

2016-2017 Activity Report

INSTITUTE FOR RESEARCH
IN IMMUNOLOGY AND CANCER

A reference in fundamental and applied research to conquer cancer



ABOUT THE INSTITUTE FOR RESEARCH IN IMMUNOLOGY AND CANCER

— IRIC

An ultra-modern research hub and training centre located in the heart of the Université de Montréal, the Institute for Research in Immunology and Cancer of the Université de Montréal was created in 2003 to shed light on the mechanisms of cancer and discover new, more effective therapies to counter this disease. The IRIC operates according to a model that is unique in Canada. Its innovative approach to research has already led to discoveries that will, over the coming years, have a significant impact on the fight against cancer.

iric.ca

ABOUT UNIVERSITÉ DE MONTRÉAL — *UdeM*

Université de Montréal and its two affiliated schools, École Polytechnique (engineering) and HEC Montréal (business), are amongst the world's top universities, according to international rankings. Founded in 1878, the campus today has over 67,000 students and 2,700 professors, making Université de Montréal the second largest university in Canada. Its students are drawn to the university by its deep roots in cosmopolitan Montreal and in consideration of its tenacious dedication to its international mission.

umontreal.ca

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CANCER

— a social issue

Cancer is a devastating disease and a major social issue. According to the Canadian Cancer Society, 1 out of 2 Canadians is expected to develop cancer during their lifetime, and 1 out of 4 Canadians is expected to die from this disease. Cancer is the leading cause of death in Canada. It is estimated that in 2017 alone, more than 200,000 new cases will be diagnosed in Canada, and that close to 90,000 Canadians will die from cancer. Beyond its dire consequences on patients and their families, cancer also places an enormous strain on society by its adverse impact on the health care system as well as the country's economy.



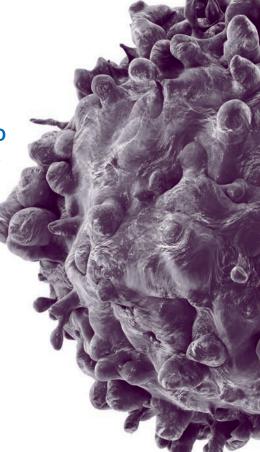
1 OUT OF 2 CANADIANS IS EXPECTED TO DEVELOP CANCER DURING THEIR LIFETIME



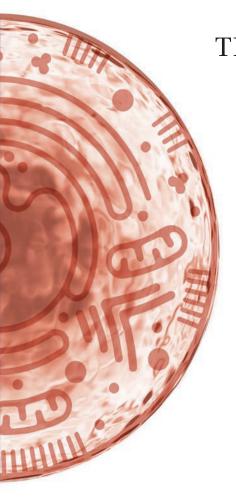
1 OUT OF 4 CANADIANS IS EXPECTED TO DIE FROM THIS DISEASE











THE IRIC IS...

A multidisciplinary approach and complementary expertise

29 fundamental, translational and applied research investigators

Cutting-edge research environment and facilities

11 core facilities available to investigators from here and abroad

Innovative teaching methods to train the next generation of scientists

More than 200 students a year benefiting from unique mentoring

An access to a research commercialization hub, specialized in drug discovery (IRICoR)

Close collaborations with the clinical community and with the industry

A network that includes collaborators across the country





29 principal investigators

professors in 8 departments of the UdeM's Faculty of Medicine and Faculty of Arts and Sciences, holding among them 10 Canada Research Chairs and 1 private research chair CLOSE TO 1,000 SCIENTIFIC PUBLICATIONS THUS FAR

with a significant percentage published in the most prestigious journals

11 HIGH-TECH CORE FACILITIES

constructed and equipped at a cost of \$110M and operated by highly skilled professionals

A yearly average of \$15M in research funding from government agencies

STRATEGIC PARTNERSHIPS

LICENCE AGREEMENTS

PATENT FAMILIES

PROMISING PROJECTS

in preclinical development

CLINICAL TRIALS (phase I and II)

IRI@oR

access to a drug discovery chain in a university setting resulting in great success

CREATION OF SPIN-OFF COMPANIES



Robert Tessier
IRIC CHAIRMAN
OF THE BOARD

MESSAGE FROM THE CHAIRMAN OF THE BOARD

— Robert Tessier

More than a decade of scientific advances

The IRIC is a reference in basic, translational and applied research in the fight against cancer. It is also a major player in the discovery of therapeutic solutions to defeat the disease.

With its 29 research units and its 11 cutting-edge technological core facilities – including the largest medicinal chemistry facility in an academic setting in the country – the IRIC is positioned as a key player not only with respect to the advancement of knowledge, but also when it comes to training the next generation of scientists.

As a result, the Institute sets itself apart by offering innovative teaching methods and a unique program. Another of its assets is a centre for the commercialization of research, IRICOR, which on an annual basis brings to fruition research partnerships, licensing agreements with the biopharmaceutical industry, protects patent families and contributes to creating companies.

Thanks to its innovative model, the Institute has positioned itself not only on the provincial stage, but also on the national and international stage.

The Board of Directors, made up of prominent members of the university community and independent members from civil society, is excited about supporting the Institute's projects, activities and strategic guidelines.

It also provides an opportunity to recruit the best investigators and the best students, and to obtain adequate funding for research activities.

To ensure the proper continuation of its activities, every year the IRIC invests energy and effort with governments and granting agencies, and makes sure to showcase its notoriety through public relations initiatives. The Institute must also rely on philanthropy and the support of major donors, who faithfully and generously encourage cancer research efforts.

With this in mind, I personally wish to thank all of the organizations and all of the people who, through their donations, contribute to making a difference in the fight against cancer.





MESSAGE FROM THE CHIEF EXECUTIVE OFFICER AND THE SCIENTIFIC DIRECTOR

— Michel Bouvier and Marc Therrien

A full and promising year

Serving as Chief Executive Officer and Scientific Director of the IRIC means getting a chance to work with 29 exceptional investigators who work in a collegial setting that fosters collaboration. It's also an opportunity to contribute to training the next generation of scientists. And finally, it's taking part in the advancement of knowledge and fostering the discovery of innovative therapeutic solutions that will help short-circuit cancer.

Managing the IRIC also means marveling at our teams of investigators and students, who all work to ensure the complementarity of their respective expertise.

The 2016-2017 year was rich in news. We can proudly paint a positive portrait of the year, which produced several discoveries that provided us with a better understanding of the mechanisms of cancer. Here are a few of the highlights: advances in immunotherapy that are progressively leading us towards personalized medicine, partnerships and collaborations with other research institutes and the expansion of the medicinal chemistry core facility, resulting in the discovery of new drugs.

The year was also marked by several publications from our investigators who were also the recipients of prestigious awards, including the Cinader Award,



Michel Bouvier
CHIEF EXECUTIVE OFFICER

11/1/20

given to Claude Perreault. Several IRIC investigators were also honored and rewarded for their efforts. The breakthroughs that emerged from this productive year are the fruit of the passion and scientific rigor of the IRIC's investigators and of the privileged access that they have to 11 leading-edge technological core facilities run by highly qualified staff.

This year, we were also fortunate to welcome Delphine Bouilly, a physicist who, through her talent and rigor, will take part in our research efforts that will allow us to have a major impact on cancer treatment.

As a result, the IRIC is – on an annual basis - a rich program of scientific and



Marc Therrien
SCIENTIFIC DIRECTOR

educational activities orchestrated by the investigators and the Academic Affairs team.

The fact that the Institute sets itself apart through its success and its unique character can be attributed to the dedicated people who all pull in the same direction. We are ardent ambassadors for the achievements of IRIC members. We cannot overlook the support of our partners and donors who, each and every year, bring our research activities to life.

Through your support, your passion and your commitment, you contribute to the success of our organization.



PRINCIPAL INVESTIGATORS



Vincent Archambault, Ph. D.Cell Cycle Regulation



Katherine L.B. Borden, Ph. D. Structure and Function of the Cell Nucleus



Michel Bouvier, Ph. D., FCAHS, FRSC Molecular Pharmacology Chief Executive Officer



Gregory Emery, Ph. D.Vesicular Trafficking and Cell Signalling



Louis Gaboury, M.D., Ph. D., F.R.C.P.(c), F.C.A.P. Histology and Molecular Pathology



Étienne Gagnon, Ph. D.Cancer Immunobiology



Jean-Claude Labbé, Ph. D.Cell Division and Differentiation



Sébastien Lemieux, Ph. D.Functional and Structural Bioinformatics



Julie Lessard, Ph. D. Chromatin Structure and Stem Cell Biology



Sylvain Meloche, Ph. D Signalling and Cell Growth



Claude Perreault, M.D., F.R.C.P.(c) Immunobiology



Martine Raymond, Ph. D. Yeast Molecular Biology Director, Academic Affairs



Marc Therrien, Ph. D.
Intracellular Signalling
Scientific Director



Pierre Thibault, Ph. D.Proteomics and Bioanalytical Mass Spectrometry



Michael Tyers, Ph. D., FRSC, FRSE Systems Biology and Synthetic Biology



Delphine Bouilly, Ph. D. Design and Application of Electronic Nanobiosensors





Lea Harrington, Ph. D. Telomere Length Homeostasis and Genomic Instability



Sylvie Mader, Ph. D. Molecular Targeting in Breast Cancer



Philippe P. Roux, Ph. D. Cell Signalling and Proteomics



Alain Verreault, Ph. D. Chromosome Biogenesis



Sébastien Carréno, Ph. D. Cellular Mechanisms of Morphogenesis during Mitosis and Cell Motility



Trang Hoang, Ph. D. Hematopoiesis and Leukemia



François Major, Ph. D. Ribonucleic Acid Engineering



Guy Sauvageau, M.D., Ph. D., F.R.C.P.(c) Molecular Genetics of Stem Cells



Brian Wilhelm, Ph. D. High-Throughput Genomics



Damien D'Amours, Ph. D. Cell Cycle Regulation and Chromosome Structure



Benjamin Kwok, Ph. D. Chemical Biology of Cell Division



Anne Marinier, Ph. D. Medicinal Chemistry



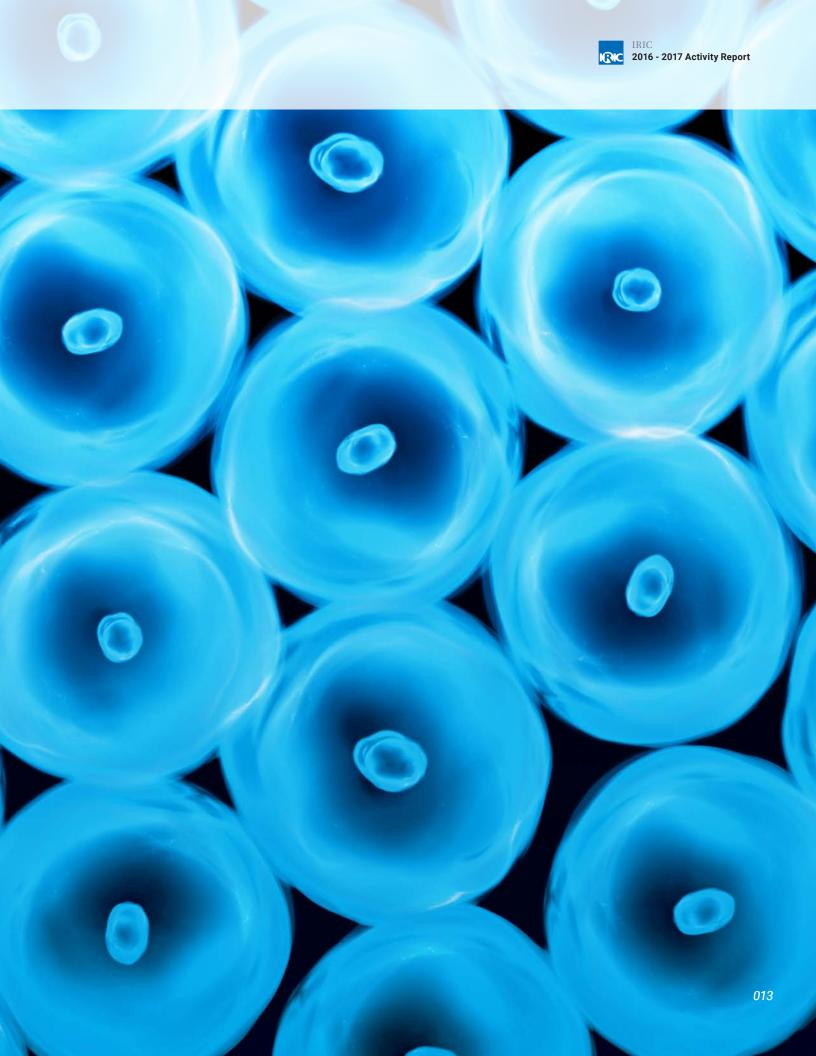
Matthew J. Smith, Ph. D. Signalling and Structural Biology of Cancer

A RESEARCH

The 29 IRIC research teams work to better understand the complex mechanisms of cancer in order to develop new targeted and personalized therapies to fight this disease.

Investigators use a wide variety of experimental approaches and models and pool their expertise in order to bring about the development of new diagnostic tools and new innovative drugs. They have access to a cutting-edge infrastructure, including the largest medicinal chemistry laboratory in a university setting in Canada.

Their work leads to major discoveries, most of which are presented in high-impact scientific journals. Furthermore, the number of collaborations with other research institutes, universities and hospitals continues to rise and create the pursuit of knowledge.



DISCOVERY OF A NEW PROTEIN COMPLEX PLAYING A ROLE IN G PROTEIN-COUPLED RECEPTORS (GPCRs)

— Published in Cell

The laboratory of Michel Bouvier, in partnership with the laboratories of Dr. R.J. Lefkowitz (2012 Nobel Prize in Chemistry) at Duke University and Professor Skiniotis at the University of Michigan, discovered and revealed the structure of a new protein complex playing a role in G protein-coupled receptors (GPCRs). The work was published in the scientific journal Cell.

Given the importance of GPCRs as a therapeutic target, this discovery could have considerable impact on the development of new drugs with better therapeutic profiles and fewer side effects.

GPCRs act as a communication conduit between the inner and outer cell. Outside the cell, receptors bind with various molecules (such as hormones or neurotransmitters), which triggers a reaction from the G proteins inside that cell and initiates a cascade of reactions leading to cell changes.

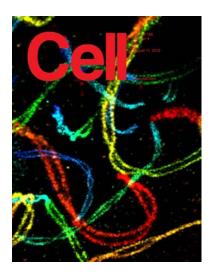
As for the β -Arrestin proteins, which are also inside the cell, they can have several functions: either by alleviating the reaction to external signals, or by activating other cell reactions that are independent from G proteins. Before this study, however, it was believed that GPCRs acted only with G proteins

or only with β -Arrestin proteins. The findings presented in the publication show that they can interact with both at the same time and that this protein complex contributes to more sustainable signals occurring inside the cell

"This new mechanism at the basis of the activation of more sustainable cell signals could be used to provide new pharmacological solutions for treating diseases in which such long-term signaling could be problematic."

Bianca Plouffe

Postdoctoral fellow in the laboratory of Michel Bouvier, who successfully spearheaded the project for the Montreal team.







The discovery of this new protein complex, made up of a receptor, G proteins and β -Arrestin proteins, challenges the previously held view that G proteins and β -Arrestin proteins could not interact simultaneously with a receptor.

Michel Bouvier

[CEO, IRIC]

Referenced study

GPCR-G Protein-β-Arrestin Super-Complex Mediates Sustained G Protein Signaling.

Thomsen AR, Plouffe B, Cahill TJ, Shukla AK, Tarrasch JT, Dosey AM, Kahsai AW, Strachan RT, Pani B, Mahoney JP, Huang L, Breton B, Heydenreich FM, Sunahara RK, Skiniotis G, Bouvier M, Lefkowitz RJ

Cell 2016;166(4):907-19.



CHEMICAL COMPOUNDS IDENTIFIED TO TARGET PRELEUKEMIC STEM CELLS

— Published in The Journal of Clinical Investigation

A study published in The Journal of Clinical Investigation brings to light the breakthroughs made in the laboratory of Trang Hoang. The study examines T cell acute lymphoblastic leukemia (T-ALL), which represents 20% of all childhood leukemia diagnoses and is characterized by an overabundance of immature T-cells in the blood and bone marrow.

T-cells are a type of white blood cells and a vital component of the immune system. Current chemotherapies effectively reduce the leukemic burden; in the event of relapse, however, leukemia becomes harder to treat. This is attributable to the survival of preleukemic stem cells, which escaped chemotherapy and acted as reservoirs to produce new cancer cells.

This study shows two things: first, it confirms the hypothesis that preleukemic cells are much less sensitive to the chemotherapy treatments used for treating T-ALL. Second, thanks to setting up a new high-throughput screening procedure that recreates the cell's microenvironment, Professor Hoang's team identified chemical compounds that specifically target preleukemic stem cells, without affecting healthy stem cells.

This represents a highly promising and innovative method. Since its release, this study has been cited and commented on in several medical journals: American Association for Cancer Research, Medical Xpress, Hematopiesis News and Cancer Stem Cell News.



The study was notably conducted by Bastien Gerby, project leader on Professor Hoang's team. It is the result of a multidisciplinary collaboration between several teams led by the IRIC's Principal Investigators: Philippe Roux, Benjamin Kwok, Anne Marinier and Guy Sauvageau – and Josée Hébert, Director of the Quebec Leukemia Cell Bank at the Maisonneuve-Rosemont Hospital, as well as Paul Maddox from the Department of Biology at the University of North Carolina at Chapel Hill.

Referenced study

High-throughput screening in niche-based assay identifies compounds to target preleukemic stem cells.

Gerby B, Veiga DF, Krosl J, Nourreddine S, Ouellette J, Haman A, Lavoie G, Fares I, Tremblay M, Litalien V, Ottoni E, Kosic M, Geoffrion D, Ryan J, Maddox PS, Chagraoui J, Marinier A, Hébert J, Sauvageau G, Kwok BH, Roux PP, Hoang T

The Journal of Clinical Investigation 2016-12-01;126(12):4569-4584.



Identification and development of a new molecule to treat thrombotic diseases discovered through a partnership with Bristol-Myers Squibb (BMS).

This molecule, BMS-986120, acts on the cellular receptor PAR4 involved in the activation of blood platelets in clot formation. Thus, it considerably reduces the risk of blood clots (thrombosis). PAR4 is part of a molecular receptor family for which the IRIC has developed world-renowned expertise. Basic research work first helped establish the promising inhibitory potential of PAR4 in a therapeutic setting.

Subsequently, the high-throughput screening of over one million chemical compounds and tremendous efforts in medicinal chemistry led to the development of BMS-986120, a PAR4 antagonist that can be administered orally. In an animal model of arterial thrombosis, molecule BMS-986120 demonstrated potent and highly efficacious antithrombotic activity. It also exhibits a low bleeding liability and therefore a wider therapeutic window than the most commonly used standard antiplatelet agent.

This study, which involved Principal Investigators Anne Marinier and Michel Bouvier, as well as several other members of the medicinal chemistry team, showed that targeting PAR4 is a promising strategy for treating patients at high risk of atherothrombosis with superior safety compared with current treatments. This discovery was also made possible thanks to the support of IRICOR.

Promising results have already led to two Phase I clinical studies for molecule BMS-986120, and an optimized version of the molecule will be subject to a Phase II study that was announced in December of 2016, focusing on more than 1,300 patients in hospitals here and abroad.

Referenced study

Blockade of protease-activated receptor-4 (PAR4) provides robust antithrombotic activity with low bleeding.

Wong PC, Seiffert D, Bird JE, Watson CA, Bostwick JS, Giancarli M, Allegretto N, Hua J, Harden D, Guay J, Callejo M, Miller MM, Lawrence RM, Banville J, Guy J, Maxwell BD, Priestley ES, Marinier A, Wexler RR, Bouvier M, Gordon DA, Schumacher WA, Yang J

Science Translational Medicine 2017;9(371).

IDENTIFICATION OF A KEY FACTOR CONTROLLING THE PRODUCTION OF BLOOD CELLS

— Published in Nature Genetics



Julie Lessard's team published a study in the scientific journal Nature Genetics, conducted in collaboration with Dr. Louis Gaboury and Dr. Guy Sauvageau. The study describes the discovery of a key mechanism in the production of white blood cells specialized in defending the body against infections.

Gene SMARCD2 is essential to the production of neutrophils and eosinophils – specialized cells that defend the body against pathogens (also called the innate immune system). They are abundant in human blood: in a normal individual, they represent around 50-60% of immune cells. These guards are usually the first cells to arrive at the site of an infection.

The bone marrow of a healthy adult produces more than 100 billion neutrophils every day, a number that can be multiplied by ten during an acute infection. In Julie Lessard's laboratory, the team found that suppressing gene SMARCD2 in mice causes a blockage in the production of immune cells in the bone marrow,

leading to the animal's premature death.

This observation recalls a human congenital disorder called "specific granule deficiency" (SGD), which not only causes severe infections due to the lack of neutrophils, but is also often linked to a myelodysplastic syndrome that can develop into leukemia. Although the first five patients affected were identified in the early 1970s, the molecular basis of this disease of the immune system is yet to be fully understood.

A study completed by the team of Dr. Christoph Klein, in Germany, published in the same scientific journal, identified mutations in gene SMARCD2 in patients suffering from the disease, thus demonstrating that the functions of this gene are maintained in humans.

"Our studies led to the discovery of a critical regulator of the innate immune response and provide a better understanding of the molecular defects responsible for a disease of the immune system."

Pierre Priam

Ph.D. student in Julie Lessard's laboratory, and first author of this paper.

Referenced study

SMARCD2 subunit of SWI/SNF chromatin-remodeling complexes mediates granulopoiesis through a CEBP ϵ dependent mechanism. Priam P, Krasteva V, Rousseau P, D'Angelo G, Gaboury L, Sauvageau G, Lessard JA

Nature Genetics 2017-05-01;49(5):753-764.

— In brief

Guy Sauvageau - Marc Therrien

Some forms of acute myeloid leukemia are caused by a mutation that fuses the NUP98 and HOXA9 genes, but the mechanism underlying the development of the disease in these cases is not well understood. Investigators used the fruit fly (Drosophila) as an experimental model to better understand this mechanism by generating transgenic Drosophila expressing the human mutant protein. As a result, they reproduced several aspects of the disease in the hematopoietic system of these flies and confirmed certain observations at the molecular level. This very convenient experimental system will help elucidate the genetic interactions involved in the disease.





Referenced study

Human NUP98-HOXA9 promotes hyperplastic growth of hematopoietic tissues in Drosophila.

Baril C, Gavory G, Bidla G, Knævelsrud H, Sauvageau G. Therrien M

Developmental Biology 2017;421(1):16-26.

Sébastien Carréno – Philippe Roux – Gregory Emery

The 14-3-3 protein family orchestrates a complex network of molecular interactions that regulate, among other things, the cell cycle and the trafficking of proteins. To identify the proteins that act in concert with 14-3-3, the investigators used a proteomic approach and compared the 14-3-3 interactomes (the network of 14-3-3 interacting partners), in human and Drosophila cells. They identified a group of effector proteins, Rab11-FIPs, which plays an evolutionarily conserved role and is essential in regulating one of the last stages of cell division.







Referenced study

Proteomics Screen Identifies Class I Rab11 Family Interacting Proteins as Key Regulators of Cytokinesis.

Laflamme C, Galan JA, Ben El Kadhi K, Méant A, Zeledon C, Carréno S, Roux PP, Emery G

Molecular and Cellular Biology 2017;37(3).

François Major

MicroRNAs (miRNAs) are important regulators of the expression of many genes. The investigators modeled the dynamics of maturation for miR-125a, a miRNA associated with certain breast cancers. Their analysis showed how a mutation in miR-125a disrupts the network of transient structures that can form during maturation. This leads to the absence of mature miR-125a in cells and abnormal gene expression. The modeling approach developed for this analysis will help in understanding the biology of miRNAs in other cases associated with diseases.



Referenced study

Structural dynamics control the MicroRNA maturation nathway.

Dallaire P, Tan H, Szulwach K, Ma C, Jin P, Major F Nucleic Acids Research 2016;44(20):9956-9964.

Jean-Claude Labbé

Investigators used the nematode worm as an experimental system to better understand the regulation of germinal stem cell growth and proliferation. They discovered a new signaling pathway governing this process, the components of which are conserved in complex organisms. This mechanism could be involved in maintaining cancer stem cells in humans.



Referenced study

DAF-18/PTEN signals through AAK-1/AMPK to inhibit MPK-1/MAPK in feedback control of germline stem cell proliferation.

Narbonne P, Maddox PS, Labbé JC PLoS Genetics 2017;13(4):e1006738.

Alain Verreault - Pierre Thibault

In the cell nucleus, DNA is wrapped around proteins called histones whose function is modulated by different chemical modifications. HDAC enzymes play an important role in this process as they eliminate one of the chemical modifications (acetylation) of histones. To better understand the mechanisms underlying the function of HDACs, investigators used fission yeast as an experimental model, where they were able to profile the acetylation and methylation changes induced by certain mutations. The results of this study greatly enhance our understanding of the mechanisms involved in HDAC-induced gene regulation, which has been reported to be abnormal in various types of cancer.





Referenced study

Unraveling Site-Specific and Combinatorial Histone Modifications Using High-Resolution Mass Spectrometry in Histone Deacetylase Mutants of Fission Yeast.

Abshiru N, Rajan RE, Verreault A, Thibault P

Journal of Proteome Research 2016;15(7):2132-42.



Four IRIC investigators

- receive awards from the Fonds de recherche Québec - Santé

Four IRIC investigators received salary awards as part of the 2016-2017 Chercheurs-boursiers program of the Fonds de recherche du Québec – Santé (FRQS), designed to support the career of independent healthcare researchers.

They are:

Vincent Archambault (Junior 2 Award) for his project "Comprendre et cibler la régulation spatiotemporelle de la division cellulaire";

Philippe Roux (Senior Award) for his project "Régulation oncogénique de la croissance cellulaire par la voie de signalisation mTOR";

Matthew J. Smith (Junior 1 Award) for his project "Analyses structurales et systémiques des protéines modulatrices de la signalisation RAS oncogénique pour de nouvelles approches thérapeutiques contre les cancers humains";

Brian Wilhelm (Junior 2 Award) for his project "Identification de nouveaux mécanismes moléculaires impliqués dans les leucémies myéloïdes aiguës en pédiatrie".

Michel Bouvier

— recipient of the Julius Axelrod Award for his contributions as a scientist and mentor

Professor Bouvier, Chief Executive Officer of the IRIC, received the 2017 Julius Axelrod Award in Pharmacology, handed out by the American Society for Pharmacology and Experimental Therapeutics (ASPET). This award is presented annually to an eminent researcher to highlight significant contributions to understanding the biochemical mechanisms underlying the pharmacological actions of drugs and for contributions to mentoring other pharmacologists.

The award acknowledged his major contributions to the field of G protein-coupled receptors (GPCRs), the largest family of drug-targeted cell receptors, and the profound impact that he has had as a mentor to many students and postdoctoral fellows.

Professor Bouvier and his laboratory have greatly influenced the field of GPCRs, particularly through their vital contributions to several innovative concepts such as inverse agonism and biased signaling, as well as to the development of pharmacological chaperones for the potential treatment of several genetic diseases, including nephrogenic diabetes insipidus and early-onset severe obesity.

Claude Perreault

— recipient of the Bernhard Cinader Award from the Canadian Society for Immunology (CSI)

It was in Banff, Alberta, that Dr. Claude Perreault, hematologist and Principal Investigator at the IRIC, received the Bernhard Cinader Award, as part of the $30^{\rm th}$ Annual Conference of the Canadian Society for Immunology (CSI). The CSI presents the award annually to a Canadian researcher showing excellence in immunology and who demonstrates a keen interest in other fields.

The breadth of Dr. Perreault's career was honored for his significant contributions to the fight against cancer, and his mentoring of the next generation of scientists. The jury also highlighted his passion for the evolution of life and ideas, and for the recent developments in the interactions between humans and artificial intelligence.

The Bernhard Cinader Award was named in honor of Dr. Hardy Cinader, the award's first recipient 30 years ago. He is considered to be one of the "creators" of immunology in Canada in the 1960s.



Pierre Thibault

—honored by the Canadian National Proteomics Network

Pierre Thibault is an internationally renowned leader in mass spectrometry-based proteomics.

His research contributions have spanned the elucidation of major environmental toxins, to the deep analysis of the immunopeptidome of cancer cells, to the global characterization of dynamic post-translational modifications. He leads one of Canada's premiere mass spectrometry platforms at the IRIC.

His contribution was highlighted by the Canadian National Proteomics Network, from whom he received the 2017 Tony Pawson Proteomics Award, in recognition of his remarkable achievements in the understanding and the practice of proteomics in biological sciences.

Pierre Thibault also holds a Tier 1 Canada Research Chair in Proteomics and Bioanalytical Mass Spectometry and received the Maxxam Award for Analytical Chemistry in 2012 for his many contributions



HIRING — Principal Investigator



Delphine Bouilly PRINCIPAL INVESTIGATOR

DESIGN AND APPLICATION OF ELECTRONIC NANOBIOSENSORS

Delphine Bouilly: new Principal Investigator at the IRIC

Delphine Bouilly joined the IRIC as a Principal Investigator on January 5, 2017, as part of the Design and Application of Electronic Nanobiosensors Research Unit. She also serves as a Professor in the Physics Department of the Faculty of Arts and Science at the Université de Montréal.

Delphine Bouilly earned a Ph.D. in Physics from the Université de Montréal in 2013 before completing a postdoctoral fellowship at Columbia University, in New York City. She received several awards and scholarships over the course of her studies, including the prestigious Banting Postdoctoral Fellowship, which rewards the most qualified postdoctoral fellows with a highly promising research potential.

At the IRIC, Delphine Bouilly and her team assemble ultra-miniature electronic circuits and sensors to explore the dynamics of the interactions between biological molecules (DNA and proteins) or the fluctuation within a single molecule. The goal is to develop new tools to identify biomarkers associated with various types of cancer and to better understand the mechanics of basic macromolecules. The results of this work will support and develop the creation of new therapies. Delphine Bouilly's research program is complementary to the expertise of the IRIC's investigators and provides the Institute with many opportunities for collaboration.

The addition of Delphine is great news for both the IRIC community and management. Her research methods, her innovative ideas and her spirit of collaboration are a perfect fit for the philosophy of the IRIC.

B CORE FACILITIES

The IRIC research teams have access to an impressive equipment park at the leading edge of technology. The IRIC has 11 core facilities operated by highly skilled professionals.

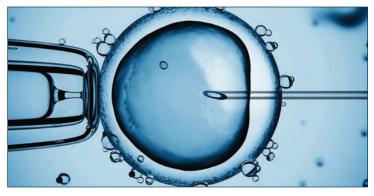
Moreover, the Institute and the Maisonneuve-Rosemont Hospital jointly operate the Cytogenetics core facility of the Quebec Leukemia Cell Bank.

These facilities are available to Principal Investigators and to the entire scientific community from the Université de Montréal, other affiliated centres, university centres, public organizations and industry.

Also, thanks to the development and expansion of its medicinal chemistry facility, the IRIC set up the first Canadian cancer drug discovery chain in a university setting.



11 CORE FACILITIES— supporting research



IN VIVO BIOLOGY

In vivo modelling of pharmacokinetics and therapeutic efficacy, transgenesis, in vitro fertilization, genotyping, and cryopreservation.



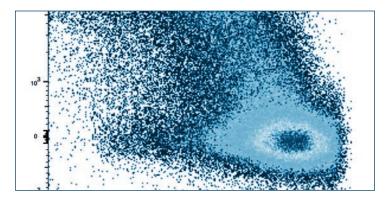
BIOPHYSICS

NMR spectroscopy for experiments on the structure of proteins, protein-ligand interactions and characterization of small molecules.



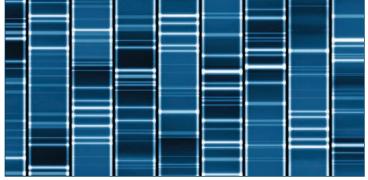
MEDICINAL CHEMISTRY

Synthesis of small, original and specific molecules leading to the discovery of chemical entities with therapeutic potential.



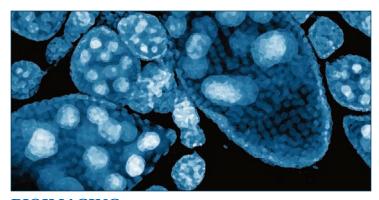
FLOW CYTOMETRY

Analysis of various physical properties of cells, study of the cell cycle and apoptosis, immunophenotyping.



GENOMICS

Cutting-edge technologies in next-generation sequencing, capillary sequencing and real-time PCR.



BIOIMAGING

Cutting-edge optical microscopy equipment and image analysis stations.



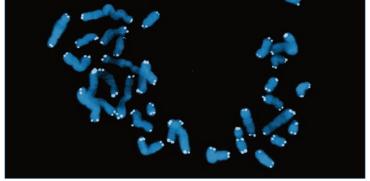
BIOINFORMATICS

Innovative tools for analyzing, integrating and consulting biological databases with the use of high-performance computing clusters.



HIGH-THROUGHPUT SCREENING

A portfolio of over 125,000 molecules, and integrated robotic system used for a variety of biochemical and cell-based studies with different biological systems and models.



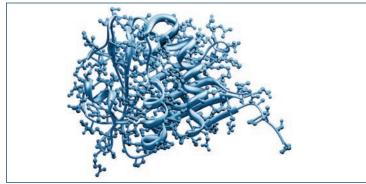
CYTOGENETICS

Chromosomal analysis of human and mouse cells through traditional cytogenetic techniques and spectral karyotyping.



HISTOLOGY

Histology, image acquisition, laser microdissection, immunohistochemistry and generation of tissue microarrays.



PROTEOMICS

Identification and quantification of proteins, and analysis of their post-translational modifications by mass spectrometry.



HIGHLIGHTS EXPANSION OF THE MEDICINAL CHEMISTRY CORE FACILITY

- 1 increases drug discovery activities
- contributes to speeding up the expansion of its chemical compounds library

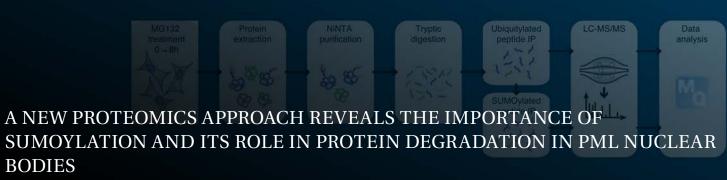
The December 2016 inauguration also provided an opportunity to officially announce the launch of Phase II clinical trials for BMS-986141 (UDM-003183), a molecule being studied for the treatment of thrombotic diseases in partnership with Bristol-Myers Squibb.

New laboratories for the medicinal chemistry core facility were inaugurated at the IRIC in December of 2016. These new labs increase drug discovery capacity and help speed up the expansion of the chemical compounds library.

The expansion is the result of a partnership between UdeM's Faculty of Pharmacy and the Institute, thus strengthening the synergy between these two units. The medicinal chemistry core facility was expanded thanks to grants from the Canada Foundation for Innovation (CFI) and the Government of Quebec.

It is both proof and recognition of past achievements from the medicinal chemistry team, which is made up in large part of experienced scientists from the pharmaceutical industry. The announcement clearly illustrates the rapid progress made in several discovery projects and in the development of new molecules for therapeutic applications.

Since the creation of this core facility in 2008, three molecules that were first synthesized at the IRIC resulted in clinical trials. These achievements attest to the efficiency of the IRIC's innovative model of drug discovery in an academic setting.



— Published in Nature Communications

The team of Pierre Thibault, in collaboration with colleagues from the University of Paris-Descartes, published in the journal Nature Communications a new approach for the global-scale analysis of protein SUMOylation with unprecedented sensitivity and depth.

This important type of protein modification regulates many cellular processes such as cell division, intracellular trafficking, protein degradation and senescence. An imbalance of this modification can result in cell proliferation and the development of tumors.

Within cells, the activity of several proteins is governed by reversible chemical modifications. Ubiquitylation and SUMOylation are two such modifications that involve the transfer of small proteins, respectively called Ubiquitlin (Ub) and SUMO (Small Ubiquitlin-like Modifier) to specific sites on the targeted proteins. In

particular, Ub often acts as a tag that marks proteins for degradation by the proteasome, a normal and vital process. Indeed, in cells, there is a continual turnover of proteins, which involves a permanent process of synthesis and degradation. This dynamic between synthesis and degradation ensures the quality control of proteins and allows the cell to quickly adapt to changes in its environment.

Researchers found that many proteins are modified by both SUMOylation and ubiquitylation and that there is a functional crosstalk between these changes. This study opens new avenues for the identification of protein

substrates, their specific modification sites, the interaction between SUMOylation and ubiquitylation, and their regulation in different diseases.

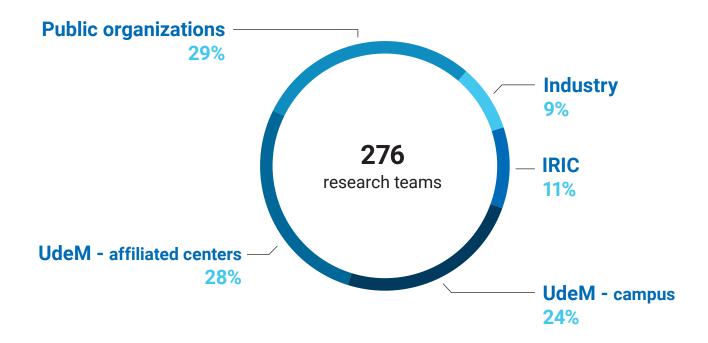
Referenced study



2016-2017 STATISTICAL DATA

IRIC'S CORE FACILITIES

— Source of users



IRIC: 29

UdeM - campus: 67

UdeM - affiliated centers: 76

Public organizations: 80

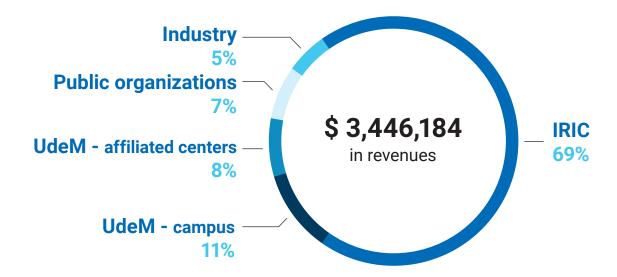
Industry: 24



2016-2017 STATISTICAL DATA

IRIC'S CORE FACILITIES

— Source of revenues



IRIC: \$ 2,391,899

UdeM - campus: \$ 369,009

UdeM – affiliated centers: \$ 259,956 Public organizations: \$ 238,065

Industry: \$187,254

© NEXT GENERATION OF SCIENTISTS

The Office of Academic Affairs is committed to assisting students along their path from the time they arrive at the Institute right through their graduation. Everything is set up for them to receive the best possible training. They have access to the Institute's state-of-the-art facilities, several conferences and seminar series, as well as personalized university and administrative support. Whether enrolled at the IRIC for an undergraduate internship, a master's or a doctorate, students actively participate in better understanding cancer while fully developing as the next generation of scientists.

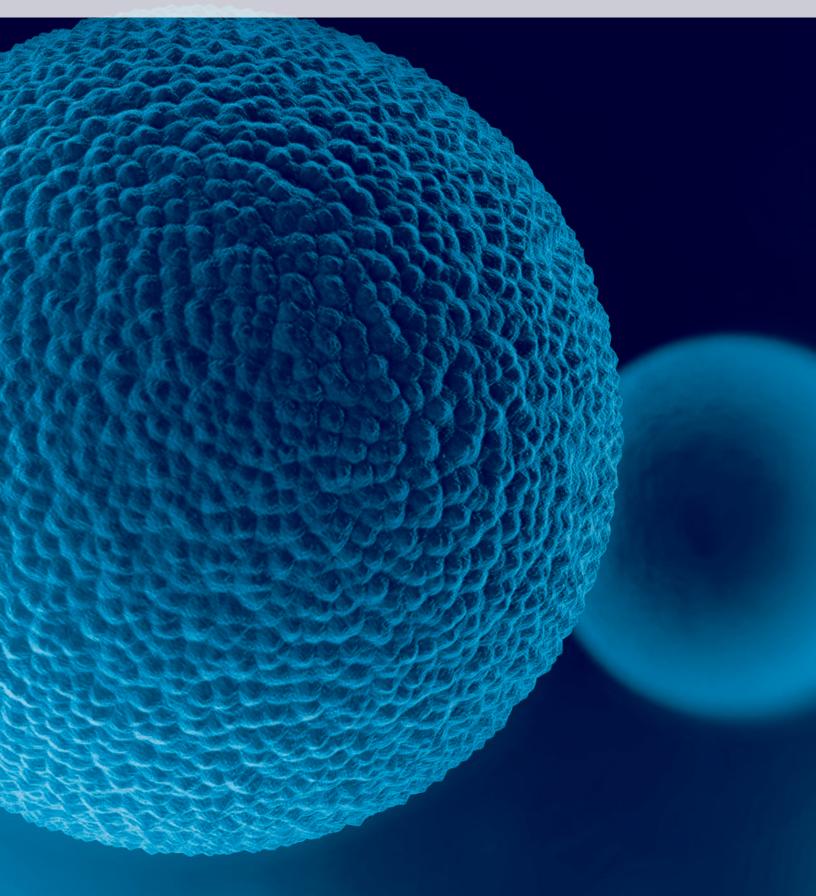
Innovative teaching method and personalized programs

In choosing to pursue their training at the IRIC, the next generation of scientists receive multi-disciplinary training in the field of cancer research and benefit from the varied expertise of IRIC's investigators.

In 2016-2017, 100 new students joined the IRIC to pursue their training and actively participate in advancing research conducted at the Institute. They came from 50 academic institutions located in 18 different countries.

Numbers like those attest to the reputation for excellence enjoyed by the IRIC and UdeM both nationally and internationally, and their ability to attract the finest students seeking scientific training in cancer research. At the graduate level, students have access to a wide variety of study programs offered by UdeM. In 2016-2017, approximately 65% of master's and doctoral students were enrolled in the Systems Biology training program developed by IRIC investigators.

Integrated into the Molecular Biology programs of UdeM's Faculty of Medicine, this training offers an accelerated one-year master's degree and a five-year doctorate that includes, among others, cellular and molecular biology, immunology, biochemistry, genetics, bioinformatics, proteomics, drug development and the more clinical aspects of cancer research. The IRIC also offers master's and doctoral programs in the following fields of study: molecular biology, biochemistry and molecular medicine, bioinformatics, chemistry, microbiology and immunology, as well as pharmacology.





2016 STUDENT RECRUITMENT EVENT

— recruitment







For the third straight year, the IRIC organized its student recruitment event to attract and recruit the finest prospects in the field of biomedical research. Attesting to the excitement generated by the event, which took place from June 15 to 18, 2016, over 146 applications from 80 universities spread over 26 countries were welcomed for this year's edition.

With its innovative programming and interactive formula, this recruitment activity allows participants to visit the IRIC's laboratories and core facilities, meet and discuss with investigators and students, learn about the study programs and graduate projects, and participate in one-on-one interviews with the investigators of their choice.

That's how 37 applicants from various countries (6) were selected to take part in three days of activities. More than 185 one-on-one interviews between applicants and investigators were held during the course of the event. Twenty students (11 for master's degrees and 9 for doctorates) were recruited as a result of this activity and joined an IRIC research team.

IRIC ON THE ROAD

— recruitment



In the fall of 2016, the IRIC took part in 8 higher education fairs organized at various Canadian universities located in Alberta, Ontario and Quebec.

These recruitment activities provide students with an opportunity to meet representatives of educational institutions and research centres to learn more about study programs, available internships, admission criteria and scholarship possibilities.

Furthermore, an IRIC representative also joined UdeM's Office of Admissions and Recruitment to take part in a tour in France. Jointly organized by several Quebec universities, the "Étudier au Québec" tour is designed to promote Quebec universities in the major French university hubs, in order to recruit undergraduate, master's and Ph.D. students who wish to continue their studies in Quebec.



SUMMER SCHOOL — in Systems Biology

Organized since 2006, the IRIC's Summer School in Systems Biology is aimed at offering top-notch training in cancer research.

It includes a series of theoretical courses covering a variety of themes connected to the cell and molecular biology of cancer, the molecular genetics of eukaryotes, immuno-oncology, model organisms and experimental approaches based on systems biology.

The School also offers practical laboratory courses designed to teach various techniques linked to molecular biology, cell analysis, protein expression and purification, analysis of the biochemical and biophysical properties of proteins, functional genomics, bioinformatics and the use of model organisms. During these practical courses, students carry out a number of small-scale research projects requiring the use of the IRIC's core facilities. In 2016, 41 students (including 30 from the IRIC) were able to take courses at the Summer School.

THE IRIC NEXT GENERATION — Awards Program

Offered for a sixth straight year, the IRIC Next Generation Awards Program enabled 19 Canadian students at the undergraduate level with an outstanding academic record to receive a scholarship in order to do a research internship with an IRIC team during the summer of 2016.

The awards are worth \$4,250 for a 12-week internship or \$5,670 for a 16-week internship.

The granting of these awards is made possible thanks to the participants and the generous donors of IRIC's Great Challenges Against Cancer, organized annually to benefit the IRIC Great Challenges Fund, including a generous donation from the Fondation Famille Diane et Léon Gosselin.

THE IRIC AWARDS COMPETITIONS

For the second year in a row, the IRIC conferred doctoral scholarships and Conference Awards to students at the Institute.

The doctoral scholarship competition aims to support Ph.D. students at the IRIC with an outstanding academic and research record, but who do not benefit from any other substantial scholarships. The IRIC was able to hand out 13 half-scholarships worth \$11,000 each (the second half being provided by the investigators).

The aim of the Conference Awards competition is to support master's and doctoral students, as well as postdoctoral fellows, who wish to present their research findings at scientific conferences outside Quebec. As a result, the IRIC was able to hand out 5 conference awards worth \$1,000 each.

The awards competition was made possible thanks to the funds raised through the 'Audacious' benefit event.

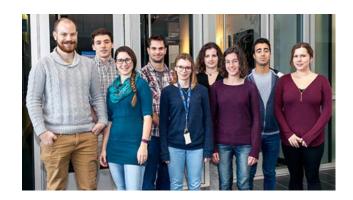
IRIC STUDENT ASSOCIATION — AEIRIC

The AEIRIC mandate is to represent master's and doctoral students, interns and postdoctoral researchers in institutional matters.

The AEIRIC contributes to the IRIC's development and to maintaining the quality of student life through active participation, on the one hand, by carrying out institutional programs and projects, and on the other hand, by fostering interactions between students, postdoctoral fellows and other members of the IRIC team, through various organized university, scientific and social activities.

NETWORKING EVENT — Alumni wine and cheese

Organized by the Office of Academic Affairs in collaboration with IRIC students, the first edition of the Alumni wine and cheese networking event took place on March 30, 2017. The purpose of the evening is to inform postdoctoral fellows about future career opportunities in the field of life sciences. Seven graduates from all backgrounds, working in the public, private or academic sector, were invited to attend. They got the chance to discuss and exchange with the various guests during the event.



PROMINENCE AND RECOGNITION

Each year, many IRIC students distinguish themselves by receiving a great deal of awards at several scientific retreats and at national and international seminars (notably oral or poster presentation awards).

Several IRIC students were rewarded for the quality and importance of their publications and their research work.

Two IRIC students stood out at the Étudiants-chercheurs étoiles awards from the Fonds de recherche du Ouébec in the "Health" section.

Céline Laumont, Ph.D. candidate in molecular biology in Dr. Claude Perreault's laboratory, was the laureate for the month of May 2016 for her study published in the scientific journal Nature Communications titled: "Global proteogenomic analysis of human MHC class I-associated peptides derived from noncanonical reading frames".

Bianca Plouffe, a postdoctoral student in biochemistry in Michel Bouvier's laboratory, was the laureate for the month of October 2016 for her study published in the scientific journal Cell titled: "GPCR-G Protein- β -Arrestin Super-Complex Mediates Sustained G Protein Signaling".



Céline Laumont
PH.D. CANDIDATE IN
MOLECULAR BIOLOGY

Dr. Claude Perreault's laboratory



Bianca Plouffe
POSTDOCTORAL
STUDENT IN
BIOCHEMISTRY

Michel Bouvier's laboratory



NEW IRIC RECRUITS

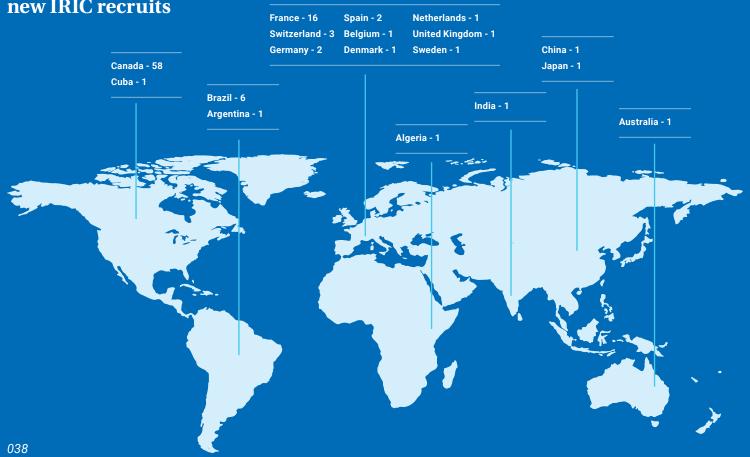
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Breakdown of new recruits based on level*

*Some students are included in more than one category (e.g., in the same year, an intern becomes a student).



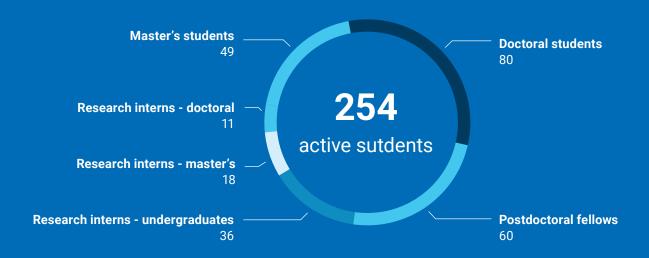
Countries of origin of new IRIC recruits





BREAKDOWN OF ACTIVE STUDENTS

— for 2016-2017 based on level



BREAKDOWN OF GRADUATES — for 2016-2017 based on level



GRANTS AND NOMINATIVE AWARDS

QUEBEC

Cole Foundation

Doctoral

Yayha Benslimane Karine Bourdages

Céline Laumont Nandita Noronha Pierre Priam

Camille Simon

Clinician

Vincent-Philippe Lavallée

Postdoctoral Adam-Nicolas

Pelletier

Fonds de recherche du Québec - Santé (FRQS)

Master's

Gwenaëlle Gavorv Elizabeth Ottoni Guillaume Laflamme Louis-Philippe Picard Myreille Larouche Assya Trofimov Laura Rivest-Khan Charles St-Pierre Yu Wei Zhang

José-Carlos Zeledon Doctral Orellana

Karine Bourdages Jessica Gagnon

Postdoctoral Eugénie Goupil

Fonds de recherche du Québec -Nature et technologies (FRQNT)

Master's

Doctoral

Blandine Monjarret

Yayha Benslimane Nicholas Iannantuonno

Merit Scholarship Program for Foreign Students (PBEEE)

Doctoral

Neethi Nandagopal Chongyang Li

Dhanaraman Seetharaman Thillai

Fondation du Grand défi Pierre Lavoie

Khaled Ben El Kadhi

CANADA

Canadian Diabetes Association

Postdoctoral

Bianca Plouffe

MITACS

Undergraduate

Kévin Xi

Postdoctoral

Arhamatoulaye Maiga

Canadian Institutes of Health Research (CIHR)

Undergraduate

Olivier Mailhot

Doctoral

Fanny Bergeron-Labreque Maude Dumont-Lagacé

Peter Kubiniok

Postdoctoral

Céline Moison

Jasmin Coulombe-Huntington

Natural Sciences and Engineering Research Council of Canada (NSERC)

Undergraduate

Guillaume Poirier-Morency

Master's

Blandine Monjarret

Doctoral

Samuel Rochette

OTHER COUNTRIES

Switzerland

Sibvlle Pfammatter

Franziska Marie Heydenreich

France

Clément Agret Irène Baccelli

Oman

Shaima Al-Khabouri

IRIC

IRIC Next Generation Awards (undergraduate)

Michelle Barbagallo Gabriela Bernal Astrain Anne-Sophie Castonguay

Jeanne Chan Fiona Dickson Thomas Dodsworth Megan Fass

Kevin Fortier
Trevor Henderson
Jennifer Jean-Louis
Sarah Mirza
Olivia Paserin

Marie Ashley Ste-Croix

Badr Sokrat

Luc St Laurent Niklas von Krosigk Megan Wheatley Jay Yin

Master's Perseverence Awards

Anca Apavaloaei

Simon Bergeron-Fortier

Moana Boulangé

Reece Dowling

Stephanie Fedorov

Ema Elissen Flores Diaz

Audrey Herrmann

Charles Homsi

Marion Lacroix

Chithra Muthuramu

Lindsay Noonan

Frédéric Perriot

Vincent Poupart

Céline Schott

Badr Sokrat

Srivatsava Viswanadha

Xingjian (Jim) Xu

Doctoral Awards

Nicholas Iannantuono Myreille Larouche Laura Simon

UdeM

Molecular Biology Program Awards

Merit Awards – Master's Simon Bergeron-Fortier

Moana Boulangé Reece Dowling Stephanie Fedorov Ema Elissen Flores

Diaz Audrev H

Audrey Herrmann Marion Lacroix Frédéric Perriot Vincent Poupart Céline Schott Badr Sokrat

Srivatsava Viswanadha Xingjian (Jim) Xu

Writing Awards – Master's Beichen Gao Merit Awards – Doctoral Mélanie Criqui

Marine Diennet Kevin Leguay Thomas Milan Camille Simon Camille de Jamblinne

de Meux

Marjorie Lapouge Sara Marullo Virginie Mondin Sami Nourreddine

Writing Awards –

Pierre Priam

Khaled Ben El Kadhi Mohamed El Ezzy Elizabeth Rajan Yogitha Thattikota

Faculty of Medicine Recruitment Awards

Master's

Michelle Barbagallo Ema Elissen Flores Diaz Srivatsava Viswanadhai

Emergency bursary from the Faculty of Medicine

Aline Khayat

COPSE Award from the Faculty of Medicine

Mégane Tanguay

Merit Award from the Department of Computer Science and Operations Research

Doctoral

Mathieu Dupont

Merit Award from the Faculty of Graduate and Postdoctoral Studies

Elizabeth Ottoni

UdeM

A Awards for fast-track from master's to doctoral from the Faculty of Graduate and Postdoctoral Studies

Blandine Monjarret Sibylle Pfammatter

B Awards for direct access from bachelor's to doctoral from the Faculty of Graduate and Postdoctoral Studies

Olivier Mailhot Louis-Philippe Picard

End-of-study scholarships from the Faculty of Graduate and Postdoctoral Studies

Doctora

Frédéric Lamoliatte Justine Paradis Tatiana Traboulsi

Master's awards for Canadian candidates non-residents of Quebec (D awards) from the Faculty of Graduate and Postdoctoral Studies

Stéphanie Fedorov Chithra Muthuramu Swati Singh

Awards for exemption from additional tuition fees for international students from the Faculty of Medicine and the Faculty of Graduate and Postdoctoral studies

Ema Elissen Flores Diaz Amir Medjtoh Gustavo Borges Lucas de Lima Carvalho Mayra dos Santos Carneiro

IRICoR

Research commercialization hub specialized in drug discovery

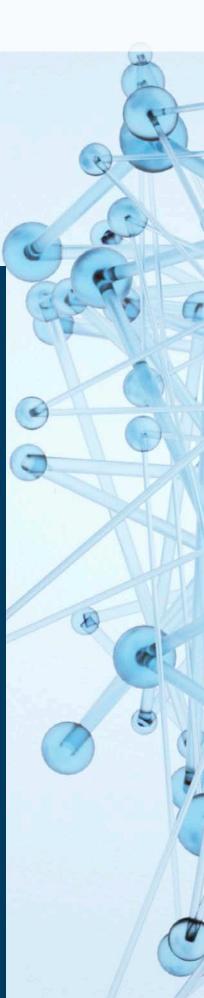
IRICoR's objective is to translate research projects into innovative therapies, notably in the fields of oncology and immunotherapy. Its mission is to accelerate the commercialization of those therapies by establishing partnerships with industry or by creating new companies, for the purpose of making personalized therapeutic solutions available to patients.

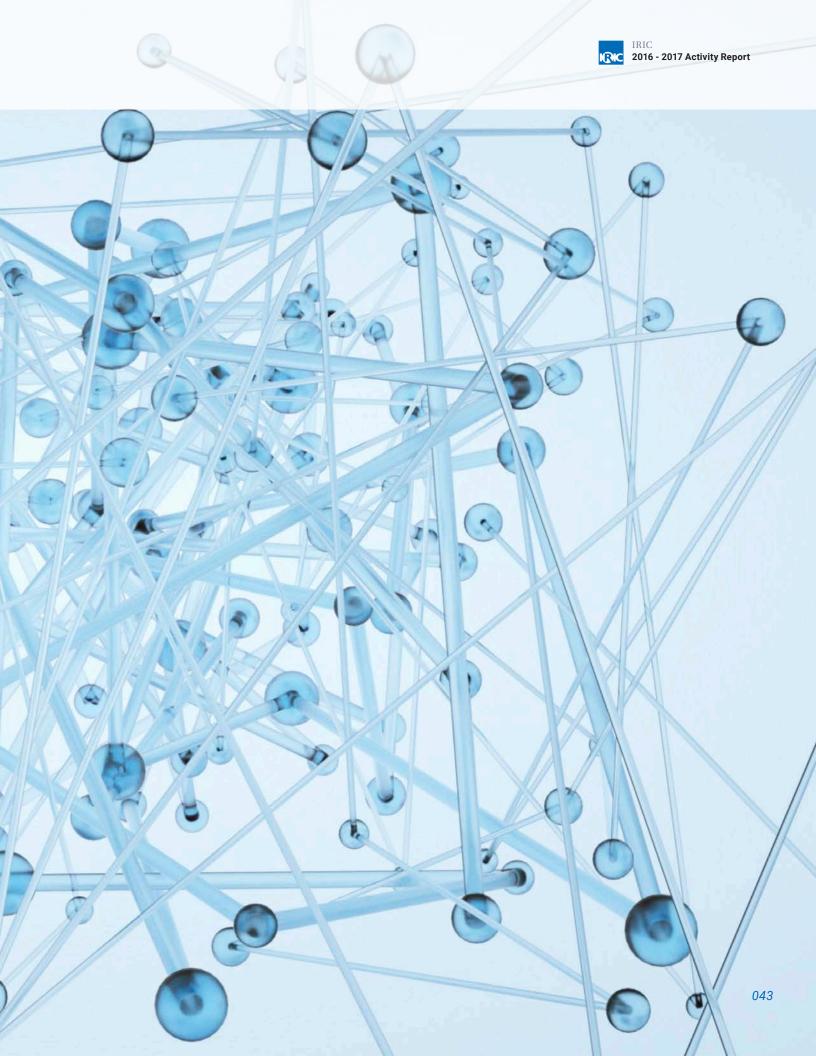
IRICoR's unique model resides in access to diversified research projects, privileged access to the IRIC's core facilities, great expertise in project commercialization and know-how with respect to the commercialization of research. IRICoR relies on a team with solid experience in the fields of drug discovery, business development, risk capital, protection of intellectual property and project management.

IRICoR also enjoys privileged access to one of the largest academia-based medicinal chemistry units in Canada, with 40 qualified chemists and biologists working on drug discovery and located at the IRIC.

IRICoR strives to attract the best drug discovery projects in Quebec, Canadian and foreign universities, helping to transfer research into innovation in order to accelerate their migration towards commercialization. IRICoR pursues its mission by establishing a close relationship between university research and the complementary resources of the private sector.

This hybrid research-business model also allows the 200 students of the next generation of scientists trained annually at the IRIC to be exposed and sensitized to the key factors involved in the commercialization of research, thus contributing to their cross-training and nourishing a culture of innovation.







BUSINESS MODEL

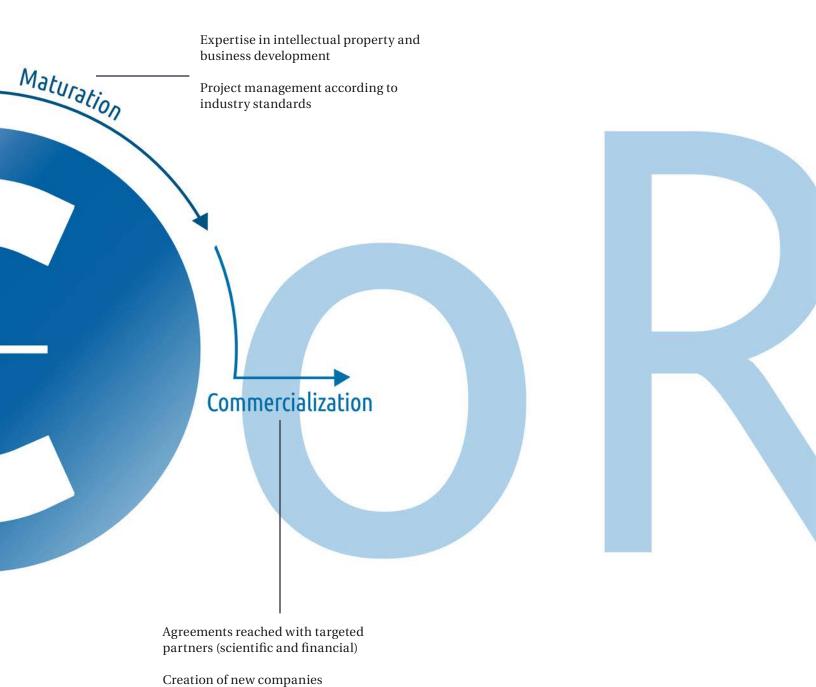
Opportunity to access scientific core facilities at the cutting-edge of technology covering the drug discovery chain

Privileged access to the largest medicinal chemistry team in an academic setting in Canada with industry expertise (40 chemists and biologists)





Assessment and selection of projects with high commercial potential aimed at sustaining a portfolio of innovative projects





HIGHLIGHTS: IRICOR AT THE HEART OF STRATEGIC PARTNERSHIPS



The emergence of new proteomics technologies is a key driver in developing personalized medicine, resulting in better meeting patients' needs.

Mass spectrometry (MS) thus offers new perspectives in personalized medicine by providing a high-capacity technology, enabling the detailed characterization of thousands of proteins present in patient specimens. However, the performance of MS instruments is currently mitigated by the overwhelming sample capacity that limits the comprehensiveness and dynamic range of MS analyses.

Pierre Thibault's laboratory, in partnership with Jean-Jacques Dunyach of Thermo Fisher Scientific, undertook a project targeting the development of new technologies that improve the sensitivity and specificity of mass spectrometers for numerous applications in life sciences. In particular, this project aims to bridge the gap in proteomics in order to identify biomarkers specific to human cancer cells with unprecedented sensitivity.

This project also benefits from a grant from Genome Canada and Génome Québec.

The project focuses on developing a high-sensitivity platform for the identification of antigens for leukemia immunotherapy programs, and the targeted identification of mutations in cancer cells.

In the end, the expected socio-economic benefits of this project include privileged access to state-of-the-art technology, an increase in the sensitivity and the speed of MS analysis, and potential savings for Canadian laboratories, over a wide range of analytic and biomedical applications.



HIGHLIGHTS: IRICOR AT THE HEART OF STRATEGIC PARTNERSHIPS



During the course of the year, IRICoR and the Centre for Commercialization of Cancer Immunotherapy (C3i) announced a major collaboration to identify novel tumor-specific antigens (TSAs) in a certain number of solid and hematological cancers.

Under the leadership of Dr. Lambert Busque, a hematologist involved in clinical research and biomarkers development at Maisonneuve-Rosemont Hospital, the C3i team added its expertise in genomic sequencing and clinical validation for the targeted indications.

Also, with support from IRICoR, Dr. Claude Perreault and his colleagues worked to develop a novel approach for rapidly identifying clinically relevant TSAs which can stimulate MHC Class I-specific T-cell responses.

By having access to human tumor samples as well as the cell therapy and clinical expertise at C3i, this collaboration will allow to generate proof-of-concept data.

This partnership laid the foundation for a long and successful strategic collaboration between IRICoR and C3i. Identifying tumor-specific neoantigens is vital to the development of targeted therapies that maximize antitumor efficacy and minimize off-target toxicities and is fully aligned with its mandate to discover and commercialize cancer immunotherapies.



ACCOMPLISHMENTS

— IRICoR



IRICoR selects its projects on the basis of their scientific excellence and their commercial potential, provides them with strategic support and invests in them directly with a view to moving them rapidly towards commercialization.

By the end of the 2016-2017 period, 14 new projects were funded, bringing the number of projects in the IRICoR portfolio to 42. They cover the entire drug discovery chain, from identifying therapeutic targets to clinical trials. IRICoR's supported projects this year led to the filing of 38 patent applications representing 20 patent families.

Projects supported by IRICoR have also led to the development of three

drug candidates currently at the clinical evaluation phase. During the course of the 2016-2017 year, a project in partnership with AmorChem, a Montreal-based venture capital firm, involving a high-throughput method to identify new human minor histocompatibility antigens (MiHAs), began its clinical development (Phase I/II) at Maisonneuve-Rosemont Hospital (MRH), and the stroke – platelet aggregation project, developed based on a target identified at Bristol-Myers

Squibb, entered into Phase II, which will involve several hospitals around the world. Also, the clinical study that got underway in February of 2016 on the expansion of stem cells for transplantation into leukemia patients is underway at the MRH and has progressed according to expectations.



HIGH IMPACT ACHIEVEMENTS — thus far

Companies created ~50 Patent families generated Strategic partnerships with industry ~50 Partnership projects ~80 Project financings 23 License agreements Active clinical trials



FUNDING AND REVENUES

For the 2016-2017 period, funding for IRICoR's activities totalled \$5.6 million from private partners and \$6.5 million from public funds. Moreover, licensing revenues stemming from collaboration contracts now reach over \$3.9 million.

After nine years of existence, in close cooperation with IRIC/UdeM, IRICoR is at the heart of the Quebec and Canadian ecosystem in the commercialization of academic research. IRICoR is proud that it has successfully set up an environment that is conducive to creating value.



CREATION OF COMPANY

In October of 2016, SpecificiT Pharma Inc. was created. It's a spin-off company of the UdeM based on the discovery and use of immunodominant minor histocompatibility antigens (MiHAs) stemming from the work carried out by the teams led by Drs. Claude Perreault, Denis-Claude Roy and Jean-Sébastien Delisle, as well as Pierre Thibault.

The company's goal is to use MiHAs to identify a treatment in hematological cancers. The project is proof of the acceleration that has taken place in the transformation of basic research into clinical applications.



VISIBILITY

The IRICoR team was invited to present its business model and its project portfolio at 25 national and international gatherings.

IRICOR was also selected as a finalist for the 2016 Life Sciences – Innovation Awards, part of the 26th edition of the Gala des Prix Innovation de l'Association pour le développement de la recherche et de l'innovation du Québec (ADRIQ).



PARTNERSHIPS

During the course of the 2016-2017 period, IRICoR managed to create or maintain the following 10 strategic partnerships with the pharmaceutical industry: Amorchem, Bristol-Myers Squibb, Caprion Biosciences, Cyclenium Pharma, Domain Therapeutics, Encycle Therapeutics, Merck (Sharp and Dohme), Pfizer, Pharmascience and Stem Cell Technologies.

IRICOR, Domain Therapeutics, the Université de Montréal and McGill University also extended their licensing and partnership agreement on G protein-coupled receptor (GPCR) biosensor technology (the first licensing agreement was signed at the end of 2013, upon completion of a project

funded by CQDM's FOCUS program). This exclusive second licensing agreement, based on the pre-existing BioSens-AllTM technology, makes it possible to assess more intracellular signaling pathways and to more accurately discriminate the functional activation associated with specific GPCRs, which will accelerate the discovery and development of biased ligands for this class of receptors. As a result, Domain Therapeutics will have exclusive access to a new array of more powerful biosensors, developed by a team of researchers led by Michel Bouvier of the IRIC and Stéphane Laporte of McGill University.



GOVERNANCE

In 2016-2017, four new administrators were appointed to IRICoR's Board of Directors.

Fréderic Alberro – Director, Quebec, Innovative Medicines Canada

Jacques Bernier - President and Managing Partner of Teralys Capital

Andrew Casey - President and CEO of BIOTECanada

 $\label{lem:pierce} Pierre Fontaine - Executive \ Assistant \ Director \ of \ Research - CIUSSS \ de \ l'Est-de-l'Île-de-Montréal$

All four new administrators bring a wide range of experience that complements the one already in place on the Board, particularly with respect to questions concerning the biotechnology sector, the pharmaceutical industry and risk capital, while also taking governmental issues into account.

Under Nadine Beauger's leadership, IRICoR has become a key player in academic-based drug discovery and now enjoys international visibility which translates into major socio-economic and scientific benefits.

NATIONAL AND INTERNATIONAL NETWORK (SOME OF OUR COLLABORATORS)

Karolinska Institutet

Université Laval

Institut Cochin

University of Toronto

MD Anderson Cancer Center

Centre for Commercialisation of Cancer Immunotherapy

Max-Planck-Gesellschaft

Quebec Leukemia Cell Bank

Université de Sherbrooke

Research Center of the Sainte-Justine University Hospital

Memorial Sloan Kettering Cancer Center

McGill University

MRC Laboratory of Molecular Biology

HOSPITALS

— clinical studies of discoveries

CHUM

Maisonneuve-Rosemont Hospital

Jewish General Hospital

Princess Margaret Cancer Centre

BC Cancer Agency

PHARMA AND BIOTECHS
— strategic partnerships

Pfizer

Pharmascience

Bristol-Myers Squibb

Vertex

Merck

Ono Pharmaceutical Co., LTD.

Domain Therapeutics

ExCellThera

FINANCIAL AND GOVERNMENT PARTNERSHIPS

Networks of Centres of

Excellence of Canada

AmorChem

Genome Canada

Génome Québec

Gouvernement du Québec

CENTRES OF EXCELLENCE FOR COMMERCIALIZATION AND RESEARCH

MaRS Innovation

NEOMED Institute

CQDM

Centre for Drug Research and Development

Centre for Commercialization of Regenerative Medicine

IRIC IRICoR

E PHILANTHROPY AND COMMUNICATIONS

PHILANTHROPY: SERVING THE CAUSE

The generous patrons who support the IRIC allow the scientific community to accomplish its threefold mission of research, training the next generation and drug discovery. By providing substantial support for cancer research, donors directly contribute to accelerating the discovery of more effective cancer treatments.

As a result, events such as the Audacious benefit evening, IRIC Great Challenges Against Cancer and the annual campaign mounted as part of World Cancer Day enable the IRIC to benefit from the unwavering support of loyal donors from both the business community and the general public.

The IRIC community is more than grateful for the support of its donors and for the interest that they have shown in the research being carried out at the Institute.

COMMUNICATIONS: SERVING RESEARCH

Each year, these events, orchestrated by the Communications team, are an opportunity to both increase the support of loyal donors and provide the Institute with greater visibility.

The 2016-2017 year made way for a great many opportunities to showcase the work being done at the IRIC, while also seeking out networks in a position to support its mission.

Fostering the emergence of greater visibility for the Institute can not only kindle the interest of new donors, but also contributes to shining light on the work being carried out by Principal Investigators and their students, to boost the collective interest being shown in research.



WORLD CANCER DAY

—2017

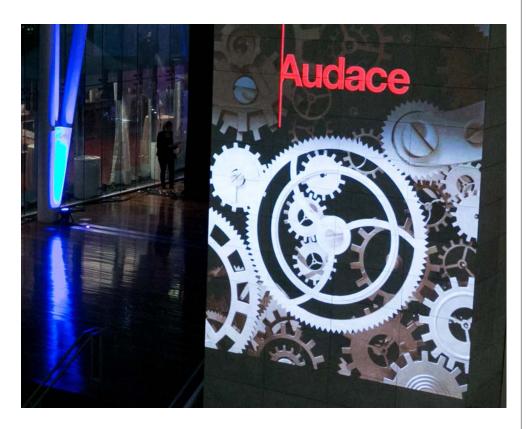


As part of World Cancer Day 2017, the Institute led a campaign with its donors.

For the occasion, thanks to the support of its partners Fairmont Le Château Frontenac and Ivanhoé Cambridge, the IRIC launched a contest among the donors who supported the campaign and held a conference on cancer immunotherapy.

BENEFIT EVENING TO SUPPORT RESEARCH

— AUDACIOUS 2016



Four hundred and fifty guests gathered on the Parquet of the Caisse de dépôt et placement du Québec for the third edition of Audacious, the IRIC's annual benefit event. Hosted by Stéphane Bellavance, the event raised over \$1.1 million to support the Institute's activities in the fight against cancer.

Under the co-chairmanship of Sylvain Brosseau, President and Chief Operating Officer, Fiera Capital, Roland Lescure, Executive Vice-President and Chief Investment Officer, Caisse de dépôt et placement du Québec and Pierre Pomerleau, President and CEO, Pomerleau Inc., the event provided an opportunity to pay tribute to Dr. Guy Sauvageau, named La Presse Scientist of the Year in the science category in 2014.

The Institute wishes to give special thanks for the remarkable work done by the members of the Fundraising Committee, who greatly contributed to the success of the evening, as well for the support of its many main partners, including the Caisse de dépôt et placement du Québec, CGI, CIBC, Desjardins Group, Fiera Capital, Ivanhoé Cambridge and Pomerleau Inc.

We would also like to point out the vital support of our intermediary partners, sponsors and volunteers.







HIGHLIGHTS

3rd édition

of the event

450

guests

Over 1.1 million

dollars

A DEVOTED FAMILY

— Outaouais / Blais Family Fund golf tournament



New record of \$60,000 raised at the Outaouais / Blais Family Fund golf tournament benefiting the IRIC

The IRIC is fortunate to be able to rely on loyal donors who are passionate about the cause. That certainly applies to the Blais Family, who organized the 7^{th} edition of their golf tournament to benefit the IRIC.

A record sum of \$60,000 was raised in 2016 from the event, which was chaired by Jean Labrie (Habitations Alta) and brought together over 150 golfers. Since being created, the Blais Family Fund has raised \$267,000 for the Institute's innovative research projects.

GREAT CHALLENGES TO FIGHT CANCER

— IRIC Great Challenges Against Cancer







The seventh edition of the IRIC Great Challenges Against Cancer raised over \$240,000 to support the training of the IRIC's next generation of scientists through the issuing of several Perseverance Awards and IRIC Next Generation Awards.

More than 220 participants raised funds and took part in one of the three sporting events that were organized: the IRIC Ascent Challenge and the IRIC Mount Royal Tour, held in partnership with the Grand Prix Cycliste de Montréal, as well as the Défis du Parc national de la Mauricie.

An evening in their honor was organized to thank them. They were welcomed by Dr. Robert Patenaude, founder of IRIC's Great Challenges Against Cancer, himself a survivor of chronic myeloid leukemia thanks to a treatment provided by Dr. Claude Perreault.

The evening also served as an opportunity for the IRIC to announce the 16 winners of the Perseverance Awards. The Institute wishes to thank all of the participants, donors, volunteers and sponsors for their support, as well as its main partners, namely Université de Montréal, the Grands Prix Cyclistes | Québec et Montréal Notre-Dame-des-Neiges Cemetery, the City of Montreal and the Parc national de la Mauricie.

HIGHLIGHTS

7th edition

of the event

220

participants

\$240,000

to support training

DONATIONS WITH TANGIBLE RESULTS, A TRUE SOURCE OF INSPIRATION — for the IRIC



The IRIC is pleased to be able to count on the commitment of exceptional donors who recognize the importance of cancer research.

The Marcelle and Jean Coutu Foundation: a mobilizing generosity

The Marcelle and Jean Coutu
Foundation, continuing its
longstanding relationship with the
Institute, renewed its invaluable
support. Their exemplary assistance
has enabled the IRIC to recruit the
best Princcipal Investigators and fund
specific high-risk, high-impact projects.





THE NEW GUY JL SAUVAGEAU FUND — direct financial support for laboratory work

In order to accelerate the discovery of more effective new therapies to fight cancer, the IRIC prioritizes visionary and creative research projects with high potential impact on innovative drug discovery. However, as a result of their relatively high level of risk, it is difficult to find funding for these projects from traditional funding agencies, at least initially.

Over the years, several donors have made the choice to support these strategic projects with great potential, right from the early phases of development, and several emerged thanks to that financial support. Some, such as the chemolibrary and Leucegene, have provided a way to create great leverage that resulted in greater interest and an increase in available funding.

Along those lines, in 2017, the IRIC received a substantial donation to kick-start the Guy JL Sauvageau Fund with an initial amount of \$250,000, which was used for a project in Marc Therrien's laboratory. The donation enabled his team to continue developing a new generation of molecule inhibitors directed against an oncogene frequently mutated in cancer.

LIST OF DONORS

The IRIC executive wholeheartedly thanks all the individuals, foundations and companies who believe in its unique model and contribute generously to the success of the Institute through the pursuit of its mission.

Don	ations	of	\$51
and	over		

Fondation Marcelle et Jean Coutu

Donations of \$1M to \$4,999,999

CGI

Fondation Famille Diane et Léon Gosselin

Donations of \$100,000 to \$999,999

Anonymous (2)

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2016-2017 REVENUES — total of \$38,594,933

	Operating	Research	Capital assets	Total
Université de Montréal	\$5,437,187	\$3,220,982		\$8,658,168
Grants	\$5,059,165	\$13,863,315	\$1,000,000	\$19,922,481
Student and postdoctoral awards		\$1,489,480		\$1,489,480 ¹
Chairs and salary awards		\$2,237,723		\$2,237,723
Contracts with industry		\$3,355,422		\$3,355,422
Core facilities - external clients	\$1,111,488			\$1,111,488 2
Donations and sponsorships		\$1,780,603		\$1,780,603 ³
Other	\$39,568			\$39,568
TOTAL	\$11,647,408	\$25,947,525	\$1,000,000	\$38,594,933

2016-2017 EXPENSES — total of \$37,335,413

	Operating	Research	Capital assets	Total
Salaries and employee benefits	\$6,525,679	\$18,301,180		\$24,826,860 4
Supplies and services	\$1,761,355	\$6,313,253		\$8,074,608
Maintenance and repairs	\$2,950,110	\$ 245,078		\$3,195,188
Scientific equipment	\$172,297	\$ 66,461	\$1,000,000	\$1,238,758
TOTAL	\$11,409,441	\$24,925,972	\$1,000,000	\$37,335,413

¹Includes the IRIC Great Challenges Against Cancer scholarships, IRIC members Ph.D. awards, IRIC Next Generation Internship Awards, and IRIC Awards.

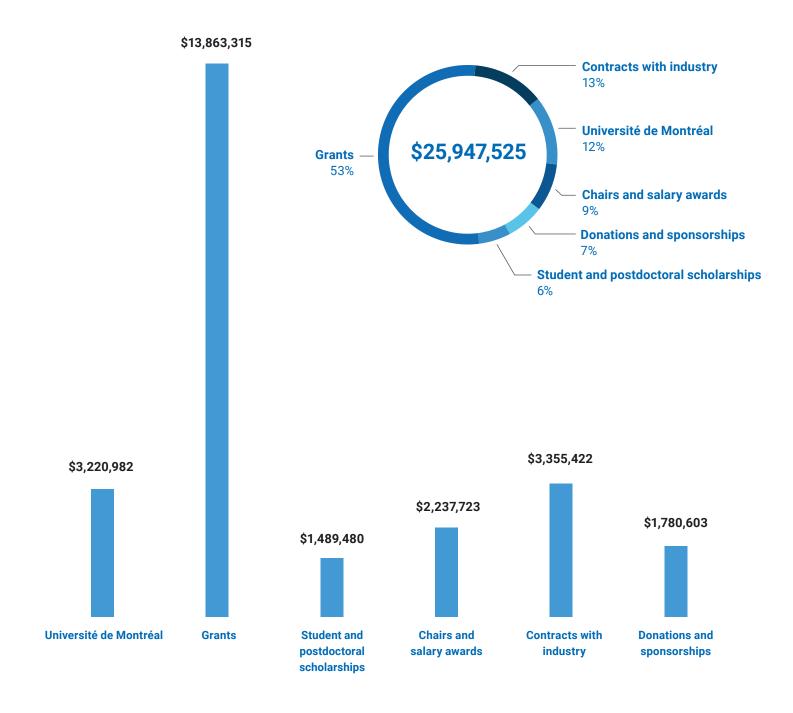
 $^{^2\,}Excludes\,the\,amounts\,from\,IRIC\,researchers\,(\$1,653,436.76),\,these\,being\,included\,in\,research\,grant\,revenues.$

³ Solely donations and sponsorships received. Excludes the IRIC Great Challenges Against Cancer scholarships, IRIC Members Ph.D. awards, IRIC Next Generation Internship Awards, and IRIC Awards.

⁴ Includes Principal Investigator salaries paid by UdeM.



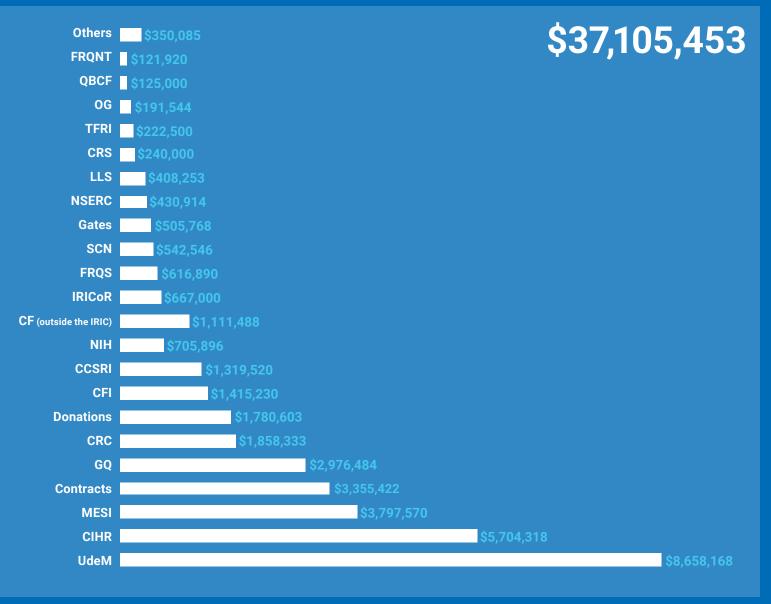
RESEARCH FUNDING SOURCES — in 2016-2017





FUNDING SOURCES

— in 2016-2017 (excluding scholarships)



FRQNT = Fonds de recherche du Québec - Nature et Technologies

QBCF= Quebec Breast Cancer Foundation

OG = Ontario Genomics

 $TFRI = Terry\ Fox\ Research\ Institute$

CRS= Cancer Research Societ

LLS = Leukemia and Lymphoma Society - USA / CAN

NSERC = Natural Sciences and Engineering Research Council of Canada

Gates = Fondation Bill & Melinda Gates

SCN = Stem Cell Network

FRQS = Fonds de recherche du Québec - Santé

CF = Core facilities (outside the IRIC)

NIH = National Institutes of Health

 $CCSRI = Canadian\ Cancer\ Society\ Research\ Institute$

 $CFI = Canadian\ Foundation\ for\ Innovation$

CRC = Canada Research Chairs

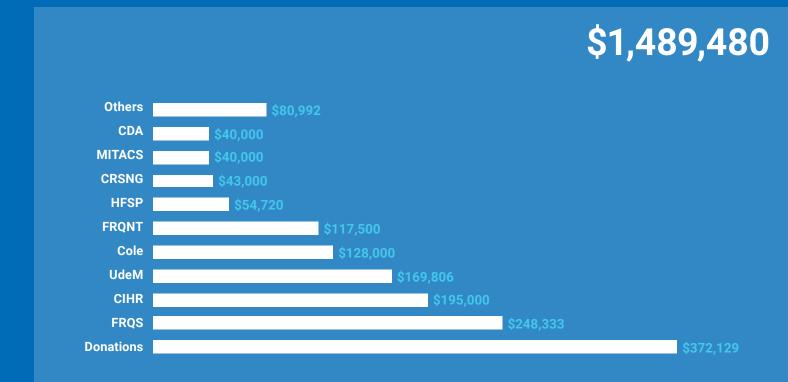
GQ = Genome Canada / Génome Québec

MESI = Ministère de l'Économie de la Science et de l'Innovation

CIHR = Canadian Institutes of Health Research

STUDENT SCHOLARSHIPS AND POSTDOCTORAL FELLOWSHIPS — in 2016-2017

Research funding coming from organizations with peer committees for nominative student and postdoctoral fellow awards



CDA = Canadian Diabetes Association Cole = Cole Foundation HFSP = Human Frontier Science Program

MAIN ORGANIZATIONS WITH PEER COMMITTEES HAVING PROVIDED RESEARCH FUNDS AND SCHOLARSHIPS

— in 2016-2017

Bill and Melinda Gates Foundation (Gates)			
Canada Foundation for Innovation (CFI)			
Canada Research Chairs (CRC)			
Canadian Cancer Society Research Institute (CCSRI)			
Canadian Diabetes Association (CDA)			
Canadian Institutes of Health Research (CIHR)			
Cancer Research Society (CRS)			
Fonds de recherche du Québec – Nature et technologies (FRQNT)			
Fonds de recherche du Québec – Santé (FRQS)			
Genome Canada and Génome Québec (GC and GQ)			
Human Frontier Science Program (HFSP)			
Leukemia and Lymphoma Society - USA / CAN (LLS)			
Ministère de l'Économie, de la Science et de l'Innovation (MESI)			
National Institutes of Health (NIH)			
Natural Sciences and Engineering Research Council of Canada (NSERC)			
Ontario Genomics (OG)			
Quebec Breast Cancer Foundation (QBCF)			
Stem Cell Network (SCN)			
Terry Fox Research Institute (TFRI)			

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