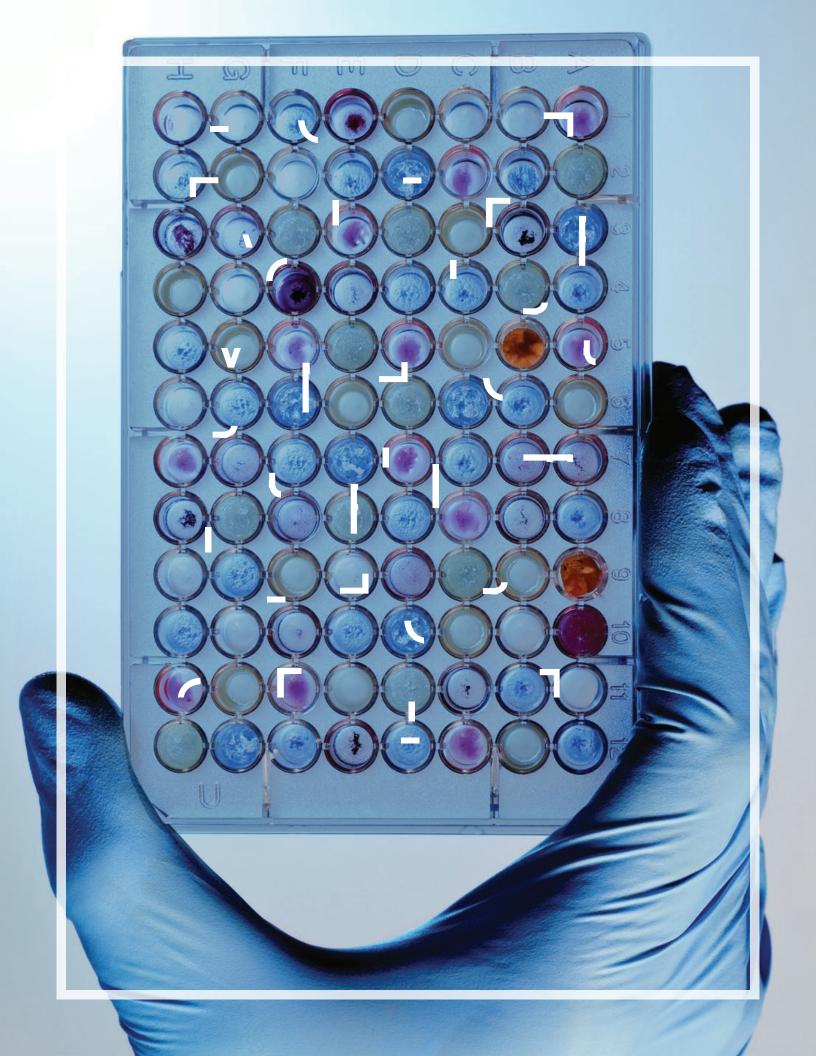
IRIC: VANQUISTING CANCER D'FFERENTLY







About the Institute for Research in Immunology and Cancer

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

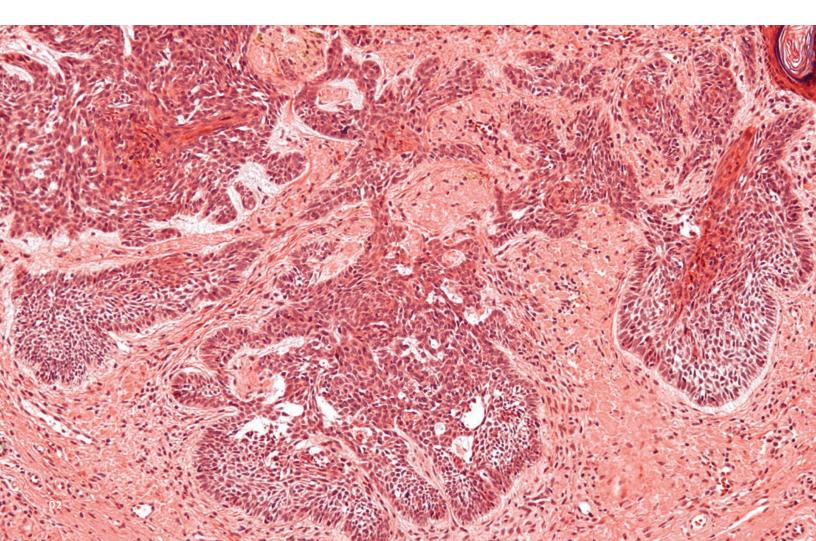
About the Université de Montréal

Deeply rooted in Montréal and dedicated to its international mission, the Université de Montréal is one of the top universities in the French-speaking world. Founded in 1878, the Université de Montréal today has 16 faculties and schools, and together with its two affiliated schools, HEC Montréal and Polytechnique Montréal, constitutes the largest centre of higher education and research in Québec and one of the major centres in North America. It brings together 2,500 professors and researchers and welcomes more than 60,000 students.

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CANCER IS...

200	different illnesses
196,900	new cases in Canada in 2015
78,000	people will lose their lives to
30%	of all deaths in Canada





IRIC IS...

A concentration of cancer researchers	A multidisciplinary training program
A complementarity of areas of expertise	An integrated development and commercialization unit
A drug discovery chain	An ultramodern technology park

cutting-edge facilities

principal investigators and research units

integrated drug discovery chain

481

people, including interns



professional and administrative employees

38

million dollars annual budget

Canada Research Chairs research

students

graduate program in systems biology

private research chair

Inspiring accomplishments for a promising future



Robert Tessier

Chairman of the Board of IRIC

Charman of the Board of the

Throughout the past decade, IRIC has boldly gone about achieving exceptional progress. Being an enthusiastic admirer of this institution and its accomplishments, it was with great pleasure that I accepted the mandate of chairmanship of its board of directors.

---IRIC is a valuable asset whose potential we must carry on developing while preserving the highest standards of excellence. The importance of its mission, the dynamism of its team, and the quality of its facilities have made it one of the highest-performing and most admired research centres in Canada and throughout the world. These factors are reflected today in proven results likely to have a decisive impact on the fight against cancer and illnesses affecting the immune system.
---In this regard, I would like to call attention to the success achieved by Dr. Guy Sauvageau and his team,

attention to the success achieved by Dr. Guy Sauvageau and his team, whose research has led to an important discovery, the UM171 molecule, which enables multiplication of stem cells in umbilical cord blood. A principal investigator and former chief executive officer of IRIC, Dr. Sauvageau was among, other distinctions, named *La Presse* Scientific Personality of the Year and Radio-Canada Scientist of the Year following his remarkable achievement. The breakthrough was also recognized as Discovery of the Year by readers of *Québec Science*.

--- In the course of the past year, IRIC received generous and essential support from its many donors. The first Audacious benefit evening, celebrating the tenth anniversary of the Institute, was a resounding success, raising \$730,000 in funding, not counting a contribution of \$196,000 in equipment from Thermo Fisher Scientific.

---I would also like to take the opportunity to highlight the appointment of Michel Bouvier as Chief Executive Officer and to congratulate him for his excellent work to date, taking over from Dr. Guy Sauvageau. I also take my hat off to Marc-André Blanchard, my predecessor as Chairman of the Board, who succeeded in taking IRIC to new heights.

--- Finally, I wish to thank the members of the management team and the entire staff of IRIC for their passion and for the quality of their involvement.

Boldness in the service of innovation



Michel Bouvier Ph.D., FCAHS, FRSC

Chief Executive Officer of IRIC

Chief Executive Officer of INIC

It was with great pride that in the summer of 2014 I accepted the responsibilities that come with directing IRIC. For a number of years, I have been inspired by the success of this ground-breaking institute, which never ceases to stir a passion in me. That same passion can be found in all of our teams, who make IRIC a one-of-a-kind research centre, a place where boldness is constantly placed at the service of innovation.

--- For over ten years now, IRIC has distinguished itself through its ability to achieve the difficult balance between the demands of basic research and the practical imperatives of applied research. To make progress in the fight against cancer, we must focus our efforts on basic research to arrive at a better understanding of the malfunctioning biological mechanisms that characterize the illness. The results thus obtained must also be applicable to the resolution of specific problems, so that we are in a position to quickly offer effective new therapies. For that to happen, IRIC has developed very special partnerships, enabling it to optimize the transition between theoretical results and their practical application. That ground-breaking approach has already borne fruit, and continues to carry great promise for the years ahead.

--- In this regard, we must not ignore the discovery of molecule UM171 by Dr. Guy Sauvageau and his team. I would like to congratulate them for this outstanding feat, which earned Dr. Sauvageau, my predecessor at the head of IRIC, the fully deserved titles of *La Presse* Scientific Personality of the Year and Radio-Canada Scientist of the Year. That discovery also highlights the remarkable quality of the rising generation of researchers working at IRIC, which, like its academic side, brings together great talents from here and elsewhere.

--- For these achievements, IRIC can count on the outstanding contribution of a host of donors whose renewed support is a guarantee of future success. I therefore wish to thank our donors for the generosity they have shown for, among other things, the first Audacious benefit evening and the fifth Great Challenges Against Cancer presentation. --- In closing, I would also like to thank Mr. Robert Tessier for the quality of his commitment since his appointment as Chairman of the Board of IRIC, taking over from Mr. Marc-André Blanchard, whose contribution proved to be just as inspiring during his mandate. --- My thanks to the entire team.

--- My thanks to the entire team. It is because of each and every one of you that IRIC's future looks to be especially promising.

Scientific affairs: pivot of the institute

The mandate of IRIC's Scientific Affairs is to formulate recommendations on all the Institute's research and training activities.

I am extremely satisfied and proud to once more be able to provide a highly positive assessment of our research activities for the past year.



Marc Therrien, Ph.D.

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Scientific Director and Principal Investigator at IRIC The successes of the Institute are above all the result of the work of 27 dedicated research teams, whose members each play an important role: students, postdoctoral researchers, professionals and principal investigators. These teams rely as well on the expertise and professionalism of the technology core facility staff, who not only offer services of the highest calibre, but also participate in their own way in training future researchers.

Some of the many achievements of our researchers are described in the following pages. They include important breakthroughs in our understanding of the cell mechanisms underlying cancer, the development of new and innovative research tools, and decisive developments in the transformation of fundamental discoveries into therapeutic applications. One of IRIC's great strengths lies in its ability to excel in each of these different, though complementary research activities.

IRIC's ultimate objective is to obtain concrete results likely to improve cancer treatments; however, we must not lose sight of the fact that every new clinical breakthrough is necessarily indebted to the basic research that preceded it. In the face of an illness as complex and tenacious as cancer, no potential avenue should remain unexplored. This is why, since the very beginnings of the Institute, scientific leadership has been guided by a continuous concern for supporting the efforts of its researchers, both in basic research and in translational research. This work is made possible by the complementary areas of expertise of our researchers and by our state-ofthe-art technology.

Researchers must also have at their disposal the resources and support needed to translate their discoveries into practical applications liable to reach clinical-trial phase. This is why IRIC has integrated its facilities within a drug discovery chain unique in a Canadian academic setting. The Institute has also equipped itself with a value-creation and commercialization unit acting as a catalyst for the acceleration of the transfer of knowledge to clinical trials and then, ultimately, to the market. This ground-breaking model, particular to IRIC, has proven its worth and makes it possible to maximize the impact of the Institute's research.

While IRIC has already acquired an enviable reputation in the Canadian and international scientific community, the future looks to be even more promising. With the combined effect of a mature scientific program, the recruitment of new researchers, and the launch of a number of clinical trials in the year ahead, we can rest assured that the Institute will leave its mark on the fight against cancer.

Various activities of the Scientific Assembly

The Institute's Scientific Director is supported in his work by the Scientific Assembly.

The assembly met on nine occasions during the past year to discuss questions related to the following elements:

- --- strategic plan and scientific programming
- --- recruiting and assessment of researchers
- --- recruiting and monitoring of graduate students and postdoctoral fellows
- --- institutional fund request strategies
- acquisition plan and usage policies of major research infrastructures.

The Institute's principal investigators sit on various committees managing academic and scientific affairs, as well as committees managing the 12 high-tech core facilities. The various aspects of research at IRIC are thus managed collectively and are the subject of ongoing consultations with researchers.

The principal investigators also had the opportunity to exchange ideas at a scientific retreat held on December 4 and 5, 2014. They took advantage of the get-together to discuss recent technological advances in various spheres and the relevance of acquiring the equipment necessary for IRIC's scientific programming. The retreat also made it possible to present innovative research projects in the early stages of development so that their scientific potential and the relevance of creating new collaborations at IRIC or with other institutions could be evaluated. Lastly, questions of the recruitment and the retention of students and postdoctoral fellows, as well as issues pertaining to communications and philanthropy, were also considered.

Responsibilities of the various committees Scientific Program Committee Étienne Gagnon, Principal Investigator

Fund Allocation Committee

Marc Therrien, Scientific Director and Principal Investigator

Mentoring Committee

Trang Hoang, Principal Investigator

Principal Investigator Recruitment Committee

Marc Therrien, Scientific Director and Principal Investigator

Space and Equipment Committee

Jean-Claude Labbé, Principal Investigator

Awards and Distinctions Committee

Vincent Archambault, Principal Investigator

Strategic Projects Committee

Philippe Roux, Principal Investigator

Publishing in 2014-2015

This year, IRIC researchers and their collaborators published 96 articles.

A number of these articles benefited from the outstanding visibility offered by prestigious high-impact scientific journals such as Nature, Nature Communications, Nature Structural & Molecular Biology, Science, Developmental Cell, Molecular Cell, Cell Reports, Genes & Development, Blood, Leukemia, Journal of Cell Biology, Proceedings of the National Academy of Sciences of the USA, and Current Biology.

These publications presented several discoveries made at IRIC representing major advances in our understanding of cancer. In a number of cases, these discoveries pave the way to developing more specifically targeted therapeutic solutions. As is the case every year, a large number of these publications are the result of collaborations among principal investigators and/or associates of the Institute—a fact that reflects the collegiality, the complementarity of areas of expertise, and the pooling of resources that characterize the scientific research undertaken at IRIC.

Multidisciplinary team

2014-2015 principal investigators

IRIC brings together renowned scientists from Canada, the United States, and Europe, who engage in bold collaborations at the junction of a number of complementary disciplines. The Institute boasts 27 principal investigators who are impassioned by their work and who are committed to the goal of discovering new therapies to defeat cancer.



Vincent Archambault, Ph.D. Cell Cycle Regulation



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



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



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



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



Trang Hoang, Ph.D. Hematopoiesis and Leukemia



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



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



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



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



Étienne Gagnon, Ph.D.Cancer Immunobiology



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



Sébastien Lemieux, Ph.D.Functional and Structural Bioinformatics



Sylvain Meloche, Ph.D.Signalling and Cell Growth



Marc Therrien, Ph.D.
Intracellular Signalling



Julie Lessard, Ph.D. Chromatin structure and stem cell biology



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



Pierre Thibault, Ph.D.
Proteomics and Mass Spectrometry



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



Martine Raymond, Ph.D. Yeast Molecular Biology



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



François Major, Ph.D. RNA Engineering



Philippe Roux, Ph.D.
Cell Signalling and Proteomics



Alain Verreault, Ph.D. Chromosome Biogenesis



Anne Marinier, Ph.D. Medicinal Chemistry



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



Brian Wilhelm, Ph.D.High-Throughput Genomics



Focus 1:
Biology of cancer

Cell division is a strictly controlled process, and anomalies that affect it are often associated with the development and growth of tumours. A number of our researchers are therefore endeavouring to understand the slightest details of this extremely complex process. In so doing, they hope to open new avenues for the development of cancer therapies.

The 16 research units in this focus are divided into two more specialized groups. The first group studies the processes through which cells perceive the signals emanating from their environment and modulate the expression of their genes. The second group studies the mechanics of cell division and the molecular mechanisms of its regulation.

Research units

Signalling/transcription

Chromosome Biogenesis
Molecular Targeting in Breast Cancer Treatment
Proteomics and Mass Spectrometry
Cell Signalling and Proteomics
Signalling and Cell Growth
Intracellular Signalling
Vesicular Trafficking and Cell Signalling

Cell division regulation and mechanisms

Chemical Biology of Cell Division
Systems Biology and Synthetic Biology
Cell Division and Differentiation
Telomere Length Homeostasis and Genomic Instability
Mechanisms of Morphogenesis during Mitosis
Cell Cycle Regulation
Cell Cycle Regulation and Chromosome Structure

Principal investigators

Alain Verreault Sylvie Mader Pierre Thibault Philippe Roux Sylvain Meloche Marc Therrien Gregory Emery

Benjamin Kwok Michael Tyers Jean-Claude Labbé Lea Harrington Sébastien Carréno Vincent Archambault Damien D'Amours

In 2014-2015



research units



51 students



19 postdoctoral fellows



\$10,043,374 in research funding



50 publications

Associate investigators

Manfred Auer (University of Edinburgh, UK)

Dr. André Robidoux (Centre hospitalier de l'Université de Montréal)

Highlights—IRIC acquires a powerful microscope for the study of living tissue



Vincent Archambault, Principal Investigator, and Myreille Larouche, master's student.

Professor Vincent Archambault obtained an important grant from the Canada Foundation for Innovation (CFI) for the acquisition of a powerful microscope to study the molecular machinery that coordinates cell division. This new confocal spinning-disc microscope, manufactured by the Zeiss company, is a highly specialized apparatus that makes it possible to observe, in real time and with great accuracy, the changes in location and activity of the proteins that regulate cell division."This type of microscope is one of the few that combines the high resolution, the fast rate of image acquisition, and the

low photo-toxicity required for imaging molecular events inside cells and living tissue," explains Professor Archambault. The cutting-edge instrument will enable the researcher and his team to better understand the role of the proteins that regulate cell division. It will also help them identify targets for new cancer drugs. Other IRIC and UdeM researchers will use it in the framework of their own research projects. This new acquisition joins IRIC's important high-tech core facilities, contributing at the same time to its reputation for excellence on the national and international scene.

Showcased discoveries—A new cell-division regulation mechanism revealed, courtesy of a nematode worm

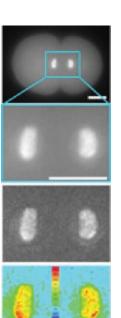
Research cited:

Benkemoun L.,
Descoteaux C.,
Chartier N.T., Pintard L.,
Labbé J.C., "PAR-4/LKB1
regulates DNA replication
during asynchronous
division of the early
C. elegans embryo,"
Journal of Cell Biology,
205:447-455, 2014

The enzyme LKB1 is an important regulator of cell proliferation. Certain mutations entailing a loss of LKB1 function are associated with a number of types of cancer (lung, uterus, intestines, testicles, pancreas, and skin).

To better understand how LKB1 controls cell division and to identify partners in its activity, the laboratory of Jean-Claude Labbé uses the nematode worm *C. elegans* as an experimental model. Thanks to a detailed analysis using genetic approaches and quantitative imaging of the first cell divisions of the *C. elegans* embryo, IRIC researchers demonstrated

for the first time that LKB1 can delay the start of DNA replication, which has the result of slowing down cell growth and proliferation. Jean-Claude Labbé and his collaborators are focusing now on characterizing the DNA replication regulators specifically targeted by LKB1 and identifying those could prove to be promising therapeutic targets. This knowledge provides a basis for understanding the molecular and cellular anomalies responsible for a number of human pathologies characterized by abnormal cell proliferation, notable among them cancer.



Showcased discoveries—A molecular switch responsible for chromosome assembly

Research cited:

Robellet X., Thattikota Y., Wang F., Wee T.L., Pascariu M., Shankar S., Bonneil É., Brown C.M., **D'Amours D.**, "A highsensitivity phosphoswitch triggered by Cdk1 governs chromosome morphogenesis during cell division," *Genes & Development*, 29:426–439, 2015 The compaction of DNA to form condensed chromosomes visible in the nucleus is a process essential to any normal cell division. It is necessary to prevent chromosome breakage, an anomaly often associated with cancer. But the mechanisms leading to the formation of condensed chromosomes are still poorly understood.



The rDNA locus (in green) on DNA (in red) undergoes different conformational changes during condensation of mitotic chromosomes. During the cell cycle, uncondensed rDNA (puff, on the left) transforms into a highly organized structure (loop, on the right). This process is essential to the maintenance of chromosome integrity when division occurs. As part of this study, we identified a new intermediate condensation configuration ("intertwist", centre).

Recently, the team from the research unit of Damien D'Amours identified the principal switch responsible for this process and showed how it connects chromosome condensation with cell cycle progression. By using a unicellular organism as an experimental model, in this case yeast, IRIC researchers identified the way in which the enzyme Cdk1, principal cell cycle regulator, activates a protein complex called a condensin to form chromosomes. They also demonstrated that a condensing is hypersensitive to Cdk1 activity, reacting very easily to directly induce quantitative changes in the morphology of the chromosome, this happening before the start of any other event in the cell cycle. The condensin acts as a rheostat to integrate the level of kinase Cdk1 activity and the chromosome configuration changes.

Overall, the study by Damien D'Amours and his collaborators reveals the basic mechanism responsible for the formation of chromosomes visible during the mitotic program—one of the cornerstones of the process of cell division.

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Visualization of DNA replication in the embryo of the $\it C.\ elegans$ nematode.

Fluorescence microscopy images of a *C. elegans* embryo expressing the PCNA protein coupled to the green fluorescent protein. The top image shows the embryo in its entirety. The following images present a magnified representation of the chromosomes: before a deconvolution (second image from the top), after a deconvolution (third image from the top) and further to the application of luminous intensity ratios (fourth image from the top).

The six research units in this focus are at the leading edge of leukemia and stem cell research. Building on an internationally recognized expertise, they seek to elucidate the causes of leukemia at the molecular level, develop targeted therapies, and improve current treatments. A number of researchers in this focus work in close collaboration with partners from various clinical centres, in particular Montréal's Maisonneuve-Rosemont Hospital and Jewish General Hospital.

Research units

Molecular Genetics of Stem Cells
High-Throughput Genomics
Hematopoiesis and Leukemia
Immunobiology
Chromatin Structure and Stem Cell Biology
Structure and Function of the Cell Nucleus

Principal investigators

Guy Sauvageau Brian Wilhelm Trang Hoang Claude Perreault Julie Lessard Katherine Borden

In 2014-2015



6 research units



26 students



16 postdoctoral fellows



\$9,639,635 in research funding



27 publications

Associate investigators

Frédéric Barabé (Université Laval)

Dr. Josée Hébert (Centre de recherche de l'Hôpital Maisonneuve-Rosemont)

Dr. Denis-Claude Roy (Centre de recherche de l'Hôpital Maisonneuve-Rosemont)

Highlights—World breakthrough: a new molecule to increase stem-cell transplants

Research cited:

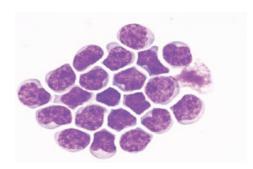
Fares I., Chagraoui J., Gareau Y., Gingras S., Ruel R., Mayotte N., Csaszar E., Knapp D.J., Miller P., Ngom M., Imren S., Roy D.C., Watts K.L., Kiem H.P., Herrington R., Iscove N.N., Humphries R.K., Eaves C.J., Cohen S., Marinier A., Zandstra P.W., Sauvageau G., "Pyrimidoindole derivatives are agonists of human hematopoietic stem cell self-renewal," Science, 345(6203): 1509-12, 2014

2014-2015 saw the culmination of many years of research in the biology of hematopoietic stem cells (HSC) by the team of Dr. Sauvageau and his collaborators. This effort devoted to basic research resulted in a major discovery that will have a significant impact on the treatment of hematological cancers (leukemia, myeloma, lymphoma).

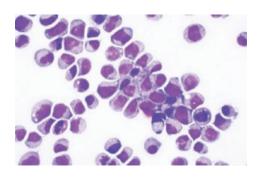
Dr. Guy Sauvageau, with Anne Marinier, Principal Investigator and Director of Medicinal Chemistry at IRIC, along with their colleagues, achieved a major breakthrough with the discovery of a new molecule—named UM171 in honour of the Université de Montréal—which enables multiplication of stem cells in a unit of umbilical cord blood in the laboratory. This type of stem cell is used in transplants that are a treatment of last resort for many patients.

Initiated by Dr. Guy Sauvageau,
Principal Investigator at IRIC, Professor
at Université de Montréal's Faculty of
Medicine, and hematologist at the
Maisonneuve-Rosemont Hospital, this
breakthrough has the potential to multiply
by 10 the number of umbilical cord blood
units available for transplant in humans,
while at the same time considerably
reducing the complications associated
with stem cell transplantation.

According to Dr. Guy Sauvageau, "This new molecule will give thousands of patients around the world access to safer stem cell transplants. Considering that many patients currently cannot benefit from stem cell transplants due to a lack of matching donors, this discovery seems highly promising for the treatment of various types of cancer."



Fresh stem cells



Multiplied stem cells due to the molecule UM171

Umbilical cord blood from newborn children is an excellent source of hematopoietic stem cells intended for transplants. At this stage, their immune system is still immature, and the stem cells have a lower probability of inducing an adverse immune reaction in the recipient.

It is therefore not necessary for the immunological compatibility between donor and recipient to be perfect, unlike the conditions required in a bone marrow transplant.

However, in most cases, the number of stem cells obtained from an umbilical cord is much too small for treating an adult, and its use is confined above all to the treatment of children. With the new molecule UM171, it will be possible to multiply stem cells in culture and to produce enough of them to treat adults (especially non-Caucasians), who have limited access to transplants because of a lack of donors.

By the beginning of 2016, a clinical trial using molecule UM171 and a new type of bioreactor developed for the culture of stem cells will be initiated in collaboration with the University of Toronto. The Centre of Excellence for Cellular Therapy at the Maisonneuve-Rosemont Hospital will serve as stem-cell production unit. After that stage, grafts will be distributed to patients in Montréal, Québec City, and Vancouver as part of this first Canadian clinical trial. Tangible results should be announced at some point next year.

Conclusive clinical results could revolutionize the treatment of leukemia and other blood-related diseases. This potential reflects the importance of this new discovery, for which Dr. Sauvageau was named *La Presse* 2014 Personality of the Year in the science category and 2014 Radio-Canada Scientist of the Year. The findings of Dr. Sauvageau and his team were also named 2014 *Québec Science* Discovery of the Year. (See page 54)

Showcased discoveries—Towards the development of cancer immunotherapies

Research cited:

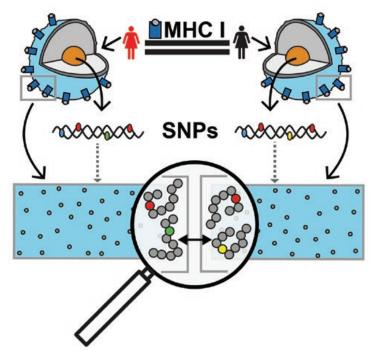
Granados D.P.,
Sriranganadane D.,
Daouda T., Zieger A.,
Laumont C.M.,
Caron-Lizotte O.,
Boucher G., Hardy M.P.,
Gendron P., Côté C.,
Lemieux S., Thibault P.,
Perreault C., "Impact of
genomic polymorphisms
on the repertoire of
human MHC class
I-associated peptides,"
Nature Communications,
5:3600, 2014

Approaches that use the immune system to arrest or slow the growth of cancer cells are largely considered today to be among the most promising avenues in oncology. We now know that T-cells in the immune system, which recognize a suitable antigen in cancer cells, can detect and eliminate these abnormal cells. Nevertheless, identification of antigens appropriate to the development of effective cancer immunotherapies remains a major challenge.

The teams of Dr. Claude Perreault and Professor Pierre Thibault took up that challenge by developing an entirely new strategy. This combines high-throughput mass spectrometry with personalized genomic approaches in order to identify fragments of immunogenic proteins called minor histocompatibility antigens (MHAs),

which are found on the surface of leukemic cells. The revolutionary strategy made it possible to identify 34 new potential antigens in just one year, which amounts to as many as the entire scientific community has succeeded in identifying over the last 30 years. It will thus be possible to use these antigens to teach T-cells from a donor to recognize the cancer cells in a recipient during a transplant for treating leukemia.

This approach will make treatment significantly more effective and safer. In the longer term, it can be offered for other types of cancer, and could lead to true cancer vaccines. Over 400 MHAs have now been identified, several of which will soon be evaluated as part of a clinical trial at Maisonneuve-Rosemont Hospital.



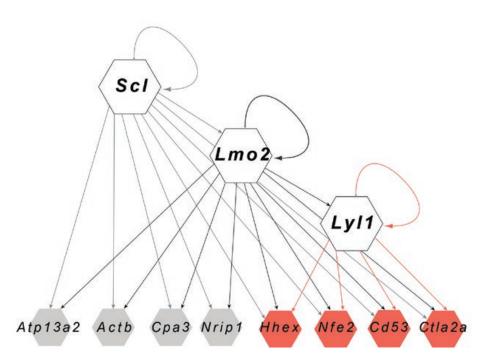
IRIC researchers developed a new approach for characterizing peptides presented to the immune system on cell surfaces, and demonstrated for the first time how our genetic polymorphisms determine our individual immunological identity. This breakthrough will accelerate the discovery of specific peptides that will make it possible to develop new anti-cancer immunotherapies.

Showcased discoveries—Uncovering pre-Leukemic stem cells

Research cited:

Gerby B., Tremblay C.S., Tremblay M., Rojas-Sutterlin S., Herblot S., Hébert J., Sauvageau G., Lemieux S., Lécuyer E., Veiga D.F., Hoang T. "SCL, LMO1 and Notch1 Reprogram Thymocytes into Self-Renewing Cells", PLoS Genetics, 10:e1004768, 2014 Researchers from the laboratory of Trang Hoang recently demonstrated how a limited number of oncogenes can cooperate to trigger the earliest steps in the development of T-cell acute lymphoblastic leukemia (T-ALL), a form of the disease that accounts for approximately 20 percent of all childhood leukemia. The IRIC investigators also precisely identified the population of cells that accumulate these mutations, leading to a chaotic proliferation and to cancer. By using a transgenic animal model in which human oncogenes are activated specifically in certain cell

populations, the researchers demonstrated that the gene anomalies could reprogram more mature cells into pre-leukemic cells with a capacity for sustained self-renewal. These observations were validated on human samples from the Québec Leukemia Cell Bank, headed by Dr. Josée Hébert. The discoveries shed new light on the process leading to T-ALL and provide valuable clues for the development of new therapeutic strategies that may effectively eradicate leukemic stem cells that are self-renewing and resistant to current treatments.



A network of self-renewal genes (bottom row) is induced by SCL and LMO, and reprograms thymocyte progenitors that normally have a finite life span, into pre-leukemic stem cells with extensive self-renewal capacities.



RNA engineering and the study of pathogenic yeasts.

Their efforts focus on the development of new diagnostic tools, as well as targeted therapies and innovative drugs. By supporting these approaches, IRIC is fulfilling an important aspect of its mission: to make a significant impact on the treatment of cancer.

Research units

Functional and Structural Bioinformatics Yeast Molecular Biology Medicinal Chemistry Histology and Molecular Pathology Cancer Immunobiology RNA Engineering Molecular Pharmacology

Principal investigators

Sébastien Lemieux Martine Raymond Anne Marinier Louis Gaboury Étienne Gagnon François Major Michel Bouvier

In 2014-2015



research units



24 students



10 postdoctoral fellows



\$8,721,057 in research funding



20 publications

Associate investigators

Jacques Archambault (Institut de recherches cliniques de Montréal)

Olivier Lichtarge (Baylor College of Medicine, Houston, Texas)

Highlights—Expansion of the Medicinal Chemistry Laboratory at the NEOMED Institute

A victim of its own success, IRIC's Medicinal Chemistry Unit had to expand to meet the ever-growing demand for its unique expertise in drug discovery. With no space available at IRIC's Marcelle-Coutu Pavilion, the unit set up its laboratory on the premises of the NEOMED Institute, a research and development centre at Technoparc Montréal.

This expansion was carried out under the existing strategic collaboration agreement signed in 2013 between NEOMED, the UdeM, and IRICOR (IRIC's Research Commercialization Unit). In the framework of an understanding aimed at accelerating the development and transfer of promising drugs between academia and the biopharmaceutical

industry, the participating institutions agree to share access to each other's facilities, equipment, expertise, and resources. NEOMED thus acts as an open-access drug discovery hub hosting commercial firms and providing a unique environment to foster collaboration, innovation and creativity.

"Due to the growing number of ongoing internal projects with several partners," said Anne Marinier, Principal Investigator, Director of Medicinal Chemistry at IRIC, and Associate Professor at the Université de Montréal's Department of Chemistry, "this addition to our research infrastructure was needed to fulfill our mandate of developing new drugs against cancer and other therapeutic targets associated with this disease."

Highlights— Agreements with Encycle Therapeutics and Cyclenium Pharma for the development of a type of molecule

IRICoR entered into two collaborativeresearch agreements this year with emerging companies specializing in the discovery and development of new drug candidates based on macrocyclic molecules. These molecules are more massive and often more complex than the majority of synthetic molecules used in drug discovery, but offer biological and physico-chemical properties that are interesting for research into new solutions for more and more difficult targets. These agreements will enable IRIC's medicinal chemists to acquire fresh expertise in exploring a different "chemical space."



Éric Jolicoeur and Sasmita Tripathy, Research Officers at the Medicinal Chemistry core facility.

Highlights— Collaboration with Encycle Therapeutics

Encycle Therapeutics is a Toronto biotechnology firm that is currently working on an orally-bioavailable macrocycle drug to target a protein involved in the inflammatory process in a number of diseases. Encycle Therapeutics has established a collaborative partnership with IRICOR, the Université de Montréal, and MaRS Innovation in Toronto to advance the molecule towards clinical trials. This collaboration builds on a \$4 million public-private funding partnership with Merck Canada.

Announced in April 2013, the agreement aims to create collaborative research projects with three Canadian academic commercialization centres in Québec and Ontario. It will make it possible to welcome a certain number of experienced medicinal chemists to IRIC with the aim of optimizing the molecule identified by **Encycle Therapeutics. These partnerships** will allow the IRIC team of chemists to develop advanced expertise in the analysis of this type of molecule. Additional studies will be held at the Platform of Biopharmacy in the Université de Montréal's Faculty of Pharmacy, while Encycle Therapeutics will carry out other activities connected with the project, including evaluation of the effectiveness of preclinical trials.

Highlights—Agreement with Cyclenium Pharma

IRICOR also signed an agreement with the Cyclenium Pharma company. This understanding will allow for the combination of a library of next-generation macrocyclic molecules—exclusive to Cyclenium—and the expertise of its hit-to-lead team with IRIC's state-of-the-art capabilities in the screening, identification, and characterization of biological targets. The objective of the collaboration is to discover and develop new drug candidates for the treatment of cancer and immunological disorders.

"We are extremely pleased to be working with Cyclenium," said Michel Bouvier, Chief Executive Officer of both IRIC and IRICoR. "We clearly see multiple areas of synergy between IRIC's drug discovery, screening, and therapeutic chemistry expertise and Cyclenium's leadership position in macrocycle-based drug development."



Showcased discoveries— Discovery of PTEN regulation

Research cited:

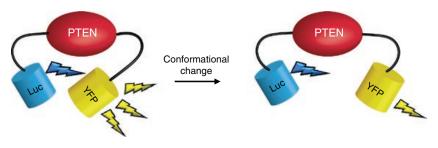
Lima-Fernandes E.,
Misticone S., Boularan C.,
Paradis J.S., Enslen H.,
Roux P.P., Bouvier M.,
Baillie G.S., Marullo S.,
Scott M.G., "A biosensor
to monitor dynamic
regulation and function
of tumour suppressor
PTEN in living cells,"
Nat Communications,
5:4431, 2014

The enzyme PTEN is a tumour suppressor, since its activity stops cell proliferation, whereas loss of its activity, even partial, is associated with an increased susceptibility to cancer. The ability to measure PTEN activity in living cells directly, accurately, and in real time would be a key factor in the development of cancer drugs aimed at improving or restoring PTEN function in cancerous cells.

To achieve this goal, the teams of Professors Michel Bouvier and Philippe Roux collaborated with their Parisian partners at the Institut Cochin on the development of a new type of extremely sensitive biosensor. The researchers adapted the BRET (bioluminescent resonance energy transfer) technology initially developed by Professor Bouvier. This technology measures the light emitted during the change in molecule conformation inside the cells. The new biosensor keeps the intrinsic PTEN properties, allowing for fine kinetic

analyses of its activation. The use of this biosensor has, among other things, led to the discovery of PTEN regulation by several G protein-coupled receptors (GPCRs), a previously unknown phenomenon, but one of great importance, since GPCRs are themselves the target of a great number of drugs.

This study also demonstrated that trastuzumab, used to treat certain breast cancers, kindles the activation of PTEN, a significant discovery when we know that a number of mutations associated with cancer lead to a loss of PTEN activity. These observations demonstrate that the new biosensor can be used to identify the PTEN regulatory pathways or molecules that heighten its antitumor activity.



New highly sensitive biosensors can detect changes in the conformation of the PTEN protein that are indicative of changes in its activity. In the "closed" conformation (left) corresponding to the inactive form of PTEN, the proximity of the bioluminescent domains (Luc and YFP) induces yellow light emission. In the "open" conformation (right) corresponding to the active form of PTEN, the bioluminescent domains are too distant to interact and emission of yellow light is reduced. Changes in the wavelength of the emitted light can be accurately measured and used to quantify the activity of the PTEN protein in the cells.

Showcased discoveries—A new understanding of the structure of the oncoprotein RAF

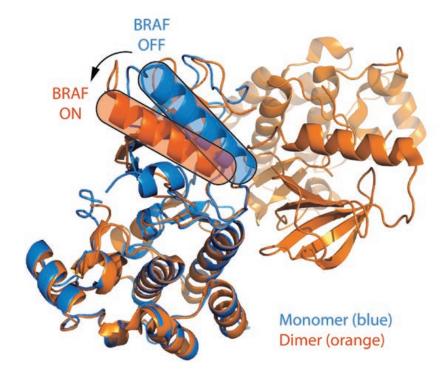
Research cited:

Thevakumaran N., Lavoie H., Critton D.A., Tebben A., Marinier A., Sicheri F., Therrien M., "Crystal structure of a BRAF kinase domain monomer explains basis for allosteric regulation," Nature Structural and Molecular Biology| 22, 37–43, 2015 The team of Marc Therrien—with the help of Anne Marinier and their colleagues from the pharmaceutical company Bristol-Myers Squibb and the Lunenfeld-Tanenbaum Research Institute at Mount Sinai Hospital in Toronto—recently elucidated the molecular structure of the enzyme RAF involved in many cancers. This discovery furnishes valuable clues for the development of a new generation of therapeutic RAF inhibitors.

RAF is one of the principal regulators of cell survival and proliferation.
The enzyme can adopt different conformations that correspond to its active or inactive form. The transition between these two forms is therefore tightly controlled in healthy cells. In the case of cancerous cells, the mutant

forms of RAF are often blocked in an active configuration, leading to a chaotic cell proliferation.

IRIC investigators and their colleagues identified, for the first time, the details of inactive conformation and the structure that stabilizes this conformation. This new understanding of the configuration of RAF will lead to the design of new inhibitors that may arrest the enzyme in its inactive form. They will thus have the potential to constitute an effective treatment against a broad spectrum of cancers whose survival depends on RAF activity.



Overlap of the active (ON) and inactive (OFF) forms of one of the RAF proteins (BRAF). The paired configuration (or dimer) shown in orange is active. The single configuration (monomer), shown in blue, is inactive because one of the helical sections of the protein is locked in an open position that prevents the formation of productive contacts with its target substrates in the cell.

Cutting-edge scientific facilities

The highly qualified professionals of IRIC's 12 core facilities have access to an equipment park at the leading edge of technology, allowing them to offer high-level specialized services to researchers at the Institute, the Université de Montréal, and elsewhere in academia and industry. These facilities constitute one of the few integrated drug discovery chains in a university setting in Canada.

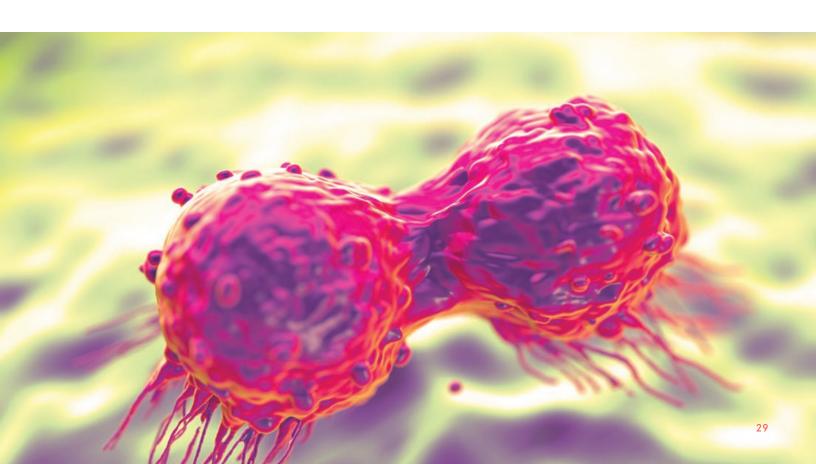
At the heart of the world-class basic integrative research in immunology and cancer carried out at IRIC, each of the core facilities has its own advisory committee chaired by a particular researcher. Facility managers oversee the operations of state-of-the-art equipment and provide an advisory service for carrying out research work. The overall activities of the core facilities are coordinated by Manon Valiquette, Head of Scientific Platforms.

Highlights

In the framework of Genome Canada's Canada-wide Geonomics Innovation Network competition, IRIC's proteomics facility, directed by Pierre Thibault, was selected as a centre of advanced proteomic analysis. This recognition, and the \$756,000 award that comes with it, will allow IRIC to supply access to leading-edge technologies that Canadian and international researchers need for their research work in proteomics.

Grants from the Canadian Foundation for Innovation worth a total of \$560,000 were received by Vincent Archambault and Claude Perreault. These allowed for the acquisition of a Zeiss confocal spinning-disk microscope for the bio-imaging facility and the upgrading of a BD FACSAria II sorter equipped with a biological safety cabinet for the flow cytometry facility.

Thanks to \$109,000 in provincial financial support from the Ministry of Economic Development, Innovation and Export Trade, a second robotics suite was installed at the high-throughput screening core facility. This support made it possible to increase our screening capacity, which benefits the internal and external scientific community.



Cutting-edge scientific facilities

Animal facility in the

Marcelle and Jean Coutu pavilions

IRIC houses one of Canada's largest animal facilities, which include a specific pathogen-free area, a conventional area, and a separate quarantine area. In addition to managing the facilities and providing technical and veterinary support for animal research and health, IRIC's animal facility offers pharmacokinetics, bioanalysis, and toxicology services in collaboration with the biopharmacy core facility of the Université de Montréal's Faculty of Pharmacy.

Bio-imaging

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.

Biophysics

State-of-the-art solutions in 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 that can serve as pharmaceutical tools and that have therapeutic potential.

High-throughput screening

Portfolio of over 115,000 molecules; integrated robotic systems used in a wide range of biochemical and cell-based studies in various biological systems and models.

Cytogenetics

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

Flow cytometry

Use of FACS equipment to analyze various physical properties of cells in immunophenotyping, among others, and study of both the cell cycle and apoptosis.

Genomics

Consulting services and access to cuttingedge technologies in next-generation sequencing, capillary sequencing, and real-time PCR.

Histology

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

Proteomics

Identification and quantification of proteins and their post-translational modifications based on cell extracts, tissue, and biological fluid.

Transgenesis

DNA microinjection, directed gene targeting, ES cell injection into blastocysts, embryo and sperm cryopreservation, mouse line rederivation, and in vitro fertilization.

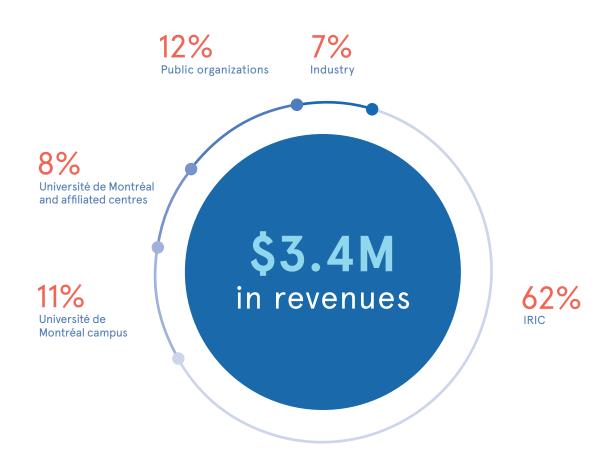
Statistical data

Author: Dariel Ashton-Beaucage
Title: Drosophilia's eye

Statistical data— Source of users of IRIC's high-tech core facilities in 2014-2015



Statistical data— Source of revenue for IRIC's core facilities in 2014-2015



IRICOR: multiple partnerships with both the private and public sectors

The Institute for Research in Immunology and Cancer – Commercialization of Research (IRICOR) is a not-for-profit organization focusing on the discovery, development, and commercialization of drugs. Since 2008, IRICOR's objective has been to rapidly translate cutting-edge research projects into innovative and highly valuable therapies. The mission of this centre is to promote the development of partnerships with the private sector, and the creation of new firms, in order to accelerate the transfer of university-research innovation to patients.

IRICOR relies on a team with solid experience in the following fields: drug discovery, business development, risk capital, protection of intellectual property, and project management. Integrated into IRIC, IRICOR professionals have an in-depth knowledge of the Institute's technological capacities and that of its partners, and keep abreast of the Institute's most recent discoveries.

Note that IRIC has one Canada's largest academic units in medicinal chemistry, the majority of whose members are from the pharmaceutical industry. These experienced chemists and biologists lend the Institute a unique added value.

IRICOR is based on a versatile business model, tailored to the needs of both the academic and private sectors.

Its goal is to bridge the traditionally observed gap between basic research and biopharmaceutical industrial research. The IRICoR model ensures the mitigation of risks connected with the discovery and commercialization of new therapeutic approaches. It is built around the four main pillars presented in the following diagram:

In-house Financial and professional support cutting-edge technologies, to selected projects platforms and affiliated clinical facilities **Business** Model Investment Identification and in innovative Establishment of commercializationtargeted partnerships focused projects

Project portfolio

IRICOR selects its projects on the basis of their scientific excellence and their commercial potential, supports them strategically, and invests in them directly with a view to moving them rapidly towards commercialization.

At the conclusion of 2014-2015, 11 new projects were funded, bringing their number to 29 in the IRICOR portfolio. These cover the full gamut of the drug discovery chain, from the identification of therapeutic targets to clinical trials. Support of projects covers many aspects, from funding to the negotiation of partnerships and licences, special access to IRIC's scientific core facilities, project management, and protection of intellectual property. IRICoRsupported projects this year led to the filing of 30 patent applications representing 14 patent families.

Projects supported by IRICoR have also led to the development of three drug candidates that are currently at the clinical evaluation stage. Two other projects in partnership with Amorchem will enter the clinical phase during the coming year.

Partnerships

IRICOR entered into or extended eight licensing agreements related to 19 projects.

- --- IRICoR's expertise also made possible the implementation of joint projects with the Centre for Drug Research and Development in Vancouver and with MaRS Innovation in Toronto. It additionally enabled the introduction of a drug development program in the field of rare diseases in partnership with Pfizer. This program invests in the research and development activities conducted at IRIC that are relevant to its objectives.
- Collaboration with the Montréal biopharmaceutical company Pharmascience and the Leukemia and Lymphoma Society in the United States continued with a Phase II clinical trial in acute myeloid leukemia (AML).
- --- The partnership agreement with the venture-capital firm Amorchem for the funding of two projects as part of Genome Canada's (GC) and Génome Québec's (GQ) Large Scale Applied Research Project Competition in Genomics and Personalized Health continues according to the stages planned at the outset. Funded originally by IRICoR, these two multi-institutional projects benefit, in addition to GC/ GQ's important financial support, from a \$1.5 million investment for a period of four years as part of the grant.

- ·The first project is headed by Dr. Guy Sauvageau, Principal Investigator at IRIC, and Dr. Josée Hébert, Associate Investigator at IRIC and Director of the Québec Leukemia Cell Bank, both hematologists at Maisonneuve-Rosemont Hospital (HMR). The aim of the project is the development of new diagnostic and prognostic tools for patients with acute myeloid leukemia (AML). The investment received will allow for the establishment of an improved method for tracking residual cancer cells, which often remain present in patients after the termination of treatment and can give rise to recurrence.
- The second project is headed by two IRIC principal investigators, Dr. Pierre Thibault and Dr. Claude Perreault, the latter also a hematologist at HMR. In the field of immuno-oncology, it focuses on the identification of new minor human leukocyte antigens for the treatment of AML and will enter clinical phase at HMR by the end of the year.

IRICoR has also been a key player in the creation of Domain Therapeutics in North America (Domain Therapeutics NA), a spinoff company of Domain Therapeutics in France. Located in Montréal on the premises of the NEOMED Institute, the biopharmaceutical company specializes in the research and development of new drug candidates targeting G proteincoupled receptors (GPCRs). Domain Therapeutics runs BioSensAll™, a technology initially supported by IRICoR and by the Focus program of the Québec Consortium for Drug Discovery (CQDM). BioSensAll™ was developed by researchers from IRIC and from the research centres of Ste-Justine Hospital, McGill University, and the Université de

Sherbrooke. The company offers services making use of some 30 biosensors developed in the academic sector. These will allow for, among other things, identification of the functional selectivity of a ligand by characterizing its specific signalling pathway.

Finally, IRICOR is working on the development of the UM171 "proprietary" component in partnership with the Centre for Commercialization of Regenerative Medicine in Toronto. The molecule UM171 allows for the expansion of hematopoietic stem cells for transplants and will enter clinical trials (phase I/II) at some point in the upcoming year.

IRICOR activities are carried out by nearly 90 full-time employees, including highly qualified research, commercialization, and administrative staff.

Visibility

The IRICoR team was invited to present its business model and its project portfolio at six national and international gatherings, in addition to taking part in the organization of two meetings on drug discovery, one at the national level and the other at the international level.

Funding

For the 2014-2015 period, IRICoR's cash flow came from the direct funding of research and development activities by private partners (\$6M) and by public funds (\$12M), and from research licensing/contract revenues (\$1.2M).

Statistical data— From 2008 to April 30, 2015

- \$42.6M in direct R&D funding from public partners
- \$21.2 M in direct R&D funding from private partners
 - \$2.2M in licence and milestone revenues
 - \$1M in research contract revenues
 - 152 patent applications
 - full-time jobs in science and management created and maintained
 - projects funded (funding/management/PI/grants)
 - patent families developed internally
 - projects in partnerships/licencing signed with industry
 - private partners (BMS, Pfizer, Pharmascience, Merck, Domain, Amorchem, Cyclenium, Encycle Therapeutics)
 - patents granted
 - 3 companies created

The next generation of researchers: students are the future

At IRIC, the rising generation of scientists have at their disposal an exceptional training environment, worthy of the finest academic institutions in the field. Whether they join IRIC with a view to a master's degree, a Ph.D., a postdoctoral fellowship, or a research internship, IRIC students benefit from the highest level of supervision and from research resources and facilities that foster learning, scientific creativity, and the raising of personal bars. They have access to different ground-breaking research projects that offer them a unique opportunity to contribute in an active way to advancing the understanding of cancer and the development of new therapies. They can also rely, throughout their training, on the academic and administrative support of the members of the Office of Academic Affairs headed by Martine Raymond, Principal Investigator in the Yeast Molecular Biology Research Unit and in charge of systems-biology training.

Top-level multidisciplinary training in the field of cancer research

121 recruits in 2015



In choosing to pursue their training at IRIC, young researchers receive top-level multidisciplinary training in the field of cancer research and benefit from the varied expertise and exceptional guidance offered by IRIC's principal investigators.

In 2014-2015, 121 recruits joined IRIC to undergo training and participate actively in advancing the research work conducted at the Institute, representing an increase of 18 percent compared to the previous year. They came from 48 academic institutions located in 16 different countries and from the four corners of the planet to be part of the research teams. Figures like these are evidence of the reputation for excellence of IRIC and the Université de Montréal at the national and international levels and their ability to attract the finest students searching for top-level scientific training in cancer research.

At the graduate level, students have access to a wide variety of study programs offered by the Université de Montréal. In 2014-2015, 69 percent of master's and Ph.D. students were enrolled in the systems biology training program developed by IRIC investigators. Integrated into the molecular biology programs of the Université de Montréal's Faculty of Medicine, this training offers an accelerated one-year master's degree and a five-year doctorate that includes cellular and molecular biology, immunology, biochemistry, genetics and bioinformatics, biophysics, drug development, and the more clinical aspects of cancer research. The other study programs represented at IRIC are master's and Ph.D. programs in the following areas: molecular biology, biochemistry and molecular medicine, bioinformatics, information technology, chemistry, pathology and cellular biology, pharmacology, immunology, and microbiology.

18%

increase in the number of recruits

IRIC's 2014 student recruitment event



students recruited at the master's and doctoral level

The activities organized as part of IRIC's first Annual Student Recruitment Event were held at the Institute from June 19 to 22, 2014, on the campus of the Université de Montréal. Launched in the fall of 2013 with the goal of recruiting the brightest hopes among younger researchers, the international event is piloted by Sébastien Carréno, Principal Investigator in the Mechanisms of Morphogenesis during Mitosis and Cell Motility Research Unit and President of IRIC's Student Recruitment Committee. The event hosted 41 high-level candidates seeking to earn a master's or Ph.D. in cancer research. These candidates were selected from among 114 applicants hailing from 57 universities and 18 countries for their outstanding academic performance, their previous contributions in the field of research, and their motivation to be part of the IRIC team.

With its innovative programming and interactive formula, the recruitment event offered participants the unique opportunity to visit IRIC's laboratories and core facilities, to meet and discuss with investigators and their students, to learn out about the study programs and research projects offered, to take part in different social activities, and to discover the attractions of the UdeM campus and the city of Montréal. At the conclusion of their stay, participants could participate in individual interviews with the researcher of their choice. In all, more than 170 interviews took place, leading to the recruitment of 21 students (18 for master's degrees and 3 for doctorates), unprecedented for an IRIC recruiting activity.



Participants and members of the organizing committee for IRIC's 2014 edition of the Student Recruitment Event.

2014 IRIC Next Generation Awards program

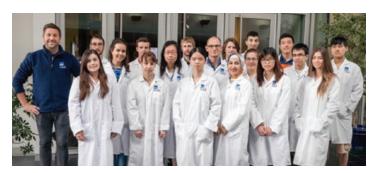
For a fourth consecutive year, IRIC welcomed the winners of the IRIC Next Generation Awards program. This year, 18 Canadian undergraduates were offered a merit scholarship of \$4,250 and a 12-week research internship at IRIC in recognition of their keen interest in cancer research and the quality of

their academic records. As a sign of the growing enthusiasm stirred by IRIC among Canada's young scientists, more than 176 applications from 25 Canadian universities were analyzed by the selection committee—a record number since the launch of the program in 2011.

With this program, IRIC's aim is to allow students the opportunity to experience a complete immersion in the research field in an academic setting and thus encourage them to pursue their graduate training at IRIC. Besides being entrusted with projects that allow them to be actively involved in the research activities

of their host laboratory, the grantfunded interns are invited to take part in all the academic, scientific, and social activities organized at the Institute.

The grants in the IRIC Next Generation Awards program are offered thanks to the generous contribution of donors to IRIC's Perseverance Challenge Fund, including an outstanding donation from Fondation Famille Diane et Léon Gosselin.



Awardees of the 2014 IRIC Next Generation Internship program.

From left to right: Patrick Lacasse (IRIC, Program Coordinator), Audrey Bouchard (Université de Montréal), Louis-Philippe Picard (Université de Montréal), Christine Desroches Altamirano (Dalhousie University), David Haberl (Queen's University), Gabrielle Bourque (University of Ottawa), Rachelle Lee (University of Calgary), Franck Simon (Université du Québec à Montréal), Yu Yan He (McGill University), Alexandre St-Pierre-See (Université de Montréal), Jordan Quenneville (McGill University), Shima Mohsen-Pour (McGill University), Annie Karakeussian Rimbaud (Université de Sherbrooke), Abe Albaghjati (University of Ottawa), Celia Li (Queen's University), Beichen Gao (Western University), Francis Wong (Carleton University).

2014 Summer School in Systems Biology

In the summer of 2014, 18 students from IRIC and other research centres in the greater Montréal area took part in the Summer School in Systems Biology. Organized since 2006 and directed by Sylvie Mader, Principal Investigator in IRIC's Molecular Targeting in Breast Cancer Treatment Research Unit, the school offers students multidisciplinary training geared to cancer. It includes a series of theoretical and practical courses covering a variety of subjects such as the

cell cycle, gene expression, signalling pathways, the molecular genetics of eukaryotes, the use of model organisms, the mechanisms of immune defence, drug development, bioinformatics, the therapeutic use of stem cells, and immunotherapy. These classes also enable students to familiarize themselves with the most recent experimental approaches and the state-of-the-art technologies used in the field of biomedical research.



Participants in the 2014 Summer School in Systems Biology.

From left to right: Alexandra Laverde-Saad, Samuel Jacques, Marine Blackman, Laura Rivest-Khan, Francis Lussier, Yahya Benslimane, Peter Kubiniok, Amogh Gopinathan Nair, Swati Shetti, Myreille Larouche. Absent: Marie Armande Ang Houle, Sarah Cherkaoui, Félix Comtois, Élise Cournoyer, Abdellatif Daghrach, Catherine Descôteaux, Arturo Papaluca, Jonathan Seguin

IRIC's International Summer School in Brazil



The seven Brazilian students invited to attend IRIC's Systems Biology Summer School.

From left to right: Luana Campos Soares, Maisa Pinheiro, Antuani Baptistella, Hellen Kuasne, Geysson Javier Fernandez, Mariana Franco Fragoso, and Fabio Marchi.

In the wake of the resounding success of its Systems Biology Summer School, IRIC launched an international version of that summer school in 2014-2015. Its objective is to offer top-level training in cancer research to students attending research institutions outside the country.

Piloted by Trang Hoang, Principal Investigator in IRIC's Hematopoiesis and Leukemia Research Unit, and by Julie Mantovani, IRIC Academic Affairs Advisor, the first IRIC International Summer School was held in collaboration with the Faculty of Medicine at the Universidade Estadual Paulista (UNESP) and the research centre of the A.C. Camargo Hospital. It ran from April 22 to 29, 2014, in São Paulo, Brazil. Six teacher-researchers from IRIC offered a series of classes to some 30 Brazilian

participants, presenting the contributions of genetics to systems biology and the various types of cancer. The seven best Brazilian students from the group were next invited to take part in the 2014 edition of the Systems Biology Summer School organized at IRIC.

This project received financial support from the Université de Montréal's Office of International Relations, the government of Québec's Ministry of International Relations and La Francophonie, and from IRIC. Funding from Brazilian partners came from the São Paulo Research Foundation (FAPESP), the research centre of the A.C. Camargo Hospital, the Faculty of Medicine at UNESP, and the National Council for the Development of Science and Technology (CNPq).



Teacher-researchers from IRIC, UNESP, and the research centre of the A.C. Camargo Hospital alongside the group of students who took part in the first IRIC International Summer School, organized in São Paulo, Brazil.



Patrick Lacasse, Project Manager for Student Recruiting.

IRIC on the road

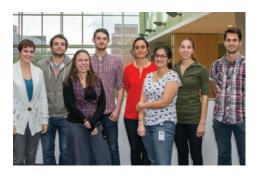
In the fall, representatives of the Academic Affairs team at IRIC visited a number of Canadian provinces to take part in seven student recruitment fairs organized by several graduate and professional schools. These fairs offer students an excellent opportunity to discover the programs of study offered by the various universities and to learn more about admission criteria, services offered, and scholarship possibilities. They can also get advice on preparing their applications.

In October 2014, representatives of the IRIC Academic Affairs team joined the team from the Université de Montréal's Office of Admissions and Recruitment to take part in a student recruitment tour in France. Jointly organized by several Québec schools, the "Study in Québec" tour is designed to promote Québec universities in major French university centres and to recruit undergraduate, master's, and Ph.D. students hoping to continue their studies in Québec. The tour took place mainly in the south of France and included four regional recruiting days (Aix-en-Provence, Lyon, Toulouse, Bordeaux), as well as two more in Paris.

IRIC Student Association (AEIRIC)

The mandate of the IRIC Student
Association (AEIRIC) is to represent
master's and doctoral students, interns,
and postdoctoral investigators in
institutional matters. AEIRIC contributes
to IRIC's development and to maintaining
the quality of student life through active
participation in various committees and
by organizing institutional projects. Its
mandate is also to foster interactions
among students, postdoctoral fellows,
and other members of the IRIC team by
organizing various academic, scientific,
and social activities.

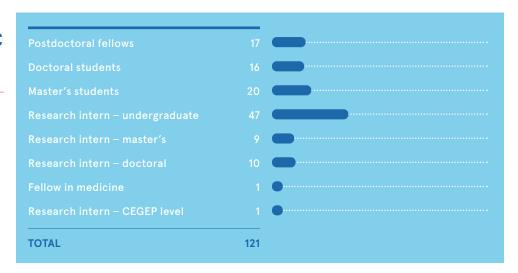
Over the past year, AEIRIC set up a number of social events (January wine and cheese, summer barbecue, etc.) in addition to taking part in such activities as the Christmas and Halloween parties, the Audacious evening, and the IRIC Scientific Day. They were also responsible for the success of the International Symposium and the agreement with Brasseurs Illimités for the creation of the beer La Tête Chercheuse, profits from the sale of which will be distributed in the form of scholarships to IRIC students so that they can attend conferences in their areas of expertise.



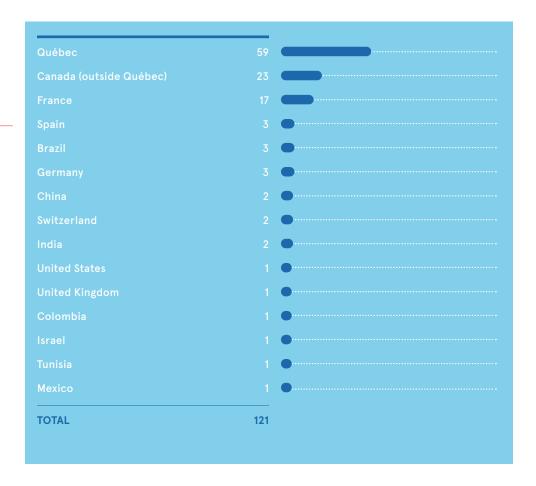
Members of the 2014-2015 AEIRIC.
From left to righ: Catherine Descôteaux (treasurer),
Simon Mathien (secretary), Magalie Celton (social life),
Camille Simon (academic affairs), Laura Rivest-Khan
(scientific affairs), Shaima Al-Khabouri (social life),
Maude Dumont-Lagacé (president), Éric VaillancourtJean (student recruitment). Absent: Magalie Tardif
(internal affairs), Karine Bourdages (summer school).

Statistical data

Distribution of new IRIC recruits in 2014-2015

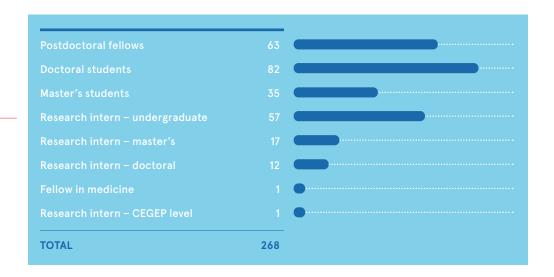


Countries of origin of new IRIC recruits for 2014-2015

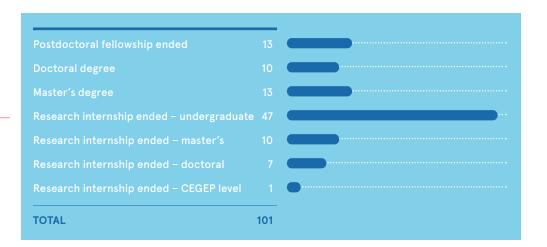


Statistical data

Distribution of active students at IRIC in 2014-2015



Distribution of IRIC graduates in 2014-2015



Grants and nominative awards from granting agencies and private foundations in 2014-2015

Québec

Outside Canada

Cole Fondation

Doctoral

Jérôme Roger

Alexandre Rouette

Postdoctoral David Kachaner

Vincent-Philippe Lavallée Clarisse Thiollier

Canadian Institutes of Health Research (CIHR) / **ICR Publication Prizes**

Doctoral

Hiba Zahreddine

Canada

École Normale Supérieure Cachan - Université Paris Sud Orsay (France)

Master's

Marthe Laisné

Gairdner Foundation - Canada Gairdner Awards

Fonds de recherche du Québec - Nature and Technology Funds (FRQ-NT) / Merit Scholarship for

Foreign Students Program, Québec-China category

Doctoral

Chongyang Li

Diana Paola Granados

Human Frontier Science Program (HFSP) (France)

Irène Baccelli

Ministry of Higher Education (Oman)

Doctoral

Shaima Al-Khabouri

Fonds de recherche du Québec - Health Funds (FRQ-S)

Master's

Guillaume Lépine

Charles St-Pierre Éric Vaillancourt-Jean **Postdoctoral** Diego Serrano Tan-Ning (Sarah) Tsao

Fonds de recherche du Québec - Health Funds (FRQ-S) / Étudiants-chercheurs étoiles

Doctoral

Fadi Hariri Hiba Zahreddine **Iman Fares**

Grants and nominative awards from IRIC and the Université de Montréal in 2014-2015

IRIC Perseverance Awards

Master's

Marianne Archambault Kaleem Atchia Louise Chui Florencio Marie-Hélène Corre Marine Diennet

Amogh Gopinathan Nair

David Haberl Milena Kosic Peter Kubiniok Myreille Larouche Alexandra Laverde-Saad Armen Tchohanian

Master's award for Canadian candidates non-resident of Québec (Award D) of the **Faculty of Graduate and Postdoctoral Studies**

Master's

Kaleem Atchia Amani Daoud Beichen Gao

Milena Kosic **Hilary Pearson** Armen Tchobanian

End of studies awards from the Faculty of **Graduate and Postdoctoral Studies**

Doctoral

Einas Yousef

IRIC Next Generation Awards

Abe Albaghiati **Audrey Bouchard** Gabrielle Bourque Sébastien Dang **Christine Desroches**

Undergraduate interns

Altamirano Beichen Gao David Haberl Yu Yan He

Kaleem Atchia

Amogh Gopinathan Nair

Amani Daoud

Annie Karakeussian Rimbaud Rachelle Lee Arielle Leone Celia Li Shima Mohsen-Pour Louis-Philippe Picard Jordan Quenneville Frank Simon Alexandre St-Pierre-See Francis Wong

Guillaume Laflamme

Neethi Nandagopal

Laura Simon

Excellence awards from the Molecular Biology programs Doctoral

Kaleem Atchia Marine Diennet Amogh Gopinathan Nair David Haberl Milena Kosic Peter Kubiniok Myreille Larouche Alexandra Laverde-Saad Armen Tchobanian

Marianne Archambault

Yahya Benslimane Forum Bhanshali Karine Bourdages Mohamed El Ezzy Gwenaëlle Gavory Justyna Kulpa Guillaume Laflamme Pierre Priam **Alexandre Rouette** Dhanaraman T. Seetharaman Swati Shetty

Krystel Vincent

Exemption of supplementary tuition fees for international students of the Faculty of Medicine and the Faculty of Graduate and **Postdoctoral Studies**

Faculty of Medicine recruiting scholarship

Master's

Louise Chui Florencio Peter Kubiniok Khady Ndeye Thiombane Saeideh Torabi Dalivandan

Doctoral

Amogh Gopinathan Nair Neethi Nandagopal Dhanaraman T. Seetharaman Swati Shetti Laura Simon

Writing awards from the Molecular Biology programs

Master's

Laura Rivest-Khan

Doctoral

José Carlos

Shanti Rojas-Sutterlin Aline Khayat Xiaocui Zhang

Zeledon-Orellana

IRIC 5th Scientific Day -

Fisher Scientific Award - Poster presentation

Master's

Peter Kubiniok

Postdoctoral fellows Abigail Gerhold

Doctoral

Céline Laumont Julien Patenaude Roshan Elizabeth Rajan

Peng Wang Hiba Zahreddine

IRIC 5th Scientific Day — Award for Excellence in memory of Jean-Guy Mongeau - Oral presentation

Doctoral

Gloria Assaker Justine Paradis

Postdoctoral fellows Diana Paola Granados **David Kachaner**

Patrick Narbonne

20th Scientific Day of the Molecular **Biology Programs**

Master's

Magalie Tardif

Doctoral Karine Bourdages Antoine Méant **Justine Paradis**

20th Scientific Day of the Molecular Biology Programs - Award for the best oral presentation

Doctoral

Carl Laflamme

Prominence and recognition

Members of IRIC contribute to the advancement of knowledge and in so doing to the Institute's prominence. Moreover, in the course of the year, some of them received awards for their research work or for their contribution to the community. Such visibility is indispensable for further solidifying the Institute's reputation for excellence and its ability to attract the finest talents. Raising awareness of IRIC and carrying out various media-relations communications projects came under the direction of Manon Pepin.

Science à la carte

Each year, IRIC presents the "Distinguished Scientists Lecture Series." Under the direction of the Scientific Program Committee (chaired by Étienne Gagnon, Principal Investigator in the Cancer Immunobiology Research Unit), this lecture program, intended for graduate and postdoctoral students and members of Montréal's biomedical community, invites well-known researchers from Canada and abroad to present their most recent scientific breakthroughs.

During the period covered by this report, some 30 lecturers came to present their findings at IRIC. The eighth IRIC International Symposium, entitled

"Molecular Targets in Cancer Genomics," was organized exceptionally by a committee made up of students and postdoctoral fellows, and headed by Étienne Gagnon and Nora Mostefaï, project manager associated with the Scientific Program Committee. Held at IRIC on May 14 and 15, 2015, the event brought together international experts working in areas related and complementary to cancer research. This symposium allowed 16 well-known researchers to present their most recent work on various aspects of cancer research, such as genomic instability, epigenetic regulation, small RNA regulators, and integrative approaches in genomics. Over 250 students from

Canada, the U.S., and Europe attended. The goal of the event was to promote fruitful exchanges among researchers and students whose complementary areas of expertise are essential to a better understanding of tumour establishment and growth. A report of this symposium was published by a group of IRIC students and postdoctoral fellows: Laumont, C.M., Haberl, D., Ghugari, R. and Tsao, S.: "Meeting report – 9th IRIC International Symposium on Molecular Targets in Cancer Genomics," *J Cell Sci.* 128(19):3521–3524, 2015.

Visibility: a record year for production





Each year, IRIC's presence in the media and on social networks increases. Over 50 press releases were published in the course of the year, a record since the creation of the Institute. These publications were picked up by a host of media outlets, boosting visibility of IRIC and spreading word of its research and its various fundraising activities

The Office of Communications and Media Relations moreover supervised the development of visual signatures and videos of the first Audacious benefit evening and the Great Challenges Against Cancer presentation, as well as coordinating the public-relations aspects of these activities.

In addition to the institutional video entitled "Conquering cancer differently," two promotional videos were produced by Campus Montréal to raise awareness of IRIC and solicit donations.

These activities attracted the attention of the media and social networks. Also important to highlight were the many TV reports that followed the discovery of molecule UM171 by the team of Dr. Guy Sauvageau, and the publication of over 60 articles on the subject. The teams of Dr. Claude Perrault and Michel Bouvier were also the subject of TV reports related to their respective research work on a vaccine to prevent cancer and cell signalling.

Mobilization of the IRIC community

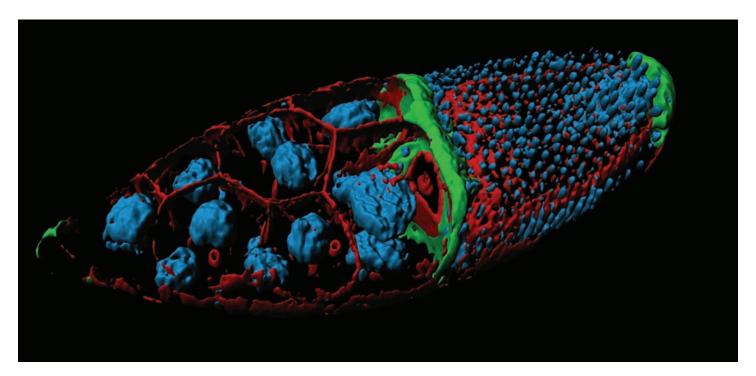
Also worthy of mention is the commitment of IRIC's Social Life Committee, which throughout the year promotes the visibility and mobilization of the IRIC community by way of a series of social activities. The committee is coordinated by Marie-Christine Ménard, Head of Human Resources.

"Réflexion Science" competition for scientific work

With the goal of extending knowledge of science, the internal Scientific Promotion Committee, chaired by principal investigator Pierre Thibault, inaugurated the annual "Réflexion Science" competition for scientific

work. For this first edition, the committee selected the eight best scientific works from among the proposals received (photography, microscopy, immunofluorescence, varied structures). The works selected were printed and

distributed at strategic locations around the Institute and will be offered to sponsors at the annual Audacious benefit evening. This competition is sponsored by Zeiss, a world leader in imaging.



Author: Sarah Keil

Title: Egg chamber of Drosophila melanogaster in 3D

Highlights—Dr. Robert Patenaude receives the Humanism Award from the Collège des médecins du Québec

Recognized for his dynamism and the quality of his social commitment in the fight against cancer, Dr. Robert Patenaude, spokesperson for IRIC, received the Humanism Award from the Collège des médecins du Québec on May 9, 2014.

An emergency physician for over 25 years, Dr. Patenaude is a model of determination, having struggled with cancer himself in his early twenties and being the recipient of one of the first bone marrow transplants performed by Dr. Claude Perreault, Principal Investigator at IRIC. Subsequently, Dr. Patenaude has shown his humanitarian calling through his extraordinary contribution to the fight against cancer, first by establishing the Fondation de la greffe de la moelle osseuse (Bone Marrow Transplant Foundation), and then by serving as spokesperson for IRIC. In 2007 he founded the IRIC Perseverance Challenge to raise money to fund the IRIC Next

Generation Internship Awards and the IRIC Perseverance Challenge scholarships. Renamed "IRIC Great Challenges against Cancer," this booming fundraising program now encompasses several challenges. Over the years, Dr. Patenaude has raised over \$1.1 million for the fight against cancer through these activities.



Dr. Charles Bernard, Chief Executive Officer of the Collège des médecins, and Dr. Robert Patenaude, spokesperson for IRIC

Highlights—Michel Bouvier, one of the most cited scientists internationally, is elected Fellow of the Royal Society of Canada



Michel Bouvier, Chief Executive Officer and Principal Investigator at IRIC

As Chief Executive Officer of IRIC. Principal Investigator at IRIC, Chief Executive Officer of IRICoR, and Professor in the Department of Biochemistry and Molecular Medicine of the Faculty of Medicine, Michel Bouvier figured on the 2014 list of scientists most cited internationally, all disciplines taken together, according to the science indicators of Thomson Reuters, the world leader in information for businesses and professionals. The scientists appearing on the list number around 3,000 and rank among the top one percent of researchers cited. An internationally recognized expert in the field of cell signalling, Professor Bouvier along with his team have made a number of significant breakthroughs in this field with regard to G-protein coupled receptors (GPCRs), his work having led to the development of concepts and tools enabling the discovery of more effective drugs, with fewer undesirable effects.

Mr. Bouvier was also elected Fellow of the Academy of Sciences of the Royal Society of Canada. The newly elected Fellows, who have diverse backgrounds and disciplines, are elected by their peers for the excellence of their outstanding scholarly, scientific, or artistic achievement. Election to the Royal Society of Canada is the highest honour a scholar can achieve in the arts, humanities, and sciences.

Highlights—Four IRIC investigators awarded grants by the Leukemia and Lymphoma Society

The Leukemia & Lymphoma Society (LLS) awarded grants to four IRIC researchers during the "Journey of Hope" event organized by the LLS. The award recipients, all affiliated with the Faculty of Medicine, are: Katherine Borden, Principal Investigator in the Structure and Function of the Cell Nucleus Research Unit and Professor in the Department of Pathology and Cell Biology; Trang Hoang, Principal Investigator in the Hematopoiesis and Leukemia Research Unit and Professor in the Department of Pharmacology; Guy Sauvageau, Principal Investigator in the Molecular Genetics of Stem Cells Research Unit and Professor in the Department of Medicine; and Brian Wilhelm, Principal Investigator in the

High-Throughput Genomics Research Unit and Research Assistant Professor in the Faculty of Medicine.

The chief executive officer of IRIC, Michel Bouvier, took advantage of the occasion to thank the Leukemia & Lymphoma Society for its support of the Institute's investigators. "These bursaries," he said, "are an essential help in the discovery of mechanisms at the origin of cancers of the blood and the development of new therapeutic approaches aimed at treating these cancers. The event was also an opportunity to meet with investigators from other research centres, LLSC volunteers, and cancer patients and their families. The spirit of collaboration and camaraderie reflects our core values and is a reminder that research results are a source of hope for patients."



From left to right: Brian Wilhelm, Principal Investigator at IRIC, Michel Bouvier, Chief Executive Officer of IRIC, Daniel Lajeunesse, Vice-Dean of Basic Sciences and Higher Education of the Université de Montréal's Faculty of Medicine, Trang Hoang, Principal Investigator at IRIC, Cynthia Price, Executive Director of LLS-Québec, Katherine Borden, Principal Investigator at IRIC, and Gilles Legault, Senior Counsel, CN, Chairman of the Board of LLS (absent from the photo: Guy Sauvageau, Principal Investigator at IRIC).

Highlights—Dr. Guy Sauvageau and his team receive several prestigious awards for their revolutionary discovery relating to blood cancer and other illnesses of this type

Dr. Guy Sauvageau's team made an unprecedented breakthrough with the discovery of a new molecule that allows for the multiplication of stem cells in umbilical cord blood. Use of this molecule—named UM171 in honour of the Université de Montréal—will notably allow for a significant increase in the availability of compatible stem cells for treating patients with such illnesses as leukemia, lymphoma, and myeloma. This work, published in the prestigious journal Science, could revolutionize the treatment of leukemia and other blood-related diseases (see page 18).

This new discovery earned Dr. Sauvageau the titles of *La Presse* 2014 Scientific Personality of the Year and Radio-Canada 2014 Scientist of the Year. The work of Dr. Sauvageau and his team was also recognized as Québec Science 2014 Discovery of the Year.

"Dr. Sauvageau's research gives cause for hope to thousands of patients and their families," commented Guy Breton, Rector of the Université de Montréal. "This research is carried out in collaboration with numerous partners and thanks to the coming together of several disciplines, which is the source of the great strength of IRIC and the Université de Montréal. We're immensely proud of Dr. Sauvageau, who is an outstanding ambassador for our university."

Such discoveries are the result of a true team effort. Réjean Ruel, Yves Gareau, and Stéphane Gingras, chemists at IRIC's Medicinal Chemistry platform led by Dr. Anne Marinier, and the screening platform team led by Jean Duchaine, played an important role in this discovery, as did postdoctoral student Iman Farès and research officer Jalila Chagraoui, who collaborated on writing the original study, which appeared in the prestigious journal Science. The discovery also came to fruition in part thanks to invaluable collaborators, namely Maisonneuve-Rosemont Hospital, Héma-Québec, and IRIC's Drug Discovery and Research Commercialization Unit (IRICOR).

Such advances are never the result of the work of one person but rather the efforts of several research teams. Doctoral student Iman Farès and research officer Jalila Chagraoui, with the help of members of the High-Throughput Screening core facility directed by Jean Duchaine and the Flow Cytometry facility headed by Danièle

Gagné, developed the biological test, screened the IRIC library of compounds, and identified the starting small molecule. Under the direction of Anne Marinier of the Medicinal Chemistry core facility, chemists Yves Gareau, Stéphane Gingras, and Réjean Ruel from this team then designed the molecule UM171 by optimization of the starting molecule, and developed a synthesis. Maisonneuve-Rosemont Hospital, Héma-Québec, and IRICoR were also invaluable collaborators in contributing to bring this discovery to fruition. In addition, collaborators from the British Columbia Cancer Agency, the Ontario Cancer Institute, and the Fred **Hutchinson Cancer Research Centre** played an important role in evaluating the biological properties of UM171. Collaborators from the University of Toronto also contributed to the development of a bioreactor for the production of cells as part of clinical trials.



Guébec Science 2014 Discovery of the Year From left to right: Stéphane Gingras, chemist at IRIC; Jalila Chagraoui, Research Officer at IRIC; Iman Farès, Ph.D. student at IRIC; Dr. Guy Sauvageau, Principal Investigator at IRIC; Dr. Anne Marinier, Medicinal Chemistry Director and Principal Investigator at IRIC; Réjean Ruel, chemist at IRIC; Yves Gareau, chemist at IRIC

(absent from the photo: Sandra Cohen, Elizabeth Csaszar, Jean Duchaine, Connie J. Eaves, Robert Herrington, R. Keith Humphries, Suzan Imren, Norman N. Iscove, Hans-Peter Kiem, David J. H. F. Knapp, Nadine Mayotte, Paul Miller, Mor Ngom, Denis-Claude Roy, Kori L. Watts).

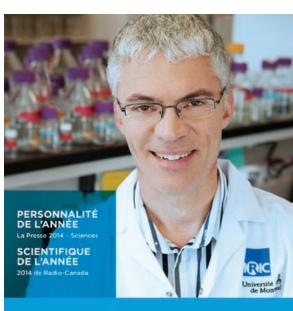
Highlights— 20th Scientific Day of the molecular biology programs



IRIC students distinguished themselves at the 20th Scientific Day of the molecular biology programs, hosted by the Faculty of Medicine on May 2, 2014, at the CHUM research centre (CRCHUM). They earned six prizes out of the 10 prizes awarded during this day for the quality of their oral and poster presentations (See page 47 the list of winners).

Also as part of this activity, Trang Hoang, Principal Investigator at IRIC, received a diploma of recognition for her commitment of over 16 years as director of molecular biology programs.

An annual event, the Scientific Day of the molecular biology programs allows students who are pursuing their research in the various affiliated research centres of the Université de Montréal to meet and present their work.



BRAVO!

Bravo au D' Guy Sauvageau, professeur à la Faculté de médecine et chercheur à l'Institut de recherche en immunologie et en cancérologie (IRIC) de l'Université de Montréal, pour la découverte de la molécule UM171. Cette percée figure parmi les 10 découvertes de l'année 2014 de Québec Science.

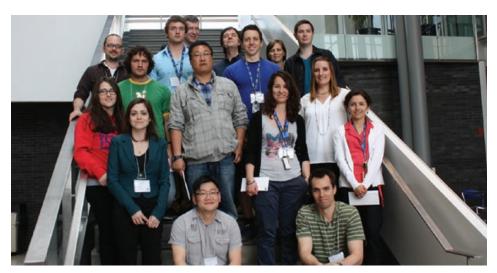
La molécule UM171 a la propriété de multiplier les cellules souches contenues dans le sang de cordons ombilicaux. Un plus grand nombre de cellules souches signifie que davantage de patients atteints de cancer pourront ainsi être traités.

iric.ca medecine.umontreal.ca



Print by the Université de Montréal for Dr Guy Sauvageau's award: La Presse 2014 Scientific Personality of the Year and Radio-Canada 2014 Scientific of the Year.

Highlights—Fifth IRIC Scientific Day: Training at the heart of the action



Winners of the Awards for Excellence in memory of Jean-Guy Mongeau, and the Fisher Scientific Award, conferred for the best presentations during the 5th edition of the IRIC Scientific Day, accompanied by IRIC senior investigators Benjamin Kwok and Vincent Archambault, and members of the organizing committee for the event.

The 5th IRIC Scientific Day took place on May 23 and 24, 2014. The event celebrates the role of training at the heart of the Institute's activities, and its goal is to provide a forum where the members of the IRIC community can meet and deliberate over ongoing scientific activities within the Institute. Organized every two years, the Scientific Day is also an opportunity for graduate students, postdoctoral fellows, research associates, and staff to present their projects orally or as posters.

For the keynote address, Dr. Prasad Jallepalli of New York's Memorial Sloan Kettering Cancer Centre delivered the lecture, "Surfing mitosis with chemical genetics." This was an opportunity for participants to expand their knowledge in this area of expertise and discuss the topic with an expert known worldwide for his research into chromosome anomalies in human cells.

In the course of the event attended by over 175 people, participants also had access to 20 oral presentations and 58 poster presentations. In that context, several IRIC members especially distinguished themselves with the quality of their presentations, and received awards for excellence (see page 47).

The organizing committee was made up of principal investigators Vincent Archambault, Étienne Gagnon and Benjamin Kwok, and representatives of the Office of Academic Affairs Patrick Lacasse, Pascale Le Thérizien, and Julie Mantovani, along with Nora Mostefaï, project manager associated with the Scientific Program Committee, and Ph.D. student Céline Laumont. The 5th IRIC Scientific Day was made possible thanks to the financial support of Fisher Scientific.

Highlights—Several IRIC students rewarded for the quality and importance of their publications and research work

In 2014-2015, three IRIC students enrolled in the Molecular Biology Ph.D. program, systems biology option, were selected as winners of the competition Étudiants-chercheurs étoiles du Fonds de recherche du Québec – Health Funds, in recognition of the excellence of their research.

One student also received a prestigious grant from the Merit Scholarship for Foreign Students program in the Québec-India category from the Fonds de recherche du Québec – Nature and Technology Funds, which aims to attract the best foreign students to highereducation institutions in Québec.

Another student received the award from Genome Canada and the Gairdner Foundation, recognizing the achievements of researchers in medicine whose work contributes in a significant way to improving the quality of human life.

Five grants were also awarded to students and postdoctoral fellows by the Cole Foundation.

Given the intense nature of these competitions, this outstanding result testifies once again to the quality of IRIC students and the research projects entrusted to them.



Recipient of the Étudiants-chercheurs étoiles award of the Fonds de recherche du Québec - Health Fund, for the month of April 2015, for the publication of the article: Pyrimidoindole derivatives are agonist of human hematopoietic stem cell self-renewal

This publication presents the use of the molecule UM171, which permits the multiplication of stem cells in a unit of cord blood, these being used for transplants aimed at healing a number of blood-related illnesses, including leukemia, myeloma, and lymphoma.

Research cited:

Fares I., Chagraoui J., Gareau Y., Gingras S., Ruel R., Mayotte N., Csaszar E., Knapp D.J., Miller P., Ngom M., Imren S., Roy D.C., Watts K.L., Kiem H.P., Herrington R., Iscove N.N., Humphries R.K., Eaves C.J., Cohen S., Marinier A., Zandstra P.W., Sauvageau G., "Pyrimidoindole derivatives are agonists of human hematopoietic stem cell self-renewal". *Science*, 345(6203): 1509-12. 2014

Recipient of the Étudiants-chercheurs étoiles award of the Fonds de recherche du Québec – Health Fund, for the month of August 2014, for the publication of the article: The eukaryotic translation initiation factor elF4E is a direct transcriptional target of NF-kB and is aberrantly regulated in acute myeloid leukemia

This research on the structure and function of the cell nucleus is directed at understanding the role of the protein eIF4E in acute myeloid leukemia (AML) and other cancer subtypes.

Research cited:

Hariri F., Arguello M., Volpon L., Culjkovic-Kraljacic B., Nielsen TH., Hiscott J., Mann K.K., Borden K.L., *Leukemia* 27(10): 2047-55. 2013 Recipient of the Étudiants-chercheurs étoiles Award of the Fonds de recherche du Québec – Health Fund, for the month of December 2014, and of the Canadian Institutes of Health Research Publication Program for the article: The sonic hedgehog factor Gli1 imparts drug resistance through inducible glucuronidation

This publication made it possible to identify a new mechanism causing resistance to cancer drugs in acute myeloid leukemia (AML) and other subtypes of cancer.

Research cited:

Zahreddine H.A., Culjkovic-Kraljacic B., Assouline S., Gendron P., Romeo A.A., Morris S.J., Cormack G., Jaquith J.B., Cerchietti L, Cocolakis E., Bergeron J., Leber B., Becker M.W., Pei S., Jordan C.T., Miller W.H., Borden K.L., *Nature* 2014; 511(7507): 90-3.



Iman Farès, Ph.D. student at IRIC under the supervision of Dr. Guy Sauvageau



Fadi Hariri, Ph.D. student at IRIC under the supervision of Katherine Borden



Hiba Zahreddine, Ph.D. student at IRIC under the supervision of Katherine Borden

Winner of an award at the "Genomics: the Power and the Promise" congress organized by Genome Canada and the Gairdner Foundation for a poster: Discovery of Minor Histocompatibility Antigens for Leukemia Immunotherapy with a Novel Proteogenomics Approach

The poster presents a study to develop a personalized approach for the treatment of leukemia.

Recipient of a grant from the Merit Scholarship for Foreign Students program in the Québec-India category from the Fonds de recherché du Québec, Nature and Technology Fund (in partnership with the Ministry of Higher Education, Research and Science [MESRS]).

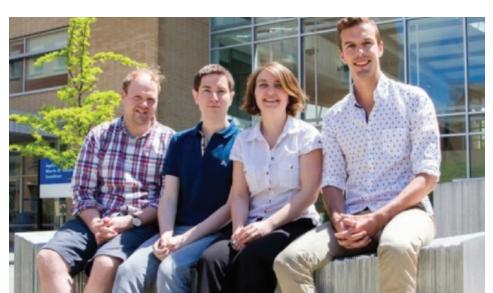
The aim of this program is to support the internationalization of research activities in institutions of higher learning in Québec, to attract the best researchers and the finest foreign students, and to promote awareness of Québec universities and college technology transfer centres.



Diana Paola Granados, postdoctoral fellow at IRIC under the supervision of Dr. Claude Perreault



Neethi Nandagopal, Ph.D. student at IRIC under the direction of Philippe Roux



Students and postdoctoral fellows who received scholarships from the Cole Foundation for research having an impact on leukemia and lymphoma in children and young adults.

Left to right:

Jérôme Roger, master's student under the supervision of Philippe Roux, David Kachaner, postdoctoral fellow under the supervision of Vincent Archambault, Clarisse Thiollier, postdoctoral fellow under the supervision of Dr. Guy Sauvageau, Vincent-Philippe Lavallée, postdoctoral fellow under the supervision of Dr. Guy Sauvageau, Alexandre Rouette (absent from the photo), Ph.D. student under the supervision of Dr. Claude Perreault

Philanthropy: vanquishing cancer differently

For over ten years, we have been witness to the strength of commitment and the growing number of donors eager to support IRIC. These essential partners contribute to accelerating the discovery of more effective cancer drugs and treatments. Events such as the Audacious benefit evening and the IRIC Great Challenges Against Cancer have enabled us to significantly expand the base of our support among donors from both the business community and the general public. That philanthropic commitment is important support not only for research but also for patients with the illness.

Development of IRIC's philanthropic component is handled by the duo of Pierre Thibault, Deputy Director, Philanthropy, and Robert Turgeon, the Institute's Development Director. They are backed in their mandate by Anne Lebel, Development Officer with the Université de Montréal's Office of Development and Alumni Affairs, and Manon Pepin, IRIC's Director of Communications and Media Relations.

Highlights—Success of the first annual Audacious benefit evening: objective exceeded with \$730,000 raised

At the first annual Audacious benefit evening, the Québec business community celebrated IRIC's 10th birthday and the extraordinary commitment of its ambassadors and donors extraordinary, Marcelle and Jean Coutu.

Thanks to the audaciousness and commitment of the members of the fundraising committee, partners, sponsors, numerous donors,

and volunteers, the evening—under the honorary presidency of Mr. Stéphane Achard, Senior Executive Vice-President and General Manager, Business and Institutional, Card and Payment Services, Desjardins Group, and Mr. Daniel Fournier, Chairman and Chief Executive Officer, Ivanhoé Cambridge—welcomed 425 people to the Parquet floor at the Caisse de dépôt et placement du Québec and raised a total of \$730,000,

not counting a contribution of \$196,000 in equipment from Thermo Fisher Scientific.

The money raised was turned over to the Audacious Fund, whose mandate is to invest in the four major priorities of IRIC, namely research, university training, strategic projects, and fixed assets.



From left to right, some members of the Audacious Fundraising Committee and guests: Pierre Thibault, Principal Investigator at IRIC; Marcel Dutil, Chairman of the Board of Canam Group; Marie-Josée Coutu, President of the Marcelle and Jean Coutu Foundation; Pierre Pomerleau, President and CEO of Pomerleau; Guy Breton, Rector of the Université de Montréal; Réal Raymond, Corporate Director; Marcelle Coutu, ambassador for IRIC; Guy Sauvageau, CEO and Principal Investigator at IRIC; Jean Coutu, ambassador for IRIC; Robert Tessier, Chairman of the Board of the Caisse de dépôt et placement du Québec; Louise Roy, Chancellor of the Université of Montréal; Marc-André Blanchard, Chairman of the Board at IRIC and Chairman and CEO of McCarthy Tétrault;

Benoît Brière, host of the evening and actor; Stéphane Achard, Co-chair of the Fundraising Committee and Senior Vice-President and General Manager, Business and Institutional Services, Card and Payment Services at Desjardins Group; Daniel Fournier, Co-chair of the Fundraising Committee and Chairman and CEO of Ivanhoé Cambridge; Robert Lacroix, Professor, Rector Emeritus of the Université de Montréal and CIRANO Fellow; Steven Klein, Vice-President, Business Development at IRICOR













Highlights—Blais Family Golf Tournament: the commitment of an outstanding ambassador in the Outaouais community

In the framework of the 5th annual Blais Family Fund Outaouais Golf Tournament held on July 18, 2014, at the Buckingham Golf Club, members of the organizing committee handed over the record amount of \$40,700 to IRIC.



Left to right: Cyntia Plouffe, member of the Tournament organizing committee; Guy Sauvageau, Principal Investigator at IRIC; Gyslain Boudreault, partner in Tapis J2G and co-president of the Tournament, Jean-Guy Laframboise, partner in Tapis J2G and co-president of the Tournament; Pierre Blais, IRIC ambassador and founder of the Blais Family Tournament.

With Gyslain Boudreault and Jean-Guy Laframboise, both partners in Tapis J2G, serving as co-presidents, this fifth edition brought together more than 150 people, including a number of representatives of the Outaouais region, members of the business community, and principal investigators and staff members from IRIC.

Mr. Blais is living proof that investing in medical research contributes to saving lives. Diagnosed a few years ago with chronic leukemia, the Outaouais citizen survived thanks to an experimental treatment recommended by IRIC Chief Executive Officer, Dr. Guy Sauvageau.

Highlights—IRIC Great Challenges Against Cancer: participant perseverance gains record commitment from the public

Led by Dr. Robert Patenaude, founder of IRIC's Great Challenges Against Cancer and spokesman for the Institute, close to 400 cyclists and runners entered the fifth edition of this annual fundraiser as part of the IRIC Mount Royal Tour and the Défis du Parc in La Mauricie. A record amount of over \$415,000 was collected on the occasion. Moneys raised made it possible to award 12 Perseverance Awards to master's students in the molecular biology program and to offer 18 IRIC Next Generation Internship Awards to bachelor's students so that they could take part in summer internships. Dr. Patenaude also highlighted "the remarkable

commitment and generosity of the Diane and Léon Gosselin Family, who through their recurring donation, contribute incontestably to accelerating the discovery of new cancer drugs."

In addition, for a third straight year, 205 members of the women's team at the Parc national de la Mauricie also participated in the event on the initiative of the two co-founders, Dr. Chantal Guimont, an emergency medicine specialist, and Marie-Josée Gervais. These participants not only took up a fitness challenge, but also turned over a record total of \$120,000 for cancer research at IRIC.



Highlights — National Bank and Metro make major donations

IRIC is pleased to be able to count on the support of two important new corporate donors. The National Bank of Canada has made a donation of \$500,000 for the creation of research laboratories and technology platforms, important tools for accelerating the discovery of cancer drugs. Represented by its president and chief executive officer, Éric La Flèche, Metro, for its part, turned over an amount of \$250,000 in support of IRIC.



Left to right: John Parisella, Executive Director of Campus Montréal; Michel Bouvier, Chief Executive Officer of IRIC; Robert McCollough, Vice-President, Government Affairs, National Bank; Yves Beauchamp, Vice-Rector at the new campus and of Development of the Université de Montréal; and Robert Tessier, Chairman of the Board of Directors of IRIC.



Left to right: Yves Beauchamp, Vice-Rector at the new campus and Development of the Université de Montréal; Michel Bouvier, Chief Executive Officer of IRIC; Dr. Guy Breton, Rector of the Université de Montréal; and Eric R. La Flèche, President and Chief Executive Officer of Metro.

Highlights—B2Discovery: new commitments to fund novel high-potential research projects

Established in 2010, the B2Discovery program brings together donors from the business community and funds high-potential ground-breaking projects for cancer drug and therapy discovery. For help in selecting these projects, IRIC relies on a Strategic Priorities Committee made up of five of the Institute's researchers.

For the current year, \$325,000 in donations has been received from our donors. The following initiatives have benefited from funding in this way: expansion and enrichment of IRIC's compound collection (funded by a donation from Fondation Marcel et Rolande Gosselin), the project on the inhibition of the adenosine 2A receptor for the treatment of leukemia, and the project on improving the technology of chimeric receptors for the treatment of leukemia by immunotherapy. Over the past five years, close to \$550,000 has been allocated to various projects.



Highlights-Campus Montréal: to see further ahead

HEC Montréal, Polytechnique Montréal and the Université de Montréal jointly conducted a major fundraising campaign under the name Campus Montréal.

The goal of Campus Montréal is to support promising projects for the design and development of innovative solutions to complex issues. The campaign also strives to create the right conditions for training and knowledge transfer. To that end, Campus Montréal seeks to connect with the community by generating partnerships that are both creative and productive.

To be successful in this huge social project, its objective is to raise \$500 million.

To realize that amount, the CM3 campaign has launched an appeal to the generosity and sense of commitment of the major players in Québec society. Be they business personalities or philanthropists from other sectors, all are invited to participate in this collective project.

In the framework of Campus Montréal, the IRIC team aspires to achieve the following four major priorities by raising over \$25 million in Québec:

--- \$15 million in research funds to recruit eminent researchers and provide equipment for their laboratories;

- --- \$3.5 million in student training funds to offer more competitive research grants for master's, doctoral and postdoctoral programs, attract the best researchers of tomorrow, and meet the growing demand of the student body;
- --- \$2.5 million in strategic-project and B2Discovery funds allowing for the funding of research projects that cannot be subsidized by traditional granting agencies, but whose high cancer drug and therapy discovery potential is promising;
- --- \$4 million in capital project funds to acquire and maintain cutting-edge equipment for the scientific core facilities.

10 ways of helping to beat cancer

- --- Make an annual donation.
- --- Match your donation to your company's donation.
- --- Make a donation in memory or honour of a loved one.
- --- Create a fund, scholarship or award that will bear the donor's name or the name of a loved one.
- --- Make a gift of market securities.
- --- Donate material or equipment.
- --- Plan a legacy gift.
- --- Donate a life insurance policy.
- --- Donate a charitable annuity.
- --- Take part in IRIC fundraising activities.

Making a donation to IRIC means helping support research efforts that may have an impact on the lives of thousands of people. It is also essential for IRIC that donations have a leverage effect to ensure the sustainability of the organization. There are several options available for donating to the Institute, and donors can choose the option that suits them best. The team of IRIC's Philanthropic Development service can provide information on the broad range of methods for maximizing donations while taking advantage of interesting tax benefits.

Donors can make single or annual donations, take part in activities, or set up a planned gift.

List of donors

The IRIC executive wholeheartedly thanks all the individuals, foundations, and companies who believe in the unique and innovative model of the Institute and who contribute generously to the advancement of cancer research.

The following table lists cumulative donations of \$1,000 or more on April 30, 2015. Entries in each section are in alphabetical order.

Donations of \$5M and over

Marcelle and Jean Coutu Foundation

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

CG

Fondation Famille Diane et Léon Gosselin

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

Canam Group

Fondation Marcel et Rolande Gosselin Laporte, Roger M.

Merck Canada Inc.

Metro Inc.

National Bank of Canada

Pomerleau Inc.

Raymond, Élaine et Réal

Sauvageau, Monique and Guy Sr.

Wood Family Foundation

Donations of \$25,000 TO \$99,999

Agilent Technologies Foundation

Anonymous (1)

Blais, Pierre

Bouvier, Michel

CAE Inc.

Fondation J.-Louis Lévesque

Goldring, C. Warren

Katelyn Bedard Bone Marrow

Association

Lacroix, Chantal and Sauvageau, Guy

Le Groupe Jean Coutu (PJC) inc.

Marinier, Anne

Pfizer Canada Inc.

Plessis-Bélair, Michel

SNC-Lavalin Inc.

Thibault, Pierre

Transcontinental Inc.

Donations of \$10,000 to \$24,999

3249531 Canada Inc.

Anonymous (1)

Bisson, André

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Hoang, Trang

Lacroix, Robert

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Lavigne, Robert

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Mader, Sylvie

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Manulife

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Family Foundation

Otéra

Panet-Raymond, Robert

Perreault, Claude

Provencher, France

RBC Foundation

Saputo Inc.

Société de gestion COGIR S.E.N.C.

Transat A.T. Inc.

Verreault, Alain

Donations of \$1,000 to \$9,999

2699222 Canada Inc. 4518080 Canada Inc. 6858031 Canada Inc.

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AIM Holdings LP

Amaya Gaming Group Inc.

Anonymous (37)

Aon Reed Stenhouse Inc.

Atelier de menuiserie Allaire & fils Inc.

Aubry, Muriel

Autorité des marchés financiers

Banville, Jacques Barnes & Thornburg LLP BCF S.E.N.C.R.L. **Bell Canada** Benoit, Claire

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Bertrand, Maryse and Brock, William

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Caisse populaire Desjardins de la

Basse-Lièvre

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Filteau, Éric

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Lebel, Anne Leboeuf, Jean-Marc Legault, François M. Lemmel, Albert Lépine, Yves

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Placement Gabriel Gagnon Inc.

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Roy, Jean Roy, Louise Roy, Martine Rov. Sébastien Sabbatini, Luc Sabourin, Thomas Saine, François

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TVM Life Science Management Inc.

Tyers, Michael Unibéton Uni-Select Inc. Vachon, Louis Vibien, Anne Vignault, François Walter Technologies Wallingford-Blais, Gail Wilson, Rénald Yelle, Marcel Zumwalt, Michael



The funding IRIC receives is used to carry out many of its essential activities, including laboratory operations, salary support for researchers, development of research support programs, and rewarding of scholarships. Thanks to these funding sources and IRIC's unique model, the average annual budget per research unit is \$1,052,000.

Under the responsibility of Richard Martin, the Administrative Services team includes Patrick Gendron, Head of Information Technologies; Vincent Huard, Head of Finances; Marie-Christine Ménard, Head of Human Resources; Manon Pepin, Director of Communications and Media Relations; Stéphane Pinsonneault, Manager of Infrastructure and Specialized Equipment, and Manon Valiquette, Head of Scientific Core Facilities.

Revenues	Operating	Research	Capital assets	Total
Université de Montréal	\$5,451,447	\$2,750,055		\$8,201,502
Grants	\$4,139,793	\$12,445,065	\$360,000	\$16,944,858
Student and postdoctoral awards		\$1,153,333		\$1,153,333
Chairs and salary awards		\$2,270,962		\$2,270,962
Contracts with industry		\$6,608,348		\$6,608,348
Core facilities – external clients	\$1,393,004			\$1,393,004
Donations		\$1,345,524		\$1,345,524
Sponsorship and other	\$41,103			\$41,103
TOTAL	\$11,025,347	\$26,573,288 4	\$360,000	\$37,958,636

Expenses						
Salaries and employee benefits	\$6,243,841	\$18,371,220		\$24,615,061		
Supplies and services	\$1,825,068	\$8,302,284		\$10,127,352		
Maintenance and repairs	\$2,831,068	\$451,437		\$3,282,505		
Scientific equipment	\$174,061	\$364,544	\$360,000	\$898,605		
TOTAL	\$11,074,038	\$27,489,485	\$360,000	\$38,923,523		

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

 $^{2\} Excludes\ the\ amounts\ from\ IRIC\ researchers\ (\$1,830,777),\ these\ being\ included\ in\ research\ grant\ revenues$

³ Solely donations granted

⁴ Includes principal investigators' salaries paid by the Université de Montréal

Statistical data

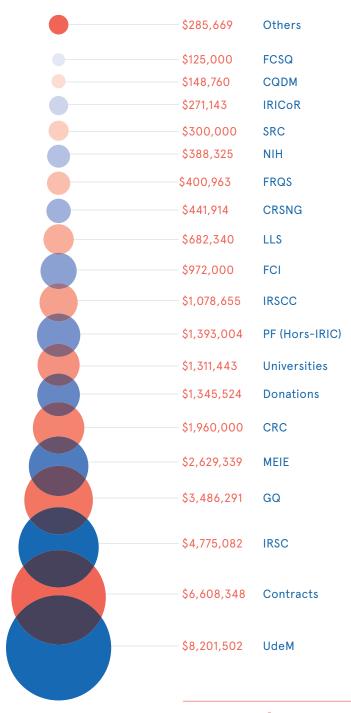


Main organizations with peer committees providing research funds and scholarships in 2014-2015

Canada Research Chairs (CRC)
Natural Sciences and Engineering Research Council of Canada (NSERC)
Québec Consortium for Drug Discovery (CQDM)
Canada Foundation for Innovation (CFI)
Cole Foundation
Fonds de research du Québec, Nature and Technology Fund (FRQNT)
Fonds de research du Québec, Health Fund (FRQS)
Génome Québec (GQ)
Institute for Research in Immunology and Cancer – Commercialization of Research (IRICoR)
Canadian Cancer Society Research Institute (CCSRI)
Canadian Institutes of Health Research (CIHR)
Québec Ministry of Economic Development, Innovation and Export Trade (MEIE)
National Institutes of Health (NIH)
Stem Cell Network (SCN)
Networks of Centres of Excellence of Canada (NCE)
The Leukemia & Lymphoma Society (LLS) of Canada and the United States
Cancer Research Society (CRS)
Université de Montréal (UdeM)

Funding sources in 2014-2015

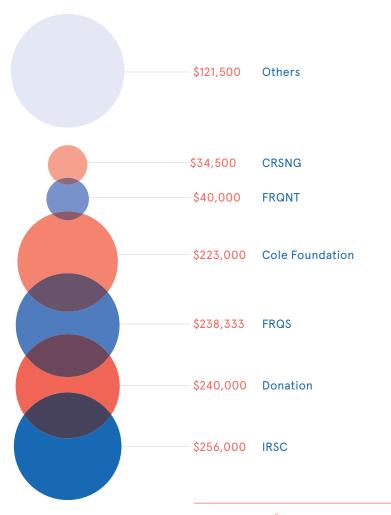
Excluding scholarships



Total: \$36,805,302

Student scholarships and postdoctoral fellowships in 2014-2015

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



Total: \$1,153,333

Management team

IRIC represents the culmination of the efforts of a host of people sharing a common vision—creating a research centre armed with an innovative approach that enables it to generate tangible results in the fight against cancer. Thanks to its many collaborations and its distinctive model, IRIC is today one of principal hubs in the fight against cancer in Canada.

We would like to take the opportunity to sincerely thank Mr. Réal Raymond and Dr. Guy Sauvageau, who concluded their mandates as members of the IRIC board of directors. Their commitment to the Institute is invaluable. Note that Mr. Marc-André Blanchard remains a member of the board, but yields the chairmanship to Mr. Robert Tessier.

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