CHU SAINTE-JUSTINE RESEARCH CENTER

ANNUAL REPORT 2017-2018

Summary

Produced by the Communications Service of CHU Sainte-Justine Reasearch Center, 3175 chemin de la Côte-Sainte-Catherine, Montréal Qc H3T 1C5.

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CHU Sainte-Justine Research Center
Mother and Child University Hospital Center

Université de Montréal

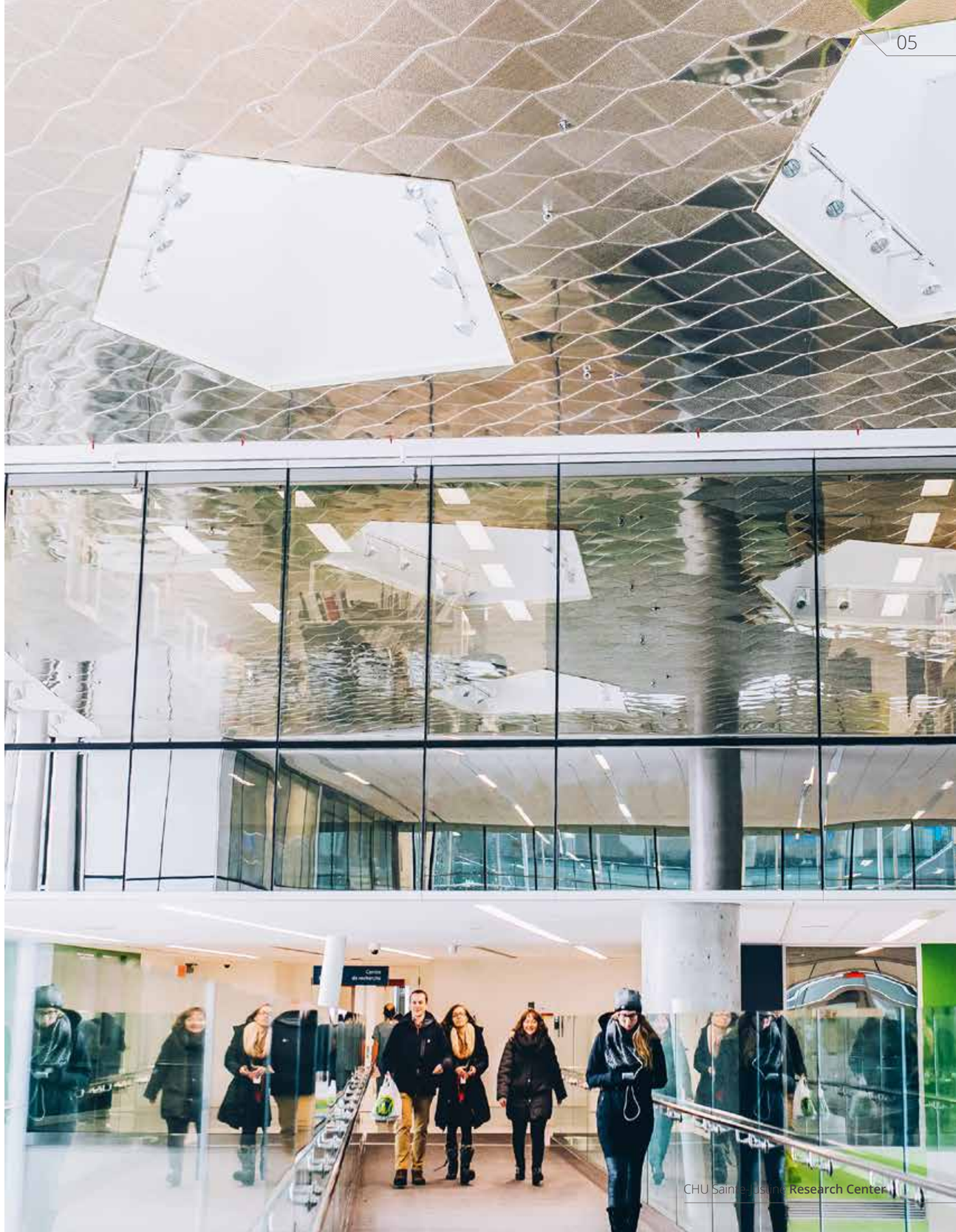
A Message From Our Director...
Dr. Jacques L. Michaud

Dr. Jacques L. Michaud

It is now over a year that I was appointed as Director of Research. This first year has been very exciting and certainly busy. The CHU Sainte-Justine Research Center (Research Center) has the wind in its sails as indicated in the high success rates in national and provincial competitions, key recruitments and partnerships with academic and industrial leaders. We have initiated major changes by reorganising the structure of our research axes and focussing our efforts on initiatives that will transform our Institution. I am privileged that with the start of my mandate the new state-of-the-art Research Center had just opened its doors. With more than 26,700m^2 supporting multidisciplinary research communities with cutting-edge infrastructure, **this center marks 2017 as a new start to shape the future of multidisciplinary perinatal and pediatric research in Quebec**. In this exciting momentum, we also succeeded to launch a brand new microscopy platform through collaboration with Leica Microsystems. Investigators now have access to the newest microscopic technologies to advance their research.

The mission of the CHU Sainte-Justine (CHUSJ) is to improve the management and care of patients. As such, we are concentrating our efforts to translate discoveries toward the clinic. In this respect significant progress on a number of strategic priorities and initiatives have been made, including a centralized biobank facility for rare pediatric diseases. We have significantly invested in clinical research by improving the infrastructure and procedures for clinical trials through funding from the Ministry of Economy, Science and Innovation (MESI). Finally, we are in the midst of developing a Big Data strategy for our Institution that will enhance our current expertise in machine learning and leverage clinical information that will become available over the coming year.

Finally, I want to say a word of thank to our dedicated partners, in particular the Fondation Charles-Bruneau who has committed $22M to support cutting-edge research in pediatric oncology and the Sanfilippo Children's Research Foundation for its support to develop new therapeutics for Sanfilippo neurodegenerative disease. Without such support from foundations and donors, research would not be where it is right now. Last, but not least, I have a special word of thanks for the CHU Sainte-Justine Foundation (CHUSJ Foundation), with engaged members and volunteers, who are doing tremendous work to raise interest in our cause with the public. Their enthusiasm for the research is stimulating and I am pleased to have them at our site for our cause that **today's research leads to the care of tomorrow**.



...and Main Partners

Ms. Isabelle Demers

Ms. Isabelle Demers, Chief Executive Officer, CHUSJ

Over the last year, the achievements of the Research Center have fostered a real boom in the proposal of new scientific knowledge aimed at improving the health of mothers and children in Quebec. This makes it a leading player in the fulfillment of CHUSJ's mission. Among these highlights, the recruitment of world-renowned researchers, the implementation of state-of-the-art infrastructures, the implementation of innovative projects and the support of provincial, federal and international institutions have allowed us to provide real leadership in the field of mother-child health. Added to this is the collaborative work done through many partnerships established not only in Canada but in more than 50 countries. The integration of these expertise and the synergy that results from it contribute to advance knowledge and accelerate their transfer to the bedside.

Because of the uniqueness of the CHUSJ and its continuum of care, from conception to adulthood, the research work carried out here above all makes it possible to offer innovative diagnostic, prognostic and therapeutic tools that transform mother-child care not only in Quebec but also in Canada and abroad.

Ms. Maud Cohen, President and Chief Executive Officer, CHU Sainte-Justine Foundation

Research at CHUSJ is an undeniable strength of the institution. A strength to which our donor community wants to associate and contribute. The success of our *Healing More Better* campaign, concluded in March 2018, is in part based on your daring, collaboration, and passion. The last few years have shown us the incredible potential of scientific and philanthropic community collaboration such as ours. The leverage effect created by the commitment of our donors, combined with the vision and talent of your teams, has the power to accelerate the pace of discovery. Justine Lacoste-Beaubien dreamed of a healing center, but also of a scientific environment of studies and research. One hundred and ten years later, there is no doubt: mission accomplished!

Each of our encounters is a source of great pride. Thank you for inspiring us. Thank you for embodying a vision of innovation, future, hope. Your dreams are wild, and ambitious, but with you behind, everything is possible. More than anything, we are determined to help you achieve them.

With you, the future of Sainte-Justine is safe.

Ms. Maud Cohen

Ms. Marie-Josée Hébert, Vice-Rector for Research, Discovery, Creation and Innovation, UdeM

Ms. Marie-Josée Hébert

The Université de Montréal is very proud to have the CHU Sainte-Justine Research Center among its closest partners. The Research Center is an important leader on the global stage of research with the ultimate goal to improve the health of mothers, adolescents and children. Passionate researchers, international students, dedicated highly qualified personnel and state-of-the-art infrastructure enable the pursuit of innovative projects that have a real impact on health. The Research Center is also an essential cornerstone for the training of the next generation of scientific leaders. If the Université de Montréal ranks third in university research in Canada, it is partly thanks to you, dear friends and colleagues.

This partnership cherishes our vision of excellence and gives us confidence that we will be able to meet the challenges of tomorrow. We will continue to work together with your research teams to improve health in Quebec and around the world.

Thank you!

Prevent disease with early screening;
Diagnose clearly and precisely;
Treat with precision;
Heal with novel and humanistic approaches stemming from research.

408 Research Contracts & Agreements

Mission, Values and Goals

Ensuring Mothers, Children and Teens Health

Founded in 1974, the **Research Center** is a leading Canadian mother-child research institution affiliated with Université de Montréal. It nurtures the vision of a Quebec where mother, child and adolescent health ranks among the best in the world. With this in mind, it is intent on fulfilling its mission of **advancing knowledge and applying new findings with faster and less invasive methods and devices aimed at disease prevention, diagnosis, treatment, and long-term follow-up starting at conception and pregnancy and continuing right through to adulthood**.

Bursting With Talent

Working closely with healthcare teams, CHUSJ's research teams are engaged in fundamental, clinical, and translational research within either of the Center's six research axes: **Brain and Child Development**, **Fetomaternal and Neonatal Pathologies**, **Immune Diseases and Cancer**, **Infectious Diseases and Acute Care**, **Metabolic and Cardiovascular Health** and **Musculoskeletal Health, Rehabilitation and Medical Technologies**.

+1200 Individuals

543 Students

+600 Publications

14 Patents Filed

+200 Researchers

11 Inventions & Disclosures

6 Research Axes

Research Axes
Brain and Child Development

The CHUSJ is the major pediatric center in Quebec for the **clinical evaluation of neurodevelopmental disorders**, such as intellectual disability, epilepsy and autism spectrum disorders. A second important focus is to **understand the development of psychopathologies**. It has been estimated that one out of five children has attention or communication problems, anxiety, is hyperactive of impulsive or shows aggressive behaviour before adolescence.

Researchers within the axis have diverse expertise in neurosciences and developmental psychopathology and take advantage of data from longitudinal studies to provide breakthroughs in diagnostics as well as management and interventions for these complex diseases.

The main goals of this integrated research program are to:

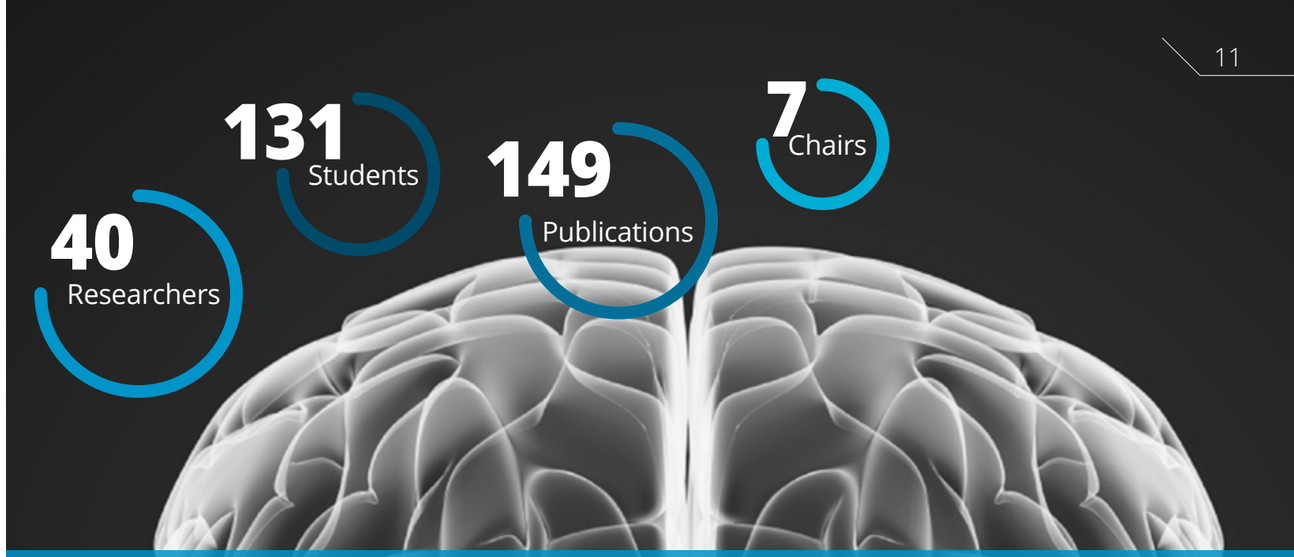
1. **identify genetic and environmental determinants of neurodevelopmental disorders;**
2. **understand the impact of these determinants on the development of neuronal circuits;**
3. **characterize neurodevelopment phenotypes in children using diverse approaches including imaging, electrophysiology and neuropsychological approaches with the goal to find biomarkers allowing early diagnosis and intervention of children at risk and:**
4. **combine the data obtained through patient phenotypes and functional analysis to inform the development of new therapeutic approaches/interventions.**

For example, our researchers have demonstrated that the pre-adolescent difficulties are good predictors for several forms of psychopathologies, including depression, substance addiction, anxiety or borderline syndrome, emerging at adolescent or adult age. Different large initiatives have been put in place such as the **Co-Venture Project**, a cluster randomized trial investigating the effects of delaying the onset of substance use on adolescent cognitive development, involving several high schools in the Montréal area.

Researchers from the axis have a leadership role within the **GRIP (Groupe de recherche et d'intervention psychosociale)**, a multidisciplinary group that contributes to the understanding of the development of adjustment problems in children and youths, and to the identification of the most effective means to prevent these problems. GRIP researchers work with families, school personnel and school boards.
They have established partnerships with provincial and federal departments, and private foundations, to conduct longitudinal studies and transfer new knowledge to policy makers, and to the general public.

Themes

- **Neurodevelopmental diseases**
- **Development of psychopathologies**



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Clinician
+ 2017-2018 Recruitment

Recruitments

Decoding the Enigma of Memories and Behaviour

Dr. Bénédicte Amilhon is a neurobiologist, who has trained with Dr. Salah El Mestikawy at the University Pierre and Marie Curie in Paris, where she studied the role of *VGLUT3*, an atypic glutamate vesicular transporter, in cholinergic neurons of the striatum and serotonine neurons of the raphe. She continued her studies as post-doctoral fellow with Dr. Sylvain Williams at the Douglas Mental Health Institute of McGill University on modulation of the theta rhythm of interneurons in the hippocampus that has a central role in her current research program.

How memories influence our behaviour has always intrigued Dr. Amilhon. The communication between brain regions through specific neuronal networks is what ultimately allows the neuronal activity to translate into behaviour. Understanding how these networks operate and lead to specific behaviours is one of the biggest challenges in neurosciences. It has been long recognized that memory plays a key role in determining how we respond to certain situations, particularly the ones that are formed in a heavy emotional context, either positive or negative. Response to those traumatic situations can also lead to dysfunction in memory formation resulting in general anxiety or post-traumatic stress disorder. Dr. Amilhon **investigates how the brain is linking emotion and memory by studying the neural circuit of the ventral hippocampal, the region in the brain that plays a central role in learning and memory**. Her research will provide a wealth of fundamental data on the physiology of ventral hippocampus networks, and circuit interactions in context with emotional behaviour and memory.

Dr. Inge Meijer

Dr. Inge Meijer is a child neurologist, who trained with Dr. Guy Rouleau to study the genetic basis of neurodegenerative diseases and obtained a medical doctor's degree in child neurology. She specialized in pediatric movement disorders at the Mount Sinai Beth Israel in New York, the most renowned movement disorder center in the world on a fellowship from the American Academy of Neurology. Dr. Meijer's research program will focus on pediatric movement disorders. She is particularly interested on a novel dystonia gene she identified together with her colleagues from CHUSJ, Drs. Julie Gauthier and Philippe Campeau.

Dr. Meijer's goal is to combine her knowledge in neurogenetics and pediatric movement disorders to **study the genetic basis of pediatric dystonia** and further **characterize the function of the newly identified *VPS13D* gene to discover new dystonia treatments**. She will also **develop a prospective Tourette syndrome cohort to better understand the fluctuation of tics and how to improve their treatment**.

Profile

Cellular and Network Basis of *CACNA1A* - Associated Epileptic Encephalopathies

Epilepsy is a common disorder affecting 0.5-1% of the general population with more than 30% of the patients not responding to standard therapies. Epileptic encephalopathies, presented in early childhood, comprise the more severe cases; however, the molecular basis of these pathologies is poorly understood hindering the development of efficient therapies. **Dr. Elsa Rossignol**, a clinician-researcher is investigating the mechanisms that lead to epilepsy. She discovered that **mutations causing loss or gain of function in the *CACNA1A* gene are associated with epileptic encephalopathies**.

Dr. Rossignol found that deletion of this gene reduces cortical inhibition and induces seizures in mice. Recently, she identified mutations in the *CACNA1A* gene in children with epileptic encephalopathy and profound intellectual deficiency. She hypothesizes that the cortical inhibition/excitation ratio is reduced by the mutations and postulates that this can be reverted by stimulating the cortical interneurons. With recent support from the Canadian Institutes of Health Research (CIHR), Dr. Rossignol will now generate human stem cell-derived neurons and introduce patient-specific mutations using gene-editing and test the impact of the *CACNA1A* mutations on the calcium channel function in these neurons and on the functional integrity of neuronal networks. Dr. Rossignol received the 2015 Junior Investigator Award from the Canadian League against epilepsy and has been funded through national funding agencies.

Selected Publication

A New Model to Predict the Effect of Genetic Mutations on Intelligence

How to measure the impact of genetic mutations on cognitive functions has been a major challenge in neurodevelopment, as the effect of 90% of such mutations in neurodevelopmental and psychiatric disorders are unknown. In a collaboration with researchers from the Institute Pasteur in France, **Dr. Sébastien Jacquemont** developed a **model that permits to predict the effect of genetic variants on general intelligence of an individual** (*JAMA Psychiatry*). The model allows to estimate the reduction of intellectual quotient points induced by a deletion based on the biological function of the protein encoded by the affected gene. Results show an increasing risk to develop neurodevelopmental disorders with increasing number of genes associated with cognitive functions carrying mutations. The model has been validated with data from previous studies and shows concordance rates of 75% with reported IQ loss across the different cohorts. This new approach to analyse the effect of mutations on general intelligence is of particular value for studying rare mutations, which cannot be addressed using conventional methods. The information obtained by the model will allow for better clinical management of children that are at risk of developing neurodevelopmental disorders.

Research Axes
Infectious Diseases and Acute Care

CHUSJ is a reference center for the prevention, diagnosis and management of infectious diseases that affect pediatric patients and pregnant women in the Province of Quebec. It is also the main center for pediatric emergency medicine, trauma, and intensive care. Our institution is the only one in Quebec to group these specific fields of expertise.

In this context, the mission of the axis consists of the following priorities:

1. **develop decision-making tools for acute/severe diseases**
2. **develop guidelines and implement programs on prevention of infections**
3. **develop personalized pharmacological approaches for the treatment of infectious diseases**
4. **investigate and understand the mechanisms of resistance to antimicrobial agents.**

By bringing together clinical researchers and researchers in basic sciences working at CHUSJ in the above-mentioned themes, the axis main goal is to **ensure translation from research to bedside but also reverse translation by bringing questions from the bedside to bench**.

In addition to being key players at CHUSJ and its Research Center, many of the axis members are researchers recognized in their particular fields of expertise. Some of them have played key roles in nucleation of networks and major projects at the provincial, national, and international levels.

Themes

- **Infection, immunity and inflammation**
- **Respiratory health**
- **Critical care, trauma and transfusions**
- **Prevention of infections**
- **Clinical pharmacology**

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Clinician
+ 2017-2018 Recruitment

Recruitment


Dr. Caroline Quach-Thanh

Tackling Prevention and Control of Infectious Diseases

In Canada, the total economic burden of healthcare-associated infections (HAI) is estimated at close to $110 billion CAD/year, with 11.6% of hospitalized adults developing at least one HAI. A major problem to cure infectious diseases is the widespread antimicrobial resistance (AMR). **Dr. Caroline Quach-Thanh,** a pediatrician, microbiologist and infectious disease specialist aims to tackle HAI issues. She recently became the physician responsible for infection prevention and control at the CHUSJ and pediatric medical director at OPTILAB Montréal-CHUM. Dr. Quach-Thanh graduated at UdeM, completed her pediatric residency at CHUSJ and her postgraduate training in microbiology and infectious diseases at McGill University, where she worked for more than 10 years. Dr. Quach-Thanh's research has as objective to **reduce and ideally overcome infections, in particular HAI, and decrease AMR, through 1)** the understanding of modifiable risk factors leading to infections, **2)** validation of systems used for HAI surveillance, and **3)** evaluation of implemented interventions.

She has performed ground-breaking work that merited awards and distinctions, such as the 2015 SHEA William Jarvis Award for the best international paper in infection prevention and control and the highly competitive Chercheur-boursier de mérite from the Fonds de recherche du Québec - Santé (FRQS). Her expertise is recognized at the national and international level as the Chair of the Quebec Immunization Committee and the Chair of the National Advisory Committee on Immunization, representing Canada on the CDC – Advisory Committee for Immunization Practices and on the WHO Global NITAG (National Immunization Technical Advisory Group) Network. **These leadership positions are allowing Dr. Quach-Thanh to identify knowledge gaps, establish new research collaborations, but also to have direct knowledge translation of her work, from research to policy**.

Profile

Improving Care for Asthmatic Children All Over the World

Dr. Francine Ducharme, a clinical researcher, pediatrician and epidemiologist at CHUSJ and Professor in the Department of Pediatrics at UdeM, has dedicated her career to improving the management of pediatric asthma. Her research program has been deployed on several fronts. Dr. Ducharme has **developed instruments to evaluate young children with asthma** who were previously excluded from major studies for lack of validated tools. She also set up **large interventional and observational clinical trials on asthma**. Finally, she **developed methods aimed at improving adherence to guidelines by health professionals, patients and their families**. Dr. Ducharme's journey is simply remarkable. Her work has resulted in 175 peer-reviewed publications as well as 15 editorials and commentaries in high-impact journals, such as the *New England Journal of Medicine*, the *Lancet*, the *British Medical Journal*, and the *Journal of the American Medical Association*. She held a leadership role in the **development of Evidence-Based Canadian Asthma Guidelines** and has also developed recommendations for pulmonary function tests and evaluation of infants and young children with respiratory diseases who were sponsored by the American Thoracic Society and the European Respiratory Society. Dr. Ducharme's research program led to the development and integration of guidelines in current practice, improving care for asthmatic children all over the world. There is no doubt that she has greatly helped bridgeing the gap between evidence-based medicine and current care provided to children in Canada and abroad and reducing congestion in the emergency room.

Publication

Vertical Transmission of Hepatitis C Virus in Early Pregnancy

Hepatitis C is a chronic disease of the liver affecting more than 250,000 Canadians that is caused by hepatitis C virus (HCV). This disease can lead to cirrhosis, hepatic dysfunction, and, in certain cases, necessitates the patient to undergo liver transplantation. Hepatitis C tends to worsen after pregnancy in infected women. In addition, HCV can be transmitted to the child during pregnancy and childbirth. However, the timing and precise biological mechanisms of this process are poorly understood, as are the determinants that influence transmission of particular HCV variants. The work of **Pr. Hugo Soudeyns** and his team are aimed at **understanding the mechanisms that lead to the worsening of hepatitis C**, at **defining the role of the immune system in the control of this disease**, and at **identifying the precise manner (where, when and how) by which HCV is passed from the mother to the child**. A study recently published in *Journal of Virology* now sheds light into this question and shows transmission could take place comparatively early in pregnancy. Furthermore, it was found that when the mother also carried human immunodeficiency virus type 1 (HIV-1), many more HCV variants were shared between her and her child, suggesting that the mechanism and/or the route of transmission of HCV differed in the presence of coinfection with HIV-1. These results could explain why caesarean section is ineffective in preventing vertical HCV transmission and guide the development of interventions to avert pediatric HCV infection.

Research Axes
Immune Diseases and Cancer

The CHUSJ is responsible for the diagnosis and treatment of more than 65% of pediatric cancers in Quebec and is the only accredited pediatric bone marrow transplantation center in Quebec. Also, the CHUSJ is one of the world leaders for research and management of patients with immune diseases. To address the medical issues related to immune disorders and cancer, the axis has strategically prioritized **research in hematopoietic malignancies** as well as **functional genomics** and **cell/gene therapy** for both immune diseases and cancer.

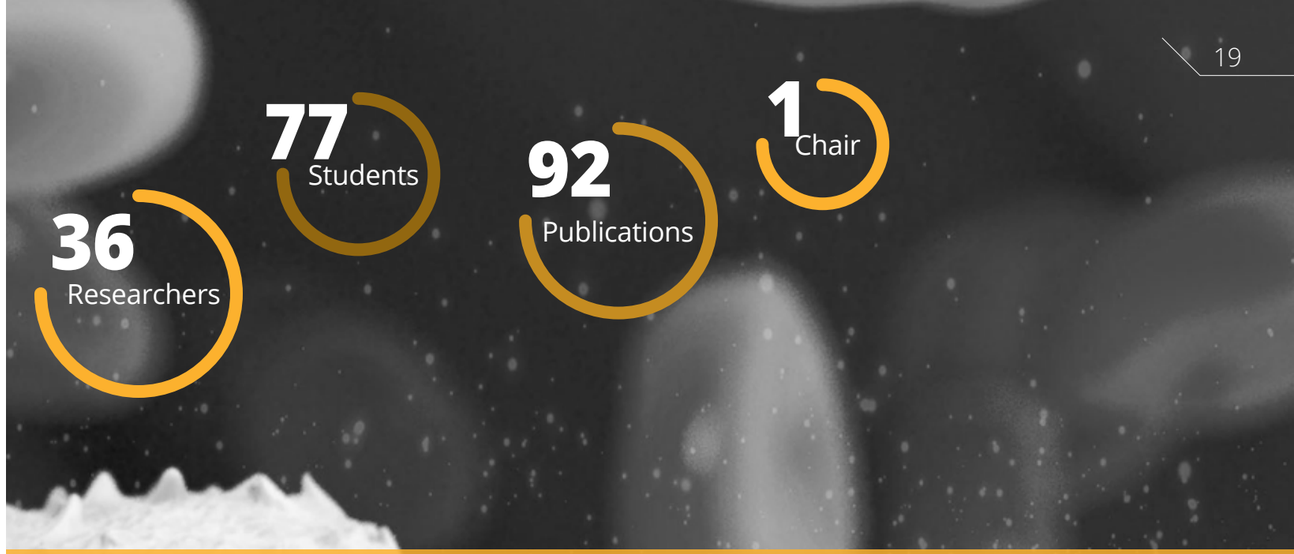
Cell-based immune therapy, such as the **chimeric antigen receptor (CAR) T cells**, is currently the most promising therapy for treatment of certain types of cancer. This year the world saw the first CAR T cell trial being approved by the Food and Drug Administration (FDA) to treat children. Our researchers are developing new and creative solutions for more efficient, safer and sustainable CAR-based cell therapies going beyond the T cells. Furthermore, identification of proteins that leukemia stem cells need to survive and thrive is a major goal in the field, because such proteins represent new targets for treatment. **Genomics**, **proteomics**, **single-cell analysis**, and **disease modelling** are part of the functional genomics strategy to **understand the molecular signature of pediatric cancers** and **develop more efficient therapeutic approaches**.

The axis has also a strong expertise in fundamental immune biology to be exploited for **studying the mechanisms of immune diseases** and for the **development of new immunotherapies for a range of immune disorders and malignancies**. Efforts are also made to advance gene therapy for immune deficiencies and non-malignant hemopathies applying cutting-edge gene-editing approaches.

The axis has established important national and international collaborations, such as the Primary Immunodeficiency Treatment Consortium, the Children's Oncology Group (COG), the Dana Farber Cancer Institute, the Pediatric Blood and Marrow Transplant Consortium and as such has been strongly involved in Phase I and II clinical trials for pediatric cancer patients, patients suffering immune disease or transplant complications.

Themes

- **Immune diseases: mechanisms, new therapeutic approaches and disease outcomes**
- **Cancers: mechanisms, new therapeutic approaches and disease outcomes**
- **Severe hematologic diseases**



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Clinician
+ 2017-2018 Recruitment

Recruitments

Empowering Predictive Medicine Using Artificial Intelligence

Dr. Philippe Broët has a MD in Public Health from the University Pierre-et-Marie-Curie and holds a PhD in Biostatistics from the University of Paris-Sud. Before being recruited at CHUSJ, he was team leader at the Genome Institute of Singapore and has been involved in EU consortia (Abirisk) and Europe-Asian partnership (Merlion). Dr. Broët is Professor at the Department of Social and Preventive Medicine at the School of Public Health (ESPUM) at the UdeM and he is co-scientific director of the CARTaGENE cohort. His research activities at the CHUSJ focus on **predictive medicine and its clinical applications in oncogenomics**.

In the era of genomics, statistical modeling has been developed as a powerful tool to decipher complex diseases. As a medical doctor and biostatistician, Dr. Broët embarked early in this field first by using association studies and later by developing new statistical methodologies to analyze genomic profiles of lung adenocarcinomas and their alterations. Currently, he is focussed on **predictive medicine with clinical applications in oncogenomics and immunogenomics using machine learning and artificial intelligence**. Recently, he generated a **strategy to identify common immunogenetic pathways adapted for time-to-event** with the aim to predict how individual patients with autoimmune disease are likely to produce antibodies against biotherapies. Now, Dr. Broët wants to combine several approaches for prediction for tailored applications in real-world medicine problems in situations with small number of patients (rare diseases) where high-dimensional data, such as genomics, are available. He will interrogate data from the PETALE cohort of pediatric leukemia survivors and CARTaGENE for predictions related to immune diseases and lung cancer.

The axis also recruited **Dr. Thai Hoa Tran**, a clinician-researcher, who is interested on translating genomic discoveries into novel therapies for pediatric leukemia patients. Dr. Tran did his medical training at McGill University and a fellowship at the Hospital for Sick Children in Toronto. In the lab of Dr. Mignon Loh at the University of California San Francisco he investigated the drug resistance of a leukemia subtype characterized by a gene expression profile resembling those of leukemias with the Philadelphia (Ph) chromosome. Dr. Tran continues to investigate these Ph+ like leukemias. His research program entails to:

1. **validate whether new generation sequencing (NGS) can be used to diagnose these leukemias**
2. **perform a prospective feasibility clinical study to test whether this NGS approach can be performed in a timely matter**
3. **investigate whether adding relevant tyrosine kinase inhibitors to the treatment will improve the disease outcome.**

Profile

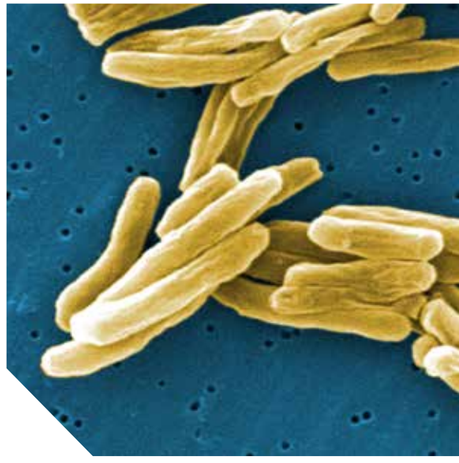
Innovative Immunotherapy to Prevent Leukemia Relapse

Hematopoietic stem cell transplantation is the therapy of choice for chemotherapy-resistant leukemias. However, leukemia relapse remains the first cause of death after haematopoietic stem cell (HSC) transplantation. Immunotherapy has proven its efficacy against chemotherapy refractory cancers, but several limitations for current therapies remain. **Dr. Michel Duval** has dedicated his work to pioneer an **immunotherapy with plasmacytoid dendritic cells (pDC)**. These cells are required to present tumor antigen to T cells, which in turn will mount an immune response against cancerous cells. In a preclinical animal model, Dr. Duval has demonstrated that pDCs activated in vitro can eliminate human leukemic cells. Dr. Duval is now further fine-tuning the therapeutics conditions to prevent T cell mediated graft-versus-host disease, which is the major side-effect of hematopoietic stem cell transplantations. Dr. Duval collaborates with the Centre d'excellence en thérapie cellulaire at the Hospital Maisonneuve-Rosemont to produce GMP-grade pDCs for use in humans in preparation of a Phase I/II clinical trial to treat leukemia patients following HSC transplantation. Dr. Duval is the director of the Cord Blood Transplantation research lab and has successfully led multiple clinical trials. He has been supported by funds from organizations including CIHR, FRQS and the Fondation Charles-Bruneau and recently by BioCanRx for the translation of the pDC immunotherapy.

Publication

First Evidence for Memory Immune Responses Generated by the Innate Immune Cells

Pr. Luis Barreiro's team shed light on the capacity of the innate immune system to generate memory immune responses. This study published in the journal *Cell* demonstrated that exposure of hematopoietic stem cells (HSC) to bacteria Bacillus Calmette-Guérin (BCG) leads to a change in the HSC transcriptional profile and that of their immediate descendants resulting in a higher propensity to differentiate into myeloid cells at the expanse of lymphopoiesis. Importantly, the macrophages produced by the BCG-exposed HSCs provided better protection against virulent tuberculosis infection than naïve macrophages. These results show that **innate memory response can be generated through HSCs, which may provide a novel strategy for vaccine development**.



M. Tuberculosis

Research Axes
Fetomaternal and Neonatal Pathologies

Every year in Quebec, 8,000 at-risk pregnancies expose both mother and child to serious complications. In addition, 10% of children are born prematurely <37 weeks of gestation and 3% have a congenital malformation or a neonatal condition (asphyxia, infection) requiring specialized care. The health of the mother and child is at the heart of the hospital's mission and CHUSJ is positioned as the **largest mother-child center in Canada**; it has unique expertise in treating mothers with at-risk pregnancies, which represent more than half of the hospital's 3,600 annual deliveries, and the sickest newborns (1,000 admissions/year, 2/3 of which are prematurity). In line with this medical need, the axis research themes focus primarily on **embryonic and fetal developmental abnormalities**, **pregnancy and birth complications**, and their **long-term consequences**.

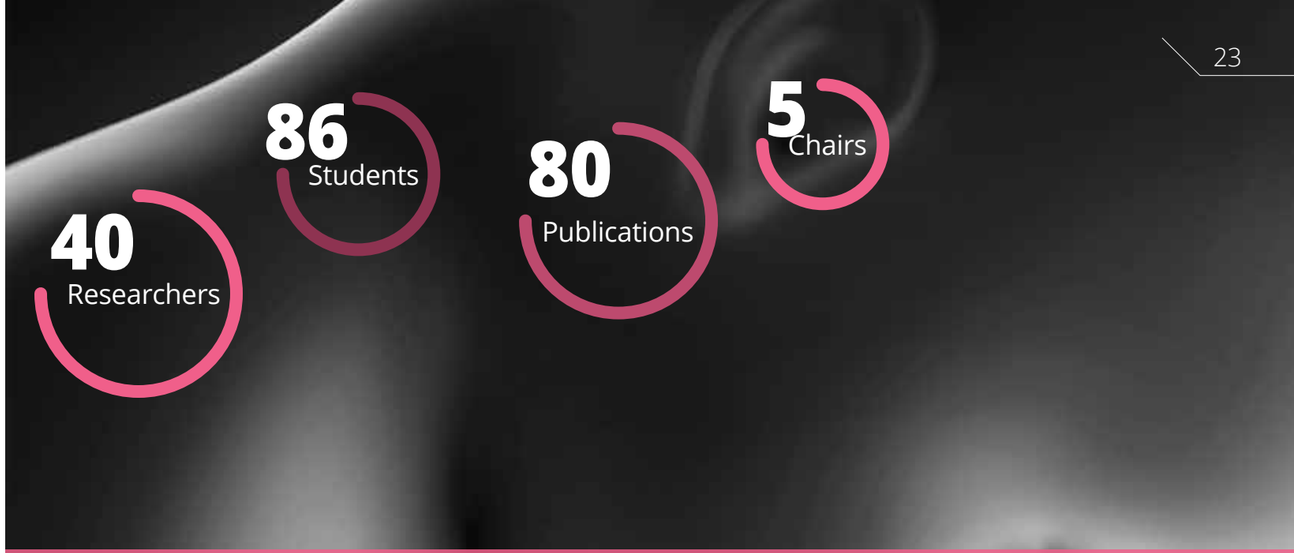
The future of children is determined from conception by the **health, first and foremost, of the mother**, the **intrauterine environment**, and the **conditions surrounding birth and the first days of life**. The axis interested in this critical period of **ontogeny** with a more focused interest in organic systems such as the heart, vessels, and brain. Collectively, the goals are to:

1. **identify the environmental and genetic risk factors associated with fetal-maternal complications and congenital and neonatal diseases**
2. **understand the pathophysiological, cellular, and molecular mechanisms underlying these disorders**
3. **develop and validate interventions to change the future of mothers and children**
4. **reflect on the ethical issues surrounding our care decisions sometimes at the limit of human viability.**

The axis builds upon **major cohorts** such as the Cohort of Quebec Pregnancies (450,000) and Health of Adults born Preterm Investigation (HAPI), to **biobanking of samples from rare diseases** as well as **national networks** such as the Canadian Neonatal Brain Platform and **international networks** (Human Cell Atlas). Their approach conceptualizes health as a continuum that begins with conception and continues into adulthood. The various research programs are grouped around this theme and serve a common goal: the **development of interventions that will improve the health of mothers and children**.

Themes

- **High-risk pregnancies**
- **Fetal development and prematurity**
- **Mechanisms of congenital abnormalities**
- **Bioethics and family study group**



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CHAILLET, Nils
CHEMTOB, Sylvain
DAVID, Michèle
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DUMONT, Alexandre
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FRASER, William D.
GOSSELIN, Julie
HARDY, Pierre
HATEM, Marie
INFANTE, Claire
JANVIER, Annie
LEDUC, Line
LEFEBVRE, Francine
LODYGENSKY, Gregory A.
MCGRAW, Serge
+ MOUSSA, Ahmed
NUYT, Anne Monique
OLIGNY, Luc Laurier
PAYOT, Antoine
PHAN, Véronique
REY, Evelyne
SANSREGRET, Andrée
SIMARD, Marie-Noelle
+ TREMBLAY, Sophie
VAN VLIET, Guy
WEI, SHU QIN

Clinician
+ 2017-2018 Recruitment

Recruitments

Advances in Preterm Births: from Medical Simulation Teaching to Neuroprotective Strategies

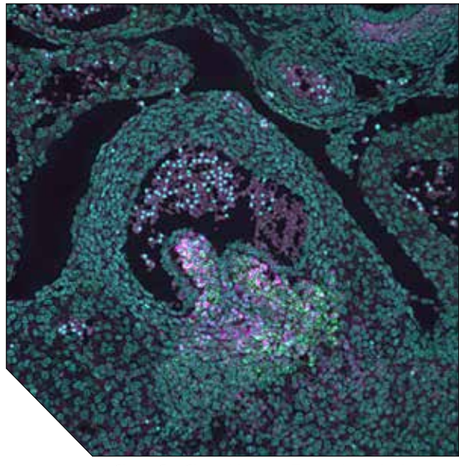
At birth, 10% of newborns require resuscitation, many are then hospitalized in the Neonatal Intensive Care Unit because of their critical condition. Healthcare providers involved must master resuscitation techniques, teamwork/communication skills, and optimal relational skills to communicate with parents. **How do we best teach healthcare providers these competencies? Dr. Ahmed Moussa** has a unique tract-record on research in medical education. Following the completion of his medical degree at UdeM, he completed his residency training in Paediatrics, UdeM and subspecialty training in Neonatology at University of British Columbia in Vancouver and later completed a MSc degree in Medical Education at Dundee University in the UK. He was then recruited as a neonatologist at the CHUSJ and a clinical associate professor at the Department of Paediatrics, UdeM, and more recently at the Research Center. Dr. Moussa fulfills his research work at the Mother-Child Simulation Centre and in diverse clinical units. His research objectives include: **1)** how simulation-based education can improve teaching of endotracheal intubation; **2)** how simulation-based education can improve teamwork/communication skills of interdisciplinary teams during acute critical events; **3)** how collaborating with parents can improve simulation-based education related to critical communication skills as well as optimization of organisational practises.

The axis has also recruited, **Dr. Sophie Tremblay**, a clinician-researcher, who has always been passionate about the nervous system. Dr. Tremblay holds a BSc in Biotechnology from the Université de Sherbrooke and an MSc in Neurosciences from Laval University. She then did her medical training at UdeM with a specialization in Perinatal and Neonatal Medicine at CHUSJ and she pursued a PhD in neurosciences at the University of British Columbia. Her research program focuses on **better defining the role of microglia, a type of brain cells, in various perinatal insults affecting the cerebellum of children born extremely premature to develop neuroprotective strategies**.

Profile

Cardiovascular Genetics: Healing Hearts one Cell at a Time

The genetic origin of approximately 90% of congenital heart-related abnormalities are still unknown today and 1% of new babies are born with such abnormalities. 1 in 1000 babies will be operated on and to date those operations do not offer a cure but only palliation.
Dr. Gregor Andelfinger is a cardiologist and researcher-clinician, who has dedicated his career in deciphering the genetic architecture underlying congenital heart disease. He received his MD from the University of Ulm (Germany) and his pediatric specialty at the University of Geneva. After his pediatric cardiology fellowship, he trained in Cardiovascular Genetics at the Cincinnati Children's Hospital and Molecular Cardiovascular Biology at the Institut de recherches cliniques de Montréal (IRCM), Montréal. Since 2006, he has established the first Canadian biobank specifically geared towards the investigation of the genetics of congenital heart disease in a province-wide effort. Dr. Andelfinger also uses stem cells to advance the knowledge in this field: ***Considering the opportunities offered to us through today's new technologies, such as induced pluripotent stem cells and single-cell genomics, we focus on the identification of mechanisms underlying serious cardiovascular diseases and the identification of new approaches for their prevention and therapy***. As part of the Human Cell Atlas Project, his lab is currently **deciphering and mapping cardiac progenitors cells using single-cell sequencing**, contributing to an international effort to create comprehensive reference maps of all human cells as a basis for both understanding human health and diagnosing, monitoring, and treating disease.



Single Cell Single Molecule Transcriptomics in the Developing Aortic Valve

Selected Publication

Combating Premature Births

Prematurity, which accounts for ~10% of births, is the world's leading cause of death and handicaps in newborns. This challenge may soon be history thanks to a **new molecule which prevents from being born too soon**. Interleukin-1 (IL-1) has been identified as a major mediator in triggering preterm labor. **Dr. Sylvain Chemtob** and his team have developed a heptapeptide (Rytvela) that inhibits the action of IL-1. Rytvela suppresses uteroplacental and fetal inflammation (murine model), prolongs pregnancy thus allowing fetal maturation, increases fetal survival and preserves fetal organ integrity including of brain. In a study published in *Journal of Immunology*, Dr. Chemtob's team investigated the effects exerted by antenatal exposure to IL-1β on the development of offspring. They focused on changes induced by antenatal inflammation, particularly on the onset of a fetal inflammatory response and gestational outcome. Their data in models of preterm birth uncover a major detrimental role of antenatal IL-1 on the development of adverse perinatal, neonatal, and developmental outcomes in progeny, and they suggest that Rytvela represents an effective therapeutic candidate for administration preferably during pregnancy to decrease neonatal morbidities. This project was a joined effort from Drs. Girard and Joyal at CHUSJ and Drs. Olson, University of Alberta and Adams-Waldorf, University of Washington. The PSRv4 grant from the MESI and the CIHR Foundation scheme grant obtained by Dr. Chemtob in 2017 supports the in-depth development of this innovative therapeutic approach. The next goals are: **1)** to complete pre-clinical efficacy by determining dose-response, and establish optimal treatment timing of Rytvela; **2)** Demonstrate effectiveness of Rytvela in a primate model; **3)** Validate its efficacy in human *ex vivo* placental conditions. Tackling as proposed premature delivery is projected to contribute significantly to the well-being of mothers and children, in line with the mission of the CHUSJ.

Research Axes
Metabolic and Cardiovascular Health

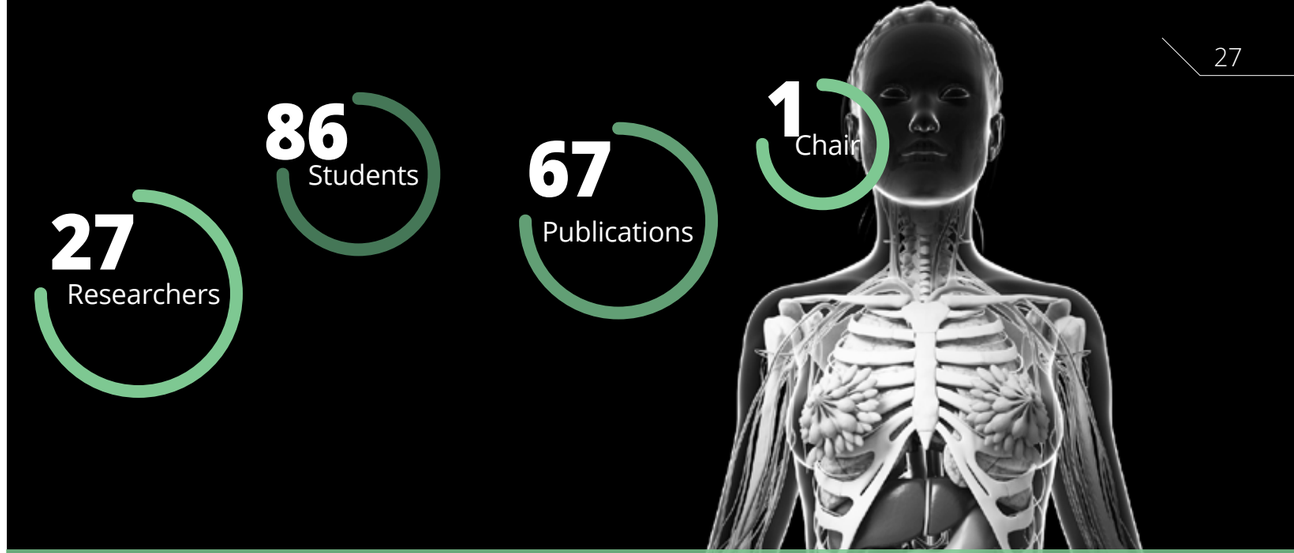
Although individually rare, collectively, inherited metabolic diseases represent a substantial population health burden in Canada and internationally. The axis represents the principal research unit in Quebec on **genetic pediatric diseases**, **non-transmittable chronic cardiometabolic** and **several nutritional disorders**. The CHUSJ has taken an important leadership role not only in pursuing research to identify the **genetic determinants of these diseases** and **develop efficient therapies and interventions** but also in pioneering **knowledge translation of findings in paediatric metabolic health** in Quebec. For example, cutting-edge work on identifying the genetic causes and mechanisms underlying hereditary tyrosinemia and neonatal hyperthyroid disease has led to implementation of new guidelines and changes in clinical practice.

The axis has created **important clinical cohorts** and has access to different types of biological samples from the local biobank with clinical data to address mechanistical and clinical questions related to metabolic diseases and nutrition. For example, **CIRCUIT** (Pediatric Intervention Centre for Heart Disease Prevention and Rehabilitation) was created to **improve health in children with a high risk of cardiovascular disease**, as well as **personalized intervention strategies related to the resources of their community** to **optimize their level of health**. CIRCUIT targets in particular recruitment of young people with conditions such as obesity, hypertension, diabetes, dyslipidemia or congenital heart disease.

On a global level our researchers contribute to major national and international initiatives and organisations in obesity, diabetes and cardiovascular health such as EPODE International, a world-wide network on childhood obesity.

Themes

- **Cardiometabolic and vascular health: from genetics to environmental approaches**
- **Genetic and metabolic diseases in Quebec: diagnosis, mechanisms and interventions**
- **Energy metabolism, stress and mitochondrial dysfunction**
- **Pediatric gastro-intestinal and liver diseases**



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+ DROUIN, Olivier
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LEVY, Émile Haim
MARCIL, Valérie
MATHIEU, Marie-Eve
MITCHELL, Grant
PSHEZHETSKY, Alexey
SAMUELS, Mark
ST-PIERRE, David H.

Clinician
+ 2017-2018 Recruitment

Recruitment


Dr. Olivier Drouin

Research in Lifestyle Behaviour to Prevent Disease and Improve Treatment Adherence

In line with the priorities on nutrition and metabolic health, the axis recruited **Dr. Olivier Drouin** as a clinical researcher for his **expertise in public health**, **lifestyle behaviour**, **general pediatrics** and **chronic disease prevention**. Dr. Drouin obtained a BSc and MSc in biochemistry from the University of Sherbrooke and McGill, respectively. He continued his studies in medicine at McGill University, where he also did a fellowship at the Institute for Health and Social Policy, and completed his residency in pediatrics at both Montreal Children's Hospital and CHUSJ. Dr. Drouin then moved to Boston at the Massachusetts General Hospital where he worked as a fellow with Drs. Winickoff and Taveras on the use of technology and behavioural sciences to help improve lifestyle behaviours in children. In parallel, he obtained a MSc in Public Health in Clinical Effectiveness at the Harvard TH Chan School of Public Health.

Dr. Drouin joined CHUSJ in 2017 to establish his research program to **develop new strategies to promote adherence to medication in childhood asthma** in collaboration with Dr. Francine Ducharme. He is also heavily involved in the CIRCUIT project and **explores innovative approaches to tackle pediatric obesity and cardiometabolic diseases**.

Profile

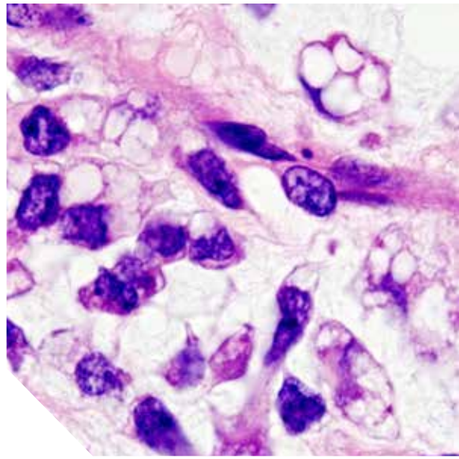
Risk Factors for Cardiovascular Disease and Diabetes

Dr. Mélanie Henderson is a pediatric endocrinologist with a PhD in epidemiology. Her research program focuses on the **etiology of obesity and their metabolic and cardiovascular consequences** as well as their **prevention in various populations including healthy and diabetic children**. In particular, she is interested in the **influence of lifestyle habits and obesity on metabolic health in youth**. Understanding how physical activity, sedentary habits, diet and sleep affect metabolic health in large cohorts is critical in developing effective preventive strategies for clinical practice and public health.

Recently, data analysis from the **QUALITY cohort** (Quebec Adipose and Lifestyle Investigation in Youth), which includes children with parental history of obesity, showed that children with at least one obese parent and who experienced faster weight gain in the first two years of life led to the presence of cardiovascular risk factors in early adolescence through its effect on childhood adiposity. Furthermore, data from the same cohort also showed a link between birth weight, rate of weight gain early in life and excess of childhood adiposity with risk factors for type 2 diabetes. These findings stress the need for monitoring children at risk to prevent childhood obesity and its deleterious consequences. In line with this work, Dr. Henderson has a leadership role in the **CIRCUIT program** and collaborates on several important initiatives, such as the **CARDEA project** (study to cardiovascular risk factors in youth with type 1 diabetes), **child metabolic health and foetal programming** and a **national initiative on stigmatisation of children with type 1 diabetes**.

Publication

A New Model to Study Liposarcoma


Myxoid Liposarcoma

Liposarcomas are malignant tumors of the fat. It is the commonest soft tissue sarcoma and the annual incidence is 2.5 cases per million. Specific biomarkers for early diagnosis and specific curative treatments are currently not available. The mechanisms underlying liposarcoma development and progression are poorly understood, but there is evidence that lipolysis, the pathway by which triglycerides are degraded, is implicated in cancer, both as a source of fatty acids for tumor growth and as a mechanism of cancer-associated wasting. In a publication in *PLoS Genetics*, **Dr. Grant Mitchell** reports the creation of mice with adipose tissue deficiency that may shed light on the involvement of lipolysis in tumor development. He has knocked out the genes *Pnpla2* and *Lipe* encoding for two major enzymes involved in the first steps of lipolysis, **adipose triglyceride lipase** (ATGL) and **hormone-sensitive lipase** (HSL), respectively. Mice that were lacking both enzymes all developed liposarcoma around one year of age, while no tumors occurred in mice knockout for only one of the genes. Analysis at the molecular level showed a dysregulation of a subset of genes already at three months of age in the adipose tissue. The same genes were found to be aberrantly expressed in human liposarcoma, suggesting a **potential use of these genes as early biomarkers of disease**. These mice thus provide a powerful new tool to study early stages of liposarcoma development, to find prognostic markers and test preventive treatments.

Research Axes
Musculoskeletal Health, Rehabilitation and Medical Technologies

The CHUSJ is a reference center for musculoskeletal diseases and pediatric rehabilitation, which is recognized by the CHUSJ as a pole of excellence. In alignment with the pole, this research axis aims to:

1. **understand the mechanisms of musculoskeletal diseases - improve prevention and early detection as well as develop diagnostic tools**
2. **design and develop innovative treatments/interventions that enable patient-tailored medicine**.

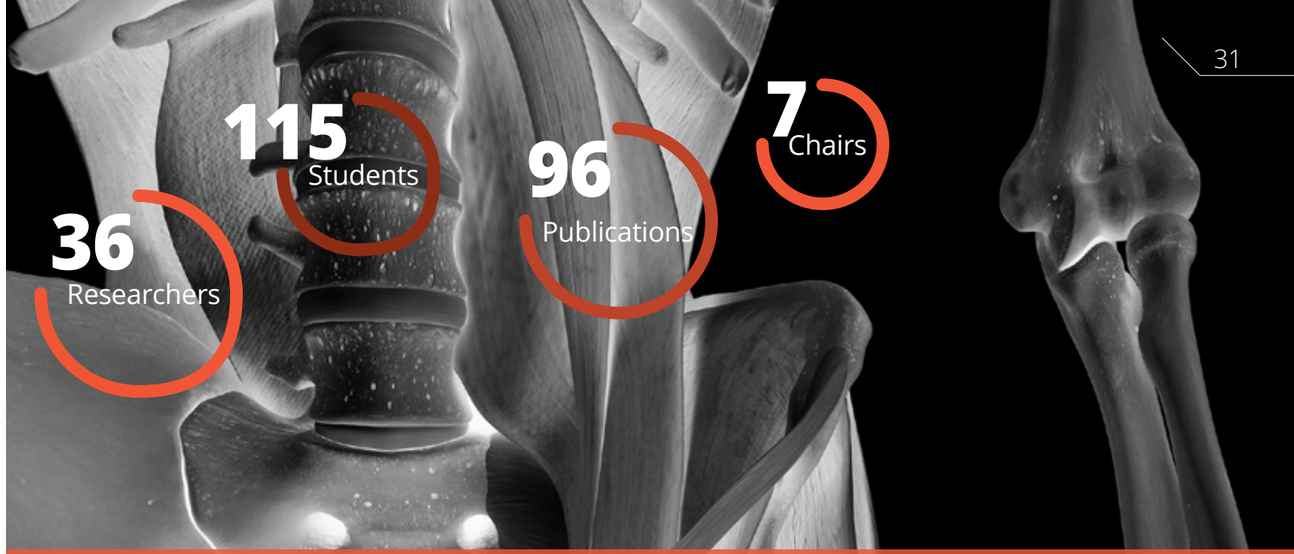
Our researchers have made several major breakthroughs in understanding the aetiopathogenic mechanisms of certain musculoskeletal diseases and paved the way for innovative and more efficient therapeutic approaches. At the level of pediatric rehabilitation at the Marie Enfant Rehabillitation Center (CRME), the convergence of disciplines and the excellence of our researchers allow us not only to **optimize the restoration of muscle and skeletal functions** for each child, but also to foresee, in some cases, the **possibility of cure the handicap**. Such achievements will ensure a better transition to the adult world. The nature of the axis is interdisciplinary, which is attested by the implementation of major initiatives such as the **Center of Excellence in Imaging and New Imaging Technologies**, the **TransMedTech Institute** ($95.6M) and the **Technopôle in Pediatric Rehabilitation** ($31M) uniting cutting-edge approaches such as:

1. **multimodal imaging and fusion;**
2. **engineering, modeling and design;**
3. **evaluative research and clinical epidemiology;**
4. **biology, genetics and mechanobiology;**
5. **evaluation and interventions.**

The axis builds upon major **industrial partnerships** with local (SAT) and international companies (Novartis, Medtronic, BostonBrace, Lagarrigue, DePuy, ParadigmSpine,) and has been successful in technology transfer and commercialization with many partners including Medtronic, EOS Imaging, BostonBrace, Rodin4D/Lagarrigue.

Themes

- **Mechanisms and more efficient approaches for spinal deformities and musculoskeletal diseases**
- **Development of diagnostic and prognostic technologies and new therapeutic approaches**
- **Pediatric rehabilitation and sports medicine**



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FORTIN, Carole
+ GAUVIN-LEPAGE, Jérôme
GRIMARD, Guy
HUYNH, Nelly
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MAC-THIONG, Jean-Marc
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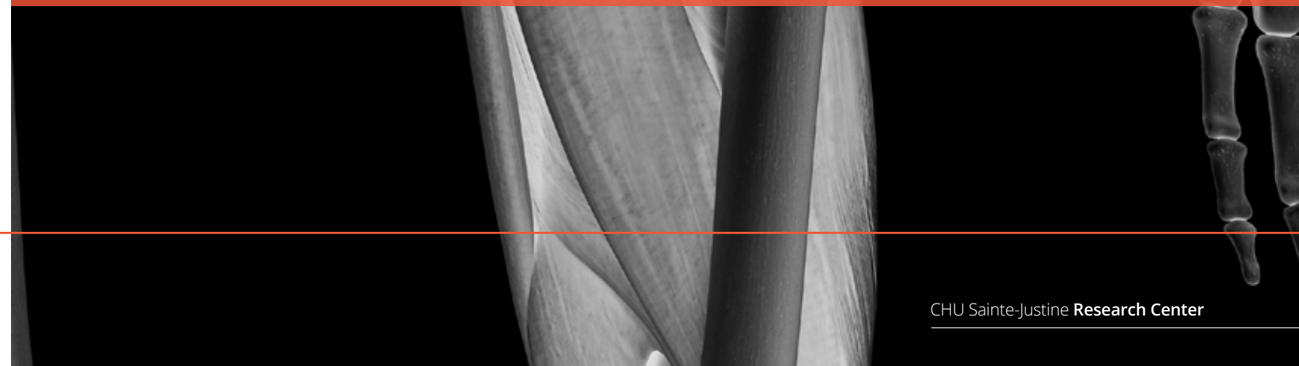
PERIE-CURNIER, Delphine
RAISON, Maxime
RAUCH, Frank
RUSHTON, Paula
SHILLER, Douglas
VILLEMURE, Isabelle
YAHIA, L'Hocine

Clinician
+ 2017-2018 Recruitment



Recruitment

Pr. Jérôme Gauvin-Lepage

Management of Neurotraumatic Lesions (NTL) through Functional Rehabilitation, Community Integration and Development of Interprofessional Interventions

With his expertise in physical rehabilitation and, more specifically, neurotraumatic lesions, **Pr. Jérôme Gauvin-Lepage** program is directly aligned with the Technopôle in Pediatric Rehabilitation. Pr. Gauvin-Lepage began his career as a nurse in the emergency room and intensive care (2001-2007) then specialized as a clinical nurse specialist in intensive functional rehabilitation (IFR; 2007-2013). He was then appointed as an Assistant Professor at the Faculty of Nursing of the UdeM following the completion of his doctoral studies. He then pursued his postdoctoral studies in rehabilitation sciences at McGill University, affiliated with the Montreal Children's Hospital.

Pr. Gauvin-Lepage's research focuses on **improving the future of youth suffering from neurotraumatic lesions in IFR** through the **development of strategies for reintegration in the community and social valorisation**. His program is part of the patient-family partnership paradigm put forward in recent years within the health system, which is an innovative approach to research and a framework in the priorities of our scientific planning. The originality and diversity of his interests allow Pr. Gauvin-Lepage to work with researchers from the Brain and Child Development research axis and the Center of Excellence in Pediatric Trauma, and to create collaborative projects with clinicians from the Clinical Research Unit in Adaptation-Rehabilitation at CRME.

Profile

Idiopathic Adolescent Scoliosis (AIS): A New Treatment Paradigm

AIS has a prevalence of 2-4%, with 280,000 young people in Canada and 66,000 in Quebec. **Dr. Hubert Labelle**, an orthopedic specialist in pediatric spine and a researcher-clinician internationally recognized for his research on spinal deformities, has dedicated his career in **understanding this condition** and **continuously developing innovative approaches to provide breakthroughs in the field**. With the continued support of CIHR since 1991 as principal investigator, he has led several projects on early detection, 3D assessment, and brace/surgery approaches of idiopathic scoliosis. He led **MENTOR**, a CIHR strategic training program in musculoskeletal diseases, bringing together 80 researchers from 5 Universities, who helped train 122 graduate students in this field.

His work has focused on the evaluation and treatment of scoliotic deformities in children and on the 3D evaluation and treatment of spinal deformities, with an emphasis on computer-assisted surgery, 3D design and evaluation of braces for the treatment of idiopathic scoliosis, as well as 3D evaluation and surgery simulations for scoliotic deformities. His leadership in the field has been recognised through the UdeM/CHUSJ Research Chair in Movement Sciences, whose activities of research are centered on the improvement of scoliosis treatments as well as president of the Canadian Orthopedic Research Society, the International Research Society of Spinal Deformities, in addition to leading the 3D Scoliosis Committee and the International Task Force on Scoliosis Screening. Over the past year, his research program was funded by the CIHR Foundation scheme to support his work on the 3D design of braces in AIS.

Selected Publication

New Genes Causing Rare Bone Malformations

Dr. Philippe Campeau's research themes are **developmental diseases of the bone**, and **DOORS syndrome**, combining epilepsy and bone abnormalities of the hands. The latter may be caused by mutations of *TBC1D24*, genes controlling the synthesis of glycolipid anchors, or epigenetic regulators. He has recently published novel genes for diseases associated with glycolipid anchors (*PIGP* and *GPAA1*) and epigenetic regulators (*ACTL6A*, *CHD4* and *BRPF1*). He also received CIHR funding for his work on *TBC1D24* and glycolipid anchors (2014-2019), and on an epigenetic regulator for the *BAF* complex (2017-2022).

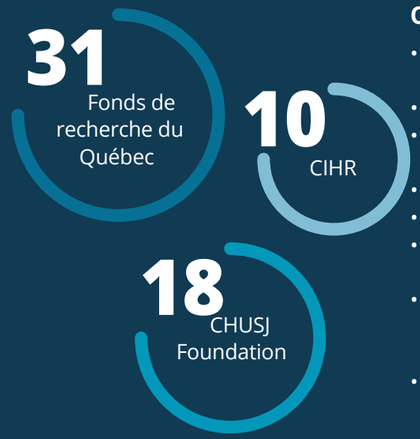
Among his many recent publications, he showed that mutations of fibronectin, a key component of the extracellular matrix, causes a new developmental bone disease with scoliosis and growth plate abnormalities (*American Journal of Human Genetics)*. This study highlights the need for collaborative efforts to tackle rare conditions and identify new treatments, and it is the result of a collaboration with clinicians and investigators from McGill (R. Hamdy, D. Reinhardt) and scoliosis experts at the CHUSJ (F. Moldovan, S. Parent). For now, twelve families around the world are identified with this disease. In the years to come there will certainly be many more families identified, guided by the publication of Dr. Campeau. Knowing the affected gene, it is now possible to understand how the mutation leads to the disease and how to eventually arrive at the therapeutic stage. Dr. Campeau's team is currently working on developing a mouse model of this disease so therapeutic approaches can be tested.

Training the Next Generation of Leaders

CHU Sainte Justine is affiliated with the **UdeM, the 3th most dynamic Canadian university in terms of academic research**, and fosters close collaborations with many other institutions of higher learning at the local, national, and international levels. The **Research Center provides a privileged place for training** graduate students, postdoctoral fellows, trainees, and interns who will make up tomorrow's workforce. The **senior investigators who mentor** our students seek to continually guide, inspire and stimulate their research teams to be at the forefront of their research domain.

PhD	MSc	Trainee	Intern	PDF
205	170	98	19	50

Scholarships



Other Sources

- Banting Postdoctoral Fellowships program
- Brain Canada Foundation
- Canadian Vascular Network
- Cole Foundation
- Défi Pierre Lavoie
- Institute for Data Valorisation (IVADO)
- Ministère de l'Éducation et de l'Enseignement supérieur (MEES)
- Mitacs Canada
- Natural Sciences and Engineering Research Council of Canada (NSERC)
- Ordre des infirmières et infirmiers du Québec (OIIQ)
- Polytechnique Montréal
- Savoy Foundation
- Social Sciences and Humanities Research Council
- Société québécoise d'hypertension artérielle
- UdeM
- Vanier Canada Graduate Scholarships Program

Spotlight on...

Joaquín Sanz Remon

2017-2019 Banting Postdoctoral Fellowship

Joaquín Sanz Remon began his postdoctoral research in bioinformatics in November 2014. **His project focuses on deciphering of genetic architecture of the interaction between M. tuberculosis and macrophages**. Joaquín was awarded a Postdoctoral Fellowship from the Fonds de recherche du Québec – Santé (FRQS) and a 2017-2019 Banting Postdoctoral Fellowship. He also co-authored two articles in *Cell*, an article in *Science* and one in *Proceedings of the National Academy of Sciences (*PNAS).

The support of this fellowship has made a huge difference in my research career, making really smooth the disciplinary leap that I pursued with my postdoc in CHUSJ. As a result, starting in spring 2019, I will begin a PI position in Spain under the umbrella of the prestigious Spanish program "Ramon y Cajal".

Lara Eid

2018-2020 Brain Canada-Kids Brain Health Network Postdoctoral Training Award

Lara Eid began her postdoctoral research in neuroscience in July 2016. **Her project focuses on altered migration of GABAergic interneurons in epileptogenic encephalopathies**. Lara was awarded a 2016-2017 Savoy Foundation Fellowship, a 2017-2018 CHUSJ Foundation Award, a FRQS Postdoctoral Fellowship, and a 2018-2020 Brain Canada-Kids Brain Health Network Postdoctoral Training Award in Developmental Neurosciences research. She recently published an article as first author in *Brain*.

This fellowship has allowed me to establish myself among the elite of academic research in Canada. During my postdoctoral training, I was able to improve my imaging expertise thanks to the Center's brand new microscopy platform.

Marie-Ève Brien

2018-2020 Brain Canada-Kids Brain Health Network Doctoral Training Award

Marie-Ève Brien initiated a PhD in microbiology and immunology in May 2017. **Her project focuses on the development of a new animal model in pathological pregnancies to study inflammation and intrauterine growth retardation**. During her graduate studies, Marie-Ève was awarded a Faculté des études supérieures et postdoctorales (FESP) Scholarship, a Departmental Fellowship from UdeM, a 2017-2018 Doctoral Excellence Scholarship from the CHUSJ Foundation as well as a 2018-2020 Brain Canada-Kids Brain Health Network Doctoral Training Award in Developmental Neurosciences Research. Marie-Eve recently published two articles as first author in J*ournal of Immunology* and *Biology of Reproduction*.

The Research Center is the most propitious place for the development of my career given the many interactions between academic research and the clinical side, both of them fascinating.

Guillaume Gaudet

2017-2018 Vanier Canada Graduate Scholarship

Guillaume Gaudet began a PhD in Mechanical Engineering at Polytechnique Montréal in September 2016. **His project focuses on the development of an active upper limb exoskeleton for children with neuromuscular disorders**. During his graduate studies, Guillaume received an Hydro-Québec, a Fonds de recherche du Québec – Nature et technologies (FRQNT) and a NSERC scholarships, a 2016-2017 Groupe de recherche en sciences et technologies biomédicales (GRSTB) Research Fellowship and a 2017-2018 Vanier Canada Graduate Scholarship. He has also published articles as first author in the *Journal of Applied Biomechanics* and *Engineering Applications of Artificial Intelligence*.

My presence at the Research Center and the Marie Enfant Rehabilitation Center allows me to maintain permanent contact with the occupational therapists who collaborate on the project and thus guarantee implementation of the final prototype to be developed.

Sören Harnois-Leblanc

2017-2018 CHU Sainte-Justine Foundation Scholarship

Sören Harnois-Leblanc began her PhD in Public Health with a specialization in Epidemiology in September 2017. **Her project focuses on the influence of physical activity trajectories and sedentary behaviors from childhood to late childhood on glucose metabolism and the risk of type 2 diabetes in children with at least one parent with obesity**. During her PhD, Sören was awarded a 2017-2018 CHUSJ Foundation Scholarship, a 2017-2018 ESPUM Fellowship and a 2018-2019 FRQS Fellowship.

Achieving my doctoral training in a center of excellence in mother-child care allows me to acquire knowledge and skills in rigorous and innovative clinical research and epidemiology with experts in lifestyle and cardiometabolic health of children, as well as holding many exciting opportunities to meet international experts and to increase my scientific communication skills.

Nadia Roumeliotis

Perras, Cholette & Cholette Graduate Scholarship

Nadia Roumeliotis completed a Fellowship in Pediatric Critical Care, a Master's degree in Biomedical Sciences and the UdeM Clinician Scientist Training Program in 2016. Currently, she is pursuing a PhD in **clinical epidemiology** and has obtained a doctoral training grant from the FRQS.

Nadia published 16 articles including 8 as first author. She has received numerous awards, including the Canadian Critical Care Trials Group Research Fellowship Award.

My master's degree at the Research Center and the UdeM allowed me to discover the world of clinical research. In addition to practical experience and theory classes, I benefited from excellent mentors who encouraged me to pursue a career as a clinician-scientist.

Fulfilling and Challenging Student Life

Several Events are Organized to Stimulate and Enrich the Academic Life

Front row, left to right: Florian Wünnemann, Rachid Abaji, Safiétou Sankhe, Andrew T. Song and Virginie Bertrand-Lehouillier.
Back row, left to right: Gwenaëlle Andrea De Clifford-Faugère, Rasheda Arman Chowdhury, Junio Dort, Emilie Heckel, Camila de Britto Para de Aragao, Prabhas Chaudhari, Estefania Marin Sierra, Mélanie Girard and Lisa-Marie Legault.

Research Congress – May 26, 2017

The Research Center, in collaboration with the Students' Association, organizes the annual **Research Congress of Graduate and Postdoctoral Students in Research at CHU Sainte-Justine Research Center.**

The 32rd edition gathered about **300 people** who attended **16 oral presentations** and **140 poster presentations**. It was an opportunity for students, trainees, interns, clinical research staff and laboratory staff to share the progress of their work in various fields. Key place for intellectual simulation, the Congress is a privileged opportunity to discuss and network.

2017 Recipients

Oral presentations (3): Rachid Abaji, Lisa-Marie Legault and Florian Wünnemann

Poster presentations (19): Virginie Bertrand-Lehouillier, Laure Boyer, Prabhas Chaudhari, Rasheda Arman Chowdhury, Nikita Cobetto, Aurélien Colamartino, Émilie Courteau, Camila de Britto Para de Aragao, Gwenaëlle Andrea De Clifford-Faugère, Junio Dort, Solène Fourdain, Mélanie Girard, Emilie Heckel, Stéphanie Larrivée Vanier, Estefania Marin Sierra, Rafael Oliveira Fernandes and Safiétou Sankhe.

Work in Progess

The Work in Progress, or WiP, are bimonthly conferences held during fall and winter semesters. Every two weeks, two students from different laboratories and research axes are asked to present the progress of their work in front of their peers. It is a formative platform where students get immediate constructive feedback while enhancing their presentation experience.

Recruitment Activities

Open Doors – November 27, 2017

In order to attract the best candidates to accelerate the development of maternal, child and adolescent health knowledge, the Research Center has opened its doors to **students seeking an internship or graduate or postgraduate study projects**.

More than **20 laboratories** were present with more than **80 research projects** available in a multitude of areas. A guided tour of the highly technological facilities was also offered.

Summer Internships Program

The Summer Internships Program is aimed at **students pursuing undergraduate studies** who wish to acquire practical biomedical research experience in a basic or clinical research laboratory.

It is also an opportunity to gain insight into what graduate life is like, discuss issues with researchers and contribute toward advancing the Research Center's multidisciplinary research projects in its six research axes.

Key Achievements
Platforms

Research Center Opens Cutting-Edge Platform for Imaging by Microscopy in Partnership with Leica Microsystems

The Research Center has partnered with Leica Microsystems to establish a **cutting-edge microscopy facility**. This platform is the latest of Leica Microsystems' partnerships with research facilities across the world dedicated to helping top academic institutions provide tools that accelerate scientific discovery.

The platform houses **11 state-of-the-art imaging systems** from simple epi-fluorescence to confocal and super-resolution light microscopy. This range enables scientists to investigate a variety of experimental systems at different scales, from single molecules to entire living organisms. The platform will address the needs of the scientific community, as well as providing a great new resource for microscopy imaging in the Montreal Region.

We are honoured to open this state-of-the-art platform and provide a direct link between the scientific researchers, the academic community and the product specialists at Leica, said Dr. Jacques L. Michaud, the Research Center's Scientific Director. ***The CHU Sainte-Justine Research Center is at the forefront of research for pediatric diseases, and having the latest equipment is essential to keep our research at the cutting edge. We will continue to work closely with Leica to develop and enhance the equipment to continually meet the needs of these scientists.***

The cutting-edge equipment and operation of the platform are supported by the CHUSJ Foundation *Grandir en santé* campaign and the Canadian Foundation for Innovation (CFI).

Graziella Di Cristo, PhD
Scientific Director

Gilles Hickson, PhD
Scientific Director

Elke Küster-Schöck, Dr.rer.nat.
Platform Manager

Integrated Unit in Clinical Engineering (UNIC)

Musculoskeletal diseases (MS) are the most prevalent chronic diseases in Canada and around the world and require considerable resources for diagnosis, treatment and rehabilitation. This sector represents the second largest expense item in direct and indirect health costs in Canada. To offer Canadians innovative solutions stemming from unique research programs in the world, we have created an "**Integrated Unit in Clinical Engineering**" (UNIC) funded by the Canadian Foundation for Innovation. Consisting of state-of-the-art imaging technology infrastructures that will be implemented in a hospital-based research ecosystem, this infrastructure is a cornerstone of the TransMedTech Institute for Biomedical Engineering and Medical Technologies ($36.5M grant from Canada Apogee Research Excellence Fund recently awarded to Polytechnique Montréal and its partners).

This major international initiative aims to **co-create the next generation of medical health technologies in MS in an open, trans-disciplinary and cross-sectoral (Living Lab) ecosystem of innovation, anchored in hospitals**. This constitutes a framework for the development, transfer and implementation of knowledge, as well as the exploitation of research results and innovations. This project is also closely linked to the Polytechnique Montréal "Life Science and Engineering" Pole of Excellence and the MS and Rehabilitation Center of Excellence at the CHUSJ.

UNIC has three major and unique equipments for 3D micro-dose and multi-energy X-ray imaging, dynamic high-performance surface topography and 2D/3D wide-field and dose-based interventional fluoroscopy. Each equipment will support an ambitious and original international medical technology R&D programming, including the **development of evaluation tools and simulations**, as well as the **design of new generations of medical technologies for the diagnosis study,** and the **treatment and rehabilitation of MMS**, by placing the patient and the users at the heart of the development process. For example, the EOS2E (EOS imaging) X-ray system, which uses a new generation of ultra-low-dose and dual-energy simultaneous bi-planar radiography technology. This will be achieved by integrating a precise 3D reconstruction of anatomical structures, while allowing to analyze the bone mineral density of the anatomical structures in 3D of the whole body and therefore to be able to take into account the physical properties of tissues in our simulation models (corrective surgeries for scoliosis, etc) or our studies in MS health (bone development, neuromuscular sequelae secondary to cancer treatments, osteoporosis, etc.). This first prototype installed in America will allow the development of a new generation of technologies for the diagnosis of MS diseases as well as the optimization of orthopedic treatments.

The integration of research infrastructure and hospital-based research infrastructure and environment will accelerate the development and evaluation of new diagnostic technology tools and therapeutic interventions using digital simulations and various advanced imaging tools, placing users at the heart of the development process (patient-clinician-research co-creation), as part of a real Living Lab.

Looking into the Future: Revolutioning Pediatric Orthopaedic Surgery with Patient-Tailored Approaches

The operating room of the future, entirely dedicated to research, makes it possible to develop **new generations of surgical procedures optimized for the treatment of spinal pathologies**. This room includes an integrated navigation and surgical visualization system, a 2D-3D fluoroscopic imaging system, a multi-functional operating table, a video communication system, and a control room accessible to students who come to develop different innovative projects.

"It takes many years of work to repel the consequences of a disease as complex as idiopathic scoliosis," says **Carl-Éric Aubin**, professor at Polytechnique Montréal, researcher and head of the axis of musculoskeletal health, rehabilitation and medical technologies of CHUSJ, and holder of the NSERC-Medtronic Research Chair in Biomechanics of the Spine.

In particular, **surgical simulators**, based on personalized numerical models with the geometry and mechanical properties of the patient, offer the surgeon the possibility of practically **performing an instrumentation surgery before the final operation, to evaluate different treatment strategies, and pre-determine the best strategy possible**. These different applications are notably developed in the framework of the NSERC/Medtronic Industrial Research Chair in Biomechanics of the Spine (Pr. C.-É. Aubin). Innovative surgeries are also being developed and tested (Dr. S. Parent). This infrastructure is leveraged through federal innovations funds (Integrated Unit in Clinical Engineering; Canada Foundation for innovation) and major funds through the CHUSJ.

Key Achievements
Clinical Research and Knowledge Transfert

A Hub for Clinical Trials

The CHUSJ is one of the founding partners in a new initiative, **CATALIS**, launched by the government of Quebec to put Quebec on the global map as a place recognized for clinical trials. In line with this view the Ministry of Economy, Science and Innovations (MESI) wishes to **increase the number of subjects participating in clinical trials as well as become a recognized hub for initiating, designing, conducting, and analyzing early clinical research trials** and as such double the private investments in this sector in Quebec over the next five years.

To achieve this mission, CATALIS has implemented an action plan based on **centralization and coordination efforts across recruiting sites** including elements as optimization of the operational procedures of clinical trials and harmonization of ethical procedures and industry contracts. This initiative will act as an facilitator between partners in the Health sector and one of its first actions is to implement a system to optimize and harmonize the evaluation process by the ethical boards. The CHUSJ is part of the three founding institutions adhering to the CATALIS initiative together with the CHUM and CUSM. As founding partner the CHUSJ is recognized in Quebec for its leadership in pediatric clinical trials particularly in the cancer and rare diseases and will have a large imprint on the development of future guidelines and process of pediatric clinical trials in Quebec.

Safer and More Effective Medication for Children - CHUSJ Part of the Innovation in Pediatric Clinical Trials Project

The **Innovation in Pediatric Clinical Trials** (IPCT) project is a major initiative led by the University of Manitoba with more than $8.4M in new research funding provided by the CIHR, Research Manitoba and the Children's Hospital Foundation of Manitoba in partnership with other institutions across Canada.

The IPCT project will address challenges specific to conducting clinical trials for children, such as the relative infrequency of many childhood illnesses that present major difficulties for recruitment of patients at one clinical site. One of the goals of the IPCT is to **explore new methods of study design that will lay the groundwork for KidsCAN** – a Canadian coordinating and advisory infrastructure network to ensure best therapies for children. The ultimate goal of IPCT is to **make trials for children feasible, better and more effective** providing doctors with accurate and robust data that can inform for prescribing medication to children.

The CIHR Strategy for Patient-Oriented Research (SPOR) network is unique in its vision not only to assemble researchers, clinicians, policy makers, academic health centers and health charities, but also engages patients. The patient perspective ensures the feasibility of the intervention for the right patient and facilitates informing patients. A total of four clinical trials will be conducted within the program at six different clinical sites. The researchers Drs. Serge Gouin and Jocelyn Gravel, both researchers in the axis Infectious Diseases and Acute Care are leading the team at the CHUSJ for these trials.

Formulatiing Better Medication for Children

The **Rosalind & Morris Goodman Family Pediatric Formulations Centre of the CHU Sainte-Justine**, (GPFC) aims to improve access to child-friendly medicines. It is the only Centre in Canada whose mandate is to **facilitate the development of commercially available age-related formulations for children**. As such, GPFC has been engaged in many initiatives over the past year to promote research in clinical practices to increase the safety of medicines administered to children. Our researchers have profound experience in the design and conduct of pediatric pharmacokinetic, efficacy and safety studies, and GPFC is currently leading many projects within KidsCAN, a Canadian network aiming to ensure best therapies for children.

Cannabis Consumption Exacerbates Psychotic Symptoms in Teens

With the legalisation of cannabis in Canada at the front door, discussions have been enflamed on the minimum age required to access this substance. In particular with respect to the potential harmful effects of cannabis used at a regular basis in adolescents and young adults. **Pr. Patricia Conrod**, who holds the Chair Dr Julien/ Fondation Marcelle and Jean Coutu in Social and Community Pediatrics of Université de Montréal, has developed a research program on cognitive, personality and biological risk factors for the development and maintenance of drug abuse and on the factors that mediate the co-concurrence of addictive behaviours with other mental disorders.

This year she made a breakthrough by confirming an **association between the consummation of marijuana and psychotic symptoms in teenagers**. The study published in *JAMA Psychiatry* is based on the results from a cohort of 4,000 13-year old youths that have been followed over a period of four years as part of the Project Co-Venture. Considering the fact that psychotic symptoms are associated with risk for psychosis and non-psychotic disorders, these results emphasize the need for targeted cannabis use prevention as jurisdictions revise their cannabis regulatory policies.

In a more recent study published in *Journal of Affective Disorders*, her group used the same cohort to examine the concurrent and subsequent effects of depressive symptoms on the initial level and evolution of four neuropsychological functioning domains such as spatial working memory, delayed recall memory, perceptual reasoning and inhibitory control. Results from multilevel model analysis suggest that **current and past year depressive symptoms were associated with poorer performance in delayed recall memory and perceptual reasoning tasks**. Past-year depressive symptoms were also associated with poorer spatial working memory performance. Detrimental effects were stronger in early adolescence.

Although it should be noted that the study examined sub-clinical depressive symptoms and not clinical depression, and therefore results may not match the accuracy of clinical based assessments. However, the indications that depression has serious consequences on the cognitive functioning are strong and increases the necessity to intervene at early stages and take measures to prevent child depression.

Centre of Excellence in Pediatric Trauma

The **CHUSJ Centre of Excellence in Pediatric Trauma** (CEPT) brings together researchers, clinicians and health professionals with diverse expertise ranging from **emergency and acute care to long term-effects of trauma and rehabilitation**. The CHUSJ is a tertiary center offering specialized and high-tech care in pediatric traumatology with approximately 12,000 visits at emergency department per year. More than 500 of these traumatized patients require hospitalization of which up to 10% are admitted to the intensive care unit.

The mandate of the CEPT is to **provide access to the most advanced technology in trauma research and care** as well as **building expertise of the team through recruitment of rising stars** and funding for projects that bring together multidisciplinary teams across the CHUSJ and in collaboration with other Institutes to provide breakthroughs in trauma research that could be ultimately transferred to the clinic.

One of this rising stars is **Pr. Miriam Beauchamp** a pediatric neuropsychologist specializing in traumatic brain injury (TBI) in children and associate professor in the Department of Psychology at the UdeM and researcher at the CHUSJ. TBI results from an external force applied to the brain and is the most common cause of disability and infant mortality. The World Health Organization has ruled on the urgency of improving the management of TBI consequences. Pr. Beauchamp's research themes are related to **neuronal, cognitive and social development, as well as the impact of TBI on these functions from birth to age 18**. Her expertise with early TBI (before age 6) is particularly recognized because of her unique findings highlighting the **high vulnerability of very young children to brain injury**. Pr. Beauchamp is currently leading or collaborating on five pan-Canadian projects supported by CIHR. Her research addresses clinical issues that are expected to have a significant impact on the health system and society.

Pr. Beauchamp's work already has made impact on clinical management. Using new and more sensitive neuroimaging tools («Susceptibility Weighted Imaging») she consistently detected micro lesions after a concussion in children. Detection of such lesions are critical in informing clinical practice and this cutting-edge imaging technology is now used for monitoring of our patients. Pr. Beauchamp is also a pioneer in the study and follow-up of very young children after a TBI (0-5 years old). She has shown that contrary to traditional beliefs in medicine, TBI are particularly prevalent and harmful at this age. Her research program aims, among other things, to **better document their consequences with a view to improving their management**. Her expertise and leadership have been recognised last year through funding from the CIHR Foundation scheme, a Canada Research Chair Tier II in Pediatric TBI and the Prix de la Relève Scientifique du Québec, the highest distinction awarded in science by the Quebec Ministry of Economy, Science and Innovation.

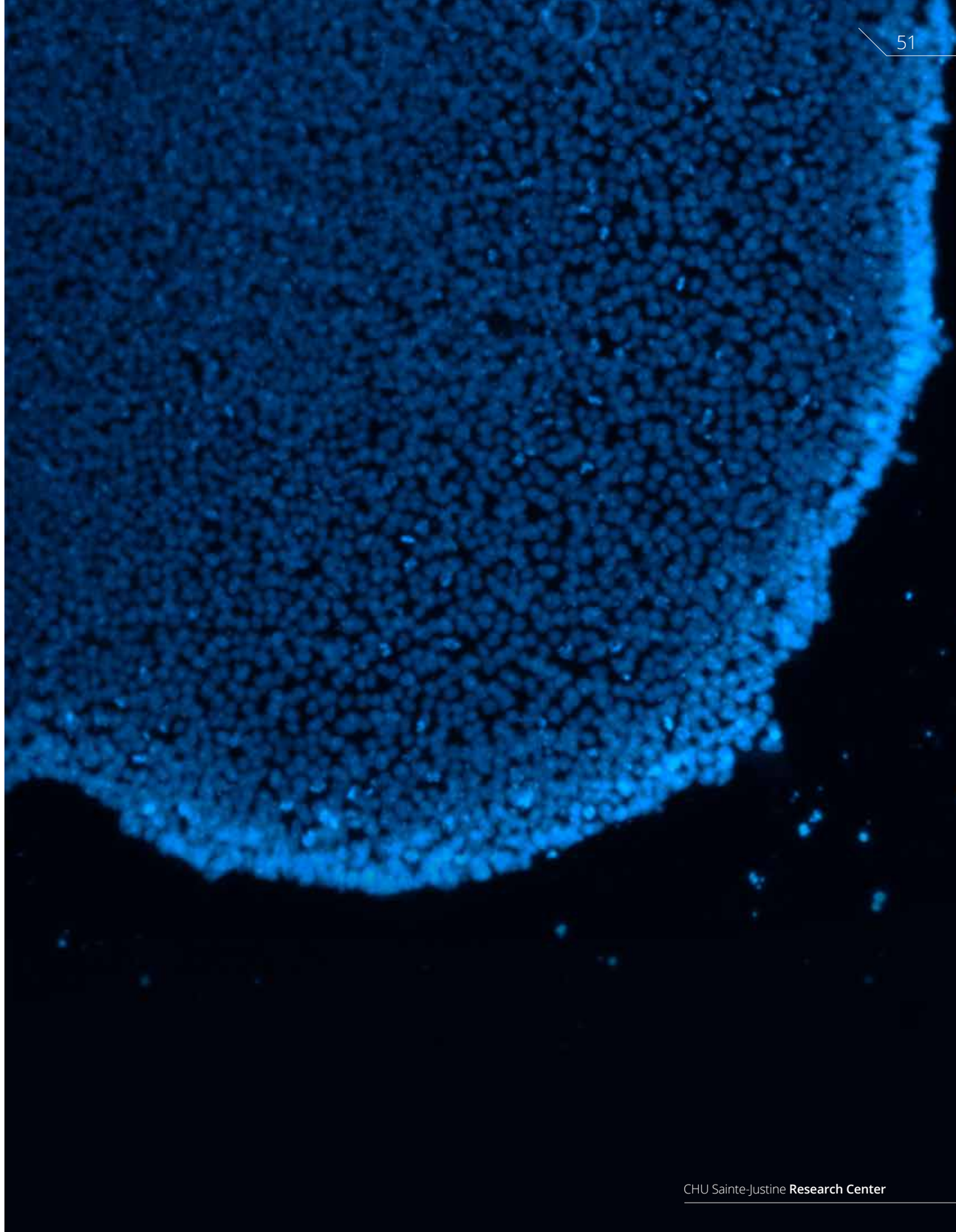
Key Achievements
Innovative Therapies

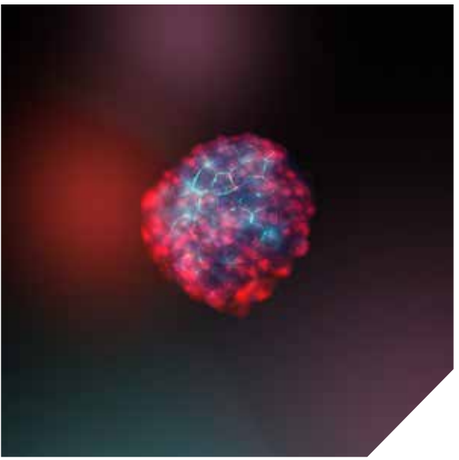
The Induced Puripotent Stem Cell (IPSC) Platform: The Generation of iPS Cells for Patient-Specific Disease Modelling and Cell Therapy

Stem cells hold a great promise for the **development of innovative cell and gene therapies**. The discovery by Yamanaka in 2006 that stem cell can be generated from mature specialized cells through the introduction of only four genes has exploded the possibilities for regenerative medicine, because these induced pluripotent stem cells can theoretically be differentiated into any cell type. Under the scientific supervision of **Pr. Christian Beauséjour** the Research Center has established a platform for the generation of IPSCs. Investigators from all the axes use this technology to either model a specific disease for drug screening purposes and understanding of the molecular mechanisms or develop personalized cell-based therapies. The applications are numerous. Some studies based on IPSC technology at the Research Center are given below.

An IPSC-Derived Tumor Model to Analyze Immune Response in Cancer

Why the immune system fails to recognise and eliminate cancer cells is an intriguing question that Pr. Beauséjour aims to address in his laboratory. Our understanding of the biology and molecular mechanisms involved in human cancer has greatly advanced through recent studies using xenograft animal models. However, these animals are typically immune deficient and thus inadequate for studying the natural immune response against cancer cells. To circumvent these barriers, Pr. Beauséjour has teamed up with **Dr. Elie Haddad** and took advantage of his expertise in the **development of humanized autologous tumor/immune system mouse models**. This approach is based on humanization of immune-deficient mice with donor-derived leucocytes and/or hematopoietic progenitor cells. Induced pluripotent stem cells (IPSC) from skin biopsy or blood cells will be generated from the same donor. These IPSCs are then differentiated in vitro into various cell types such as liver cells, myocytes and neural cells and made cancerous by transfection with a set of defined oncogenes. These cancer cells are injected in mice reconstituted with autologous immune cells and tumor growth is then monitored based on its ability to escape or not immune responses. Pr. Beausejour **aims to exploit this model to better study anticancer immune therapies**.





Hepatic Organoid

A New Stem Cell-Based Therapy to Save Lives of Patients with Acute Liver Failure

Dr. Massimiliano Paganelli, a pediatric gastroenterologist and hepatologist, is working to translate a novel **stem cell therapy for patients with acute liver failure**. The problem with acute liver failure is the urgent need for transplantation after diagnosis, and it is even more severe in children. However, the liver has the capacity to regenerate itself and it is estimated that up to 80% of the patients could avoid transplantation if temporary liver function could be assured while the patient's own liver heals.

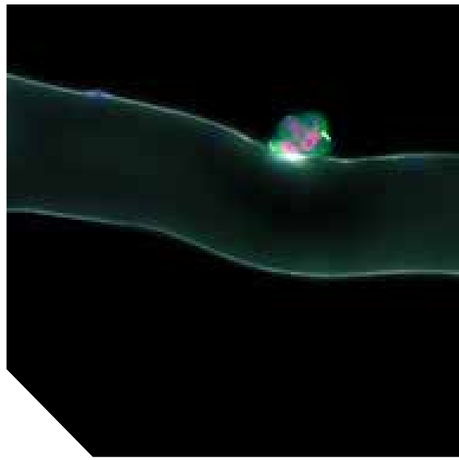
In the lab, he is **developing a new cell product that can perform liver cell functions**. Thereto, using a finely-tuned biomaterial, he created an implantable liver tissue from small livers (called organoids) he generated from human induced pluripotent stem cells. The biomaterial protects the organoids from recognition and elimination by the patient's immune system. Results show that such an encapsulated liver tissue (ELT) can perform mature liver functions as effectively as human hepatocytes, and preliminary results indicate that it is effective is saving mice with acute liver failure. Dr. Paganelli will now assess the safety and efficacy of the ELT in larger animals in preparation for a clinical trial to be conducted in patients with acute liver failure. This new technology has the potential of saving thousands of lives worldwide. Dr. Paganelli has licensed this technology and launched a spin-off company (Morphocell Technologies Inc.) with support from Univalor and the Centre for Commercialization of Regenerative Medicine.

Targeting Muscle Stem Cells to Treat Muscular Dystrophies

Duchenne Muscular Dystrophy (DMD) is a severe muscular disease leading to early death that affects approximately one boy out of 4,000 in Canada. "There is no cure for DMD," says **Pr. Nicolas Dumont**, "but stem-cell based technologies hold promise for the development of in vitro 3D-models better representing the muscle cell environment, which can be used to understand the pathology of the disease and conduct high-throughput drug screens."

Pr. Dumont has demonstrated that loss of muscle mass in DMD is not only caused by muscle cell degeneration, but also by the impaired muscle generation from stem cells. Thus one angle to find new therapies for DMD is to find molecules able to restore the regenerative capacity of the muscle stem cells. The advent of induced pluripotent stem cells (iPSCs) technology allows not only for a **personalized modeling of the disease** by generating myoblasts from patient-derived iPSC, but also **provides an unlimited source of cells** that can be used for drug screening.

Pr. Dumont's team has identified new compounds that rescue the function of iPSC-derived myoblasts isolated from DMD patients. These compounds are more efficient than the standard-of-care drugs (i.e. glucocorticoids) in preclinical mouse models of muscular dystrophy. The iPSC technology is also key in the development of cell-based gene therapeutic approaches to correct the mutation. However, a major barrier facing such cell therapies is the loss of stemness when culturing myoblasts or after infusion in vivo, hindering distribution and durability of such therapeutic approaches. Novel strategies as 3D-bioprinting are needed to address mechanistic questions of myogenesis such as regulation of quiescence.



Stem Cells on a Muscle Fiber

Racing Against Time to Battling Sanfilippo Neurodegenerative Disease

The research excellence in metabolic diseases at CHUSJ was recognized this year with a donation of $1M from the Sanfilippo Children's Research Foundation. The world-wide recognition of **Pr. Alexey V. Pshezhetsky**'s expertise in Sanfilippo disease was key for receiving this generous gift, to ensure sustainability of research on this disease and develop new therapeutic approaches. Pr. Pshezhetsky became interested in Mucopolysaccharidosis (MPS) or Sanfilippo disease 13 years ago and has since made major contributions, including the discovery of the **causative gene encoding for the enzyme HGSNAT**. This Sanfilippo disease belongs to a group of devastating rare diseases in children affecting the lysosome, a cellular compartment orchestrating degradation and recycling of large molecules. There is no therapy for patients with this disease and new clinical options to manage and treat this disease are urgently needed.

The donation will support a multidisciplinary approach to explore various therapeutic avenues. These include a lentiviral gene therapy for MPS III. Pr. Pshezhetsky aims to test whether hematopoietic cells generated to express supraphysiological levels of the deficient enzyme HGSNAT can restore the function of affected microglia cells. A second avenue is to restore the activity of the mutated HGSNAT enzyme by small molecules that prevent or repair the misfolding caused by the mutation. He has already identified such chaperone molecules, which will be tested in mouse models. Finally, in a collaborative study with Dr. Brian Bigger (University of Manchester, UK), Pr. Pshezhetsky is working on a gene therapy approach to deliver a correct gene of the HGSNAT enzyme to the brain using an adeno-associated virus delivery system.

This exceptional contribution will empower the team to better understand the disease and accelerate clinical translation, create new research opportunities and collaborations with the community, attract the brightest young scientific minds and maximize research potential by leveraging government funding. To honour the memory of Elisa Linton, the laboratory of Pr. Pshezhetsky has been named the Elisa Linton Sanfilippo Research Laboratory.

$22 million to heal more children with cancer, better

The Fondation Charles-Bruneau makes the largest donation in the CHUSJ's history to support immuno-hemato-oncology research

Hope lies in research for cancer patients

In May 2017, the Foundation Charles-Bruneau has signed a historic agreement to support research in immune-hemato-oncology at the CHUSJ with $22M for the next five years. This exceptional donation will give an enormous impulse to the research **program in personalized medicine for children suffering with cancer**. The funds will serve to advance a broad range of highly promising projects involving characterizing the molecular signature of pediatric cancers and development of more efficient therapies and ultimately translate these innovative discoveries toward the clinic.

Researchers and clinicians from the axis Immune Diseases and Cancer have initiated the **"Signature" project to identify the molecular signature of pediatric cancers at diagnosis and relapse through next-generation sequencing approaches (genome, exome, transcriptome)**. The genetic profile will allow for identification of cancer-specific mutations in each patient and could shed light on treatment resistance mechanisms as well as lead to more patient-tailored treatments. Interrogation of large genomic data sets in association with clinical outcomes also has the potential to identify new biological markers for cancer diagnosis and/or prognosis.

The second prioritized area involves development of **breakthrough therapies such as targeted therapies or immunotherapy**. Efforts are ongoing to make the very promising CAR T cell technology available for Canadians. Researchers at the CHUSJ are at the forefront in this field developing not only new generation of safer, more efficient and sustainable CAR cells beyond the CAR T, but are also pioneering cell therapies with innate immune cells, specifically NK cells and plasma dendritic cells. Other projects exploit the immune system to develop antibody or small molecule based therapies that can modify the immune response, reduce toxicity of transplantation and preserve anti-leukemia effects. Fundamental studies in T cell biology will provide essential clues on how to improve immune cell therapy by preventing T cell exhaustion.

Our greatest dream is that we never have to say to a family that the only remaining treatment option for their child is palliative care.

- Dr. Michel Duval

Another important area of the research program is the **studies to unravel the molecular pathways leading to pediatric leukemia** that could lead to the identification of new and/or more efficient drug targets. Guided by the mutations and expression profiles from the genomics data, disease models will be created to study the biology of disease and screen for promising drug candidates.

Finally, the well-being of patients remains the principal objective of this breakthrough research initiative. The CHUSJ has made it a high priority to **conduct psychosocial research** to provide social support to improve the quality of life for patients and their families. In addition to the quest for new innovative therapies, this initiative seeks to develop psychosocial programs to support children suffering cancer and their family through the emotions and difficult time that such a diagnosis provokes.

How can we measure the distress a family feels when they receive a diagnosis, or their rising hope when there is good news? Quality of life is measurable.

- Pr. Serge Sultan

Wiam

The donation will also permit the CHUSJ to **attract bright young investigators** for recruitment in the strategic areas. This will bring in novel expertise and help create a dynamic environment and stimulate cross-discipline interactions necessary to stay at the frontier of new scientific advancements.

The investment will allow to significantly **increase the quality and volume of research activities** through support in technical platforms (such as flow cytometry, gene editing and cell reprogramming, pediatric biobank to mention a few) as well as the acquisition of innovative equipments. Finally, this donation supports highly competitive research projects as well as provides a **major leverage for new strategic initiatives and developing collaborations at the national and international level**.

Key Achievement
Major Events

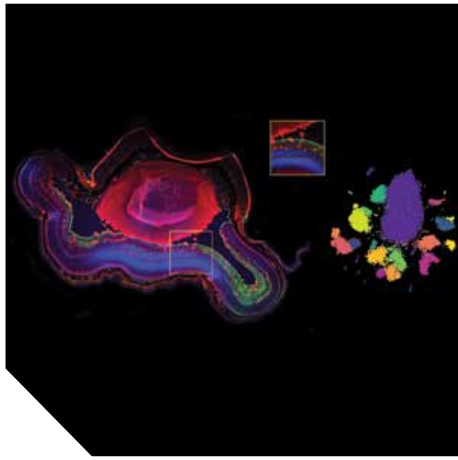
The Research Centre at the heart of Nuit Blanche: Discover the "**Night Lab – Forest of Mysteries**"

In March 2018, for a second year in a row, people were invited to the "**Night Lab – Forest of Mysteries**", during "**Nuit blanche à Montréal**," organized by **MONTRÉAL EN LUMIÈRE** festival.

Accompanied by Scientix, **nearly 850 night owls** have immerse themself in a unique world that knows how to satisfy inquisitive minds, explorers and learners of all ages. This night is an exceptional opportunity to have privileged access to state-of-the-art research infrastructure. From interactive games, instruments exhibits and video stations to observing teams at work in the lab and chatting with experts in mother-child health, people were invited to explore the Research Center as never seen before!

New during this edition: our student-researchers presented an exhibition of scientific photographs as part of a contest. The grand prize winner is **Gael Cagnone**, Ph.D., a postdoctoral fellow in the laboratory of Jean-Sébastien Joyal, MD, Ph.D., for his work entitled ***Genomic Mapping of the Retina***.

The CHU Sainte-Justine is proud to be the first research center featured as part of Nuit Blanche, and is delighted to welcome visitors. A way to inspire dozens of budding future researchers!



Genomic Mapping of the Retina

Research in Figures

New research grants obtained in 2017-2018

$11,962,146	> CIHR
$7,613,141	> FRQS
$6,686,857	> Health Canada
$4,466,769	> CFI
$3,789,592	> FRQNT
$2,236,364	> Industry
$1,548,000	> International Human Frontier Science Program
$1,495,320	> Canadian Cancer Society
$1,400,000	> Canada Research Chairs
$853,930	> Other funds
$806,939	> Heart & Stroke Foundation
$500,000	> MESI
$284,460	> SickKids Foundation
$283,000	> NSERC
$250,000	> OIIQ
$238,307	> Social Sciences and Humanities Research Council
$148,500	> IVADO
$141,937	> UdeM
$119,075	> Cancer Research Society
$100,000	> Ministère de la Santé et des Services sociaux

$45M

CHU Sainte-Justine **Research Center**