. Note: Blood safety in the context of the program refers to a safe, effective, and responsive system for blood and blood products.
References cited

Author Legend: **Bold** – Centre for Innovation investigators and senior staff; Canadian Blood Services medical directors; Directors of transfusion medicine research programs receiving funding via Transfusion Medicine Research Program Support Award.


75. Acker J, Branch D. Concentré de recherche: Où l’on optimise un test de laboratoire pour déterminer la compatibilité entre donneurs et receveurs. Blood.ca website 2018.
76. **Acker J, Branch D.** Research Unit: Improving the usefulness of a laboratory tool to match donors and patients. *Blood.ca website* 2018.


86. **Ni H.** Concentré de recherche: Important rôle de la gpibα, une protéine plaquettaire, dans la régulation de la production hépatique de thrombopoïétine. *Blood.ca website* 2018.

87. **Ni H.** Research Unit: Platelet protein gpibα plays an important role in regulating platelet-mediated production of thrombopoietin by the liver. *Blood.ca website* 2018.


## Appendix I: Grants and Awards

### Number of Centre for Innovation supported projects by program

<table>
<thead>
<tr>
<th>Research Programs</th>
<th>55</th>
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</thead>
<tbody>
<tr>
<td>Canadian Blood Services/CIHR partnership operating grants</td>
<td>13</td>
</tr>
<tr>
<td>Canadian Blood Services/CIHR partnership new investigator awards</td>
<td>1</td>
</tr>
<tr>
<td>Intramural research grants</td>
<td>11</td>
</tr>
<tr>
<td>MSM research grants</td>
<td>15</td>
</tr>
<tr>
<td>James Kreppner awards</td>
<td>3</td>
</tr>
<tr>
<td>Kenneth J. Fyke awards</td>
<td>1</td>
</tr>
<tr>
<td>Blood efficiency accelerator awards</td>
<td>8</td>
</tr>
<tr>
<td>Small project funding</td>
<td>1</td>
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<tr>
<td>Transfusion Medicine Support Award</td>
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</table>

<table>
<thead>
<tr>
<th>National Training Programs</th>
<th>20</th>
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</thead>
<tbody>
<tr>
<td>Postdoctoral fellowships</td>
<td>5</td>
</tr>
<tr>
<td>Graduate fellowships</td>
<td>12</td>
</tr>
<tr>
<td>CIHR health system impact fellowship</td>
<td>1</td>
</tr>
<tr>
<td>Transfusion medicine fellowships</td>
<td>2</td>
</tr>
</tbody>
</table>

| Research Laboratory Support Program                           | 11 |


<table>
<thead>
<tr>
<th>Development Research Programs</th>
<th>68</th>
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<tbody>
<tr>
<td>Deepening the understanding of our products and the processes used to manufacture them</td>
<td>13</td>
</tr>
<tr>
<td>Developing new or next generation products</td>
<td>10</td>
</tr>
<tr>
<td>Improving current generation products and the processes used to manufacture them</td>
<td>17</td>
</tr>
<tr>
<td>Enabling the Product and Process Development Group</td>
<td>12</td>
</tr>
<tr>
<td>On demand unit investigation</td>
<td>10</td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Education Programs</th>
<th>10</th>
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</thead>
<tbody>
<tr>
<td>BloodTechNet awards</td>
<td>8</td>
</tr>
<tr>
<td>Education research grant</td>
<td>1</td>
</tr>
<tr>
<td>Centre for Blood Research program support collaboration</td>
<td>1</td>
</tr>
</tbody>
</table>

| Clinical Guideline Development Program          | 5           |
| Externally Funded Grants and Awards            | 20          |

Total number of projects 189
Titles of projects supported by program

Note: Projects that are italicized are those for which funding was initialized in fiscal 2018–2019

**Research Programs**

**Canadian Blood Services/CIHR Partnership National Operating Grant Program**

**Purpose:** Transfusion science

Expanding treatment options for inflammatory bowel disease: a novel mechanism of antibody-based immunotherapy

Fetal and neonatal alloimmune thrombocytopenia: novel mechanisms and therapeutic approaches

Novel mechanisms of platelet aggregation: Roles of non-classical beta-3 integrin ligands and fibronectin in thrombosis and hemostasis

**Purpose:** Blood supply risk

Examining the relationship between repeated blood donations in female donors on maternal/neonatal outcomes: a cohort study

**Purpose:** Blood utilization and conservation

Aneurysmal SubArachnoid Hemorrhage - Red blood cell transfusion and outcome (SAHaRA): a pilot randomized controlled trial

Defining disease mechanisms in Immune Thrombocytopenia (ITP) and their association with clinical outcomes

Microfluidic devices to measure the deformability of stored red blood cells

Myocardial Ischemia and Transfusion. The MINT rollover trial

Polymer-based manufacturing tolerogenic miRNA-based therapeutics

Understanding transcriptional and epigenetic control by Gfi1b towards the development of a therapy for sickle cell disease
### Purpose: Transfusion-related acute lung injury

Identification of host cellular immune mechanisms responsible for the initiation and/or modulation of Transfusion Related Acute Lung Injury (TRALI)

Mechanisms of antibody-independent transfusion-related acute lung injury (TRALI)

Transfusion-Related Acute Lung Injury and delayed TRALI: a prospective study in critically ill children

### Canadian Blood Services/CIHR Partnership New Investigator Program

Code sepsis: defining and translating optimal resuscitation and care for children with septic shock

### Intramural Research Grant Program

A multifaceted intervention to optimize red blood cell transfusion practice in two provinces

*Development of a small molecule cocktail for the expansion of cord blood stem cells*

*Evaluating the role of donor characteristics and blood component manufacturing on the quality of red cell concentrates*

Human monoclonal CD44 antibodies as potential IVIg replacements

Influence of eryptosis and storage on transfused red cell recovery in sepsis

Monoclonal antibodies with anti-D-like activity in the amelioration of murine immune thrombocytopenia (ITP)

Monovalent Fc receptor blockade using novel fusion proteins: The road towards an IVIg replacement

Optimization of monoclonal anti-erythrocyte antibodies for improved immunoprophylaxis in a murine model

Plasma versus plasma protein concentrate transfusion for coagulopathic control

Role of blood component manufacturing on microvesicle-induced transfusion-related immune modulation
**TAD-POL (Transfusion-Associated-Dyspnea: Prospective observation and laboratory assessment)**

**MSM Research Grant Program**
A longitudinal analysis of behavioural and biological risk among men who have sex with men in metro Vancouver

ACB and MSM - it’s not an oxymoron: A research project that explores the importance of ACB people in MSM blood donation research

*Allowing MSM to donate in the context of pathogen reduction of blood components: mathematical modeling of the risk of HIV, HBV and HCV transmission through transfusion*

Assessing alternative CBS blood donor deferral screening policies for men who have sex with men

Assessing unintentional creation of bias against MSM as a function of exposure to blood donor screening questionnaire and assessing sexual behaviour risk factors of those successfully passing blood donor screening

Attitudes, behaviours, and acceptability related to current and future blood donation policy: A qualitative study of gay, bisexual, and other men who have sex with men in Vancouver, Toronto, and Montreal

Estimating the probability of HIV risk in MSM donor policies through biobehavioural and mathematical modelling studies

Évaluation de l’acceptabilité et de la faisabilité d’un programme de dons de plasma destiné au fractionnement, pour les hommes ayant des relations sexuelles avec d’autres hommes de la communauté gaie montréalaise

*Feasibility of implementing source plasma donation with alternative eligibility criteria for men who have sex with men*

Mathematical modeling - comparing HIV risk between MSM donation strategies

*Mathematical Modelling – Comparing HIV Risk Between MSM Donation Strategies*

Operational impact of individual risk assessment options
Safety, Acceptance, Fairness & Equality (SAFE project): Acceptable risk and donor selection

Sex Now 2018: A national survey on blood donation and undiagnosed blood borne infections

*Understanding general population impact and opportunities from changes to blood donation deferral screening and criteria for men who have sex with men*

**James Kreppner Award Program**

The role of stakeholder trust in OTDT policy change: public and professional attitudes to ante-mortem interventions in organ donation

*Of skin, sperm, and blood: A comparative analysis of exemptions in Canadian human tissue legislation*

Organ donation in Canada: Engaging with stakeholders and proposing solutions to current legal and ethical challenges

**Kenneth J. Fyke Award Program**

Developing a Canadian policy on the responsible use of umbilical cord blood for proven indications in regenerative therapy

**Blood Efficiency Accelerator Award Program**

A program to minimize preventable and inappropriate blood product transfusions in liver surgery

*Assessment of the quality of granulocyte concentrates to optimise their use in transfusion therapy*

*Blood product demand forecast modeling using clinical predictors*

*Blood utilisation epidemiological profile to evaluate appropriate use (BLUE)*

Feasibility in Canada for a non-invasive prenatal testing using single-exon fetal RHD determination

*Management of iron deficiency anemia in the pediatric emergency department: Pilot study of red blood cell transfusion IV iron therapy*
Optimizing rejuvenation to improve the product quality of pathogen-inactivation and γ-irradiated red cell concentrates

Rapid verification variant D phenotype by genotyping in a regional laboratory

**Small Projects Funding Program**

National evaluation of platelet transport bags to reduce wastage

**Transfusion Medicine Fellowship Program**

McMaster Centre for Transfusion Research

University of Toronto QUEST Research Program

**National Training Programs**

**Postdoctoral Fellowship program**

Development of a small molecule-based stem and progenitor expansion protocol to accelerate engraftment after cord blood transplantation

Donor characteristics and the quality of red cell concentrates

**Novel detection strategies for new platelet ligands and anti-platelet antibodies**

The mechanism of action of monoclonal antibody blends in the potential replacement of anti-D in HDFN

DNA aptamers for detection of red blood cells destined for rapid post-transfusion clearance

**Graduate Fellowship Program**

Anti-GPIb mediated thrombocytopenia: implications for IVIG and other therapies

Evaluation and improvement of cold stored platelets
### Impact of storage on the function of cord blood hematopoietic stem and progenitor cells

### Improving pathogen inactivation: the dengue virus-induced platelet proteome

*Investigating a new class of small molecule ice recrystallization inhibitors for red blood cell cryopreservation*

### Investigating the mechanism of anti-CD44 antibody amelioration of IVIg-treatable disease

### Novel cell-surface engineering methods to increase immune-tolerance of allogenic cell transplantation

### Platelet desialylation: novel mechanisms of platelet clearance and immune tolerance

### Recombinant Fc multimers to replace IVIG

### Small molecule ice recrystallization inhibitors as cryo-additives for red blood cell cryopreservation

### Study of the mechanisms implicated in platelet microparticle internalization by blood cells

### Synthesis of carbohydrate derivatives for the improvement of red blood cell storage

### CIHR Health System Impact Fellowship Program

**Process evaluation of the Canadian Blood Services' cord blood bank: managerial and donor perspectives**

### Research Laboratory Support Program

**Blood product manufacturing and storage research laboratory**

**Operational research engineering laboratory**

**Infectious diseases and immunopathology research laboratory**

**Platelet biology and quality research laboratory**
Immune biology research laboratory

Platelet physiology and immunology research laboratory

Stem cell development research laboratory

Infectious diseases and plasma protein research laboratory

Microbiology development research laboratory

Immune modulation research laboratory

Plasma and plasma protein research laboratory

Product and Process Development Program

Deepening the understanding of our products and the processes used to manufacture them

30-minute rule plasma study

Cord blood and registry composition analysis project

Measuring specific gravity of blood components

Plasma Freezing

Platelet LR filter from various manufacturers performance comparison project

Pooled platelet product production (dose) simulator project

Post-thaw HSC product quality attributes CBU to segment correlation project

‘Technical’ Lessons Learned from the Equipment RFP 2PD0143 Project

Understanding impact of time to test on product quality attributes for frozen plasma products project
Understanding of impact of freezing profile / freezing time (i.e. rapid versus slow cool) on plasma quality project

Understanding of, and feasibility of predicting changes in, product quality attributes (e.g. hemolysis and free iron release) during red cell storage in various anticoagulant and additive solution combinations (e.g. CPD-SAGM, CP2D-AS3)

Understanding the impact of pre-processing delay on the potency of cord blood units

‘Where are the platelets?’ – understanding causes for platelet production yield and quality attribute variation in order to identify opportunities to better optimize the process project

**Developing new or next generation products**

Blood bag (collection) RFP circa 2018/19

*Freeze dried plasma production technology development project in collaboration with Terumo*

*Leukoreduced (platelet sparing) cold stored whole blood produced using Terumo Imuflex WB-SP collection set*

*Long shelf life cold stored platelets in plasma and platelet additive solution (including NDQCT) exploratory project*

Modeling platelet unit doses after introduction of 7 day platelets and non-destructive testing project

Neo-pack and Pedi-pack divided red cell units for neonate and pediatric transfusion feasibility project

Platelet pooling bag RFP

Platelets in SSP+ platelet additive solution assessment study - Product quality perspective (including NDQCT verification)

*SSP+ platelet additive solution (apheresis plts) assessment study – product quality perspective*

SSP+ platelet additive solution assessment study – safety perspective

**Improving current generation products and the processes used to manufacture them**
Apheresis plasma project

Bringing confirmatory follow-up testing - positive BacT/ALERT cultures in-house project

Cryopreservation and characterization of DLI products

Evaluation of alternative donor skin disinfection methods

Evaluation of Rapid API for In-House Sterility Testing

Extending freezing time for frozen plasma

Increased SP Volume

Modeling and simulation of the introduction of ferritin testing and its impact on donations

NDQCT for platelet products project

NDQCT for RED CELL products project

NDQCT for red cell products supplementary studies in support of the parent 2PD red cell NDQCT project

NDQCT RBC study – safety perspective in support of the parent 2PD red cell NDQCT project

Optimization of the flow cytometry staining protocol for post-thaw cord blood samples

Post-Implementation Changes and Work Flow Improvement to In-House Sterility Testing in the C4I Micro Lab

Support the sterility stem cells BACTEC validation project

Updates to BacT Proficiency Testing Process

Warm versus Cold

Enabling the Product and Process Development group
2PD project portfolio database project

2PD test method validation project: standardization and qualification of test assays in C4I labs supporting 2PD group projects

Acquisition and installation of ACP-215 blood processing technology in 2PD project

Database design and development

eProgesa for netCAD assessment and options project

Evaluation of Vitek 2 Compact for bacteria identification

Increase the netCAD Donor Base

*netCAD2 – a blood4research 'east' applied development facility*

*Ottawa development labs relocation evaluation*

*Prepare & deliver the understanding plasma short course for 2PD and SCPM Staff*

RAM Initiative

*Transitioning In-House Sterility Testing to Testing Group*

**On Demand Unit Investigation**

*Blood box TID lap shear & 180 degree peel strength testing*

*Dartmouth Buffy Coat Indices Confirmation*

*Dartmouth large B2 Red Cells*

*Oak Pooled Platelet Investigation*

Platelet and red cell testing from Cold B1s made at a production site
Centre for Innovation
June 21 2019

Platelet rec'd from Brampton with Clot in pool

Query Plastic in Red Cell Unit

Red Cell Unit Investigation from Pembroke

Units collected with expired packs on QER 43-17-109203

Volume reduced platelet from Calgary

Other

Modeling and simulation education and training

Blood transfusion sets project

Contribute to the WHO RBC bacteria repository study

Extended shelf life platelets - post implementation optimization modelling

Hub and spoke platelet re-distribution simulator project

New Brunswick logistics modelling (redux)

Education Programs

BloodTechNet Award Program

An innovative digital strategy for dissemination of Choosing Wisely Canada guidelines in transfusion medicine

Applying educational tools of knowledge translation to reduce the inappropriate use of plasma in Ontario: a collaboration between Canadian Blood Services and Ontario hospitals

Better blood transfusion - Phase two
Development of internet modules for serology curriculum delivery

PID (Primary Immune Deficiency) Toolkit App

Podcast for FNAIT and ICTMG red cell specifications for hemoglobinopathies guidelines

Social media for knowledge translation and education 3 (SoMe-KTE3): Transfusion, thrombosis, and hemostasis

Stem Cell Transplantation Multimedia Toolkit

Education Research Grant

An evaluation of learner perspectives and outcomes following completion of the transfusion medicine area of focused competence

Centre for Blood Research program support collaboration

Clinical Guideline Development Program

Use of Albumin

Hemolytic Disease of the Newborn

Use of Platelets

Fetal and Neonatal Alloimmune Thrombocytopenia (FNAIT)

Hemoglobinopathies

External Funded Grants and Awards

Inhibiting ice recrystallization - a strategy to enable cellular therapies
Using small molecule ice recrystallization inhibitors to mitigate ice formation in complex tissue models of liver preservation.

Aneurysmal Subarachnoid Hemorrhage - red blood cell transfusion and outcome (SAHaRA): A randomized controlled trial

An innovative trial assessing donor sex on recipient mortality (iTADS)

Scalable production, delivery and assessment of human pseudosclots for research and clinical applications

Using operational research methods to improve decision making in Canada’s blood supply chain

Efficacy of Isoagglutinin-depleted IVlg to ameliorate ITP and RA in mouse models

Testing patient samples of suspected alloantibodies for potential clinical significance using a monocyte monolayer assay

Refreshing the regulatory approach to ensuring the safety and efficacy of blood transfusion products

The PSI domain of beta3 integrin: a novel mechanism and target for antithrombotic therapy

A novel approach to treating hemorrhage with mesoporous bioactive glasses

Can Tamiflu be used to treat bleeding disorders?

Apolipoprotein A-IV and platelet function: novel links with thrombosis, inflammation, and atherosclerosis

2017–2018 CIHR Foundation Grant Thrombosis and Thrombocytopenia: Novel mechanisms and treatments

The PSI domain of beta3 integrin: A novel mechanism and target for antithrombotic therapy

Proof-of-Concept: A Pilot Safety, and Efficacy Comparative Trial of Oseltamivir versus Placebo for Immune Thrombocytopenia

Inhibiting ice recrystallization - a strategy to enable cellular therapies
Translating novel factor Xa function to treat thrombosis

Polymer-grafted allogeneic leukocytes and systemic immune modulation

Targeting factor XIa for improved antithrombotic therapy
## Appendix II: Knowledge products and their impact

### Summary of peer-reviewed and non-peer-reviewed publications

<table>
<thead>
<tr>
<th>Peer-reviewed publications</th>
<th>163</th>
</tr>
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<tbody>
<tr>
<td>Journal Articles</td>
<td>115</td>
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<tr>
<td>Review Articles</td>
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<tr>
<td>Clinical Guidelines</td>
<td>6</td>
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<tr>
<td>Comment/Letters/Editorials</td>
<td>13</td>
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<tr>
<td>Books/Book Sections</td>
<td>8</td>
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<tr>
<td>Canadian Blood Services Circular of Information</td>
<td>6</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Non-peer-reviewed publications</th>
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</thead>
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<tr>
<td>Canadian Blood Services Website Publications</td>
<td>56</td>
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<tr>
<td>Technical Reports</td>
<td>26</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
</tr>
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</table>

**Total number of publications** 246
Summary of h-index factor analysis

Notes: i) H-index factors measured using Google Scholar on April 9, 2019. ii) Mean H-index calculated used H-index factors from the 16 core investigators. Core investigators include (Jason Acker, John Blake, Donald Branch, Dana Devine, Steven Drews, Margaret Fearon, Mindy Goldman, Alan Lazarus, Heyu Ni, Sheila O’Brien, Nicolas Pineault, Ed Pryzdial, Sandra Ramirez-Arcos, Mark Scott, William Sheffield, and Kathryn Webert). iii) H-index is a single bibliometric indicator that is a measure of both the productivity and impact of published work. H-index is an indicator of research users being aware of and valuing published research evidence. Average H-index for Canadian university professors in the biological sciences is 10.6.
Publications’ Details

Author Legend: Bold – Centre for Innovation investigators and senior staff; Canadian Blood Services medical directors; Directors of transfusion medicine research programs receiving funding via Transfusion Medicine Research Program Support Award.

Journal Articles


27. Gantioqui J, Stevic I, Atkinson H, Chan AKC. Rivaroxaban and dabigatran did not affect clotting profiles in plasma reconstituted with varying levels of autologous platelets to the same degree as heparin when evaluated using thromboelastography. *Blood Coagul Fibrinolysis* 2018; 29: 521-7.


111. Warkentin TE, Morin P-A, Heddle NM. Neutropenia and monocytopenia in recurrent anaphylactoid reactions after red blood cell transfusions in a woman with immunoglobulin a (IgA) deficiency and anti-IgA. *Transfusion* 2018; 58: 2320-5.


**Review Articles**


5. Leach Bennett J, Devine DV. Risk-based decision making in transfusion medicine. *Vox Sang* 2018; 113: 737-49.


**Clinical Guidelines**


Comments/Letters/Editorials


**Books/Book Sections**


5. Ning S, **Heddle NM.** Clinical outcomes and red blood cell storage. In *Hematologic Challenges in the Critically Ill*. Edited by Shander A, Corwin HL. Published in Cham by Springer International Publishing, 2018.


**Canadian Blood Services Circular of Information**


**Canadian Blood Services Website Publications**

1. **Acker J, Branch D.** Concentré de recherche: Où l’on optimise un test de laboratoire pour déterminer la compatibilité entre donneurs et receveurs. *Blood.ca website* 2018.


29. **Ni H.** Concentré de recherche: Important rôle de la GPibα, une protéine plaquettaire, dans la régulation de la production hépatique de thrombopoïétine. *Blood.ca website* 2018.

30. **Ni H.** Research Unit: Platelet protein GPibα plays an important role in regulating platelet-mediated production of thrombopoietin by the liver. *Blood.ca website* 2018.


44. **Poon MC, Goodyear MD, Rydz N, Lee A.** Concentrates for hemostatic disorders and hereditary angioedema. In *Clinical Guide to Transfusion*. Edited by **Clarke G, Chargé S.** Published in ProfessionalEducation.blood.ca by Canadian Blood Services, 2018.


**Technical Reports**


Other