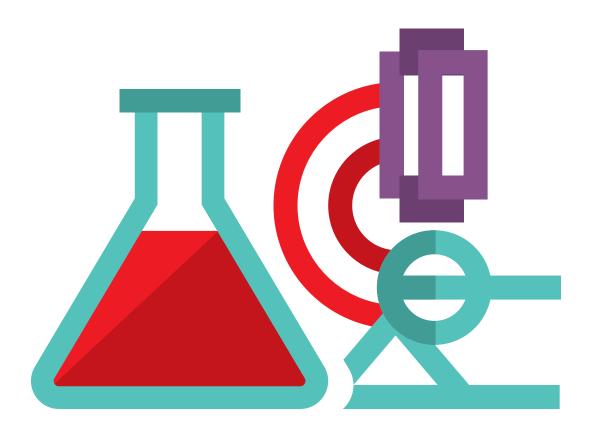


BLOOD PLASMA STEM CELLS ORGANS & TISSUES

Centre for Innovation Annual Progress Report

2020-2021



August 20, 2021

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Opening letter

Dear reader,

It is our pleasure to present the 2020-2021 Canadian Blood Services Centre for Innovation annual progress report. This was a year of unprecedented challenges as the COVID-19 pandemic impacted every aspect of our business. But in the Centre for Innovation's response to these challenges, what emerges is a story of adaptability, and a willingness to go above and beyond to help every patient, match every need and serve every Canadian. In this report, we are proud to share with you the many examples of agility and resilience, collaboration and partnership, innovation and excellence that marked the Centre for Innovation's outstanding year.

Highlights include the Centre's work to inform public health decisions with seroprevalence studies as part of the federal COVID-19 Immunity Task Force and our contributions to CONCOR clinical trials to test the effectiveness of convalescent plasma as a treatment for COVID-19. All the while, our critical work to support a safe, effective, and responsive blood system continued unabated. We are proud of the resilience and dedication displayed by the Centre for Innovation staff as they adapted our research, development, training, and education programs in a myriad of ways to ensure success and impact.

We are deeply grateful for the ongoing support we receive from our funders, Health Canada Strategic Policy Branch and the provincial and territorial ministries of health, and our partners and colleagues across the transfusion and transplantation communities. This year, we are once again inspired by the achievements of our network in rising to the challenges and working together to support Canada's Lifeline in its vigilant stewardship of the Canadian blood system.

Sincerely,



Dr. Isra Levy

VICE PRESIDENT, MEDICAL AFFAIRS AND INNOVATION

CANADIAN BLOOD SERVICES



DR. CHANTALE PAMBRUN DIRECTOR, CENTRE FOR INNOVATION CANADIAN BLOOD SERVICES

2020-2021: Year in review

Supporting the pandemic response

- Supported Health Canada-approved clinical trials to explore COVID-19 convalescent plasma as treatment option for COVID-19 patients (pages 8-9).
- Supported the COVID-19 Immunity Task Force by testing over a quarter of a million samples to generate data on the presence of COVID-19 antibodies in the Canadian population (page 14).
- Facilitated several impactful provincial and federal partnerships to inform public health and support innovation (page 13).
- Scoped the literature to provide relevant and timely information to support organizational decision making (page 10).

Introducing new blood components

 Developed a process to manufacture INTERCEPT pathogen-reduced platelets within Canadian Blood Services. This new pathogen-reduced blood component will soon be implemented for the benefit of patients, pending Health Canada approval (page 15-16).

Informing blood utilization

- Evidence from the FIBRES trial, led by University of Toronto QUEST, has led many clinicians to switch from cryoprecipitate to fibrinogen concentrate, leading to a large decrease in units of cryoprecipitate issued to Canadian hospitals (page 25).
- Evidence from the McMaster Centre for Transfusion Research shows that an oral medication that stimulates the production of platelets, called eltrombopag, is an effective alternative to IVIg to control bleeding in patients with immune thrombocytopenia needing surgery (page 24).
- Research has shown that cold storage of leukoreduced red blood cells for 21 days or more is sufficient to inactivate T-cells suggesting an alternative method to irradiation for the production of a product that keeps patients safe from Transfusion-Associated Graft versus Host Disease and improves blood inventory management (page 25).

Improving donor selection

- Changes to the malaria travel risk deferral period and the diabetes criteria were approved by Health Canada and implemented, increasing the number of eligible blood donors (page 22).
- Based on research findings, the position of the men who have sex with men screening question within the donor screening questionnaire was changed, limiting unintentional negative bias in donor screening (page <u>23</u>).
- A research-informed process to expand donor eligibility for gay, bisexual and other men who have sex with men to donate source plasma was developed and is pending Health Canada approval (page <u>23</u>).

Guiding clinical practice

- Recommendations developed by the ICTMG on red blood cell specifications for patients with hemoglobinopathies were endorsed by the National Advisory Committee on Blood and Blood Products (NAC) (page 37).
- Evidence informed the NAC statement on Fibrinogen Concentrate Use in Acquired Hypofibrinogenemia (page 25).
- Supported the training of more than 300 health care professionals to transfusion best practices through a national collaboration with Transfusion Camp (pages 33-34).
- Research led by University of Toronto QUEST informed a Using Blood Wisely program to improve red blood cell utilization in Canada (page <u>26</u>).

Engaging and disseminating

 Supported 160 investigators through competitive funding and distribution of products and data for research. The Centre's research and education network published 210 peer-reviewed publications and 33 technical reports to support knowledge dissemination and decisionmaking. Staff delivered more than 330 presentations and engaged with more than 3,300 attendees at knowledge exchange and educational events. In this report, we highlight the activities and achievements of Canadian Blood Services' Centre for Innovation over the past fiscal year (1 April 2020 – 31 March 2021). We begin by introducing the Centre and its members, then provide stories that highlight the Centre's response to the COVID-19 pandemic, our innovative research and development work to meet changing patient needs, and our ongoing work to support a safe, effective and responsive blood system. We describe our training, education, and engagement activities and conclude with a governance and operations section which includes a summary of the Centre's outputs and outcomes.

Throughout the report, the names of Canadian Blood Services staff, including our scientists, medical experts, and epidemiologists, as well as the names of organizations and individuals receiving funding from the Centre for Innovation, are bolded.

Referenced publications available online are hyperlinked in the text. For a complete list of the Centre for Innovation's 2020-2021 publications, see Appendix II.

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The Centre for Innovation

The Centre for Innovation works along the entire "life-to-life" continuum, from donors to recipients, to serve <u>Canada's Lifeline</u>. We support Canadian Blood Services to continuously improve blood components and products, and their utilization to **help every patient**, **match every need**, **and serve every Canadian**.

Our Team

We are a world-class team of discovery, development and social scientists and medical experts, supported by a dedicated administrative team. Housed within Canadian Blood Services' Medical Affairs and Innovation division, our unique position at the interface between academic discovery and operational implementation allows us to optimize our response to the needs of Canada's blood system.

Our Pillars

Research

Discovery research provides new insights into blood, blood products, plasma, and stem cells. Social science research supports donation and donor engagement.

Our Network

We engage with a broad research and education network of multidisciplinary partners both within Canadian Blood Services and in academic institutions, industry, and government. Our reach is national and international.

Connect with us and learn more

Product and process development

Applied development work improves both the blood and stem cell products we supply, and the technologies and processes used to produce them.

Knowledge mobilization and strategic alliances

Research and training are supported through competitive funding programs and knowledge mobilization activities. Health care professionals are supported through education and clinical guideline development.





Contact us at <u>centreforinnovation@blood.ca</u> Subscribe to our newsletter <u>blood.ca/research/#subscribe</u> Read our Research.Education.Discovery blog: <u>blood.ca/RED</u> Explore our education resources: <u>profedu.blood.ca/</u>

Awards and appointments

In 2020-2021, the Centre for Innovation welcomed new research appointments, and our staff and research and education network received national and international recognition.

Research and leadership appointments

Dana Devine, Canadian Blood Services' chief scientist, was appointed director of the <u>Centre for Blood Research</u> at the University of British Columbia. This new role for **Devine** deepens Canadian Blood Services' lasting collaboration with the Centre. **Devine** was also elected president-elect of AABB, an international association representing individuals and institutions in the fields of transfusion medicine and biotherapies.

The Centre for Innovation welcomed **Celina Montemayor-Garcia** as a new medical officer. **Montemayor-Garcia**'s expertise in genomics will support the Centre for Innovation in its precision medicine journey. In 2020, **Montemayor-Garcia** was elected At-Large Director to the AABB Board of Directors.



Peter Schubert was appointed principal manager of the Centre for Innovation Blood4Research Facility and senior scientist. **Schubert** applies his expertise in biochemistry and proteomics to improve the safety of blood components and products. **Schubert** is cross-appointed as a clinical professor with the department of pathology and laboratory medicine at the University of British Columbia. Prior to this appointment, **Schubert** had been with the Centre for Innovation for more than 12 years, working under **Devine**'s leadership,

Kelly Holloway was appointed a Canadian Blood Services scientist within the Centre for Innovation. **Holloway** studies the political economy of biomedical innovation and explores how donor behaviour is situated in political, social and economic contexts. **Holloway** has a cross-appointment as an assistant professor at the Institute of Health Policy, Management and Evaluation at the University of Toronto.





The Centre for Innovation appointed or reappointed the following Canadian Blood Services Adjunct Scientists in support of our research network:

- Mel Krajden (University of British Columbia)
- Christine Cserti-Gazdewich (Princess Margaret Cancer Centre)
- Ed Conway (University of British Columbia)
- Andrew Beckett (University of Toronto)
- Jeannie Callum (Queen's University and University of Toronto)
- Andrew Shih (University of British Columbia)



KELLY HOLLOWAY

Recognition and honours

The Canadian Society for Transfusion Medicine (CSTM) recognized Canadian Blood Services senior scientist **Alan Lazarus** with the 2020 Ortho Award, awarded to a CSTM member who has provided a major service or innovation in transfusion medicine. **Lazarus**' significant work examined the mechanism of action of IVIg in such diseases as immune thrombocytopenia (ITP), as well as other autoimmune states.

Canadian Blood Services' senior scientist **Heyu Ni** was appointed a Fellow of the Canadian Academy of Health Sciences. <u>The appointment</u> provides visibility to the importance of transfusion science research to the health of Canadians. **Ni** was also honoured with the Canadian Society of Atherosclerosis, Thrombosis and Vascular Biology (CSATVB) and the CIHR Institute of Circulatory and Respiratory Health (CIHR-ICRH) 2021 Distinguished Lecturer / Scientific Excellence Award in Blood and Blood Vessel Sciences. This award recognizes his extraordinary achievements in the field of blood and blood vessel sciences, including discoveries and methods that have fundamentally impacted diagnosis and therapy for bleeding disorders and significantly advanced the field of blood sciences.

The International Society of Blood Transfusion (ISBT) recognized **Devine** with the ISBT Award for her significant contribution to transfusion medicine and science, particularly her contributions in education. **Devine** served as longtime editor of ISBT journal *Vox Sanguinis* and contributed to many ISBT congresses.

Montemayor-Garcia was honoured with the 2020 AABB President's Award to recognize her outstanding work with the Cellular Therapies Spanish language program and her efforts to promote increased visibility for AABB's Spanish-speaking membership group. The President's Award recognizes extraordinary public service and contributions by an individual or organization in the health care arena.

Canadian Blood Services senior scientist **Jason Acker** was selected as the recipient of the University of Alberta's Faculty of Medicine and Dentistry's Tier 1 Basic Science Award for Excellence in Mentoring Graduate Students and Postdoctoral Fellows.

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Research & development highlights

A rapid research response in a time of crisis

In a time of crisis, keeping on top of emerging data is critical to shaping a response. Also critical is the ability to mobilize experts that together can bring forward innovative solutions. During 2020-2021, the Centre for Innovation was proud to support Canadian Blood Services' response to the pandemic. In addition, the Centre was involved in numerous initiatives that informed and supported the public health response to the pandemic.

Facilitating clinical trials

Providing convalescent plasma

Canadian Blood Services and Héma-Québec supported several Health Canada-approved clinical trials exploring COVID-19 convalescent plasma as a safe and effective treatment option for COVID-19 patients. The blood operators rallied to establish processes to recruit and collect convalescent plasma from recovering COVID-19 donors. At Canadian Blood Services, the Centre for Innovation Blood4Research Facility staff were mobilized to support the initiative. In total, Canadian Blood Services recruited 4.291 convalescent plasma donors and prepared 2,099 convalescent plasma units. 780 units were distributed to Canadian physicians caring for COVID-19 patients enrolled in the trials and more than 1,000 units were distributed to researchers to support COVID-19 research initiatives.

Convalescent plasma is collected from someone who has recovered from a virus as their plasma contains antibodies to fight the virus. It is believed these antibodies could help others with the same virus. Randomized, controlled trials, such as the ones conducted with COVID-19 convalescent plasma, are the only way to conclusively determine how effective this treatment may be.

The speed at which these trials were stood up was unprecedented, thanks to extraordinary efforts by a multidisciplinary team including experts within the transfusion research network - a thriving community with strong connections to the Centre for Innovation. The trials' lead investigators included Donald M. Arnold, the McMaster Centre director of for Transfusion Research (MCTR) and Jeannie Callum, lead for the QUEST transfusion research program at the University of Toronto. Both MCTR and **QUEST** are supported by competitive funding from the Centre for Innovation. Canadian Blood Services' medical officer and MCTR member, Michelle Zeller, and several Centre for Innovation scientists were part of the clinical trial teams and Canadian Blood Services chief scientist, Dana Devine, was a member of the trial's steering committee.

Knowing how much SARS-CoV-2 antibody is in a convalescent plasma donation, and how effective those antibodies are at neutralizing the SARS-CoV-2 virus are an important part of understanding potential effectiveness in reducing intubation or death in COVID-19 patients. Using a test called the Plaque Reduction Neutralization Test 50 assay, Canadian Blood Services associate director of microbiology, **Steven Drews** and colleagues showed that <u>levels of neutralizing antibodies drop over time</u>, and that blood operators cannot infer the levels will remain high in repeat plasma donors 3-4 months after onset of COVID-19 symptoms.

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CONCOR-1

Between April 2020 and January 2021, the CONCOR-1 trial (CONvalescent Plasma for Hospitalized Adults with Acute COVID-19 Respiratory Illness) enrolled and randomized 940 patients at 73 hospitals in Canada, the U.S. and Brazil. After an interim analysis indicated that convalescent plasma treatment was unlikely to be an effective treatment compared to the standard of care in hospitalized patients, the trial was halted. Although the analysis showed no safety concerns with the use of convalescent plasma, its benefit remains to be investigated. Could it be an effective treatment in the earlier stages of COVID-19, or in younger or immunocompromised patients? How does variation in antibody levels affect treatment efficacy? Are there promising applications for treating other diseases, like Ebola?



Find information about CONCOR1 at <u>https://concor1.ca/</u>

Lessons learned

The convalescent plasma trials have shown how blood operators can rally together to rapidly establish support for clinical trials — valuable collaborations that may be vital to supporting future trials. Moreover, valuable lessons were learned that can help blood operators prepare for future pandemics. The International Society of Blood Transfusion (ISBT) Working Group on COVID-19 published <u>a paper</u> summarizing the lessons learned from procuring and administering COVID-19 convalescent plasma. The authors, who included **Devine**, identify several areas to help improve future pandemic management and stress the need for flexibility and adaptability when dealing with a pandemic.

Centre for innovation scientist, **Kelly Holloway**, and her collaborators at the University of Toronto were awarded funding from the Social Sciences and Humanities Research Council and Mitacs to review and understand the role and experience of blood operators as they navigated the convalescent plasma clinical trials landscape. The project will provide insights to inform the involvement of blood operators in future clinical trials.

Read the R.E.D. blog post: <u>Understanding the</u> politics of clinical trials in a pandemic.

A resilient blood system

Early insights on transfusion risk

Not long after the first cases of COVID-19 were reported in Wuhan and before the World Health Organization declared COVID-19 a pandemic, **Devine** penned <u>an editorial</u> in the journal *Transfusion Medicine* that reviewed the impact of severe acute respiratory syndrome (SARS) in Canada. Her review covered the many lessons learned from the SARS outbreak in 2003, including key considerations for protecting Canadian Blood Services staff and steps taken to mitigate risk to the blood supply. As blood operators prepared for the impact of COVID-19 and as Canadian Blood Services evolved its business continuity plan, the review offered instructive reminders.

Data science

Drews and Canadian Blood Services associate director of epidemiology **Sheila O'Brien** led a team who gathered and analysed data to evaluate the risk to the sufficiency of supplies. Their work focused on modeling the risk of donors visiting a donor centre while infected with SARS-CoV-2, or the risk of collecting a blood donation containing SARS-CoV-2. As the pandemic evolved and new concerns emerged, the team was there to provide the evidence needed to inform ongoing decision-making at Canadian Blood Services.

Read the feature story: <u>How we're using data</u> science to prepare for the pandemic.

Scoping the literature

A primary concern during this pandemic was the possibility that SARS-CoV-2 could he transmissible by transfusion and create risk to blood safety. Drews and O'Brien collaborated with Héma-Québec on a literature review to identify studies that reported detection of SARS-CoV-2 RNA in blood or its components, or that reported on lab studies showing infection of blood components. The evidence showed there had not been a single reported case of transfusiontransmitted SARS-CoV-2, suggesting the risk remained theoretical.

With colleagues from Quebec, **Drews** and **O'Brien** also <u>summarized published cases</u> of transplantation of cells or organs from donors infected with SARS-CoV-2 and concluded that the evidence collected until January 2021 raises

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the possibility of SARS-CoV-2 infection and replication in some cases, which makes it impossible to exclude transmission through transplantation.

Another challenge has been the sheer volume of published literature. **Mindy Goldman**, medical director at Canadian Blood Services, was part of <u>an international study</u> published in the journal *The Lancet Haematology* that synthesized expert opinion on the supply and use of blood for transfusion during the pandemic. By developing expert consensus, their study supported transfusion services and hospitals in Canada and around the world as they grappled with the challenges brought on by the pandemic.

Read the R.E.D. blog post: <u>Blood transfusion</u> <u>during the pandemic: strategies in a time of</u> <u>uncertainty.</u>

The Centre for Innovation proudly supported the Canadian Blood Services Continuity Business Management Operational Committee (BCMC). Tasked with managing disruptive events such as the pandemic, the BCMC provides the oversight needed to safeguard ongoing operations at Canadian Blood Services, ensuring the continued delivery of blood and services. In 2020-2021, many members of the Centre for Innovation gave their time and expertise to support the BCMC's invaluable work of keeping Canada's Lifeline flowing.

Blood donation during a pandemic

Donor response to the pandemic

Centre for Innovation scientists, **Holloway** and **Jennie Haw** joined with colleagues from Australia and the Netherlands to provide some <u>early</u> <u>observations</u> on donor and public responses to the pandemic and identify areas for donor research moving forward. Their review suggested the following five areas were most important for research. They are currently collaborating with international colleagues to tackle some of these questions:

1. How are donors and non-donors responding to the crisis and appeals for blood donation, and what motivates them?

2. To what extent will first-time donors responding to specific appeals for blood during the pandemic return, and how can donor retention be encouraged?

3. How might the socially meaningful act of donation mitigate (or not) the negative effects of stay-at-home measures?

4. What are the implications for donors of convalescent plasma?

5. What is the impact of the pandemic on donors and blood collection agencies in low- and middle-income countries?

Donors and the COVID-19 vaccine

After receiving certain vaccines, people may have a waiting period, called a temporary deferral, before they can donate blood. When the global rollout of COVID-19 vaccines began in December 2020, blood operators and their regulators needed to determine whether a temporary deferral was required.

Goldman, with **Drews**, and Canadian Blood Services medical officer and medical health officer for the Fraser Health Authority, **Mark Bigham**, gathered information from multiple stakeholders on the vaccines available in Canada. They examined the known side effects of the vaccines to see if they posed potential concerns to recipient safety. They also assessed whether the vaccines might interfere with transmissible disease testing.

The team reviewed the positions of other regulatory authorities, such as the FDA in the U.S., to understand what deferrals are being implemented elsewhere. Finally, they met with the regulator, Health Canada, to ensure that everyone agreed with the policy being considered.

None of the vaccines being used in Canada contain live attenuated virus or are likely to interfere with transmissible disease testing. While some of the vaccinations cause very rare serious side effects, none have demonstrated risk to transfusion recipients. Therefore, the group advised that donors getting any of the approved vaccines in Canada should be eligible to donate.

Read the R.E.D. blog: <u>COVID-19 vaccines</u> shouldn't stop you from donating blood.



Donors donating blood during a pandemic

Impact on blood donation

Canadian Blood Services' medical officer Aditi Khandelwal looked back on the pandemic's impact on blood donations in Canada. More than one year after the pandemic was declared, data on donor attendance, donor eligibility and donation events paint a picture of a resilient blood system, thanks in part to the dedication of donors.

Read the article: Impact of COVID-19 on blood donation in Canada and **R.E.D. blog post**: The impact of COVID-19 on blood donation in Canada.

Supporting the frontline

Limiting PPE use

For health care staff working in hospitals, the pandemic raised concerns about personal protective equipment (PPE) shortages. One approach to combat these shortages was to reduce the number of bedside visits by staff. This required relocating IV pumps and monitoring equipment to outside of the ICU and extending the tubing used to administer blood transfusion, so staff could monitor patients safely while limiting PPE use.

Centre for Innovation senior scientist, **Jason Acker**, reassured clinical colleagues by examining whether using IV tubing extensions, which tend to be narrower than the tubing used to administer blood, would have an impact. The findings showed that perfusion through extended narrower tubing had no effect on the quality of red cell components. This study provided support for the practice of transfusing red cells through extended length tubing which continued throughout the pandemic in some hospitals.

Testing the limits of expiry

In response to the uncertainty at the beginning of the pandemic regarding blood shortages, **Acker**'s laboratory <u>evaluated red cell quality</u> from day 42 (current standard) to day 49 of hypothermic storage. They investigated 80 red blood cell units and showed that components produced by the red cell filtration manufacturing method at Canadian Blood Services meet Canadian regulatory standards from day 42 to day 49 of hypothermic storage. However, red cell components manufactured using the whole blood filtration method do not. These findings support health care providers and regulatory agencies in their decision making during the COVID-19 pandemic and other crisis situations.

Understanding a new disease COVID-19 and clotting

Centre for Innovation senior scientist **Ed Pryzdial** researches how viruses, including SARS-CoV-2, can affect blood clotting and hemostasis. With **Centre for Blood Research** scientist and Centre for Innovation adjunct scientist, Ed Conway, **Pryzdial** is investigating how the virus that causes COVID-19 triggers clotting. They <u>published a review</u> about the role of the complement system—a system of more than 40 proteins that together play important roles in immunity—in the thrombotic effects of COVID-19.

The complement system can activate inflammation, damage pathogens, and clear away microbes and damaged organisms. Their review notes that many of the clinical manifestations of serious COVID-19 parallel those of other clotting disorders caused by dysregulation of the complement system, suggesting that anti-complement therapies may be a valuable treatment approach for COVID-19. "Clotting and inflammation are closely linked in many conditions. COVID-19 is highlighting that

those processes are part of the same giant, puzzling mechanism," says **Pryzdial**.

Read the feature story: Exploring the mysteries of 'a beautiful system'.

Blood type and COVID-19 severity

<u>A study</u> coauthored by **Devine** looked at critically ill COVID-19 patients in the ICU of two major Vancouver hospitals. Among them, 84 per cent of patients with blood type A or AB needed to be put on a ventilator, compared to 61 per cent of patients with blood type O or B. The most common length of stay in the intensive care unit for patients with blood type A or AB was 13.5 days, while those with type O or B most commonly stayed for nine days.

This finding adds to growing evidence that blood type plays a role in whether someone will get COVID-19 and how bad the infection will be. **Devine** cautions, however, that it seems to be a minor risk factor compared to advanced age or underlying medical conditions. "More research needs to happen to understand this phenomenon better." As noted in <u>a review</u> on behalf of the ISBT COVID-19 working group that **Devine** was part of, there are insufficient data for guiding policy and more studies are needed to verify several of the proposed associations between ABO blood group and disease severity.

Read the feature story: <u>The link between blood</u> type and COVID-19 severity.

Understanding complications from COVID-19 vaccines

Researchers from McMaster University, including **Arnold**, uncovered the mechanism behind a new and perplexing rare clotting disorder associated with the AstraZeneca vaccine, an adenoviral vector vaccine against COVID-19. The research team treated the first patients in Canada to be diagnosed with the clotting disorder that came to be known as vaccine-induced thrombotic thrombocytopenia (VITT). They describe their case studies in <u>an article</u> published in *The New England Journal of Medicine*. Their groundbreaking work led to a lifesaving treatment for people suffering from VITT and a muchneeded diagnostic test.

During the pandemic, Canadian Blood Services formed provincial and federal partnerships; many were facilitated through the Centre for Innovation's Blood4Research Facility.

- The National Microbiology Laboratory (NML) conducted neutralizing antibody assays to qualify convalescent plasma collected by Canadian Blood Services for use in the CONCOR trials.
- The Blood4Research Facility provided the NML with blood to develop reference panels to test plasma. These were shared with other laboratories setting up COVID-19 tests and assay platforms.
- The Blood4Research Facility supported the British Columbia Centre for Disease Control (BCCDC) by collecting blood samples from donors who had other respiratory illnesses. These were used to test for interference with COVID-19 tests the BCCDC were establishing.
- The Blood4Research Facility worked with the National Research Council Industrial Research Assistance Program (NRC IRAP) to support their clients with biological samples to validate COVID-19 tests in development.

Understanding COVID-19 prevalence in Canada

Leveraging Canadian Blood Services' unique position in health care, the Centre for Innovation is gathering data on the presence of COVID-19 antibodies in the Canadian population.

In a research partnership with the COVID-19 Immunity Task Force, Canadian Blood Services and Héma-Québec are supporting the Government of Canada to determine the extent of SARS-CoV-2 infection in Canada. Led by Canadian Blood Services associate director of epidemiology and surveillance, **Sheila O'Brien**, our work to support the COVID-19 Immunity Task Force is the largest national SARS-CoV-2 seroprevalence study in Canada. It leverages Canadian Blood Services' unique donor base and blood testing knowledge to support future health policy decisions by answering questions like:

- Among a "healthy" population, what proportion have been infected with SARS-CoV-2?
- How are infection rates changing over time?
- What are the characteristics associated with SARS-CoV-2 infection?

Read the feature stories <u>COVID-19</u> antibody testing shows few healthy <u>Canadians have had the virus.</u>

and <u>New research project to improve understanding of COVID-19</u> immunity.

Limits in diagnostic testing capacity, test eligibility criteria, and missing cases among people who never seek testing mean COVID-19 case numbers underestimate prevalence of the virus in the population. Seroprevalence studies measure the serum levels of antibodies to SARS-CoV-2, which develop regardless of clinical symptoms. This kind of study is needed to understand the true proportion of people infected with SARS-CoV-2.

Setting up a laboratory at top speed

Setting up and conducting a project of this magnitude with relatively little lead time was no small undertaking. **Craig Jenkins**, then senior manager of the Centre for Innovation product and process development (2PD) group, remembers the urgent call from **Chantale Pambrun**, director of the Centre for Innovation who asked, "What's the likelihood we can test 10,000 samples in the first week?"

The team succeeded in setting up the study in a fraction of the time it would normally take while adhering to a high quality of service. This included transforming a lab that had been slated for closure into a functional space,



(From left to right) Lab team members Valerie Conrod, Stacey Vitali, Andy Tshiula Kalenga and Carissa Kohnen support the work of Canada's Immunity Task Force

acquiring specialized equipment—in some cases retrofitting or reprogramming existing equipment for its new purpose—and training staff.

Between April 2020 and April 2021, Canadian Blood Services tested close to a quarter of a million samples in seroprevalence studies.

Constant adaptation

As vaccines were deployed, the study had to adapt how it tracked seroprevalence since some Canadians had natural infections, and some had immunity from vaccination. Before January 2021, samples were tested using the Abbott Architect assay that detects the nucleocapsid (N) protein of SARS-CoV-2.

Starting in January 2021, the study quickly transitioned to two commercial assays from Roche that detect N antibodies and antibodies to spike (S) protein. Using both assays means it is possible to differentiate between natural exposure to SARS-CoV-2 and vaccine-induced immunity since Canada uses vaccines which produce antibodies to S.

Understanding immunity

Associate director of microbiology, **Steven Drews** received funding from CIHR, with support from Alberta Innovates, to answer questions about

immunity in people who have recovered from COVID-19. **Drews**' study looks at SARS-CoV-2 antibodies using four assays: the Abbott assay and three in-house ELISA assays developed by Anne-Claude Gingras, a collaborator from the University of Toronto. In the first wave of the pandemic, **Drews** and team estimated seroprevalence using two different statistical methods; one combined data from multiple assays and was found to give a better estimate when prevalence is low. One of the in-house ELISA assays was found to have higher sensitivity to detect positive samples than the Abbott assay. The <u>results show</u> that during the first wave, as SARS-CoV-2 antibodies wane over time, the ability for the assays to detect them also diminishes.

The evolution of a pandemic

The Immunity Task Force findings paint a picture of the pandemic in Canada. In the first pandemic wave, overall <u>seroprevalence was low at 0.7</u> <u>per cent</u>. With each successive wave, seroprevalence increased. Results from April 2021 confirm that Canada's overall levels of seroprevalence due to natural exposure remains low (3.2 per cent) while vaccine-induced immunity is estimated to be 23.6 per cent. The data from Canadian Blood Services' and Héma-Québec revealed significant regional variation among and within the provinces in seroprevalence due to natural exposure.

Canadian Blood Services is one of many blood operators around the world leading seroprevalence studies. A <u>report</u> by **Sheila O'Brien** showed that 73 per cent of surveyed blood operators were doing seroprevalence studies to inform public health.

Widening racial and social inequities

By January 2021, data from the study was highlighting a large disparity in seroprevalence showing SARS-CoV-2 infections were growing faster in poorer neighbourhoods and amongst racialized populations. As **O'Brien** notes, "racialized groups and donors living in materially deprived neighbourhoods were more likely to have been exposed to SARS-CoV-2 and the disparities are widening." Data from April 2021 also revealed vaccine inequities. Racialized donors had lower rates of vaccine-induced seroprevalence, as did donors living in the poorest neighbourhoods.

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From lab to bedside: meeting changing patient needs

One of five key focus areas for Canadian Blood Services' 2019-2024 corporate strategy is "Meet changing patient needs by providing lifesaving products and services." From the implementation of pathogen-reduced platelets to the reintroduction of whole blood and the investigation of cold-storage of platelets, these are a few new components being explored by the Centre for Innovation which hold great promise for supporting transfusion practice through enhanced safety and the provision of alternative products for specific clinical settings..

Introducing pathogen-reduced platelets to Canada

Cerus' INTERCEPT Blood System for Platelets is a pathogen inactivation system that makes blood components safer by damaging nucleic acids and preventing the replication of pathogens. This technology was licensed by Health Canada in 2018 and since then the Product and Process Development (2PD) group at the Centre for Innovation has optimized a process to bring pathogen-reduced platelet components to Canada.

Led by **Ken McTaggart**, associate director, product and process development (2PD), the team's biggest challenge was to ensure the input platelet component met very specific INTERCEPT requirements. These meant an input platelet component that differs in two ways from the buffy-coat platelet component currently manufactured by Canadian Blood Services: (1) It contains twice as many platelets (a double-dose, rather than single-dose) and (2) The platelets are



Four units of INTERCEPT pathogen-reduced platelets in a storage incubator at Canadian Blood Services

re-suspended in a platelet additive solution called SSP+ rather than plasma. The double-dose platelet component treated with INTERCEPT is ultimately split into two final single-dose pathogen-reduced platelet components prior to distribution to hospitals.

The double-dose process was developed iteratively at the Centre for Innovation Blood4Research Facility. In particular, the team had to ensure the final platelet components could consistently meet the INTERCEPT requirements for volume, levels of residual plasma, number of platelets and of residual red blood cells. Ultimately, the team had to demonstrate the final pathogen-reduced platelet components were safe and effective.

Compared to standard buffy-coat platelet components currently manufactured by Canadian Blood Services, the INTERCEPT pathogenreduced platelet component has a smaller volume and a higher platelet concentration. It is licensed for storage for up to five days, in contrast to the seven-day shelf life of platelet components currently distributed by Canadian Blood Services. However, the team tested whether a seven-day platelet component would comply with standards, in anticipation of Cerus pursuing Canadian licensure for a seven-day platelet component as it has done in other jurisdictions.

In early 2021, the 2PD process for pathogenreduced platelets was handed over to Canadian Blood Services supply chain, and successfully validated. Pending approval of a Canadian Blood Services' license amendment submission to Health Canada, this new blood component will be first implemented at one of Canadian Blood Services' manufacturing sites in Ottawa. With this implementation, Canadian Blood Services anticipates bringing this new blood component to hospitals served by the Ottawa manufacturing site and their patients in late 2021. Future work for the 2PD team will focus on developing a pathogen-reduced platelet component manufactured from an apheresis collection.



Chantal Couture operates the sterile dockers used to pool seven buffy-coat collections as part of the validation of pathogen-reduced platelets production

Whole blood for trauma patients

Renewed interest in whole blood transfusion for trauma patients – specifically use of cold stored, low-titre group O, whole blood – has prompted a need to characterize and standardize whole blood, and better understand its safety profile. In 2020-2021, Centre for Innovation senior scientist and 2PD team member, **Sandra Ramirez-Arcos**,

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conducted a pilot study investigating bacterial survival and growth in whole blood. The results of this study informed the design of a larger study now underway at Canadian Blood Services which evaluates the safety risks associated with this new component. Specifically, it is important to understand the risk of bacterial contamination following manufacturing and storage of whole blood as compared to red blood cell components that are also stored at refrigerated temperatures.

Chief scientist, Dana Devine, led a team that included associate director of research and senior scientist William Sheffield and senior scientist Peter Schubert, to study the potential impacts of pathogen inactivation technologies on blood function. Simulating trauma whole transfusion scenarios in a research laboratory setting showed that pathogen inactivation treatment has a negative impact on whole blood clot formation - a function that is important for preventing blood loss in trauma patients. Adding fibrinogen partly corrected the poorer clot formation. This advances study our understanding of the potential impacts of using pathogen inactivation technologies with whole blood - a promising technology that is not yet licensed for use in Canada.

Cold-stored platelets

Devine's laboratory, in collaboration with colleagues at the University of Colorado, looked at another next generation blood component: cold-stored platelets. Currently, platelet components are stored at room temperature as cold-stored platelets become activated and are quickly cleared from circulation after transfusion. However, the activation of platelets may be beneficial in certain clinical scenarios, for example, in trauma situations when a patient is actively bleeding. **Devine**'s <u>study</u> compared the impact of storage temperature and cold agitation

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on platelet function. They correlated these with metabolomics and lipidomics analyses to build a picture of the oxidative status of cold-stored platelets and highlight important metabolites that may contribute to the function of cold-stored platelets. A development study looking at bacterial growth in cold stored platelets is also underway. These studies will inform the clinical indications for this special platelet component and the safety risks associated with them.

The promise of genomics

Next generation sequencing makes it possible to sequence many millions of DNA molecules at the same time and at a relatively low cost. **Celina Montemayor-Garcia** is an expert in next generation sequencing and applies this powerful technology to blood group genotyping.

One of the technology's biggest challenges is the sheer volume of data it generates. In trying to illustrate just how much data is generated from sequencing one genome **Montemayor-Garcia** notes, "It's so much data that it would be equivalent of reading 45,000 scientific papers!" Another challenge is the time needed to store, back-up and analyse the data. **Montemayor-Garcia** turned to unlikely collaborators who helped her find a solution. "I met with software coders from the Silicon Valley in California, and it turns out the graphical processing units designed by the video game community to process a lot of pixels very quickly is also ideal for processing vast amounts of genomic data," she says.

Montemayor-Garcia predicts that, although next generation sequencing for blood group typing is still in development, its application to transfusion medicine is just around the corner. "We already have the tools for sequencing, but we need to develop a workflow to translate the information into a blood bank-actionable item. I'm here to help Canadian Blood Services move in that direction."



Montemayor-Garcia holds the small and portable yet powerful computer that she uses to interpret blood group antigens from vast amounts of genomic data

Read the R.E.D. blog post: <u>Dr. Celina</u> <u>Montemayor-Garcia on the potential of genomics</u> <u>to shape the future of transfusion medicine</u>.

As the Canadian Blood Services representative on the Blood Transfusion Genomics Consortium (www.bgc.io), an international partnership between blood services, research institutions and industry leaders, **Montemayor-Garcia** is working on applying genomics to blood typing. The Consortium will develop and validate a DNAbased blood test for donor and patient genotyping. It will for the first time establish an international standard for testing blood using genomics.

By improving the match between donors and transfusion patients, the work of the Consortium, and blood group genotyping in general, could significantly boost a blood operator's ability to identify genetic variants and provide even bettermatched, safer blood for transfusion patients. This is especially important for Sickle Cell Disease (SCD) patients who, even when receiving antigen-matched blood through phenotyping, may experience mismatches and develop alloimmunization.

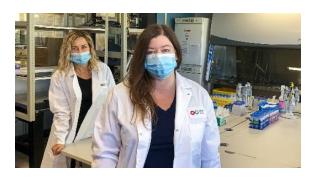
A <u>study</u> by a research team that included experts from the **MCTR** and Canadian Blood Services assessed whether genotyping could identify antigens not detected through serologic matching alone. They found that genotyping can help prevent alloimmunization in SCD patients by identifying important changes to antigen matching profiles and thus ensuring safer transfusions for SCD patients.

Read the Centre for Innovation Research Unit: <u>Protecting patients with sickle cell disease from</u> alloimmunization risk: benefits of genotyping.

Al for red blood cell shape

Research led by Centre for Innovation senior scientist **Acker** and colleagues at the Broad Institute of Harvard, MIT and Ryerson University demonstrated how <u>machine learning could usher</u> <u>in a new era</u> in red blood cell morphology assessments and research.

Red blood cell shape is linked to the quality of stored red blood cell components. But measuring red cell shape can be time- and labour-intensive and is a subjective assessment by experts who use a microscope and rely on their training to categorize each red blood cell into one of six shape types.



Olga Mykhailova (L) and **Tracey Turner** (R) in the lab

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The researchers used an AI machine learning approach to overcome these limitations. More than 52,000 red cell images collected by **Olga Mykhailova**, a postdoctoral fellow in **Acker**'s laboratory, and collaborators were manually categorized by a team of researchers trained and supervised by **Tracey Turner**, a senior research assistant and an expert in red cell morphology, also in **Acker**'s laboratory. With these images, they trained an artificial neural network which performed almost as well as humans in categorizing cell shape. This collection of images is now the world's largest freely available database of annotated red blood cells.

Even more impressive, without knowledge of the categories humans use to classify red cells, the machine determined its own progression of cell features that correspond to how long the red cells had been stored before being tested, results that the researchers discovered correlate well with a biochemical test of cell quality.

For **Acker**, this technology is especially relevant to one of his research goals: better understanding the quality of blood components to ensure the highest quality for patients. Al can provide richer, more nuanced data for research in a fraction of the time. Al also has the potential to reduce the time and number of blood donations required for essential quality monitoring.

"Ultimately, this will likely become part of blood operators' quality control processes," says **Acker**. "It provides timely information about the quality of individual components, which will help inform how best to distribute blood to Canadian patients."

Read the Centre for Innovation Research Unit: Machine learning throws away the buckets to better understand red blood cell quality and the feature story: Breakthrough study uses AI to analyze red blood cells.

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New ways to understand platelets

Platelets are small cells in the blood that are responsible for clot formation at the site of bleeding. This process could stop bleeding but may also lead to thrombosis and blockage of blood flow in the vessel. Supported by Canadian Blood Services/CIHR partnership funding, Centre for Innovation senior scientist, Heyu Ni, is identifying what role plasma and platelet proteins play in thrombosis to identify new targets for antithrombotic therapies. To support this work, Ni's team has developed new anti-fouling detection methods that avoid non-specific binding. These special probes allow for identification of new platelet ligands and anti-platelet pathogenic antibodies. It could also be useful for clinical diagnoses. Ni and colleagues have filed two patents related to this innovative technology.

Innovative alternatives to IVIg

Plasma donations are used for transfusion, or plasma is sent to fractionators to manufacture specialized medicines like intravenous immune globulin (IVIg). There is an increase in the need for plasma in Canada and globally, driven by demand for IVIg. Finding alternatives to this product is a priority for the Centre.

Senior scientist Alan Lazarus' laboratory identified a novel mechanism of anti-CD44 that explains the anti-CD44 effect in murine immune thrombocytopenia (ITP). They showed that anti-CD44 is a potent inhibitor of receptors called FcyRs on macrophages and prevents phagocytosis of platelets. These findings support the potential use of anti-CD44 in human ITP and as a potential IVIg alternative. One of the benefits of anti-CD44 antibodies is that they are effective in murine ITP at a 1,000-fold lower dose than IVIg. This means they could potentially be administered in a doctor's office rather than an infusion center (like IVIg).



Centre for Innovation senior scientist, Alan Lazarus

Engineering plasma proteins

William Sheffield studies plasma and plasma proteins-the quality and mechanism of action of transfusable plasma and replacement products. The team recently published three studies funded through the Heart and Stroke Foundation of Canada. Usina DNA manipulation and recombinant protein technology, the team created modified proteins that inhibit natural proteases - enzymes that break down proteins. Their goal was to find novel anti-thrombotic agents, to prevent or treat heart attacks and stroke.

Existing antithrombotic drugs cause bleeding as a side effect. **Sheffield**'s work targets clotting factor XIa (FXIa) — a new target for development of anti-thrombotic drugs — because patients deficient in FXI have only a mild bleeding tendency, and individuals with naturally low levels of FXI are protected from thrombosis.

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In <u>one study</u>, the **Sheffield** lab used test tube evolution to find and combine mutations in alpha-1 antitrypsin (AAT), transforming it into a more specific FXIa inhibitor. In a <u>second study</u>, the team used additional mutagenesis and computer modeling to develop AAT-RC-2, their most active and specific FXIa inhibitor yet. They are currently working on scaling up production to test AAT-RC-2 in mouse models of thrombosis and bleeding.

In the <u>third study</u>, the team used similar approaches to modify the Kunitz Protease Inhibitor (KPI) domain of Protease Nexin 2, a protease that ordinarily inactivates FXIa and the clot-busting protease plasmin, into a form that inhibits FXIa and not plasmin. They linked it to human albumin to extend its circulation time and showed that it reduced thrombosis in mice. They are currently testing it in mice that spontaneously develop heart attacks

"These studies are the culmination of years of combined effort by senior undergraduate and graduate students and expert technical staff in my lab" remarked **Sheffield**, "Continued progress could lead to licensing of these innovative engineered proteins by pharmaceutical partners, to hasten the path to the clinic."

Research & education network



investigators supported

38 with financial support102 with research and/or data products20 with both

Scientist in focus: Donald Branch

Centre for Innovation senior scientist, **Donald Branch** is an expert in immunology, hematology, cancer and cell signal transduction. But at the heart of his life's work is transfusion medicine. He has been internationally recognized for more than 40 years of major contributions to this field, and this year he celebrated a milestone 35 years working with blood services in Canada. **Branch**'s work sits at the intersection of basic science and clinical research and he is constantly seeking new ways to collaborate and help patients. One thing is evident throughout his career: **Branch** is a connector of people, ideas and technologies. He is a consummate collaborator.

A challenging but productive year

As COVID-19 shut down workplaces and laboratories across the world, **Branch** encountered an additional challenge. His team was packing up and moving their long-established laboratory to a new space at St. Michael's Hospital Li Ka Shing Knowledge Institute, Toronto. Despite this huge undertaking, **Branch** and his team had an incredibly productive year with more than 12 peer-review publications. This success is a testament to the group's dedication, as well as to **Branch**'s tenacity.

Connecting basic and clinical research

Branch has built strong connections with his clinical colleagues, in part through an annual international symposium in transfusion and hematology he hosted for over a decade with support from the Centre for Innovation. Through these connections, he saw an opportunity for the Toronto community when the Centre for Innovation launched the Transfusion Medicine Research Program Support Award. Aimed at promoting national excellence in transfusion science and medicine in service of Canadian patients, **Branch** thought "We have some of the best medical directors and transfusion experts in all of Canada right here in Toronto", and encouraged his colleagues to apply for the award. Their successful application helped support the funding of the <u>University of Toronto QUEST</u> research program.

A focus on patient safety

Branch is a pioneer of a laboratory test that can predict whether a red blood cell transfusion will be compatible before it happens. First developed in the 1980s, the "monocyte-monolayer assay" tests whether a patient's <u>antibodies will react to a donor's red blood cell antigens</u>. It can predict whether <u>a transfusion reaction may occur</u> and help keep patients safe. This assay has long been applied in research studies and in clinical cases, and Canadian Blood Services is now working to make it more broadly available

in its testing operations to support safe transfusions for hard-to-match patients.

Branch has worked to understand the mechanism behind a rare sideeffect of treatment with intravenous immune globulin (IVIg). Previously, he and his clinical collaborators in Canada, Sweden, the Netherlands, and Switzerland have shown a link between a patient's ABO genotype and IVIg-related hemolysis. **Branch**, with Jacob Pendergrast and other colleagues at **QUEST**, recently published an <u>important first prospective study</u> of IVIg-associated hemolysis incidence and risk factors. Their findings indicate hemolysis occurs at a higher incidence than previously thought and ruled in and out a number of risk factors that had been questioned by other investigators but never studied. "It is an important contribution and I'm proud to have been a part of it," says **Branch**. He's currently working with collaborators and the Centre for Innovation to educate clinicians and translate these findings into recommendations that may improve IVIg's safety profile for patients.

Read the blog post: <u>Improving patient safety: preventing a harmful side</u> <u>effect of IVIg treatment.</u>

Watch a recorded symposium: In Exploring the frontiers of IVIG-<u>associated hemolysis</u>, Pendergrast and Branch discuss incidence and risk factors, and advances in prevention.

Intravenous immune globulin or IVIg is a plasma-derived therapy that is in high demand. It is used to treat both primary and secondary immunodeficiency and autoimmune disorders. Finding alternative therapies to replace IVIg is a research priority of the Centre for Innovation.

Innovative alternatives to IVIg

Branch has dedicated much of his career to understanding IVIg and what could replace it. His finding that interleukin-11 is important for the beneficial effect of IVIg led to a collaboration with CSL Behring in Switzerland to investigate a recombinant protein as a potential replacement for IVIg. Initial research on this recombinant protein indicates it is 10–20 times more effective than IVIg for the treatment of immune thrombocytopenia (ITP) and rheumatoid arthritis in a mouse model. **Branch** and collaborators are currently working out the mechanism of action of this potential alternative to IVIg.

Branch is also investigating small molecule drugs as alternative to IVIg in certain diseases such as ITP. These small molecules prevent antibody-

mediated destruction of blood cells. Using a medicinal chemistry approach to produce derivatives of known drugs, the team has investigated more than 210 molecules and have selected two drugs that look promising in initial tests. **Melika Loriamini**, a PhD candidate in **Branch**'s laboratory is currently testing these in mouse models of ITP.

Branch has received numerous local, national, and international awards recognizing his contributions, including from the AABB, the American Society of Hematology, and the Canadian Society for Transfusion Medicine.

Breaking barriers to Alzheimer's treatment

This year, **Branch** <u>published a study</u> that suggests a novel way to help get IVIg to where it is needed in Alzheimer's patients — the brain. Published in *Proceedings of the National Academy of Sciences (PNAS)*, the study shows the promise of combining IVIg with focused ultrasound in patients with Alzheimer's disease. For **Branch**, this high-impact publication was a dream come true. "Scientists usually have a few major journals that they hope someday they can publish in and those for me and others are *Cell, Science, Nature* and *PNAS...* one down...!" he says.

Read the blog post: <u>B</u> <u>Alzheimer's disease.</u>

Reflections on a milestone year

Branch reflects on another highlight of the year - work <u>confirming the</u> <u>existence of only two types of autoimmune hemolytic anemias</u> and showing that they can be differentiated in laboratory assays. For **Branch**, an important aspect of this publication was the involvement of his daughter who worked on the project. What's next for **Branch**? He has a neverending list of projects and experiments and despite his long service, he laughs off any mention of retirement. **Branch**'s commitment to the Canadian blood system shows no signs of waning anytime soon.

"All in all, I have been with the Canadian blood system for more than 35 years, experienced the ups and downs, the good times and the not so good times, but it has all been worth it."

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Read the blog post: Breaking barriers to effective treatment for

Donald Branch

Supporting a safe, effective, responsive blood system

The Centre for Innovation helps ensure Canadian Blood Services' life-saving products are as safe and effective as possible. We continuously assess, improve, and transform the systems and processes that help Canadian Blood Services achieve its ultimate goal: improving the health of Canadians. This includes safeguarding the health of donors and recipients, working towards more inclusive donor eligibility criteria, as well as supporting appropriate utilization of blood products to safeguard sufficiency of supply.

Blood donations

Donating before pregnancy is safe

A study that included Canadian Blood Services medical director **Mindy Goldman** and associate director of epidemiology **Sheila O'Brien** examined the potential impact of repeated blood donations by women. <u>The study</u> found that repeated blood donations before pregnancy is not associated with higher risks for the baby or mother compared to women who never donate. The findings may be reassuring for women of child-bearing age and support our commitment to ensure the health of blood donors.

Read the Centre for Innovation Research Unit: Donating blood before pregnancy is safe for mothers and babies.

Preventing faint reactions

About 2-5 per cent of whole blood donors will experience а pre-faint reaction (light headedness, dizziness, sweating) while 1-3 in 1,000 will faint. Although it's not clear why blood donors sometimes faint, several studies have evaluated possible mitigation strategies. An international forum that included Goldman explored what mitigation strategies blood centres worldwide have implemented to reduce faint and pre-faint complications. Survey responses from 17 blood centres worldwide revealed that mitigation strategies vary. Sharing information among centres can help refine practices to enhance donation safety internationally and encourage more research in this area.

Expanding donor eligibility

Canadian Blood Services donor eligibility criteria are informed by science and frequently assessed and revised. In 2020-2021:

- Criteria were changed to keep up with the ever-evolving COVID-19 pandemic and ensure the safety of donors, our staff, volunteers and the blood supply
- The waiting period to donate whole blood or platelets after travelling to a malaria risk area for less than six months was reduced (from 12 to three months)
- Eligibility for donors with diabetes was expanded

Trans people and blood donation

Goldman, with Canadian Blood Services colleagues **O'Brien**; **Terrie Foster**, Medical Services Registered Nurse; and **Don Lapierre**, Manager in the MSM Plasma Program; as well as a collaborator from the University of Victoria, published an important <u>review of trans people</u>

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and their experiences as blood donors, addressing an information gap on this donor population.

The review identifies practical issues that need to be addressed: appropriate screening of trans donors within IT systems designed for binary male or female designations, questions about determining eligibility, and a general lack of regulatory standards specifically addressing eligibility of trans people in Canada. After adoption of national criteria for trans donors, the authors reported Canadian Blood Services' experience with 346 trans donors who gave 1,038 donations between November 2016 and August 2019. The results show that while trans donors are successfully donating, their findings highlight the need for cultural competence and sensitivity training for staff. Since then, resources codeveloped with trans people are now available for Canadian Blood Services staff.

MSM research

Through the Men who have Sex with Men (MSM) Research Program and the MSM Plasma Program, Canadian Blood Services is supporting 19 research projects aimed at addressing evidence gaps and evolving eligibility criteria for MSM. From the beginning, these Programs were guided by a knowledge mobilization strategy that prioritized co-creation of the research agenda with stakeholders, ensured that the right teams were brought together to conduct the research, and facilitated knowledge exchange. As increasing attention is paid to donor experiences, issues of diversity and inclusion, and the important role blood operators play in health and social systems, multidisciplinary teams that address complex questions from different vantage points is increasingly needed.

Of the 19 research projects funded under the Centre for Innovation MSM Research Program (launched in 2017) and MSM Plasma Program (launched in 2020), 12 are now completed. Four new peer-reviewed articles were published, during the year and many more are anticipated.

- Grace *et al.*: <u>It's in Me to Give: Canadian Gay,</u> <u>Bisexual, and Queer Men's Willingness to Donate</u> <u>Blood If Eligible Despite Feelings of Policy</u> <u>Discrimination</u> (read the <u>lay summary</u>).
- Vesnaver et al.: <u>Barriers and enablers to source</u> plasma donation by gay, bisexual and other men who have sex with men under revised eligibility criteria: protocol for a multiple stakeholder feasibility study.
- O'Brien et al.: Donor screening question alternatives to men who have sex with men time deferral: Potential impact on donor deferral and discomfort.
- Grace et al.: <u>Stepping Stones or Second Class</u> <u>Donors?: a qualitative analysis of gay, bisexual, and</u> <u>queer men's perspectives on plasma donation</u> <u>policy in Canada</u>.

As final results from the research projects are disseminated, they are informing Canadian Blood Services' efforts to expand eligibility criteria for whole blood and other donations by MSM in Canada. Research from this Program informed a change in the order of questions in the Canadian Blood Services' donor health questionnaire, which was implemented in 2020 to address findings of unintentional bias against MSM based on the question order. Research funded by the Program has already informed the UK's change to blood donor eligibility criteria which was implemented in June 2021. The "For the Assessment of Individual Risk" (FAIR) steering committee described an evidence-based approach to move the UK blood services to a more individualized blood donor selection policy and cited the findings of the SAFE study, one of the projects funded under our MSM Research Program.

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During 2020-2021, planning for Canadian Blood Services' plasma donation program for MSM got underway. The process of operationalizing this approach is led by a multidisciplinary team and is drawing on the research evidence. Canadian Blood Services submitted a license amendment to Health Canada to implement this change in the donor health questionnaire in fall 2021, pending regulatory approval.

Attracting new donors

Canadian Blood Services has opened new plasma donor centres to increase Canada's domestic plasma sufficiency for the manufacture intravenous immune globulin of (IVIq). Sociologist and Canadian Blood Services scientist, Kelly Holloway, is conducting a process evaluation to understand challenges and opportunities related to attracting donors to plasma donation at these sites. As part of this evaluation, Holloway is interviewing donors in the new plasma centres to shed light on what motivates them to donate. Once completed, this research will inform Canadian Blood Services strategy to engage with source plasma donors.

Safety, sufficiency and utilization

IVIg alternative for surgery patients

Patients with a bleeding disorder called immune thrombocytopenia (ITP) are at risk for blood loss if they need to have surgery. ITP patients are commonly treated before surgery with IVIg, which helps their blood clot by increasing the number of platelets. But <u>a study published in *The Lancet Haematology* and led by **Donald Arnold**, director of the **MCTR**, shows that an oral medication that stimulates the production of platelets, called eltrombopag, is an effective alternative to IVIg for this patient group.</u>



Donald Arnold, director of the McMaster Centre for Transfusion Research

Why is this important? Demand for IVIg in Canada and around the world is high and keeps growing, but the supply of this blood-derived drug is limited. According to **Arnold**, accessibility to alternative treatments such as eltrombopag could play an important role in improving IVIg availability overall. "A global shortage of immune globulin products is anticipated," he says. "And this shortage could possibly be compounded by the COVID-19 pandemic."

Read the Centre for Innovation Research Unit: Perioperative treatment for patients with immune thrombocytopenia: Eltrombopag vs IVIG and R.E.D. blog: IVIg alternative for surgery patients with bleeding disorder.

Supporting current standards

Transfusion medicine standards in Canada state that adult recipients can be safely transfused with cryoprecipitate of any ABO group, because it is commonly accepted that anti-A/B antibody levels are low in cryoprecipitate. However, the guidelines are not fully applied in practice, in part due to a lack of supporting evidence. This leads to disproportionate ordering of group AB cryoprecipitate, with knock-on effects on

management of group AB donor products. If the current standards were followed appropriately, it could increase Canadian Blood Services' availability of AB plasma by 13 per cent as it would not be used to make cryoprecipitate.

Devine and her group investigated anti-A/B antibody titres in cryoprecipitate to provide evidence about the appropriateness of the guidelines. <u>Their findings</u> provided strong evidence to support the current Canadian standards and the safety of transfusing cryoprecipitate without the need for blood matching in adult recipients.

Evaluating research impact

The FIBRES trial, completed by QUEST in 2019, showed that after cardiac surgery, fibrinogen concentrate is just as good at controlling bleeding as cryoprecipitate. This evidence informed an NAC statement on fibrinogen concentrate use and has prompted many clinicians to switch to fibrinogen concentrate. There has been a sixfold decrease in units of cryoprecipitate issued to Canadian hospitals from 2018/19 to 2020/21. This is an important shift with benefits for Canadian patients and physicians, as fibrinogen concentrate is purified and pathogen-reduced, provides consistent dosing, is faster to prepare and easier to administer.

Cold storage as an alternative to irradiation

Transfusion-Associated-Graft versus Host Disease (TA-GvHD) is a serious but preventable adverse event after transfusion. It happens when donor immune cells (T-cells) that are viable are transfused into a patient who is immune compromised. To prevent TA-GvHD, white blood cells — including T-cells — are filtered out of blood products during production in a process called leukoreduction. As an additional precaution for patients thought to be at risk of TA-GvHD, red blood cell products are irradiated to inactivate any residual white blood cells.

Centre for Innovation senior scientist **Jason Acker** and his group investigated whether leukoreduction alone is sufficient to prevent TA-GvHD. <u>Their findings</u> indicate that cold storage of leukoreduced red blood cells for 21 days or more is sufficient to inactivate T-cells suggesting an alternative TA-GvHD-safe product for patients. This approach is advantageous as it doesn't require specialized equipment to irradiate products or separate inventory management. It could save time and reduce discards of irradiated products.

Understanding red blood cells

Red cell components for transfusion consist of a population of red blood cells of varying biological "ages," from recently matured (young) to senescent (old). Acker and his team studied red cell components separated into "young" and "old" fractions. The results provide initial insights into the structural, functional and metabolomic dissimilarities between young and old red blood cells in stored blood components from female and male donors. The study was a first step towards better understanding the unique contribution that individual donors have on variability in the structure and function of red blood cells. The work suggests that red blood cell variability from individual donors contributes to how quickly the quality of blood can decrease during storage, and more importantly, help understand transfusion efficacy and/or adverse outcomes from sexmismatched transfusions.

Making research count

Reducing unnecessary transfusions protects patients from unnecessary harm and conserves a precious resource. The START (Screening by Technologists and Auditing to Reduce Transfusions) study, completed by QUEST in 2019, showed that educational interventions were remarkably effective in decreasing inappropriate red blood cell transfusions. With Canadian Blood Services as a partner, these interventions have now been incorporated into a national "Using Blood Wisely" campaign to engage hospitals in decreasing inappropriate red blood cell transfusions through interventions, including audits and benchmarking, and measurement. As of June 2021, there were 191 participating hospitals, and 57 sites have been designated as a "Using Blood Wisely Hospital."



Staff at the Health Science Centre in Winnipeg, Manitoba, one of the first hospitals to receive national "Using Blood Wisely" designation. Photo supplied by Shared Health Communications.

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Tackling platelet discards

Improper storage is the most common reason for discarding platelets components, which are the most discarded blood component in Canada. To address this problem, the University of Toronto **QUEST** research program, funded through the Centre for Innovation competitive research programs, developed the reusable Platelet Transport Bag (PTB). The PTB was designed to maintain proper storage conditions for platelets while they are transported within a hospital.



A Platelet Transport Bag

After the PTBs were implemented at 16 hospitals across Canada and educational tools were provided to frequent administrators of platelets, the study found that platelet discard rates did not decrease. However, an audit of the factors contributing to reported platelet discards, revealed that some events were avoidable. The research team plans to build on these findings to redesign their intervention.

Research impact

In 2017, research informed a new process for bacterial screening which allowed Canadian Blood Services to extend the shelf life of their platelet products from five to seven days. This change improved the safety profile of platelets and led to a system-wide reduction in the number of platelet units discarded due to outdate. As detailed in <u>a study</u> led by **Sandra Ramirez-Arcos**, overall outdating of platelets units at Canadian Blood Services and hospitals reduced from 18.9 to 13.1 per cent, and the incidence of septic transfusion events decreased about threefold.

Platelet transfusion in pediatric cancer

Platelet transfusion is an essential and very common part of supportive care for children with cancer. Much of platelet transfusion practice for children is based on adult studies, although children may have a higher risk of bleeding and increased harm compared to adults.

A team from the **MCTR** addressed this knowledge gap by examining data on cancer patients who had received at least one platelet transfusion at a children's hospital between 2009–2013.

<u>One of their key findings</u> is that children with cancer usually respond well to platelet transfusions, as measured by a satisfactory increase in their post-transfusion platelet count. Their findings also provide practical data for both parents of children newly diagnosed with cancer and their clinicians, about the likelihood and frequency of platelet transfusions during

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treatment. For treating clinicians, the study provides new insight on what is considered a normal platelet count increment following platelet transfusion in children.

Read the Centre for Innovation Research

Unit: Platelet transfusion in children with cancer.

Modelling blood inventory

Managing the inventory of blood components can be challenging for blood banks. Hospitals tend to cope with the challenges of variable demand and frequent urgent orders by holding excess inventory, which increases holding costs and risk of discards. Research funded through the Centre for Innovation's Blood Efficiencv Accelerator Award and led by Na Li, assistant professor in the department of community health sciences at the University of Calgary and adjunct lecturer at the MCTR, used real data to develop a forecasting model for red blood cells and platelets.

The red blood cell forecasting model used key clinical indicators and trends (e.g., clinical diagnoses, surgical procedures) that drive the demand for blood in hospitals. With a data-driven ordering strategy, hospitals can order red cells in a way that more accurately reflects actual demand while maintaining the safety of blood transfusions. This can reduce hospital blood bank inventory and ordering frequency, and lead to significant cost savings for the blood system. Now, the team plans to develop a software application for implementation at the hospital blood bank in their region.

Read the Centre for Innovation Research Unit: <u>A more accurate and efficient way to manage</u> <u>blood demand and supply</u>.

Improving stem cell therapies

Preserving delicate cells on ice

Centre for Innovation senior development Pineault scientist. Nicolas and Acker understand the importance of cryopreservation the science behind successfully preserving delicate lifesaving cells. "The biggest challenge for cryopreservation is managing water within the cells. If you freeze the cells without cryoprotectants, the water inside the cells will turn into ice, and when thawed the cells will break apart and die," says Pineault.

The first step to cryopreservation is preparing the cells using cryoprotectants — substances added to cells to protect them from harm. The next step is cooling the cells to the right temperature at a specific rate. In the case of stem cell this is - 196°C. Likewise they need to be thawed in the right way, and the cryoprotectant needs to be removed by dilution.

Acker and Pineault are collaborating with Robert N. Ben, a biochemist at the University of Ottawa, to develop a new type of cryoprotectant inspired by several species of fish off the coast of Newfoundland. These fish naturally produce antifreeze proteins, which bind to ice and prevent it from crystallizing. Ben's team was able to synthesize sugar molecules that mimic the proteins found in these fish. Acker and Pineault are working with Ben to develop this discovery's potential as a cryoprotectant and advance these technologies for stem cell preservation, as well as the preservation of other blood cells such as red blood cells.

Read the feature story: <u>The lifesaving science</u> <u>of keeping delicate cells on ice.</u>

Transient warming events

As part of routine cord blood bank operations, cord blood units may occasionally be temporarily removed from storage at -196°C, leading to "transient warming events" or TWEs. A study led by **Pineault** in collaboration with **Acker** sought to understand the impact of these TWEs on the quality and potency of cord blood units. <u>Their results</u> revealed that TWEs can indeed impact post-thaw viability. In particular, the viability of hematopoietic cells in smaller cord blood unit compartments were reduced.

Although the typical banking operation scenario had little effect, the "worst-case" scenario that was tested led to lower potency of the cord blood unit as indicated by reduced colony-forming unit recovery. Although TWEs are almost inevitable in cord blood banking operations, these findings show that care needs to be taken to minimize any potential effects and prevent worst-case scenario TWEs by reducing exposure time, using cold plates and adhering to strict operational protocols.

Problematic marketing by private cord blood banks

Private cord blood banking is growing around the world. A project led by **Timothy Caulfield**, Canada Research Chair in Health Law and Policy at the University of Alberta, and funded through a Centre for Innovation James Kreppner award found that private companies' claims around cord blood hype the promise of speculative uses and distort the likelihood of use.

The team analyzed the current legal and policy framework governing private cord bank marketing and found that truth in advertising law is the most useful legal tool for curbing false or misleading marketing statements they found on websites of private cord blood banks. Their research recommends <u>regulatory bodies should</u>

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<u>enforce the law</u> to help prevent public health and personal financial harm and that <u>careful</u> <u>monitoring of private cord blood companies is</u> <u>important</u> for ensuring the Canadian public is accurately informed about the services being offered.

Organs and tissues donations

Exemptions in human tissue legislation

Legislation about the sale of human tissues varies widely across Canada. While some provinces restrict the sale of plasma, others have legislation that exempts blood and blood products from provisions on sale. With for-profit plasma banks now established in Saskatoon and Moncton, concerns about the expanding market in human tissues have emerged.

With funding from a Centre for Innovation James Kreppner award, Alana Cattapan, assistant professor in the department of political science at the University of Waterloo, examined the origins of tissue exemptions in Canada. The findings of this project, including policy papers and articles, will be used to inform decision making and public opinion in jurisdictions that may want to revise existing human tissue legislation. This work will reveal whether commitments to the noncommercialization of human tissues remains strong in Canada, and how these commitments vary province-to-province. These insights will be valuable to Canadian Blood Services as it navigates the continued operation and expansion (for plasma) of a nonremunerated donation system. More about the project, including full list of publications, are available at https://www.tissueexemptions.com/.

Perceptions of cardiac donation

Cardiac transplantation is the optimal treatment for patients with end-stage heart disease. Currently, cardiac donation is limited to those who declared based on are neurological determination of death (NDD, also referred to as 'brain death'). But implementing cardiac donation after circulatory determination of death (DCDD) in Canada could improve outcomes for patients on the heart transplant waitlist. However, before widespread implementation of DCDD, it is important to identify potential ethical or other concerns of stakeholders.

With funding support from a Centre for Innovation Kenneth J. Fyke award, Ian Ball, associate scientist at the Lawson Health Research Institute, is leading research that explores perceptions of health-care providers and the public about cardiac DCDD. The research team have published their initial findings and have pilot tested educational videos that describe the processes involved in organ donation. Their research will provide an important framework for implementing life-saving cardiac DCDD programs in way that is consistent with Canadian's values. Once complete, the study findings submitted to Canadian Blood Services and provincial organ donation organizations will help inform the launch of cardiac DCDD programs.



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Training, education, and engagement highlights

Training the next generation

Building capacity in transfusion research is essential for the continued relevance and safety of the blood system. Over the past year, the Centre's 15 staff scientists supervised more than 60 students from the undergraduate to postgraduate level. In addition, through the Centre's competitive training award programs, Canadian Blood Services provided support to seven postdoctoral and 11 graduate fellows.

Successful alumni

In 2020-21, several trainees completed their training, including six who completed their graduate theses. Our alumni continue to make exciting contributions in their fields. David Donkor, former Canadian Blood Services postdoctoral fellow in the laboratory of senior scientist William Sheffield, is now field scientist at the Canadian application biotechnology company Nicoya. Miguel Neves, former Canadian Blood Services postdoctoral fellow in the laboratory of senior scientist Heyu Ni, now leads a platelet research program at University of Minho in Portugal, with collaborators in Canada.

New support for graduates

In 2020, a new financial donor expressed an interest in supporting the education and training of early career scientists working with stem cells. Canadian Blood Services' Philanthropy and the Centre for Innovation collaborated to make this donation possible by leveraging and contributing to the well-established Canadian Blood Services Graduate Fellowship Program (GFP) award. In 2020-21, **Richa Kaushal** was selected as the first recipient of this generous funding. A University of Ottawa doctoral candidate, **Richa** is studying a new solution for cord blood unit preservation under the supervision of our senior scientist **Nicolas Pineault**.

Academic skills and beyond

Developing research skills beyond technical skills learned in the laboratory are important for trainees to advance their career as academics. Our trainees are given the opportunity to participate on Canadian Blood Services grant review panels as reviewers or observers giving them the chance to learn first-hand what makes a successful grant application. In 2020-21, one graduate fellow participated as an observer on the grant review panel for the Blood Efficiency Award Program and one postdoctoral fellow served on the grant review panel for the Graduate Fellowship Program.

Every year we partner with the **Centre for Blood Research** to run a Lay Science Writing Competition to help trainees more effectively share their research. This year's theme, "Challenges 2020", gave our trainees an opportunity to showcase their research while telling their stories of challenge. It's no surprise that the competition received many heartfelt and inspiring entries. Congratulations to the winners!

Joint	Melina Messing (CBR/SBME graduate
first	student) for "Lost in lab: deciphering
prize	blood immune cells to fight COVID-19"
	Polina Petlitsyna (CBR/SBME summer
	student) for "Developing cell biology
	lessons for seniors in the age of
	COVID"
Runner-	Sarah Longo (McMaster
up	University/MCTR undergraduate
-	student) for "2020: The Year No One
	Expected - Challenges Researchers
	Face during a Global Pandemic"

In Focus: The Centre for Blood Research - Research excellence to improve blood safety

The **Centre for Blood Research (CBR)** was established in 2002, when a group of blood researchers at the University of British Columbia decided they would help make Justice Horace Krever's recommendation to pursue research excellence in blood and transfusion medicine a reality. From the outset, a partnership with Canadian Blood Services was a natural fit, due to our organization's deep interest in advancing research in blood and transfusion science. Canadian Blood Services provided 10 per cent of the start-up funding for the **CBR** and has become a permanent partner in numerous ways. The **CBR** has been home to laboratories for many of our scientists, including current occupants **Dana Devine**, **Ed Pryzdial** and **Mark Scott**.

"Canadian Blood Services is recognized as one of the leading blood operators of the world, in terms of safety, quality and efficiency. Our association with Canadian Blood Services is a great strength."

Ed Conway, former director of the Centre for Blood Research

Starting the year with a new director

In January 2021, Canadian Blood Services' chief scientist **Devine** was appointed director of the **CBR**, when former director **Ed Conway**'s 11-year tenure as director ended. **Devine**'s role as director deepens Canadian Blood Services' lasting collaboration with the Centre and is part of her longstanding pursuit of bringing new discoveries to patients in meaningful ways. **Devine** also maintains her research lab and faculty appointment at the University of British Columbia.

Read the feature stories: <u>Joining forces to improve blood research in</u> <u>Canada</u> **and** <u>Chief scientist Dr. Dana Devine takes on directorship at</u> <u>Centre for Blood Research.</u>

"As one of the founders of the Centre for Blood Research, I've watched it grow over the years. In some ways, it feels like I'm coming full circle. It's one of the largest academic blood centres in the world, and one of the most multidisciplinary. I'm really interested in ensuring it stays vibrant and keeps growing."

Dana Devine, director of the Centre for Blood Research

Facilitating training and knowledge mobilization

In 2020-2021, the Centre for Innovation and the **CBR** renewed their collaboration agreement that will run until 2024. Through this agreement, the Centre for Innovation supports the **CBR**'s education, training, and knowledge mobilization activities, including the **CBR**'s two annual symposia: the Norman Bethune Symposium and the Earl Davie Symposium. In 2020-2021, as events pivoted to virtual formats, the Centre for Innovation and **CBR** put their heads together to find ways to continue to engage trainees.

A productive **Collaboration**

The Centre for Innovation / Centre for Blood Research

collaboration supported:

- 2 virtual symposia delivered to 400+ attendees from across the globe
- 7 CBR graduate students
- I ODIT graduate students
- **5** CBR summer students
- 5 "Ask me Anything" career development Cafés3 editing workshops
- 29 CBR virtual seminars
- 9 collaborative R.E.D.
- blog posts

An innovative use of Twitter was tested with a Twitter Research Showcase event held in conjunction with the <u>Norman Bethune Symposium</u>. Workshops were developed to provide trainees with the essentials on how to communicate via this social media platform. For the <u>Earl W. Davie Symposium</u>, the **CBR** ran a virtual poster session for trainees, which was very well received. These activities gave trainees the opportunity to present their research virtually, while honing some important skills.

Excerpts from the Twitter Research Showcase. Showcase winner and CBR trainee Maria-Elizabeth Baeva describes her research with Alzheimer's and mice (left), while Centre for

Innovation trainee **Wenhui Li** shares her research about blood and donor sex (right).

The **CBR** took full advantage of the virtual format to launch a new career development "Ask Me Anything" Café series, which features non-local/international mentors. Online editing workshops for trainees were coorganized by the **CBR**, the Centre for Innovation and SciCATS, a Vancouver-based collective of science communicators who provide skillsbased science communication training, resources, and workshops. One of these workshops was timed to support trainees intending to enter the Lay Science Writing Competition (see above).

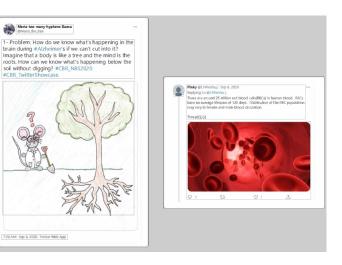
The partnership between the Centre for Innovation and the **CBR** broadens the experience of trainees from both organizations. It facilitates interactions among trainees and scientists that may not otherwise happen. It provides opportunities to engage and learn. It fosters collaboration and makes vital connections between the realms of basic science and the blood operator, fulfilling Krever's vision of nurturing expertise in transfusion medicine and science to help ensure the continuing safety of the blood system. As **Devine** notes: "Our partnership...allows [Canadian Blood Services] to be actively involved in training the next generation of transfusion scientists, empowering future generations of researchers to continue this vital work."



A group photo of some of the attendees and speakers at the 14th Earl W. Davie Symposium in 2020. With over 300 registrants, the event saw attendance from researchers, clinicians, trainees, and industry professionals from around the world.

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Supporting clinical practice

The safety of the blood system does not stop at the manufacturing of safe blood components and products – it also relies on safe and appropriate utilization. Multidisciplinary teams of health-care professionals are responsible for ensuring safe transfusion practices and optimal patient outcomes. This includes transfusion medicine specialists who support transfusion practice, physicians and nurse practitioners who prescribe blood components and products, nurses who perform the transfusions, and medical laboratory technologists in blood banks who release the blood components and products. In collaboration with Canadian Blood Services medical experts and external stakeholders, the Centre for Innovation manages programs that support a range of health-care professionals working in transfusion.

Educating health-care professionals

Elianna Saidenberg Trainees

Transfusion medicine specialists are vital to the practice of medicine. Unfortunately, few young physicians are entering the field. The Elianna Saidenberg Traineeship Award, now administered through the Centre for Innovation, facilitates the entry of young physicians into a program that trains physicians to specialize in the field of transfusion medicine.

Physicians enrolled in the Royal College of Physicians and Surgeons of Canada Area of Focused Competence diploma program in transfusion medicine are eligible for the award. This year, of the six trainees enrolled in the program, four were supported by the award. An additional three trainees were successful in securing an award to start their fellowships later in 2021 or 2022 at the University of British Columbia under the supervision of **Andrew Shih** and at the University of Toronto under the supervision of **Wendy Lau**.



Established in 1999 to address a need for more physicians in the field of transfusion medicine, 30 Canadian trainees have received their Transfusion Medicine specialty diploma to date and are now working as transfusion medicine specialists in hospitals across the country or for blood operators. Twelve of these trainees were financially supported by the Canadian Blood Services trainee award.

Transfusion Camp

Transfusion Camp was established to meet a known knowledge qap and consolidate transfusion practices across Canada. Established in 2012 by **QUEST** at the University of Toronto, Transfusion Camp's five-day curriculum is developed by QUEST faculty and collaborators. The Centre for Innovation facilitates the national expansion of Transfusion Camp by providing technology and coordination support. Transfusion Camp is delivered to postgraduate medical residents in various specialties related to transfusion. In response to increasing demand for transfusion medicine education in the nursing community, Transfusion

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Camp for Physicians was adapted in 2019 to a three-day curriculum for nurse practitioners who prescribe blood components and products in their practice.

Transfusion Camp for physicians. In 2020-21, Transfusion Camp continued to grow. Three Canadian universities (University of Sherbrooke, Université Laval and University of Alberta) were new camp participants. The program transitioned to virtual delivery during the COVID-19 pandemic and a new course portal on Canadian Blood Services' Professional Education website provided trainees with access to educational resources. A collaboration with Australian Red Cross Lifeblood was initiated so that Transfusion Camp lectures and resources could be adapted to the Australian transfusion medicine training environment.

Transfusion Camp for Physicians

- 287 trainees from 12 medical specialties, 13 Canadian universities and one UK university.
- 15 hours of didactic lectures supplemented by 13 hours of team-based learning seminars delivered by >30 faculty members.
- A new lecture on transfusion medicine and COVID-19.
- Validated assessments of transfusion medicine knowledge, conducted before and after program completion, continue to show the positive impact of Transfusion Camp Pre-Camp mean score 53 per cent vs. Post-Camp mean score 72 per cent.

Transfusion Camp for nurses. The Centre for Innovation continued to support the adaptation of the Transfusion Camp curriculum to nurse practitioners. Now in its second year, this initiative is a collaboration with transfusion medicine specialist Andrew Shih, the BC Provincial Blood Coordinating Office, Vancouver Costal Health and Fraser Health, and Transfusion Camp.

The course is delivered over two days. A third day is offered to nurses practicing in acute care settings. After completing the course, participants meet the requirements for transfusion medicine privileges in their health authority.



Screen shot of presenters at Transfusion Camp

Transfusion Camp for Nurses

- 1 camp organized by Fraser Health engaging 30 participants from five health authorities within B.C.
- >8 hours of didactic lectures supplemented by >8 hours of team-based learning seminars leveraged from Transfusion Camp for Physicians.
- Steering Committee established to provide guidance in the development, delivery, and national expansion of the program.
- Course portal launched.

Certification for medical laboratory technologists

The Centre for Innovation participated in a new initiative, led by the Canadian Society for Transfusion Medicine in collaboration with the University of Alberta and Canadian Blood Services, that aims to establish a program for advanced certification for medical laboratory technologists in the field of transfusion science. When established in 2023, this program is expected to fill a gap created when the Canadian Society for Medical Laboratory Science (CSMLS) Advanced Registered Technologist (ART) program was discontinued.

Professional education website

In addition to supporting training for health-care professionals involved in transfusion practice, the Centre for Innovation manages Canadian Blood Services' Professional Education website (profedu.ca), a resource hub for health-care professionals working in transfusion medicine and in organ and tissue donation and transplantation. In collaboration with experts from network. the Centre's Knowledge our Mobilization and Strategic Alliances team leads the development of transfusion-related content that meets the needs of the community.

In 2020-2021, new articles were published, and existing content was updated to keep abreast with advances in the field. The website recorded over 562,000 sessions (a 27 per cent increase from the previous year), engaging almost 487,000 users, primarily from Canada.

COVID-19 online resources

Developing new content to support health-care professionals in response to the COVID-19 pandemic was a key focus for the year. In particular, a <u>COVID-19</u>: FAQ for health professionals working with blood products was developed to provide answers to questions received from the community.

Clinical guide

The website's most popular resources continue to be chapters of the Clinical Guide to Transfusion, available in both French and English. Five of the Guide's 18 chapters were updated during the year.

Bacterial testing resources

In response to hospital demand, a new publication <u>FAQ</u>: <u>Canadian Blood Services</u> <u>Platelet Bacterial Testing</u> was developed to provide details on Canadian Blood Services' management of platelet bacterial testing.

BloodTechNet impact

Serology education

<u>LearnSerology.ca</u> provides interactive modules and cases for learning about immunohematology. Led by Canadian Blood Services medical officer, **Matthew Yan** and funded through a Centre for Innovation BloodTechNet award, the online curriculum was developed to <u>standardize</u> <u>serology education for hematology trainees</u> and fill learning gaps. In 2020, the website logged 10,000 unique visits.

Read the R.E.D. blog: <u>Improving transfusion</u> practice through serology education.

Increasing the diversity of stem cell donors

Because patients are more likely to find a stem cell match from donors of similar ethnicity, increasing donor diversity is crucial to improving access to matched, unrelated stem cell donors for racialized patients. Stem Cell Club is a national

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donor recruitment organization focused on addressing racial disparities in access to matched stem cell donors. Led by **Warren Fingrut** and funded through a Centre for Innovation BloodTechNet award, the club aims to increase the diversity of donors on Canadian Blood Services' stem cell registry.

To recruit donors from the demographic most needed as stem cell donors (diverse, male, between the ages of 17–35) Stem Cell Club developed resources for members of the LGBTQ community and Black Canadians. Since 2009, men who have sex with men (MSM) have been eligible to register as stem cell donors. However, few members of the LGBTQ community are familiar with stem cell donation and few healthcare providers know that MSM are eligible.

The team developed multimedia resources to highlight LGBTQ eligibility and the need for ethnically diverse donors, and to support virtual recruitment of donors from the most needed demographics. They created Twitter stories on @WhyWeSwab, TikTok and YouTube videos featuring gay, bisexual, queer-identified performers or Black Canadians championing stem cell donation (see YouTube channel: <u>http://bit.ly/2NIGwID</u>). The TikTok videos alone had impressive reach (182,000 view, 35,000 likes and 12,000 shares).



Example of multimedia image used to promote stem cell donation, developed in collaboration with performers who identify as MSM

The team also developed a toolkit to educate medical students and other health care providers about blood and stem cell donation for MSM. As of February 2021, 65 medical students from the University of Ottawa, University of British Columbia, and Dalhousie University completed training in an online module and workshop.

Guideline development

The Centre for Innovation Knowledge Mobilization and Strategic Alliances team hosts Secretariat for the International the Collaboration for Transfusion Medicine Guidelines (ICTMG). This collaborative develops clinical guidelines and complementary resources to optimize patient transfusion care, made available at ictmg.org.

ICTMG publications

Systematic review on FNAIT to determine the association between maternal HLA-DRB3*01:01 and HPA-1a-alloimmunization and neonatal outcome in children born of HPA-1a-immunized women.

Systematic review to appraise the quality of evidence-based clinical practice guidelines on platelet transfusions. This review was selected by the NHS Blood and Transplant Systematic Review Initiative as one of the top 10 publications in March 2021. Read more about this paper in our R.E.D. Blog: Improving platelet transfusion practice: examining the quality of guidelines.

<u>Commentary</u> on the guidance needed for the use of irradiated blood components.

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In November 2020, the National Advisory Committee on Blood and Blood Products published its <u>endorsement</u> of the ICTMG guidance on red blood cell specifications for patients with hemoglobinopathies. During the year, Simon Stanworth replaced **Nadine Shehata** as Executive Chair of the collaborative and will continue on the strategic vision initiated by **Shehata** to foster collaborations while ensuring rigour in guideline development. The collaborative has continued its guideline development work on use of albumin, hemolytic disease of the newborn, and platelet transfusion.

Advancing knowledge



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210 peer-reviewed publications
33 technical reports
29 blood.ca publications
4 external non-peer-reviewed publications

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An engaged network

The Centre for Innovation connects an interdisciplinary and collaborative network of experts. Through competitive funding programs, we support research to address strategic priorities. We engage with our network of researchers, clinicians, and health-care professionals to ensure the knowledge generated by the Centre increases our collective understanding of the blood system, informs best practices and influences policies.

Funding research

The Centre for Innovation Knowledge Mobilization and Strategic Alliances team develops and administers competitive research funding programs to address strategic research priorities. In 2020-21, 56 research projects received funding through 8 programs, including 14 new projects (Appendix I). In total, 44 principal investigators were supported during the year, and together with the Centre for Innovation 14 staff scientists, they represent our primary research network.

Knowledge creation

193 grants and awards research programs 56 development research programs 71 national training programs 22 externally funded grants and awards 20 research laboratory support programs 13 education programs 6 clinical guideline development programs 3 social sciences support programs 2

Fostering collaboration

Facilitating interactions between members of the Centre for Innovation research network fosters collaboration and promotes innovation.

In May 2020, our annual Research Day – normally a one-day face-to-face event – was delivered virtually. 95 individuals from our extended research network, including 23 graduate students and postdoctoral fellows participated. Centre for Innovation Research Day 2020 looked at current and future challenges, featuring sessions on "Proteins of the Future," "Donor Research," "Blood Products in Combat Operations," and "Improving Blood Products." In addition, a clinical research session focused on the importance of a transfusion research network for a major clinical trial of COVID-19 convalescent plasma.

"I think it was truly impressive for being pulled together virtually in a time characterized by rapid change and massive upheaval. Well done!"

Research Day 2020 participant

In addition, the Centre for Innovation monthly science seminar series act as "work-in-progress" sessions for our staff scientists, medical experts, adjunct scientists, and research trainees. Six seminars were held, with topics ranging from antiviral anticoagulation to next generation sequencing to the social science of donation. Trainees were particularly engaged during this year's session, a testament to our trainee engagement strategy aimed at promoting their participation in research activities.

Connecting the research community

Every spring, the Centre for Innovation supports the Canadian Society for Transfusion Medicine (CSTM) Congress. Delivered in partnership with CSTM, Canadian Blood Services and Héma-Québec, the congress is an opportunity for >300 nurses, physicians, technologists, scientists, and others involved in transfusion medicine to share information, learn about recent developments and recognize important contributions to the field. In addition to providing funding, Centre for Innovation staff scientists volunteer on the scientific planning committee and are encouraged to present and attend this national three-day Congress.

339 Learning opportunities & knowledge exchanges



3300+ stakeholders reached97% of stakeholders reportthey acquired knowledge andskills

730,000+ pageviews on our websites

The COVID-19 pandemic led to the cancellation of the 2020 annual Congress. Instead, key presenters who had been scheduled for the Congress presented their research at five virtual events organized with the support of the Centre for Innovation Knowledge Mobilization and Strategic Alliances team.

Disseminating findings

An important component of the Centre's science communication strategy is Canadian Blood Services' <u>Research.Education.Discovery. (R.E.D.)</u> <u>blog</u> where the Centre's activities are showcased. 39 R.E.D. blog posts were published last year, including 34 posts focused on Centre for Innovation stories. The R.E.D blog has seen growth year-over-year, and last year it attracted more than 71,000 views and almost 60,000 unique visitors, a 5 and 21 per cent increase, respectively, from the previous year.

Top three Centre for Innovation R.E.D. blog posts

Blood transfusion during the pandemic: strategies in a time of uncertainty Tracking the prevalence of COVID-19 at top speed Honest and compassionate leadership in a crisis: An interview with Dr. Isra Levy

Led by Canadian Blood Service's Communications team, the "<u>Stories</u>" initiative is a newer vehicle targeted at the public that tells compelling stories around the themes of information, inspiration and innovation. The Centre supports and collaborates with Communications on innovation-focused stories

Another cornerstone of our communication strategy is our monthly Research & Education Round Up e-newsletter. In 2020-2021, 11 editions of the newsletter were published. The Round Up keeps our community engaged by providing relevant and timely information about our latest publications, funding competitions and upcoming events. It continues to have excellent engagement. The open rate was 42 per cent, up from last year and almost double the industry average (22 per cent). In September 2020, we hit a milestone, surpassing 2,000 subscribers. We ended the year with 2,170 subscribers, a 19 per cent increase over the previous year.

Governance and operations

Embedded within Canadian Blood Services Medical Affairs and Innovation division, the Centre for Innovation benefits from our organization's sound governance and our financial, legal, and information technology groups. Within the Centre, a management team supported by Canadian Blood Services' leadership community, a Research Ethics Program, a specialized Blood4Research Facility, Research and Training competitive funding Programs, a performance measurement framework, and — newly implemented this year — portfolio management, together ensure appropriate governance and operations.

Governance oversight

The Canadian Blood Services' Board committee, the Safety, Research and Ethics Committee (SREC) oversees research, scientific and innovation activities, including the Research Ethics Board (REB). In 2020-2021, the SREC reviewed the Centre for Innovation and the REB annual reports and Board members continued to have confidence in the Centre to support a safe, effective and responsive system for blood and blood products in Canada.

The Scientific Research and Advisory Committee (SRAC) supports Canadian Blood Services' research direction and policy decisions. In 2020-2021, the advisory committee was instrumental in supporting pandemic-related decisions including COVID-19 related donor eligibility criteria the convalescent plasma project and seroprevalence research.

Research ethics

The Centre for Innovation Knowledge Mobilization and Strategic Alliances team manages the Research Ethics Program to facilitate research following established policies, standards, and best practices. Supported by an REB, this Program provides a framework for internal and external researchers to access biologic materials, data sets, and Canadian Blood Services donors, volunteers and staff.



Research Ethics Program reviews facilitated research activities with:

41 new studies approved (8 COVID-19 related)

9 new quality improvement/assurance studies approved (3 COVID-19 related)104 studies renewed or amended

39 studies terminated

4,030 blood products distributed



2,288 to 71 production improvement projects

1,742 to 58 Canadian researchers

3 cord blood products distributed to 4 Canadian researchers

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In 2020–2021, processes for prioritizing review of COVID-19 studies were implemented to ensure adequate support to research and public health efforts. A total of 11 COVID-19 related studies were reviewed and approved. In addition, a new process was established to suspend REB approved studies during nationally or provincially declared emergencies.

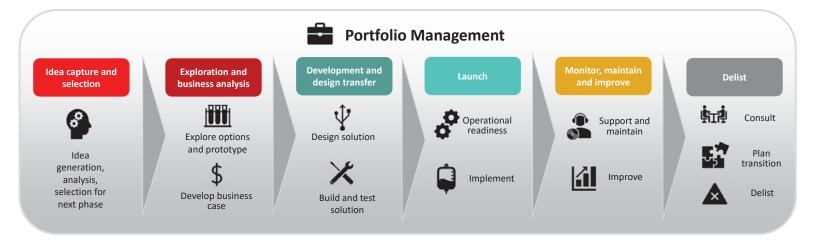
Portfolio management

The Product Innovation Operational Committee (PIOC) oversees the Canadian Blood Services portfolio through an annual review of fresh blood components, stem cell products and diagnostic services. This oversight provides direction to the development research undertaken at the Centre for Innovation. In addition, joint meetings between the Canadian Blood Services – Provincial and Territorial Blood Liaison Committee (CBS-PTBLC) and the National Advisory Committee on Blood and Blood Products (NAC) provide further directions in the development of services and products such as whole blood and pathogenreduced platelets.

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To enhance our capability to deliver timely and relevant transfusion therapeutics and services, work led by Sylvia Torrance, associate director, Centre for Innovation was completed in 2020-2021 on a new lifecycle management process. The high-level design was completed at the end of the year, with implementation efforts ongoing in 2021. This new process guides the management of blood components and products, and services from inception, through design and manufacturing, to implementation, maintenance and, in some cases, delisting. Development of the process was based on existing industry standards, FDA Design Controls and Quality by Design frameworks, and adapted for Canadian Blood Services' environment. The portfolio management approach aligns environmental scanning, research. development and operational efforts so that new products and services meet our customers' changing needs and are introduced in a timely manner.



Centre for Innovation Product lifecycle management process

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A unique facility with endless connections

The netCAD Blood4Research Facility, the heart of the Centre for Innovation's Product and Process Development (2PD) group led by **Ken McTaggart**, is dedicated to carrying out projects that support Canadian Blood Services supply chain initiatives. Another core activity is the provision of research samples to investigators across the country.

Change in management

In early 2020-2021, following the retirement of **Janet McManus** who was facility manager since 2014, a new management team was established. **Peter Schubert**, former Canadian Blood Services research associate in **Devine**'s laboratory, took on a development senior scientist position in the 2PD group and was appointed principal manager for the Blood4Research Facility. His extensive knowledge of the blood manufacturing process, acquired through his collaborations on multiple research projects while in **Devine**'s lab, prepares him well for this new challenge.



The Blood4Research Facility team (from front left to back left): Christine Shin, Rowena Maria Quintos, Joanne Ross, Le Lam, Shamim Rashidipour, Riki Roberts, Winnie Eng, Tatiana Closas, Emmanuel Zurbano, Peter Schubert (Missing: Anita Howell).

With his cross-appointment at the University of British Columbia as a principal investigator with the **Centre for Blood Research** and as a clinical associate professor at the Department for Pathology and Laboratory Medicine, **Schubert** maintains strong ties to the research community. To support **Schubert** in his new role, **Le Lam**, a former production supervisor at Canadian Blood Services' BC and Yukon Centre, was appointed as facility's operational manager.

A busy year despite restrictions

The Blood4Research Facility's output over the past year was impressive and a testament to the commitment of the team. In addition to their work to establish and evaluate pathogen-reduced platelets using the INTERCEPT system (described earlier), key projects in 2020-2021 included supporting Canadian-led COVID-19 clinical trials (CONCOR) by facilitating the recruitment of COVID-19 convalescent plasma donors (described earlier) and supporting Health Canada-approved license amendments to replace collection bag sets.

What does the future hold?

"There are many opportunities both in the innovation and development space. With the facility playing a critical role at the interface of research, development, and innovation, it is an exciting time for me to lead the work of the facility", says **Schubert**. "In the end, all innovation ideas to improve the quality and safety of our components for the optimal care of the patients we serve need a collaborative effort. I'm very grateful for our committed blood donors, our dedicated team, and the supportive environment provided by my co-workers at Canadian Blood Services and beyond."

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Competitive funding administration

There has been continued attention to good governance practices in the administration of the Centre for Innovation competitive funding programs. This year, a focus was placed on lessening the impact of COVID-19 disruptions on research and training programs funding recipients, while ensuring sound financial practices are followed and in compliance with our Health Canada contribution agreement (Strategic Policy Branch) and other funding partners.

The COVID-19 pandemic forced the closure of research laboratories nationally, forcing the transition to remote work and a pause in experimental work. To help lessen the impact of the delays that arose from these closures, The Centre for Innovation provided funding supplements to recipients of Intramural Research Grant Program (IRGP) and Canadian Blood Services-CIHR project grant funding. In addition, Canadian Blood Services provided no-cost extensions to all impacted research funding recipients.

To help minimize the impact of the pandemic on Canadian Blood Services graduate and postdoctoral fellows, all affected trainees supported by our competitive training programs were provided with additional financial support in alignment with Tri-Council Agencies approach.

Crisis leadership

Early in the COVID-19 pandemic, medical officer **Aditi Khandelwal** interviewed Canadian Blood Services' vice president of Medical Affairs and innovation **Isra Levy** on the topic of crisis leadership. **Levy** notes that during a crisis, ensuring its workforce is healthy, vibrant and safe is paramount and leaders must continually engage the employees to secure trust. "To adapt, organizations must remain resilient without becoming too slow to react. This balancing act requires leadership to be imaginative, flexible, and willing to align with redeployment during crisis," explains **Levy**.

In response to the pandemic, employee engagement at the Centre for Innovation took on increased significance as staff were supported in coping with shifting personal circumstances and demands. Employees were quickly equipped with the tools and resources they needed to work from home and were encouraged to access mental health resources provided for them. With compassionate leadership, Centre for Innovation staff exemplified the resilience and agility needed to embrace new priorities in a time of crisis.

Read the R.E.D. blog post: <u>Honest and</u> compassionate leadership in a crisis: An interview with Dr. Isra Levy.

Performance measurement

The Centre for Innovation continues to collect data to inform its performance measurement framework developed with Health Canada Strategic Policy Branch. This framework ensures that the Centre for Innovation demonstrates its contributions to the Canadian health system and the health of Canadians and meets the reporting requirements of the contribution agreement. The next page catalogues the Centre for Innovation key performance metrics over the last three years. The Centre for Innovation continues to deliver on its performance plan, a testament to its impact and contributions to a safe, effective, and responsive system for blood and blood products in Canada.

	Select Centre for Innovation program outputs and outcomes						
		Intended Outputs & Outcomes	Indicators	Target	2018-2019	2019-2020	2020-2021
		Grants and awards	Number of grants and awards provided (Appendix I)	140	189	197	193
Outputs		Learning opportunities	Number of presentations and events	375	434	385	339
		Supported network	Number of distinct Canadian investigators supported	N/A	124	102	160
		Canadian researchers advance knowledge on blood safety	Number of knowledge products published (Appendix II)	200	246	189	276
utcomes		Stakeholders access information on blood safety	Number of stakeholders attending events	5,000-7,500	3,763	2,869	3322
Immediate Outcomes			Page views of significant program websites	N/A	346,555	711,980	730,855
Imme		Stakeholders are equipped with the knowledge, skills,	Percentage of event attendees reporting knowledge gain	>85%	89%	88%	97%
		and supports required to enhance blood safety	Number of Highly Qualified Personnel completing training	5-20	14	8	9
irmediate	Outcomes	Key research stakeholders in the transfusion and transplantation community use program research findings to inform blood safety research	Percentage of staff researchers with H-index ≥ Canadian science standard of 10.6 (Appendix II)	90%	100%	100%	89%
Interm	õ	Key stakeholders make improvements in blood safety	Number of new or updated blood safety measures informed by the program	5-12	9	11	13
Ultimate	Outcome	Canadians have access to appropriate and effective health services	Percentage of stakeholders reporting that Canadian Blood Services plays an essential role in achieving patient outcomes	90%	99%	98%	100%

Note: Blood safety in the context of the program refers to a safe, effective, and responsive system for blood and blood products.

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Appendix I: Grants and Awards

Number of Centre for Innovation supported projects by program

Research Programs	56
Canadian Blood Services/CIHR partnership operating grants	3
Intramural research grants	20
MSM research grants	11
MSM plasma research grants	4
James Kreppner awards	2
Kenneth J. Fyke awards	1
Blood efficiency accelerator awards	13
Transfusion medicine program support awards	2
National Training Programs	22
Postdoctoral fellowships	7
Graduate fellowships	11
Transfusion medicine traineeship awards (now Elianna Saidenberg transfusion medicine traineeship award)	4
Research Laboratory Support Program	13
Discovery research laboratory support	8
Development research laboratory support	5
Social Sciences Support Program	2
Donor research group support	2

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Development Research Programs	71
Deepening the understanding of our products and the processes used to manufacture them	11
Developing new or next generation products	15
Improving current generation products and the processes used to manufacture them	
Improving and/or enabling the Product and Process Development Group	
On demand unit investigation	7
Other	16
Education Programs	6
BloodTechNet awards	5
Centre for Blood Research program support collaboration	1
Clinical Guideline Development Program	3
Externally Funded Grants and Awards	20
Total number of projects	193

Titles of projects supported by program

Research Programs

Canadian Blood Services/CIHR Partnership National Operating Grant Program

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

Intramural Research Grant Program

Anti-GPIb mediated thrombocytopenia: Implications for IVIg and other therapies

Anti-red blood cell monoclonal antibodies as a replacement for IVIg and anti-D in immune thrombocytopenia (new)

Assessing the impact of donor manufacturing characteristics on survival of transfused red blood cells (new)

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

Development of porcine equivalent red cell concentrates and plasma units for translatable ex vivo organ perfusion research (new)

Enabling next generation hematopoietic-based therapeutics and manufacturing (new)

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

Fc receptors and IVIg in immune thrombocytopenia

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

IN-TRUST: Using a transfusion database to explore the immune-modulatory impacts of blood transfusion and the clinical impacts of blood processing changes

Modulation of biofilm formation, virulence, and antimicrobial resistance by Staphylococcus aureus during platelet storage

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

New cryosolutions for stem cell-based therapeutics (new)

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

Plasma transfusion or plasma protein product infusion in a murine model of trauma

PREMISE: Point-of-care hemoglobin accuracy and transfusion outcomes in non-cardiac surgery (new)

Revisiting the universal donor: Does exposure to O blood products affect patient outcomes? (new)

Small molecule drug development of phagocytosis inhibitors

TAD-POL (Transfusion-Associated-Dyspnea: Prospective observation and laboratory assessment)

Translating novel clotting factor X function to treat thrombosis (new)

MSM Research Grant Program

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 Canadian Blood Services 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

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

MSM Plasma Program

Assessing the acceptability and feasibility of a plasma donation program for gbMSM in Montréal from the point of view of cis and trans gbMSM, volunteers from Héma-Québec, current donors, and plasma product recipients (new)

Assessing the acceptability, understanding and effectiveness of alternative screening questions for current donors (new)

Awareness and understanding of apheresis plasma donation and effectiveness of alternative donor screening questions for diverse gbMSM and trans populations (new)

The Calgary Plasma Study: Feasibility of implementing source plasma donation with alternative screening eligibility criteria for men who have sex with men (new)

James Kreppner Award Program

Canadian cord blood banking: Legal and policy responses

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

Kenneth J. Fyke Award Program

Canadians' attitudes and opinions regarding cardiac donation after cardiocirculatory death: A mixedmethods study

Blood Efficiency Accelerator Program

A Framework for Accelerated Synthesis of Trial Evidence - FAST Evidence - to assess efficacy of mesenchymal stromal cells and convalescent plasma for COVID-19 (new)

A machine learning based framework to analyze blood product transactional data for reducing discards

A study to understand C1 Esterase Inhibitor distribution and patterns of use in Canada

Are cervical cancer brachytherapy outcomes associated with pre-brachytherapy hemoglobin values and transfusion practice? An observational study comparing two academic centres

Blood product demand forecast modeling using clinical predictors

Blood utilization epidemiological profile to evaluate appropriate use (BLUE)

Demonstration of genetic blood group transition in patients undergoing ABO-mismatched hematopoietic stem cell transplantation by peripheral blood quantitative polymerase chain reaction targeting the ABO locus

Evaluating unintentional warming of glycerolized red cell concentrates

Informing distribution of COVID-19 convalescent plasma through implementation of CONCOR-1 in British Columbia (new)

Management of iron deficiency anemia in the pediatric emergency department: Pilot study of red blood cell transfusion IV iron therapy

Measurement of heavy metals in donor blood in Canada

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

Transfusion Medicine Program Support Award

McMaster Centre for Transfusion Research

University of Toronto QUEST Research Program

National Training Programs

Postdoctoral Fellowship Program

Development of a drug to replace IVIg, and antibody-dependent cellular cytotoxicity as cause for unexplained hemolysis post-transfusion

Donor characteristics and the quality of red cell concentrates

Identification of mechanisms leading to antibody independent red blood cell hemolysis (new)

New platform for targeted gene editing of hematopoietic stem cells for cellular therapy (new)

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

Reducing IVIG usage by developing novel prophylaxis therapies against fetal and neonatal alloimmune thrombocytopenia

The mechanism of action of monoclonal antibody blends in the potential replacement of anti-D in hemolytic disease of the fetus and newborn

Graduate Fellowship Program

A novel clot-dissolving agent derived from clotting factor Va

Deformability based cell sorting enabling quality control of stored red blood cells

Evaluation and improvement of cold stored platelets

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

Monoclonal antibodies with anti-D activity in amelioration of murine immune thrombocytopenia

New solution for cord blood unit preservation

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

Replacement of IVIg by small molecule inhibitors of phagocytosis (new)

Synthesis and live cell imaging of ice recrystallization inhibitors in red blood cells (new)

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

Transfusion Medicine Traineeship Award (now Elianna Saidenberg Transfusion Medicine Traineeship Award)

Physician completing AFC diploma in transfusion medicine at McMaster University (new)

Physician completing AFC diploma in transfusion medicine at University of Toronto (new)

Physician completing AFC diploma in transfusion medicine at McMaster University

Physician completing AFC diploma in transfusion medicine at University of Toronto

Research Laboratory Support Programs

Discovery research laboratory support

Blood product manufacturing and storage research laboratory

Immune biology research laboratory

Immune modulation research laboratory

Infectious diseases and immunopathology research laboratory

Infectious diseases and plasma protein research laboratory

Plasma and plasma protein research laboratory

Platelet biology and quality research laboratory

Platelet physiology and immunology research laboratory

Development research laboratory support

Blood for research program laboratory (new)

Genomics research laboratory (new)

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Microbiology development research laboratory

Operational research engineering laboratory

Stem cell development research laboratory

Social Sciences Support Program

Donor research

Donor research (new)

Product and Process Development Program

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

30-minute rule plasma

Autologous stem cell post thaw analysis (new)

BEST Cryoprecipitate study

Participate in multicenter study to test a new flow cytometry method to determine cord blood potency (new)

Pooled platelet product production (dose) simulator

Quality monitoring program product characterization: re-baselining post new production equipment installation

Quantification of residual red blood cells in platelets

Understanding high hemolyzers

Understanding impact of time to test on product quality attributes for frozen plasma products

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

Understanding the root cause of BacT false positive results (new)

Developing new or next generation products

Bacterial growth in cold stored whole blood (new)

Blood bag (collection) request for proposal

Cerus INTERCEPT pathogen reduced platelets in platelet additive solution

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Cord blood and registry composition analysis

COVID-19 convalescent plasma clinical trial support (new)

COVID-19 neutralizing antibody assay validation

Evaluation of products with x-ray versus irradiation

Freeze dried convalescent plasma (new)

Fresh frozen plasma eye drop aliquots

Leukoreduced (platelet sparing) cold stored whole blood produced using Terumo IMUFLEX whole blood saving platelets collection set

Modelling demand and outdate impact of introducing 5-day expiry pathogen reduced platelets in Northeastern Ontario and Nunavut

Modelling freeze dried convalescent plasma production (new)

Optimizing rejuvenation to improve the product quality of pathogen-inactivated and γ-irradiated red cell concentrates

Small platelet units - COVID-19 contingency

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

Improving current generation products and the processes used to manufacture them

Bacterial growth in cold stored platelets

Improved growth of anaerobic bacteria in platelets

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

Modelling red cell unit age at distribution after introduction of non-destructive quality control testing delayed bacterial sampling

Modelling red cell unit doses after introduction of non-destructive testing

Non-destructive quality control testing for platelet products

Non-destructive quality control testing for red cell products

Non-destructive quality control testing red blood cell study – safety perspective in support of the parent Product and Process Development red cell non-destructive quality control testing

Pool spin changes for Fresenius and Maco collection sets

Post-implementation revisions to cord blood sterility testing program

Validation and implementation of Vitek software upgrade (new)

Validation of new bottles with antibiotic neutralizer for cord blood sterility program (new)

Improving and/or enabling the Product and Process Development group

Acquisition and installation of microfluidics system at the Centre for Blood Research

Acquisition and installation of STAGO compact coagulation analyzer at netCAD

Database design and development

eProgesa for netCAD assessment and options

Increase the netCAD donor base

Product and Process Development test method validation: standardization and qualification of test assays in Centre for Innovation labs supporting Product and Process Development group

Product characterization assays and rounding rules (new)

Stabilizing the netCAD Blood4Research databases (new)

Terumo TSCD II R17091 tubing end segment closure integrity investigation (new)

Transitioning in-house sterility testing to testing group

On Demand Unit Investigation

ACP-215 hemolysis (new)

Freon leak in red cell refrigerator

Negative BacT bottles with precipitate

Oak red cell units placed in freezer

Oak red cell units with fibrin and clots

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

BacT failure October 2020 (new)

Other

British Columbia Centre for Disease Control COVID-19 antibody assay blood draws

Circular of information periodic review and overhaul

Circular of information update: B1 cryo process (new)

Circular of information update: Extending freezing time of apheresis frozen plasma (new)

Circular of information update: Fresenius whole blood collection set (new)

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Circular of information update: Intercept pathogen-reduced platelet concentrates (new)

Circular of information update: Quality control changes (new)

Circular of information update: X-ray irradiators (new)

COVID-19 banked samples (new)

COVID-19 seroprevalence study support (new)

Evaluating Incidence of bacterial contamination in platelet concentrates in Colombia

Extended shelf life platelets - post implementation optimization modelling

Modelling and simulation education & training

Modulation of bacterial growth during platelet storage

New Brunswick logistics modelling (redux)

Rebranding Product and Process Development Head Office controlled documents (new)

Education Programs

BloodTechNet Award Program

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

Blood and stem cell donations for men who have sex with men in Canada: A toolkit for healthcare professionals (new)

Development of internet modules for serology curriculum delivery

Support of HLA laboratory directors in-training for rotations in specialized laboratories (new)

Virtual transfusions competency assessment

Centre for Blood Research program support collaboration

Clinical Guideline Development Program (ICTMG)

Hemolytic disease of the fetus and newborn

Use of albumin

Use of platelets

Externally Funded Grants and Awards

An innovative Trial Assessing Donor Sex on Recipient Mortality (iTADs) (Canadian Institutes of Health Research)

Apolipoprotein A-IV and platelet function: Novel links with thrombosis, inflammation, and atherosclerosis (Heart and Stroke Foundation of Canada)

Deep supercooling of red blood cells: Towards practical long-term storage (National Institutes of Health)

Deformability based cell sorting enabling quality control of stored red blood cells (Canadian Institutes of Health Research)

Do packed red blood cells prepared by different manufacturing processes modulate inflammasome activation? (Australian Red Cross Lifeblood)

Enabling the cryopreservation of embryos from aquatic species using ice recrystallization inhibitors (new – Natural Sciences and Engineering Research Council of Canada)

Further examination of the mechanism of action of Fc-µTP-L309C in the amelioration of endogenous, chronic rheumatoid arthritis using the K/BxN mouse model (new – CSL Behring AG)

Hemostasis modulation by viruses (Heart and Stroke Foundation of Canada)

Implementation of non-invasive prenatal testing for RhD to predict fetal RhD blood type (new – Women & Children's Health Research Institute)

Into the unknown: Defining the optimal cryopreservation conditions for therapeutic thymic regulatory T cells (new – Canadian Donation and Transplantation Research Program)

Investigation of CryoProtectPure-STEM as a new dimethyl sulfoxide-free cryoprotectant for stem cells (Spectacular Diagnostics)

Novel strategies to combat thrombogenic activated factor XI (Heart and Stroke Foundation of Canada)

Sex MATTERS: Sex-Matched Transfusions to Effect Recipient Survival. A pilot randomized controlled trial (new – Canadian Institutes of Health Research)

Sickle cell disease and the need for blood: increasing donation by Black and racialized young adults (new – Social Sciences and Humanities Research Council of Canada)

Splenic macrophage Fc receptors in autoimmune hemolytic anemia and immune thrombocytopenia pathophysiology and patient outcomes (University of Toronto)

The politics of clinical trials in a pandemic: The role of the blood services in developing a treatment for COVID-19 (new - Social Sciences and Humanities Research Council of Canada)

The PSI domain of β3 integrin: A novel mechanism and target for anti-thrombotic therapy (Heart and Stroke Foundation of Canada)

Thrombosis and thrombocytopenia: Novel mechanisms and treatments. (Canadian Institutes of Health Research)

Translating novel factor Xa function to treat thrombosis (Heart and Stroke Foundation of Canada)

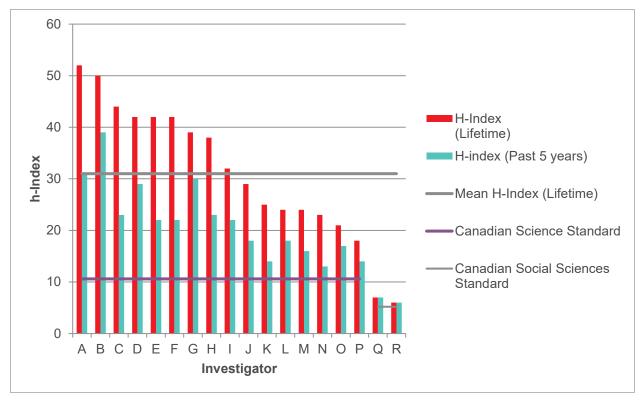
Using operational research methods to improve decision making in Canada's blood supply chain (Natural Sciences and Engineering Research Council of Canada)

Appendix II: Knowledge products and their impact

Summary of peer-reviewed and non-peer reviewed publications

Peer reviewed publications	210
Journal Articles	145
Review Articles	28
Clinical Guidelines	4
Comment/Letters/Editorials	15
Books/Book Sections	10
Canadian Blood Services Circular of Information	8
Non-peer reviewed publications	66
Canadian Blood Services Website Publications	29
Technical reports	33
Other	4
Total numb	per of publications 276

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Summary of H-index factor analysis

Notes: i) H-index factors measured using Google Scholar on April 12, 2021. ii) Mean H-index calculated used H-index factors from the 18 core investigators. Core investigators include Jason Acker, John Blake, Donald Branch, Dana Devine, Steven Drews, Mindy Goldman, Jennie Haw, Kelly Holloway, Alan Lazarus, Heyu Ni, Sheila O'Brien, Nicolas Pineault, Ed Pryzdial, Sandra Ramirez-Arcos, Peter Schubert, 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 for Canadian university professors in the biological sciences is 10.6 and average H-index for Canadian university professors in the social sciences is 5.2.

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Journal Articles

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