Centre for Discovery in Cancer Research

ANNUAL REPORT

2022/2023


Michael G. DeGroote
SCHOOL OF MEDICINE
CELEBRATING
50 YEARS
STOP
CROSSING

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Introduction

Dear Colleagues,

It's my pleasure to present this Annual Report for the Centre for Discovery in Cancer Research (CDCR).

Cancer is the leading cause of death in Canada. Nearly one in two Canadians will develop cancer in their lifetime, and approximately one in four will die from the disease. Our team at CDCR is working to change these statistics.

McMaster and Hamilton have many strong cancer experts working in clinical settings and laboratories across the city, as well as in collaborations across Canada and around the globe. The CDCR brings these scientists together to provide a 360-degree research agenda that addresses questions in the lab, clinic, and community to provide a holistic research program of global impact.

We are primarily focused on building expertise around treatment-resistant cancers, such as glioblastoma, triple-negative breast cancer, pancreatic cancer, treatment-refractory lung cancer, brain metastases, and advanced ovarian cancer.

The CDCR was established in October 2021, and since then, we have been very productive. Here are some key highlights:

- Our team of scientists and trainees are publishing outstanding cancer research, including in *Cancer Cell, Cell Reports Physical Science, Angewandte Chemie, PNAS*, and *The Journal of Cell Biology.*
- We have strengthened our scientific team by adding Professor Hong Han, an expert in cancer biology, RNA splicing regulators of cancer development, and innovative high-throughput technologies.
- We introduced the CDCR Seminar Series, bringing internationally recognized cancer researchers to lecture and interact with our trainees and scientists.
- Our outstanding trainees started the CDCR Trainee Seminar Series to share their research with their peers to help foster collaboration among our labs.
- Started a Trainee travel award program to support our Trainees to travel and present at conferences
- Launched our CDCR website, logo, and social media channels.
- We had our first Research Day Seminar, including presentations from our trainees and a keynote talk from world-renowned cancer researcher Dr. Charles Swanton (Francis Crick Institute, London).

We are proud of what we have accomplished so far and are optimistic about the impact of our research, as we develop our vision to build innovative programs of cutting edge, interdisciplinary research over the next five years.

Sincerely,

Dr. Sheila Singh
Director, CDCR
Professor of Surgery and Biochemistry, McMaster University
Pediatric Neurosurgeon, Hamilton Health Sciences

Researchers

Principal Investigators

Sheila Singh, MD, PHD

Department: Surgery

Area of Expertise: Brain cancer, cancer stem cells, immuno-oncology

Our research focuses on applying a developmental neurobiology approach to studying human brain tumours. As a pediatric neurosurgeon, I work with integrated health care teams to provide the best clinical care to brain tumour patients, using a unique perspective to guide research questions and areas of focus. With this powerful translational research approach, our lab is expanding the frontiers of brain cancer research.

My PhD thesis described the novel identification of a population of cancer stem cells that exclusively drive the formation of brain tumours. Building upon previous cell culture techniques developed for the isolation of normal neural stem cells (NSC) and applying them to brain tumours, and through the development of a xenograft model to efficiently study brain tumour initiating cell (BTIC) activity, my lab aims to understand the molecular mechanisms that govern BTIC self-renewal.

My lab is currently studying the regulation of BTIC signalling pathways in glioblastoma (GBM), brain metastases, and childhood medulloblastoma. Our ultimate goal of selectively target the BTIC with appropriately tailored combinations of small molecule therapies and immunotherapies. As BTICs are resistant to chemotherapy and radiotherapy, the lab employs a stem cell biology framework to study treatment-refractory brain cancers to identify and target the molecular mechanisms responsible for their treatment resistance. Ultimately, our lab's goal is to be able to take more targeted and effective therapies back to the clinic. To ensure that all of their findings have clinical utility, the Singh Lab has cultivated a specialty in developing robust patient-derived, pre-clinical models that recapitulate patterns of recurrence and relapse seen in patients.

Over the past seven years, I have led a pan-Canadian research collaboration of multi-disciplinary scientists who have built a translational pipeline to deeply profile recurrent GBM and its tumour immune microenvironment, to uncover novel biological targets, against which we empirically design and engineer new combinatorial immunotherapies. Our pre-clinically validated therapeutics constitute new Canadian inventions in the field of immuno-oncology, many of which are now being developed by international industry partners. Some examples include a spinout company, Empirica Therapeutics Inc., which was acquired by Century Therapeutics to create a Canadian subsidiary housed in the McMaster Innovation Park. Our team has already contributed to Canada's biotechnology sector, and has brought significant investment into Canadian GBM research development. We have created more industry and global academic partnerships to promote successful programs and drugs for GBM that could be brought to market in the future.

Ali Ashkar, DVM, PHD

Department: Medicine

Area of Expertise: Natural Killer cells, immuno-oncology, innate immune system

A major goal of our research is developing efficacious and safer treatments for hard-to-treat solid tumors. To do this, we are harnessing the tumor killing ability of Natural Killer (NK) immune cells, which have an intrinsic ability to distinguish between healthy and malignant cells. Advances in the ex vivo expansion of human NK cells has enabled the adoptive transfer of NK cells to treat patients, showing clinical success against hematologic malignancies. However, there are still two major limitations to overcome in order to successfully combat solid tumors:

Efficient homing of the adoptively transferred immune cells to the solid tumor microenvironment (TME), and, the hostile and immunosuppressive TME.

Our lab aims to overcome these two limitations to enhance NK cell-based cancer immunotherapy for solid tumors.

We have recently discovered why NK cells are dysfunctional in the TME and have established protocols to re-program their metabolism. This re-programming allows them to not only remain functional but actually thrive in the hostile TME. To further enhance NK cell functions in the TME, our lab is also engineering NK cells to express chimeric antigen receptors using CRISPR-Cas9 technology and AAV viral vectors. At present, we are testing off-the-shelf expanded NK cells in preparation for a Phase I clinical trial for treatment of ovarian cancer.

Tobias Berg, MD, PHD

Department: Oncology

Area of Expertise: Leukemia, leukemic stem cells, Minimal Residual Disease

The focus of my research is on understanding determinants of treatment response in Acute Myeloid Leukemia (AML) and on developing novel treatment approaches based on this understanding. While modern treatment approaches, including allogeneic stem cell transplantation, can often result in remission in patients with AML, many patients still experience relapse, making AML highly difficult to treat and resistant to cancer. The development of leukemia as well as relapse (in particular after allogeneic stem cell transplantation) are often driven by epigenetic processes. We, therefore, study the role of epigenetic regulators in AML and their interplay with regulators of lineage-specific differentiation, metabolism, and immune recognition. In these studies, we use functional model systems in vitro and in vivo, single-cell sequencing analysis, and functional metabolic studies. To facilitate this research, we are collecting primary samples from patients with hematological malignancies in our Hamilton Health Sciences (HHS) McMaster Cancer Research Stem Cell Bank.

Our work aims to identify novel treatment combinations and develop maintenance strategies to prevent relapse in AML after allogeneic stem cell transplantation. Our work is funded through the Boris Family Chair for Leukemia and Hemopoietic Stem

Cell Translational Research, the Canadian Foundation for Innovation, the Ontario Research Fund, and the Ontario Institute for Cancer Research (OICR).

As a hematologist, I treat patients with hematological malignancies at the Juravinski Cancer Centre (JCC). I am also a member of the Stem Cell and Cellular Therapy Program, which offers both autologous and allogeneic (related or unrelated donor) stem cell transplants and have been pioneering in chimeric antigen receptor T-cell (CART-Cell) therapy. In addition, I have been actively involved in many early clinical trials at different stages of clinical development. In these roles, I lead the Translational Oncology Program in McMaster's Centre for Discovery in Cancer Research (CDCR), facilitates collaborations and act as a bridge between the clinicians at the JCC and basic cancer researchers in the CDCR.

Jonathan Bramson, PHD

Department: Medicine

Area of Expertise: Immunology, T-Cells, immuno-oncology

I am a Professor in the Department of Medicine, the Vice Dean, Research for the Faculty of Health Sciences, and I hold the John Bienenstock Chair in Molecular Medicine. The Bramson Lab is focused on applying using synthetic biology and chemical biology approaches to direct T cells against discrete tumour targets. Among the technologies developed by the Bramson Lab, a novel synthetic antigen receptor, known as the T cell antigen coupler (TAC), is the most advanced TAC-engineered T cells have demonstrated promising biological outcomes compared to T cells engineered chimeric antigen receptors (CARs) in pre-clinical models; notably, anti-tumour efficacy was comparable but the production of pro-inflammatory cytokines by TAC-T cells is much lower, which suggests a safety advantage. I also co-founded Triumvira Immunologics, which has raised >$120M in private financing, opened two INDs to test TAC T cells, and developed several TAC receptors for novel targets. Lastly, I served as Chief Scientific Officer (CSO) for Triumvira from 2015 – 2020 and is currently the Chair of the Scientific Advisory Committee (2021 – present).

Current research in the Bramson Lab seeks to enhance the potency of engineered T cell therapies for cancer and reduce hurdles to access. To this end, the lab employs a combination of syngeneic and xenograft murine tumour models to study the anti-tumour activity of engineered T cells. The potency enhancers are a combination of genetic engineering strategies (novel synthetic antigen receptors, novel costimulatory receptors), chemical agents (small molecules that enhance T cell function and sensitize tumours to T cell killing) and oncolytic viruses. To reduce hurdles to access, the lab is investigating off-the-shelf T cells (notably gamma-delta T cells) and programmable universal synthetic antigen receptors. Conceptually, the combination of an off-the-shelf T cell with a programmable synthetic antigen receptor would allow large-scale manufacturing of a single engineered T cell product which is subsequently programmed by the hospital pharmacist to meet the antigenic profile of the tumour. Additionally, my lab is working with investigators across Canada to develop a distributed platform of automated point-of-care T cell manufacturing to reduce the cost of autologous T cell products and increase accessibility.

Juliet Daniel, PHD

Department: Biology

Area of Expertise: Breast cancer, cancer cell adhesion

My research is focused on elucidating the molecular mechanisms governing tumour progression from the benign to the malignant invasive phase, a phenomenon that is still poorly understood. Furthermore, my research is also focused on elucidating the factors (genetic, environmental and/or socio-economic) that contribute to the disparities in cancer outcomes in people of African ancestry.

The Daniel Lab team is currently studying the aggressive and difficult to treat triple negative breast cancers (TNBC) that are most prevalent in young Black and Hispanic women – groups that despite a lower incidence and lifetime risk of breast cancer than Caucasian women, have a higher mortality rate from breast cancer. This difference in TNBC prevalence and mortality seem unrelated to socio-economic status and hints at unknown genetic factors or an ancestral genetic predisposition as the cause.

My research led to the discovery and naming of a new gene "Kaiso", coined from my favorite Caribbean music "calypso". Kaiso regulates the expression of genes that control cell proliferation, cell adhesion, and cell motility. Consequently, Kaiso's malfunction in cells leads to developmental disorders, and aggressive tumour growth and spread in various human cancers (e.g., breast, colon, prostate). Depletion of Kaiso from TNBC cells prevents TNBC cell metastasis to lungs and liver in mouse models, suggesting that Kaiso plays a role in the spread of breast cancer. Indeed, high Kaiso expression correlates with aggressive breast tumours and poor survival in Black women compared to Caucasian women. Ongoing studies are focused on determining how Kaiso promotes breast tumour metastasis and elucidating Kaiso's role in the racial difference in cancer outcomes. By clarifying Kaiso's role in TNBC and outcomes, we will better understand TNBC and contribute to the development of novel tests and therapies for TNBC. Our findings will help decrease the racial differences in breast cancer outcomes and help millions of women diagnosed with TNBC worldwide regardless of ethnicity.

Lastly, I partner with The Olive Branch of Hope cancer support service in Toronto to organize "Think Beyond 'Love Pink' Breast Cancer Awareness" workshops for women of African Ancestry in Ontario and the Caribbean.

Hong Han, PHD

Department: Biochemistry and Biomedical Sciences

Area of Expertise: Brain cancer, RNA regulation, systems biology

A major challenge in biomedical research is to systematically identify genotype-phenotype relationships and therapeutic vulnerabilities. Our research focuses on high-throughput discovery and characterization of coordinated multilayer gene regulation in health and disease, and the development of novel approaches for cancer diagnosis, prognosis, and therapy.

We have pioneered the development and application of several integrated technological platforms for large-scale genetic/drug screening and ultra-high-throughput single-cell multi-omics profiling. Leveraging the power of these systematic experimental and computational approaches, together with in vitro, in vivo, and patient cohort studies, we have uncovered multilayer gene regulatory maps of key cell fate control. For example, we have discovered and characterized master alternative splicing and gene regulators of stem cell biology, lineage development, neurological disorders, and cancer progression and recurrence, including MBNL1/2, RBM38, and PUF60. In addition, we have identified small molecule modulators and mechanistic insights into possible new gene/RNA-directed therapeutics for aggressive brain, lung, and prostate cancers. We are currently further expanding the methodological advances and biological discoveries we have made to reveal coordinated multilayer gene regulatory mechanisms underlying tumor ecosystem evolution, particularly glioblastoma and metastatic prostate cancer. Our highly collaborative research program employs systematic, in-depth patient cohort and disease model studies to dissect dynamic tumor and microenvironment interactions at single-cell resolution and how they evolve in time and space to specifically impact cancer progression, therapy response, and relapse. Together, these enable us to comprehensively elucidate dynamic multilayer gene function and regulation underlying complex cancer processes. Moreover, the framework and technology platforms we build are highly translatable to investigate diverse cancer types and models to discover gene/isoform drivers and mechanisms, leading to multimodal transformative therapeutic strategies to facilitate precision medicine. Our research has been supported by funding from CIHR, Simons Foundation, Donnelly Home Research Fund, and MITACS.

Brian Lichty, PHD

Department: Medicine

Area of Expertise: Oncolytic viruses, Immuno-oncology

My research has built extensive expertise in oncolytic viruses and related immunotherapies. I am currently a professor in the Department of Pathology & Molecular Medicine and the McMaster Immunology Research Centre (MIRC) since 2004. I am one of the co-founders of Turnstone Biologics, a successful biotech company developing oncolytic viral immunotherapies.

My expertise includes influencing research in the identification of strategies to leverage oncolytic viruses to harness the patient's immune system in a sustainable manner, including vaccine design and engineering to directly engage the adaptive immune system tumour-specific and/or to enhance combinations with other immunotherapies. Lastly, I am the Director of the Robert E. Fitzhenry Vector Lab at McMaster where clinical grade viral vaccines are manufactured for human clinical trials.

Karen Mossman, PHD

Department: Medicine

Area of Expertise: Oncolytic viruses, Immuno-oncology

The focus of our research is to understand how viruses evade host intrinsic and immune defenses. When a virus infects a host, the host mounts an impressive immune response aimed at preventing the virus from multiplying and spreading. Viruses have evolved strategies to block this response to ensure their survival. Probably the most important aspect of the host immune response to virus infection is the production of an immune modulator called interferon. Interferon has a great impact on host defense mechanisms and as a result viruses have evolved multiple strategies to overcome its activities. We are currently studying the mechanisms of interferon inhibition and the countermeasures taken by different viruses in a number of mammalian systems, including bats.

These studies have led us to developing viruses for use in gene therapy and cancer therapy. The virus that we currently focus on is bovine herpesvirus type 1 (BHV-1) which is a cattle-specific pathogen that causes shipping fever in cattle. We previously found that BHV-1 targets and kills a wide variety of human cancer cells while having no effect on healthy cells. Such viruses, called "oncolytic viruses" are currently being tested as a novel approach to cancer therapy in the hopes of eliminating tumours without the toxic side effects associated with many current treatments. BHV-1 has many interesting properties, including the ability to target both pre-neoplastic and fully transformed cells, the ability to target cancer stem cells, and the ability to elicit oncolytic activity in the apparent absence of virus replication. Moreover, when screening the NCI60 panel of human cancer cell lines, we found that BHV-1 efficiently targets ~80% of the panel, with a preference to lung and colorectal cancers. Recent in vivo studies suggest that BHV-1 can be used clinically following both intra-tumour and intravenous delivery, and that BHV-1 sensitizes tumours to checkpoint blockade immunotherapy. We are currently investigating the molecular mechanisms of BHV-1-mediated killing, elucidating how BHV-1 alters the tumour microenvironment and developing BHV-1 platform vectors for clinical use.

Anthony Rullo, PHD

Department: Medicine

Area of Expertise: Covalent immune recruitment, chemical immunology

The focuses of the Rullo Chemical Immunology research program are directed at integrating the tools of organic chemistry and immunobiology to develop new molecular approaches capable of interrogating and modulating the host immune-cancer cell, interactome.

The current program encompasses three major platforms:

1. The development of covalent bi-functional molecules, "Covalent Immune Recruiters," that enhance immune recognition of diseased cells and pathogens.
2. The development of multi-valent/multi-specific tumour targeting strategies to amplify immune recruitment to heterogenic and low antigen expressing cancers.
3. New immune receptor and lectin binding ligand discovery platforms using dynamic covalent chemistry.

The Rullo Lab is founded within the scientific environment of the Center for Discovery in Cancer Research (CDCR), immersed in cancer immunotherapeutic discovery and translational science. In this environment, the Rullo Lab's therapeutic strategies are efficiently integrated with CDCR platforms, acceleration, commercialization, and translation to the clinic. Most recently, ANNA Biosciences, a McMaster university spin-off, was founded on Rullo Lab covalent antibody recruiting technology in 2020.

Yonghong Wan, PHD

Department: Medicine

Area of Expertise: Adoptive T-cell therapy, oncolytic viruses

Our research is mainly focused on the development of cancer vaccines to treat solid tumours. Specifically, we pioneered a novel approach of engineering oncolytic viruses to be anti-tumour vaccines (termed oncolytic vaccines or OVs). We have demonstrated in multiple tumour models that OVs are more potent than conventional vaccines (e.g., dendritic cell- or peptide/adjuvant-based vaccines) due to the replication capacity of oncolytic viruses. OVs can effectively engage and expand tumour-specific T cells (both endogenous and adoptively transferred) while retaining their inherent ability to directly infect and debulk the tumour and reverse the immunosuppressive tumour microenvironment. As a result, OV therapy does not only boost antigen-specific T cells to eliminate the primary tumour but also improves epitope spreading to non-target tumour antigens which promote long-term clearance of solid tumours.

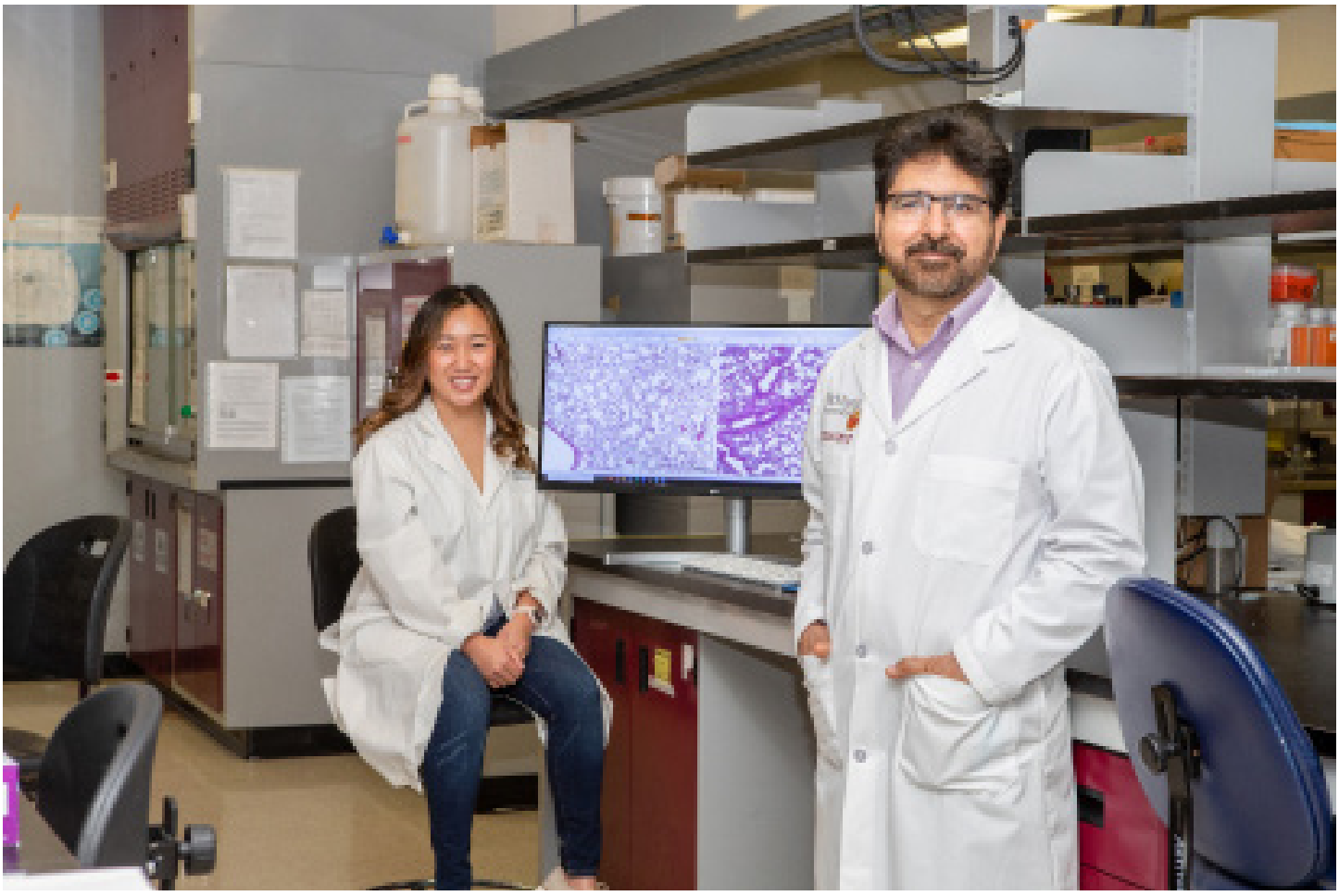
The therapeutic intensity of our OV platform has enabled us to address more difficult challenges in cancer immunotherapy. For instance, tumour burden is an inherent barrier to therapeutic responsiveness including treatment with OVs. We find that large tumours that mitigate the efficacy of OVs are associated with increased immunosuppressive pathway changes in the tumour microenvironment coinciding with prolific cellular exhaustion. Interestingly and encouragingly, concomitant delivery of class I histone deacetylase inhibitor, MS-275, can restore therapeutic efficacy by promoting tumour tissue homeostasis and subverting T cell exhaustion programming. Another example is that the potency of OVs to induce maximal CD8+ T cell responses allows us to better assess the immunogenicity and tumour rejection potential of computationally predicted neoantigens. Although neoantigens are an ideal target for cancer immunotherapy, there is a lack in knowledge of the criteria to use when selecting neoepitopes for clinical application. Indeed, we find that the immunogenicity can be enhanced by OVs, but it does not translate into a better anticancer effect. Instead, we demonstrate that it is expression level but not the immunogenicity of neoepitopes presented by tumour cells dictates tumour rejection capacity. We are currently exploring the combination of OVs with other therapeutic approaches, especially targeting neoantigens, to overcome immunosuppression and T cell dysfunction.

Obligation of Full Membership

Full members will be expected to participate in all aspects of programming and identify the new cancer research centre as their primary affiliation, which includes transferring research overheads to the cancer research centre, as per the McMaster Faculty of Health Sciences (FHS) overhead policy. Full members will share in the costs for maintaining common equipment and seek to secure group funding whenever possible.

Membership was solicited through an open call for applications at the university. Applicants must have existing research funding and a strong history of scholarly research in basic and translational cancer research, which should represent more than 50 and up to 100 percent of their overall research program.

All members are held to the highest standards of professionalism.



Associate Members

André Bédard
Department:
Biology

Richard Epand
Department:
Biochemistry and Biomedical Sciences

Amy Gillgrass
Department:
Medicine

Rosalyn Juergens
Department:
Oncology

Aly-Khan Lalani
Department:
Oncology

Jian Lu
Department:
Pathology and Molecular Medicine

Jakob Magolan
Department:
Biochemistry and Biomedical Sciences

James McNulty
Department:
Chemistry and Chemical Biology

Saman Sadeghi
Department:
Chemistry and Chemical Biology

Pablo Serrano
Department:
Surgery

Jenna Smith-Turchyn
Department:
Rehabilitation Science

Theos Tsakiridis
Department:
Oncology

Li Wang
Department:
Anesthesia

Ryan Wylie
Department:
Chemistry and Chemical Biology

Xu-Dong Zhu
Department:
Biology

Obligation of Associate Membership

Associate members are invited to participate in programming but will not be expected to contribute financially to the Centre. However, they will be allowed access to core infrastructure. Maintenance and operational costs are recovered through user fees.

All members are held to the highest standards of professionalism.

Research Productivity

The CDCR mandate fits within McMaster University's research strategic goals. McMaster lists "Research and Scholarship" as one of its five priorities in its *Institutional Priorities and Strategic Framework 2021-2024*. The Framework defines McMaster as "the go-to place for world-class researchers and collaborators who share our values and commitment to working together across disciplines, sectors, and borders to develop knowledge, tackle global issues, and advance human understanding."

The CDCR builds expertise around treatment-resistant cancers of high need, thus **developing knowledge** and **advancing human understanding**.

Global leadership and impact

- Proven track record of high-quality science by members with **787** lifetime publications
- Over **$40 million** held in current grants by CDCR members

Be a Driver of Economic Prosperity and Social Innovation

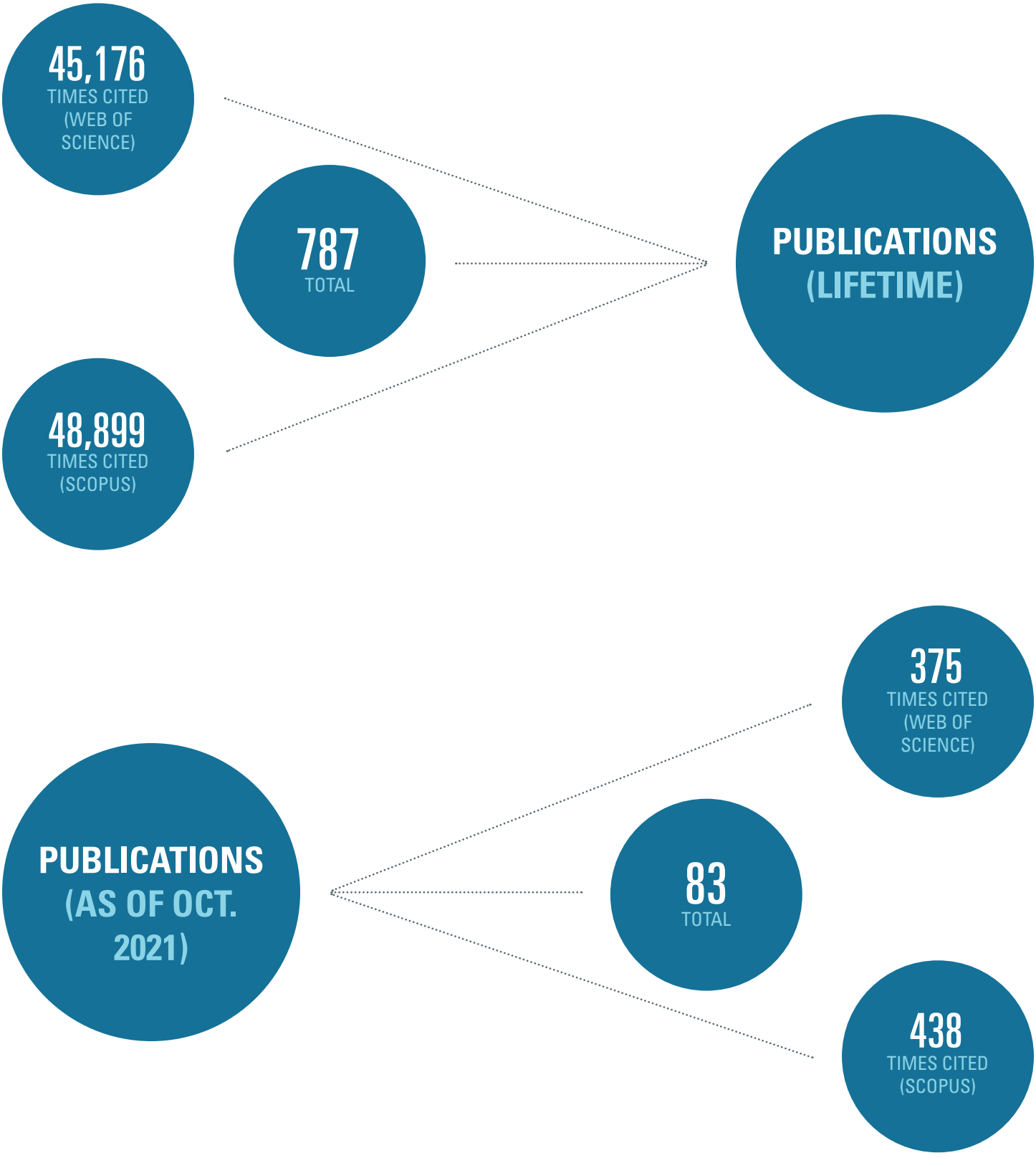
- Three biotechnology companies created by CDCR members - **Turnstone Biologics, Triumvira Immunologics, Empirica Therapeutics**
- **31 patents** held by CDCR members
- New CDCR recruits hired to develop trailblazing science

Collaboration and Partnership

- High number of national and international collaborations, including across Hamilton, Canada, the United States, and eleven other countries
- High level of activities and opportunities for CDCR trainees

https://president.mcmaster.ca/app/uploads/2022/02/Institutional-Priorities-and-Strategic-Framework_FINAL_5May21.pdf

Publications Measures



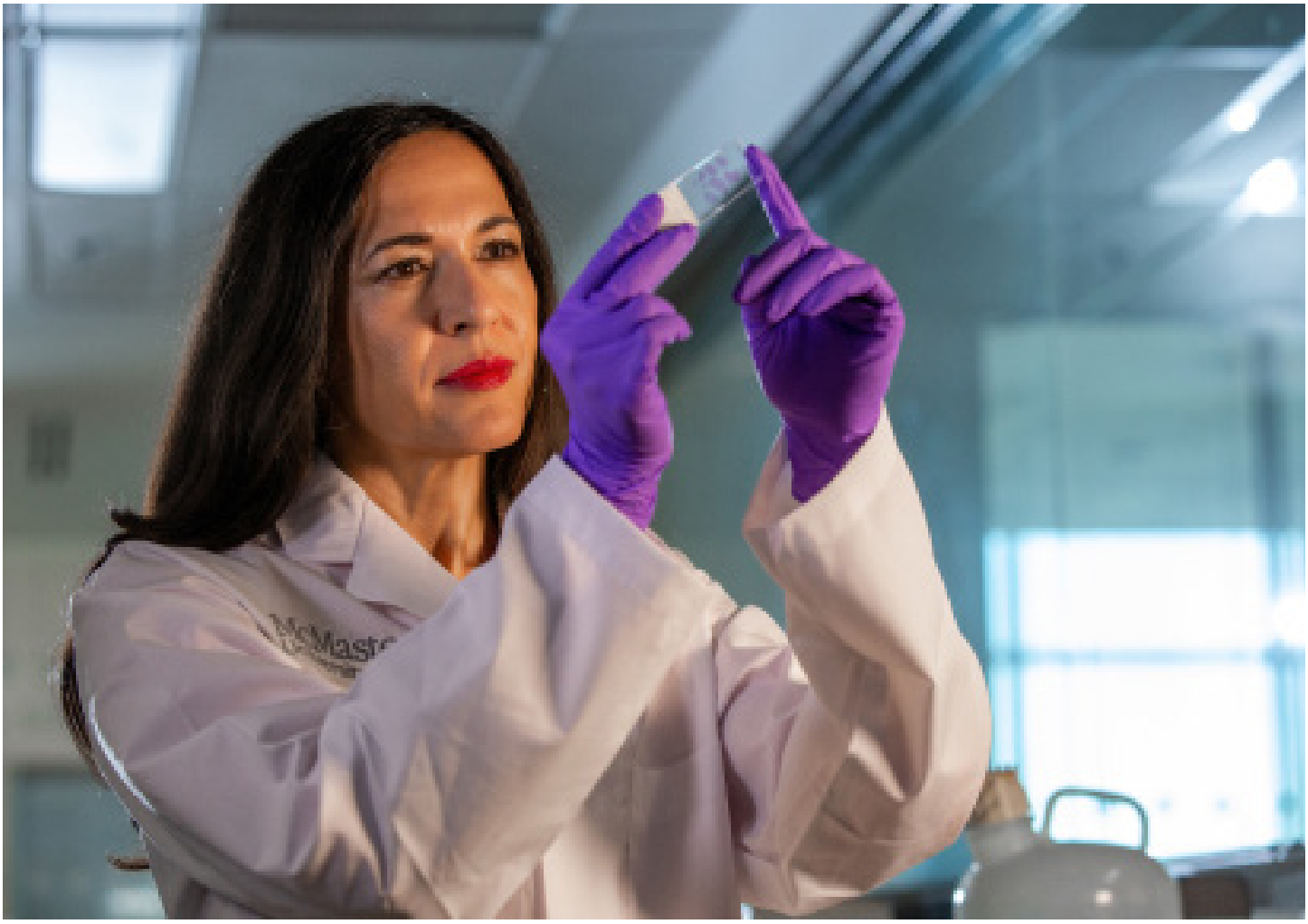
Scientific Advisory Board Report Summary

The CDCR Scientific Advisory Board (SAB) met on September 23, 2022, and provided feedback about the research output of the Centre. In the Report *[Appendix A]* :

> Based on the relatively limited resources available the SAB strongly encourages Dr. Singh and McMaster Senior leadership to focus their attention to a limited number of programs/ themes to pursue to enable them to retain a globally competitive edge and provide a distinct contribution to the Canadian research ecosystem.

The SAB on the CDCR research productivity:

> The CDCR consists of 10 Full members, 9 with established research programs and 1 new member, Dr. Hong Han who was just recruited and will be starting her own independent research program. Despite the relatively small research group they have been very productive in publishing high impact papers and securing funding from national agencies.



Research Collaboration Across the Globe

CANADA

Biomanfacturing Centre, ON
Canadian Cancer Trials Group, ON
Centre for Excellence in Cell Therapies, QC
Dalhousie University, NS
Genomics Sciences Centre, BC
McGill University, QC
National Research Council, ON
Ontario Institute for Cancer Research, ON
Ottawa Hospital Research Institute, ON
Princess Margaret Cancer Centre, ON
Structural Genomics Consortium, ON
Terry Fox Laboratory, BC
University of Alberta, AB
University of British Columbia, BC
University of Calgary, AB
University of Guelph, ON
University of Manitoba, MB
University of Ottawa, ON
University of Toronto, ON
University of Waterloo, ON
University of Western Ontario, ON
Women's College Hospital, ON

USA

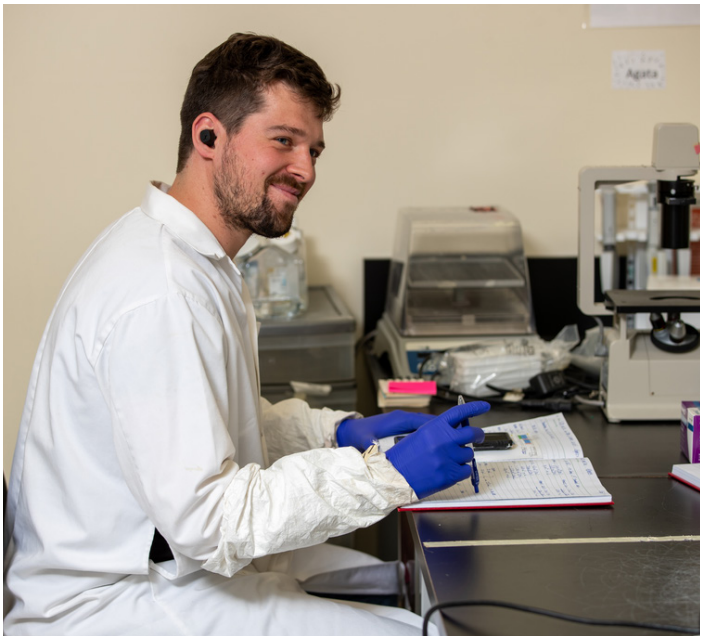
Case Comprehensive Cancer Centre, OH
AbbVie, IL
Children's Hospital of Philadelphia, PA
Children's National Hospital, DC
Columbia University, NY
Harvard Medical School/Broad Institute, MA
Imago Biosciences, CA
University of Southern California, CA
National Institutes of Health, MD
Ohio State University, OH
The State University of New Jersey, NJ
St. Jude Children's Research Hospital, TN
Stanford University, CA
University of Michigan, MI
University of Minnesota, MN
University of Pennsylvania, PA
Cornell University, NY
Yale University, CT

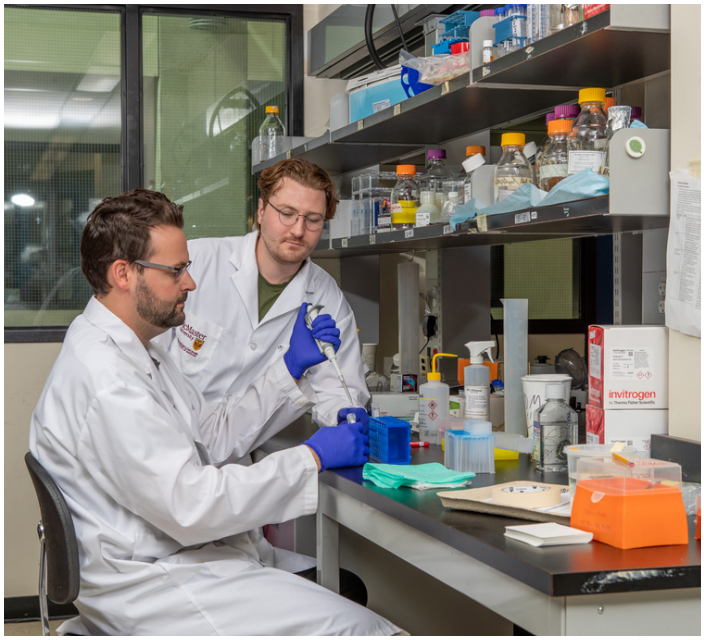
INTERNATIONAL

Calabar Teaching Hospital, Nigeria
Cancer Research UK Manchester Institute, United Kingdom
Francis Crick Institute, United Kingdom
Gebze Technical University, Turkey
Goethe University Frankfurt, Germany
Heidelberg University, Germany
Indian Institute of Technology Mandi, India
Institute of Biotechnology, Czech Republic
Kiadis Pharma, The Netherlands
Lagos Teaching Hospital, Nigeria
Nelson Mandela University, South Africa
Peter MacCallum Cancer Centre, Australia
University of Freiburg, Germany
University of Münster, Germany
University of Pretoria, South Africa
University of the West Indies, Jamaica
Utrecht Medical Center, The Netherlands

Education

10	Principal Investigators
93	Highly Qualified Personnel
15	Post Doctoral Fellows
21	PhD Students
20	Masters Students
15	Undergraduate Students
15	Technicians
1	MD Student





Training and Outreach

Our Trainee Program started in the summer of 2022. Since then, the CDCR trainees have participated in several learning, mentorship, and collaborative opportunities in the Centre, driving education and collaborative opportunities. Some of their trainee opportunities include presenting their research at our Research Day Symposium, presenting their research in the CDCR Trainee Seminar Series, and interacting with internationally renowned cancer researchers.

We will continually evaluate and assess the program's effectiveness to ensure continuous improvement and success in training the next generation of cancer researchers.

CDCR PI, Prof Anthony Rullo, oversees the Trainees as the CDCR Director of Training.

The CDCR Trainees are involved in the following organizing committees:

Academic Committee

Organizes the monthly CDCR Trainee Seminar, where two trainees provide updates on their research. The seminars offer trainees the opportunity to learn about other work being done in the Centre and help stimulate collaboration between labs.

The committee plans to organize other activities, such as bioinformatic seminars and panels with industry members.

Social Committee

Helps organize social activities for the Centre to foster collaboration, such as the bi-weekly Morning Socials and the Holiday party.

Research Day Committee

Assists the CDCR Administrative team with organizing the annual Research Day Symposium.

Organization Structure

In keeping with the University's *Guidelines for the Governance and Review of Research Institutes, Centres and Groups,* the reporting structure will be as follows:

Staff

The members of the CDCR staff include:

- Director - Sheila Singh
- Operations Manager - Paul Kutasi
- Lab Operations Coordinator - Andrew Allen
- Administrative Assistant - Dana Radcliff

Governing Board (GB)

Dr. Jonathan Bramson

Vice-Dean of Research, *Faculty of Health Sciences*
Chair of the CDCR GB

Dr. Brian Coombes

Chair of Biochemistry and Biomedical Sciences

Dr. Marie Elliot

Chair of Biology

Dr. Jonathan Sussman *

Chair of Oncology

Dr. Mohit Bhandari

Chair of Surgery

Dr. Mark Crowther

Chair of Medicine

Dr. Mark Jeschke *

Vice-President of Research, *Hamilton Health Sciences*

Dr. Lehana Thabane *

Vice-President of Reseach, *St. Joseph's Healthcare Hamilton*

Dr. John Valliant *

CEO, *Fusion Pharmaceuticals Inc.*

*ex-officio members

Scientific Advisory Board (SAB)

PROF. CAROLINE DIVE

Director of the CRUK Manchester Institute Cancer Biomarker Centre, University of Manchester; President, EACR; Commander of the Order of the British Empire; world expert in biomarker discovery and cancer biology.

PROF. JASON MOFFAT

Program Head, Genetics and Genome Biology, SickKids. Canada Research Chair, functional genomics of human cancer; world leading expert in systems biology, genetic interaction networks, CRISPR, biotechnology development.

PROF. STEPHEN ROBBINS

Director, ICR/CIHR; Director, Lady Davis Institute; Professor at McGill (former co-director of Annie Charbonneau Cancer Centre, U Calgary); leading expert in molecular genetics of cancer and TME.

PROF. CHARLES SWANTON

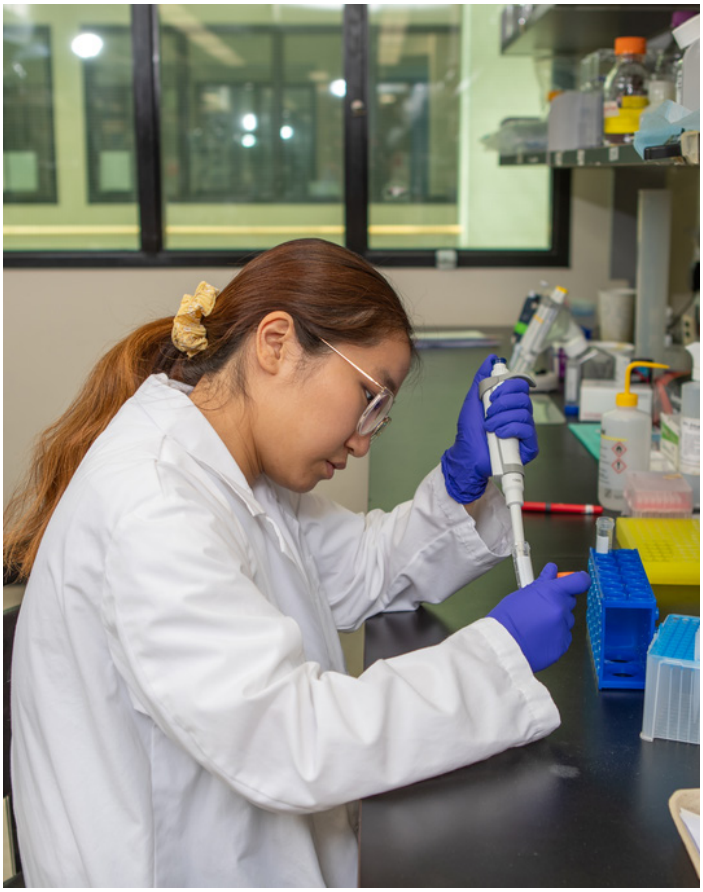
Royal Society Napier Professor of Cancer Medicine, Cancer Research UK (CRUK) Chief Clinician, Group Leader of the Translational Cancer Therapeutics laboratory, Francis Crick Institute), Chair in Personalised Cancer Medicine at the UCL Cancer Institute and Consultant Thoracic Medical Oncologist at UCL Hospitals. World leader in chromosomal instability in cancer, intratumoral heterogeneity and treatment resistance in cancer.

Approach to EDI

The CDCR is committed to promoting equity, diversity, and inclusion (EDI) in all aspects of our work. We recognize that addressing disparities and ensuring inclusivity in cancer research is essential to achieving our mission of advancing cancer prevention, diagnosis, and treatment.

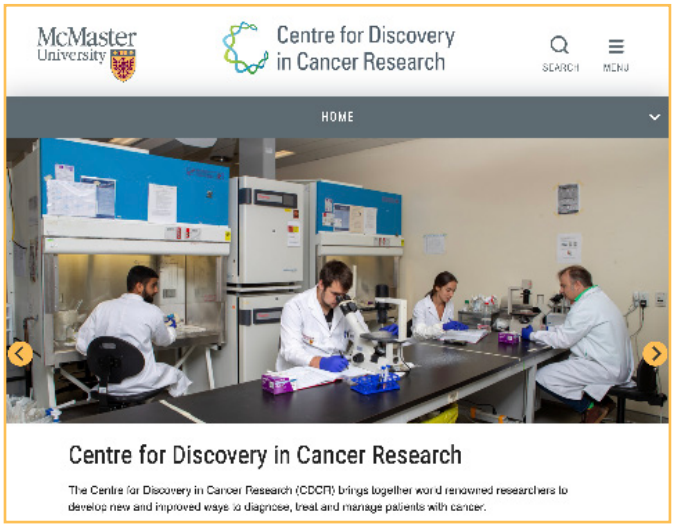
To align with the EDI goals of McMaster University, the CDCR will prioritize the recruitment and retention of diverse faculty, staff, and trainees, as well as ensure a welcoming and supportive environment for all. We will also actively seek to engage with and address the health disparities in our communities.

Furthermore, we will work to integrate EDI considerations into our research practices, including data collection, analysis, and dissemination. By prioritizing EDI in all aspects of our work, we believe we can achieve more equitable outcomes in cancer research and contribute to a more just and inclusive society.



Communication and Engagement

Website



The CDCR launched its web and social media presence. In September 2022, the CDCR launched its website.

cdcr.mcmaster.ca

4,119 — Total Website visitors

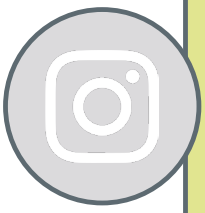
During the website launch, we also produced a video highlighting the CDCR.

https://youtu.be/6lw0ko3Y87U

187 — Total Video Views

Social Media

The CDCR launched a series of social media channels to expand reach to the McMaster and global communities.

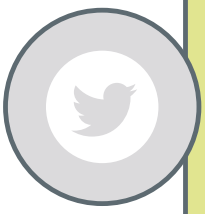


Instagram

198 Followers
396 Reach
337 Profile views

Facebook

1 Follower
65 Reach
7 Page visits



Twitter

23 Followers
1700 Impressions
137 Profile visits

YouTube

10 Subscribers
7153 Impressions
656 Video Views

Newsletter

Mailchimp Mail Out

236 Subscribers
59.5% Average Open Rate → **47.5%** Industry Average Open Rate
15.7% Average Click Rate → **8.3%** Industry Average Open Rate

Events

The CDCR has been active in running educational events since July 2022. Our Centre has run one Research Day Symposium, seven CDCR Seminar series with expert cancer researchers, and two trainee seminar series events with four trainee speakers.

Research Day Symposium

Date: September 22, 2022
Location: McMaster Innovation Park
Attendees: Approximately 120 attendees
Keynote speaker: Professor Charles Swanton (CRUK)
The Research Day Symposium showcased research by trainees with over 30 oral and poster presentations featuring research in CDCR labs from both Principal Investigators and associate members.


McMaster
University
HEALTH SCIENCES
McMASTER
INNOVATION
PARK

CDCR Seminar Series

Our monthly seminar series aims to bring renowned scientists to present their innovative research to the Centre's scientists and trainee members.

DATE: July 28, 2022
SPEAKER: Professor Rafa Montenegro-Burke (Donnelly)
TITLE: Untargeted Metabolomics: Mapping the Cancer Metabolome to Identify Therapeutic Vulnerabilities
ATTENDEES: 50 people in-person, 15 people virtually
YOUTUBE VIEWS: 74 views

DATE: August 25, 2022
SPEAKER: Professor Tobias Berg (CDCR)
TITLE: Epigenetics and AML: Impact on Metabolism and Immune Recognition
ATTENDEES: 40 people in-person, 19 people virtually
YOUTUBE VIEWS: 26 views

DATE: September 29, 2022
SPEAKER: Professor David Shackelford (UCLA)
TITLE: 3-dimensional structural and functional imaging of mitochondrial networks in lung tumors
ATTENDEES: 70 people in-person, 11 people virtually
YOUTUBE VIEWS: 65 views

DATE: October 27, 2022
SPEAKER: Professor Anthony Rullo (CDCR)
TITLE: Synthetically Modulating Tumor Immune Recognition Using Proximity Induction
ATTENDEES: 42 people in-person, 12 people virtually
YOUTUBE VIEWS: 67 views

DATE: November 24, 2022
SPEAKER: Professor Daniel Schramek (Lunenfeld)
TITLE: Using in vivo CRISPR approaches to elucidate the dark matter of the genome
ATTENDEES: 70 people in-person, 8 people virtually
YOUTUBE VIEWS: 98 views

DATE: January 26, 2023
SPEAKER: Professor Thomas Kislinger (UofT)
TITLE: Clinical Proteomics: Biomarker Discovery & Therapeutic Targets
ATTENDEES: 77 people in-person, 9 people virtually
YOUTUBE VIEWS: 67 views

DATE: February 23, 2023 *
SPEAKER: Professor Colin Kretz (TaARI)
TITLE: Investigating Protease-Substrate Relationships in the -Omics Era: ADAMTS13 and VWF as Key Mediators of Blood Coagulation

DATE: March 30, 2023 **
SPEAKER: Professor Hong Han (CDCR)
TITLE: Embracing Complexity to Achieve Precision: Multilayer Cell Fate Control in Development and Cancer

*postponed due to snowstorm
** To Be Determined

CDCR Trainee Seminar Series

A monthly seminar series showcasing our trainees and their latest research; organized by our trainees.

DATE: February 9, 2023
SPEAKER 1: Benjamin Lake (Rullo Lab)
TITLE: Directing Covalent Immune Recruitment with the Low Affinity L-Rhamnose Hapten for Proximity Induced Immune-Mediated Cancer Clearance
SPEAKER 2: Christopher Silvestri (Bramson Lab)
TITLE: Investigating the necessity of IFNy in anti tumour T cell responses
ATTENDEES: 55 people in-person, no virtual option

DATE: March 9, 2023
SPEAKER 1: Stephanie Ali Fairbairn (Daniel Lab)
TITLE: Triple-negative breast cancer – Kaiso, androgen receptor and African ancestry
SPEAKER 2: Mandeep Marway (Wylie & Zhang Labs)
TITLE: In Vitro Cancer Model for Monitoring THP-1 Monocyte Migration Using iFlowPlate™
ATTENDEES: 42 people in-person, 4 people virtually

CDCR Trainee Morning Socials

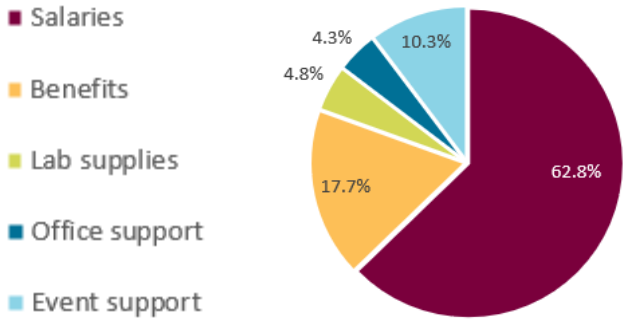
Bi-weekly meets ups with trainees in MDCL 5140 over coffee and refreshments. Average attendance is 30 trainees over two hours.

Finances

The CDCR budget is structured under three budgets: Operating budget, Overhead budget, and Trainee Development budget.

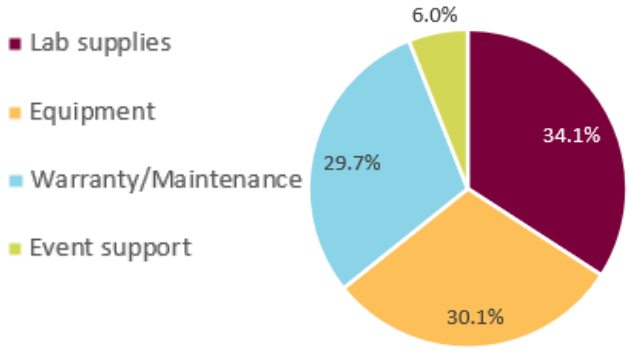
Operating Budget

Funding is secured from the Dean's Office in the Faculty of Health Sciences for five years, for a total of $1,250,000 (2021-2026). The Operating budget covers the three administrative salaries and benefits, CDCR event costs, supplies, and other operational costs to manage the Centre. Currently, the Operating budget is not sustainable to cover all these costs.



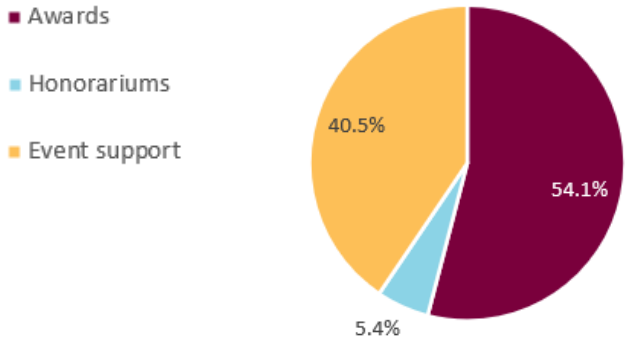
Overhead Budget

The budget is partially funded by previous funding from the dissolved SCC-RI budget and contributions from CDCR labs. The funds are used to cover, for example, common laboratory supply orders, small laboratory equipment purchases, equipment repair, warranties, and auto-claving/glass washing costs.

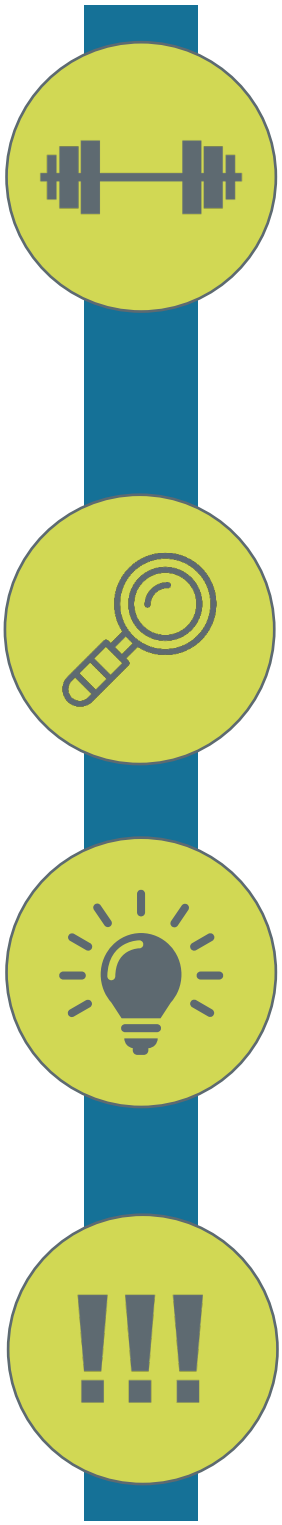


Trainee Development Budget

Funding transferred from the SCC-RI and funding from industry partner rebates goes into the trainee development funds. The Trainee Development funding will support trainee-led programming, including trainee seminar series lectures, seminar series events, debate clubs, team building, and social event activities.



Strengths and Challenges Ahead



Strengths

- Strong membership and accomplished science
- Developing greater collaborations with members and internal partners for strong team-based science
- New recruits and opportunities for new talent that offer trailblazing scientific ingenuity
- Great alignment between Biomedical Discovery & Commercialization (BDC) and cancer research
- Training program and research opportunities for trainees

Weaknesses

- Inadequate internal funding
- Not optimally positioned internally
- Lack of Advancement opportunities

Opportunities

- Securing major team grants
- Exploring joint opportunities with the Escarpment Cancer Research Institute (ECRI) and Hamilton Health Sciences (HHS)
- Creation of new McMaster Bio-bank
- Strong potential growth in innovative research and commercialization

Threats

- Lack of funding from Tri-Council and external funding agencies
- Lack of support in research-based activity in Pathology

Challenges

The most notable challenge for the CDCR is financial stability. We do have some base-funding but is inadequate with our potential growth (outlined in the Vision for the future). The SAB noted in its Report to the CDCR that, "for long-term sustainability and growth it is important that the CDCR has a predicted and stable funding source, an endowment or spend down endowment might help in this regard."

The Report further explains:

> The SAB encourages the CDCR to have some autonomy in the area of fund raising. Dr. Singh appears to have great abilities in this domain and her clinical background can help reinforce the importance of philanthropy to the success of a research group. Not to replace efforts for grant funding but to provide opportunities to do more "high-risk high-reward projects" often not appreciated by our normal grant panels.

Vision for the Future

Our bold vision is four-fold:

1) Building a comprehensive city-wide translational cancer research program
2) Translational Oncology Program
3) Coordinating major team grants
4) Building a strong team of scientists and trainees

Building a Comprehensive City-Wide Translational Cancer Research Program

We plan on building on Hamilton's institutions and industry partners to create a significant player in translational cancer research focusing on hard-to-treat cancers of unmet need. We have already established relationships with our partners in McMaster University Faculty of Health Sciences and Hamilton Health Sciences. These partners include other McMaster departments in the Faculty of Health Science, the Escarpment Cancer Research Institute (https://ecri.mcmaster.ca/) and the Ontario Clinical Oncology Group (OCOG).

Our bold plan is to become a significant global contributor to cancer research. We want to bridge the gap between basic science and translational researchers and clinical, methodological, and health service researchers. By leveraging each other's strengths, we will build a comprehensive and unique research agenda that can bring together research in the lab and clinics to create a globally impactful program.

Translational Oncology Program

The new Translational Oncology Program will connect the research groups in McMaster's new Centre for Discovery in Cancer Research (CDCR) and the clinicians and clinical researchers at the Juravinski Hospital and Cancer Centre (JHCC).

The JHCC is a regional referral centre for central-west Ontario. With many patients coming from outside of Hamilton, the JHCC collaborates with providers in the patient's home community. The JHCC is where cancer treatments such as chemotherapy, radiation, and ground-breaking clinical cancer research occur. It is also home to The Ron and Nancy Clark Stem Cell Transplantation and Cellular Therapies Unit, which provides advanced care for patients across Central South Ontario. It is specialized in the diagnosis, treatment, and care of people with leukemia, lymphoma, multiple myeloma, and other blood cancers. It offers autologous (patient's own stem cells) and allogeneic (related or unrelated donor) stem cell transplants. It is also a pioneering centre in chimeric antigen receptor T-cell (CART-Cell) therapy. These modified immune cells have been genetically engineered to recognize and fight cancer cells. While these treatments are already a reality for certain types of blood cancers, they are also under intense investigation for other tumour entities studied at the CDCR. Our Cell Therapy and Transplantation program is accredited by FACT, which sets the standards for top-quality care for patients receiving cellular therapies.

Dr. Tobias Berg is the CDCR's Director of the Translational Oncology Program.

Coordinating Major Team Grants

We plan to apply for major provincial and federal grants as a team that highlights all our strengths in translational science. Some of these will include infrastructure grants from the Canadian Foundation for Innovation (CFI) to help purchase new equipment for our members and replace aging equipment.

Building a Strong Team of Scientists and Trainees

The CDCR will recruit three new members over the next five years, including two assistant professors/early career researchers/new investigators and one mid-level/associate-level professor. These recruits would be new to McMaster University, with the first supported by a Tier 2 Canada Research Chair and identified through open competition (i.e., the same recruitment model that brought in Dr. Hong Han in November 2022). CFI allocation would be providing along with the recruitments to bring crucial new research infrastructure to the institution.

Additional salary support has been secured for the third position through an OICR (Ontario Institute for Cancer Research) Investigator Award (mid-level), and CCRM (Canadian Centre for Regenerative Medicine) and other industry or philanthropic partners will be solicited to discuss funding of a fourth position.

The three positions would comprise:

1) An expert in cancer bioinformatics and biocomputational sciences (Recruitment ongoing with BBS, CRC Tier 2) with experience in integrating multiomic datasets (genomics (host and microbiome), proteomics and metabolomics
2) An expert in metabolomics and proteomics (funding from OICR, 350K/year for 5 years, renewable)
3) An expert in advanced biologics development: antibody or vaccine engineers, medicinal chemists and pharmacology experts can contribute to a position focused on therapeutic development, in concert with the federal government's new focus on building biomanufacturing capacity and strengths in Canada (suggested funding: Industry-sponsored chair)

Grants Summary

49 Grants

=

$42,918,854
Current Value

This is just a selection of some current grant funding for our CDCR scientists.

$6M	**Canadian Institutes of Health Research (CIHR)** Anti-CD133 theranostics for molecular imaging and treatment of glioblastoma
$4.4M	**Canadian Institutes of Health Research (CIHR)** CIHR Operating grant: Therapeutic targeting of treatment-refractory childhood medulloblastoma
$3.8M	**AdMare Therapeutics Inc.** Therapeutic prevention of brain metastasis
$1.125M	**Samuel Family Foundation** Development of engineered T cells for cancer immunotherapy

$1.004M	**Canadian Institutes of Health Research (CIHR)** Investigating the metabolic drivers of hyperinflammation during viral infection
$932K	**Triumvira Immunologics** Development and optimization of TAC receptors
$930K	**Canadian Institutes of Health Research (CIHR)** Utilizing chimeric antigen receptors to direct autologous NK cell cytotoxicity to breast cancer.
$816.225K	**Canadian Institutes of Health Research (CIHR)** Targeting the heterogeneity of cancer with dual-specific T cells and oncolytic vaccines
$815K	**Canadian Institutes of Health Research (CIHR)** Investigating the regulatory functions of type I IFNs and NK cells during mucosal viral infections
$677.250K	**Terry Fox Research Institute** Project # 4. Characterizing the Influence of OV Backbone on the Therapeutic Effect of the OV Boost
$524.761K	**Ontario Institute for Cancer Research (OICR)** Development of a Personalized Epigenetic Maintenance Approach for AML and MDS Patients After Allogeneic Stem Cell Transplantation
$504.9K	**Canadian Institutes of Health Research (CIHR)** Clinical development of oncolytic BHV-1 for cancer therapy
$480K	**Luciem LLC.** Technology Development in Immune Oncology

$464.11K	**McMaster STEER** The African Caribbean Faculty Research Group Initiatives
$462K	**Canadian Institutes of Health Research (CIHR)** Mpox (monkeypox) and zoonotic Funding Opportunity
$421.428K	**3io Therapeutics Inc.** Strategic Research Agreement (Phase I and II)
$348K	**Natural Sciences and Engineering Research Council of Canada (NSERC)** Wild caught bats as a model to understand the evolution of virus host interactions
$283K	**BioCanRx** GLP support for Human Immune Testing Suite (HITS)
$225K	**Canadian Glycomics Network - GlycoNet** Glyco-chemical Programming Therapeutic Antibodies To Enhance Anti-Tumor Immune Function
$165K	**Natural Sciences and Engineering Research Council of Canada (NSERC)** The Development of Chemical Tool Technology To Modulate Immune Molecular Recognition
$161K	**Canadian Institutes of Health Research (CIHR)** Kaiso, Triple Negative Breast Cancer and Women of African Ancestry
$125K	**New Frontiers Research Fund** Genes & Geography: Disparities in Cancer Incidence & Outcomes in a Black Canadian community

$114.1K	**Canadian Institutes of Health Research (CIHR)** COVID-19 Impacts on Breast Cancer Screening and Care in the Caribbean and marginalized communities in Ontario
$108.813K	**McMaster STEER** Mac-ISTEP: McMaster Black Youth IMHOTEP STEM Enrichment Program
$108K	**Imago Biosciences Inc.** Development of a Personalized Epigenetic Maintenance Approach for AML and MDS Patients After Allogeneic Stem Cell Transplantation
$91K	**National Research Council (NRC)** Digital droplet PCR assay development for single cell analytics
$58K	**Natural Sciences and Engineering Research Council of Canada (NSERC)** POZ-ZF transcription factors in Signal Transduction and development.
$30K	**Pearl and Barnett Tomarken Excellence Fund** Medulloblastoma research program

Papers and Publications

This is a list of papers and publications since the launch of the CDCR in October of 2021.

CDCR PIs membership bolded in **maroon**.
Publication title bolded in **light maroon**.
Publication Journal *italicized*.

Hartung E, Singh K, **Berg T**. (2023). **LSD1 inhibition modulates transcription factor networks in myeloid malignancies**. *Frontiers in Oncology*, 13. doi: 10.3389/fonc.2023.1149754

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Appendix A - Scientific Advisory Board Report

Centre for Discovery in Cancer Research (CDCR) at McMaster University

Panel Members:

Dr. Caroline Dive (virtual)
Dr. Jason Moffat
Dr. Stephen Robbins
Dr. Charles Swanton

Preamble:

Scientific Advisory Board Report September 23rd, 2022
The CDCR consists of 10 Full members, 9 with established research programs and 1 new member, Dr. Hong Han who was just recruited and will be starting her own independent research program. Despite the relatively small research group they have been very productive in publishing high impact papers and securing funding from national agencies.

General Impressions:

Strong and passionate leadership, surgeon-scientist, leads by example.
Areas of documented research strength. Distinguishing features, international recognition, quality bar is appreciated.
Emerging expertise in the area of chemistry
Fertile training opportunities

Strong evidence of entrepreneurial spirit and implementation. Committee Recommendations:

1./ Based on the relatively limited resources available the SAB strongly encourages Dr. Singh and McMaster Senior leadership to focus their attention to a limited number of programs/themes to

pursue to enable them to retain a globally competitive edge and provide a distinct contribution to the Canadian research ecosystem. The panel would suggest a focus on hard-to-treat cancers such as Brain Tumors where there is great clinical linkage and national and international recognition in this area already as well as leadership from one of the world's most successful neuro-surgical physician scientists. The second area for consideration would be in the broad area of "Immuno-Oncology" based on great strength in oncolytic viruses, T cell biology and other immune-related projects. While this recommendation would not preclude other areas of research it would highlight the need to focus resources in these areas including the alignment of future recruitment of three more Principal Investigators that could enhance these research themes; for example, expertise in computational biology/data analysis, biologics development, and metabolomics. It was also discussed whether there was opportunity to recruit more researchers into the CDCR above and beyond the current commitments.

2./ Metrics of success. The SAB felt it is important to determine all of the metrics that the CDCR wants to measure and be evaluated on. While there are obvious ones such as number of publications, impact of publications, number of grants, number of students (MSc and PhD), etc there might be many others to consider to help highlight the "added value" the CDCR brings locally, nationally and internationally. Timelines for where CDCR wants to be in 5 or 10 years would be a good measure towards success.

3./ Core Infrastructure, enabling technologies or platforms. Based on the fairly small research group and the limited resources the SAB recognized that there needs to be some balancing of on-site infrastructure versus outsourcing. Mapping of the next CFI opportunities for the CDCR would be a good prioritizing activity that would engage the 10 PI's. The SAB was very supportive of McMaster Senior Leadership providing some access to the CFI envelope over the next few competitions to ensure the group can maintain their competitive edge.

4./ A very cursory look at the publication records of the group suggests that there is varied collaboration within the group and this could be enhanced with an overall goal of improving the impact and visibility of all members of the CDCR. This would also help foster more team grants in the future led by CDCR members.

5./ Certainly appears that chemistry is an emerging area of strength and how this could be leveraged in the chosen research themes to be focused on is encouraged.

6./ Explore opportunities to leverage the great expertise in the area of radionucleotides and imaging especially as it relates to the research themes selected.

7./ Explore partnership opportunities with OICR especially as it pertains to recruitment and funding projects.

8./ For long-term sustainability and growth it is important that the CDCR has a predicted and stable funding source, an endowment or spend down endowment might help in this regard. The SAB encourages the CDCR to have some autonomy in the area of fund raising. Dr. Singh appears to have great abilities in this domain and her clinical background can help reinforce the importance of philanthropy to the success of a research group. Not to replace efforts for grant funding but to provide opportunities to do more "high-risk high-reward projects" often not appreciated by our normal grant panels.

9./ Lastly, it would help define path(s) to the clinic using success stories to allow for more successes in the future, removing barriers is essential.