ANNUAL REPORT 2021-2022

Dare to look beyond the horizon

CRCHUM

RESEARCH CENTRE

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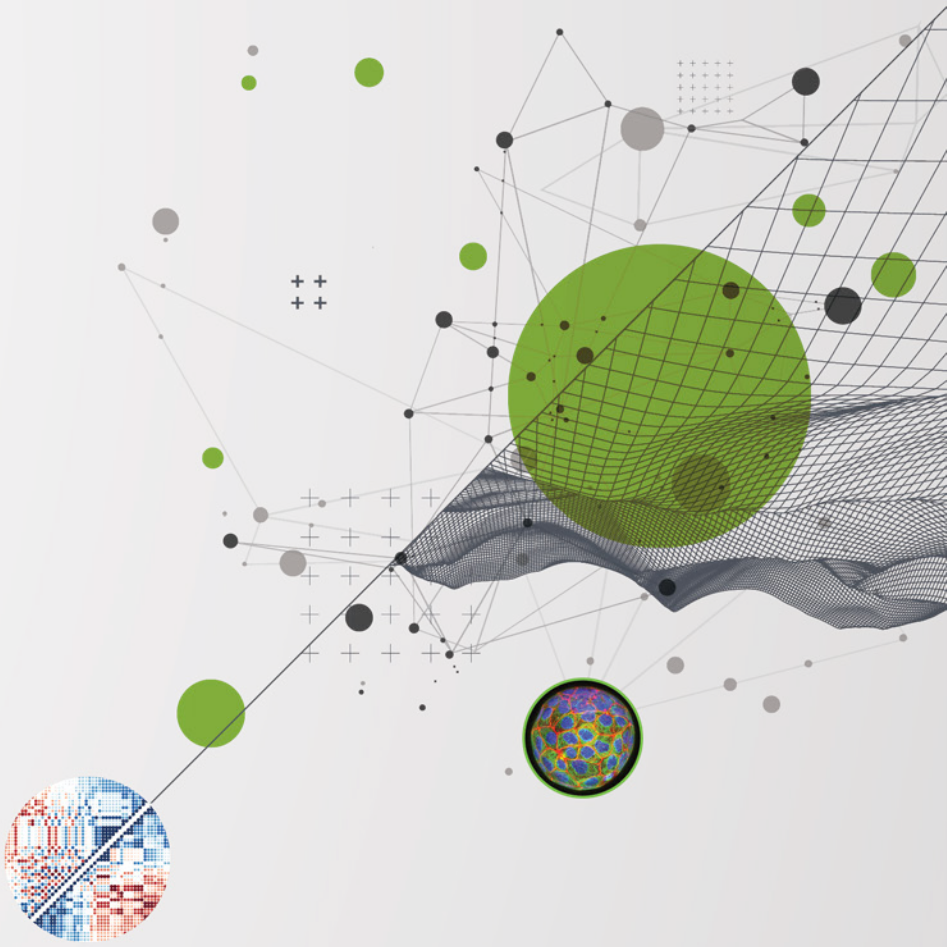

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Shingo Nakajima and **Stephanie Fulton** *(Cardiometabolic Research Theme)*

Ana Carmena Moratalla and **Nathalie Arbour** *(Neuroscience Research Theme)*

Augustine Fert and **Petronela Ancuta** *(Immunopathology Research Theme)*

Dr. Marion Tonneau and **Dr. Houda Bahig** *(Imaging and Engineering Research Theme)*

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Special thanks to:

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crchum.com

MESSAGE FROM THE DIRECTOR

THE MULTI-FACETED FACE OF RESEARCH

The Omicron variant may have disrupted our lives in the fall of 2021, but it did nothing to dampen the enthusiasm of our community to move research forward. Our lives continue, and the life of the Centre as well. As vibrant as ever.

In capital letters, Daring to Look Beyond the Horizon, our slogan, has confidently adorned the front door of the Research Centre this year, reminding everyone who enters of our good-willed ambition.

This slogan resounds like an ode to our research community, which plays an essential role in the advancement of knowledge, guides policymakers' decisions, informs our fellow citizens and fights disinformation every day.

It is our duty to relentlessly pursue this noble mission.

Through the studies and scientific projects summarized in our 2021-2022 annual report, you'll have the opportunity to discover, among others, profiles of a few members of our bright and determined younger cohort of researchers, and of our committed core facility staff.

Behind the scenes at the Research Centre is a rich, diversified and often unseen community, without whom our research activities and scientific advances would not be possible.

Advances in science are the result of small and big ideas and emerge from collaborations among people of different backgrounds. Let's take the time to appreciate and celebrate the diversity and wealth of our research community.

Together,
we are the CRCHUM!

Dr. Vincent Poitout
Director of Research at the CHUM
Scientific Director of the CRCHUM

MESSAGE FROM THE CEO

TAKING A MOMENT TO SAY THANK YOU

I like retrospectives. They reduce things to the essential, in a world that's often all hustle and bustle. A few pages, a few pictures, a few graphs and you have a great summary of the year that just ended.

Every year, the list of innovations grows with each new success. Pandemic or not, science and medicine continued their race to the future this past year. Original theories emerged. Innovations were born. Tangible advances brought hope to people affected by disease and to their loved ones.

A revolutionary drug cocktail to slow HIV. A promising therapeutic combination to fight prostate cancer. Major funding for research projects. And many other highlights for you to discover in this annual report.

Thanks to the research teams of the CRCHUM and the clinical teams of the CHUM for their collaboration, which is so vital to these achievements.

Take a few minutes to consider the colossal amount of work accomplished in 2021-2022. Get to know the people who, every day, dare to go beyond the horizon for the well-being of the public that we serve.

Stopping a little while to peruse the CRCHUM's annual report means paying tribute to your committed community.

It also means saying thank you, a word never said enough!

Dr. Fabrice Brunet, CEO of the CHUM

THE CRCHUM AT A GLANCE

The University of Montreal Hospital Research Centre (CRCHUM) is the Université de Montréal's largest biomedical and health care science research centre and one of the largest and modern in all of Canada. Here, basic, clinical and population health research are carried out side-by-side under one roof.

The Fonds de recherche du Québec — Santé, the provincial body responsible for funding research facilities, confirmed the CRCHUM's standing as a major Canadian research institution by awarding it an "exceptional" rating in its 2020-2026 strategic plan.

This position of influence is the result of all the people at the CRCHUM whose commitment, work and creativity allow us to generate and transform knowledge, making a difference in patients' lives.

+ than **160** regular researchers

+ than **330** investigators

Nearly **490** graduate students

14 Canada Research Chairs

Nearly **180** employees supporting the research teams

+ than **1010** research staff members

Nearly **1130** peer-reviewed **publications**

23 university chairs

AN ENVIRONMENT CONDUCIVE TO PERFORMANCE

A seat of internationally renowned scientific research, the CRCHUM's research is rooted in its dynamic community and offers a diversified, fair and inclusive environment for the training of scientists who will leave their marks on the world stage of research tomorrow.

Integrated into all the CHUM's hospital activities, the Research Centre's teams count on competitive infrastructure and state-of-the-art technological core facilities to improve the health of the adults of Quebec.

The CRCHUM's proximity to the university hospital makes it an intellectually rich and stimulating environment, conducive to scientific collaboration and the emergence of internationally recognized achievements and discoveries.

More than
$88M
in research revenues

DYNAMIC CLINICAL AND EPIDEMIOLOGICAL RESEARCH

385
new clinical or epidemiological trials

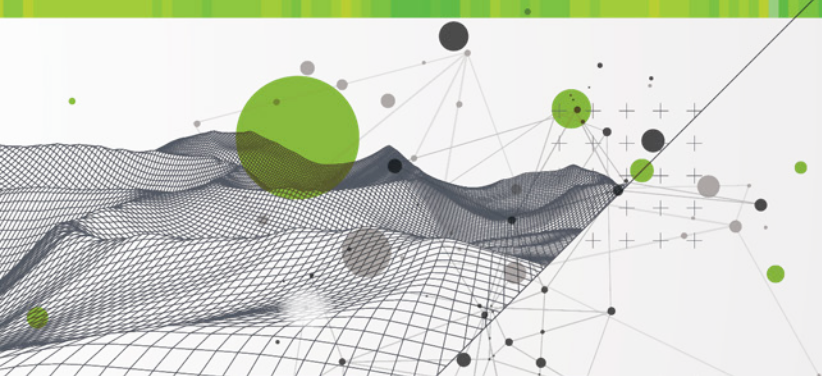
19 **core facilities providing services and research support**

For its day-to-day operations, the CRCHUM can count on the Fondation du CHUM. The Fondation helps fund the purchase of state-of-the-art equipment and contributes to the training of exceptional young researchers and the transfer of the Centre's unique knowledge.

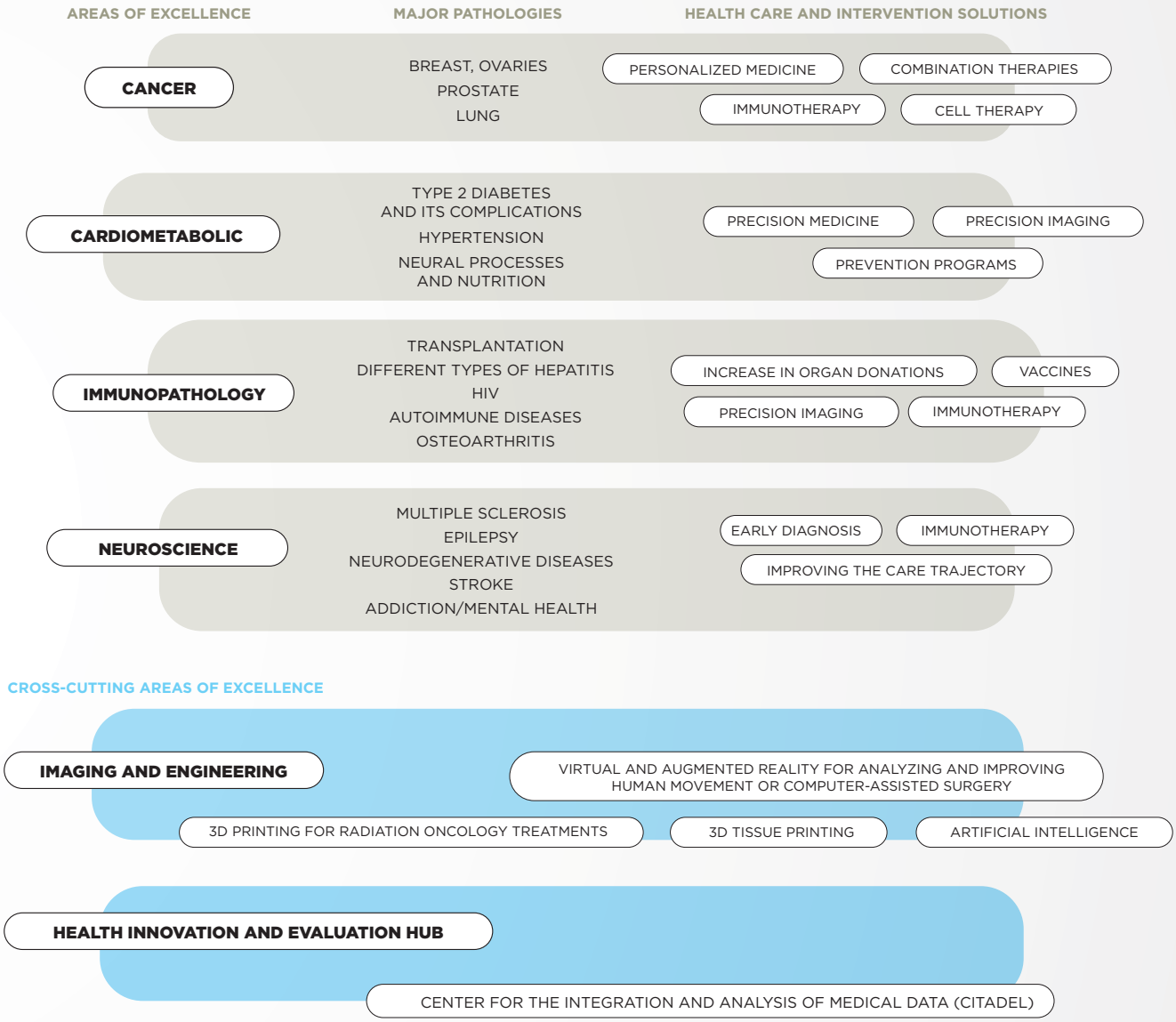
CREATING POSITIVE IMPACTS FOR OUR PATIENTS

A global leader in the improvement of health care and services and the patient experience, research at the CRCHUM falls into **six main themes**:

- CANCER
- CARDIOMETABOLIC
- NEUROSCIENCE
- IMMUNOPATHOLOGY
- IMAGING AND ENGINEERING
- HEALTH INNOVATION AND EVALUATION HUB



The research work carried out at the Centre provides health care and intervention solutions for the entire population.



With its Unit for Innovative Therapies, the CRCHUM is on the front lines of early clinical research. Its goal: to offer patients who have run out of treatment options the most advanced therapies available in oncology, neurology and immunopathology.

This 16-bed unit relies on a team of 35 people and more than 70 investigators to conduct phase 1 and 2 clinical trials. More than 55 clinical trials have been launched there since its opening in the fall of 2018, including several in collaboration with pharmaceutical companies.

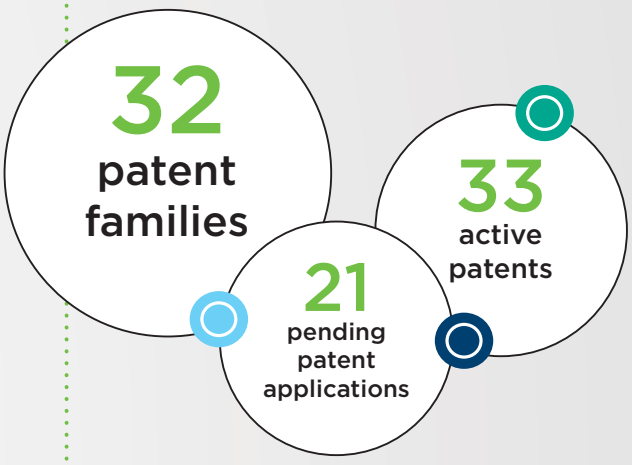
HARNESSING KNOWLEDGE AND DATA

For the teams at the CRCHUM, knowledge management is a priority activity. They harness knowledge and identify research results that will materialize in the form of innovations that benefit patients and the health system.

With its Centre for the Integration and Analysis of Medical Data, also known as CITADEL, the CHUM and the CRCHUM rely on their expertise in health data science to make good use of the nearly four million pieces of patient clinical administrative data.* Thanks to their analyses, the CITADEL team has already allowed more than 120 projects to improve population health.

13 **spinoff businesses**
active mainly in the following areas

- **Digital health**
- **Contract research** (rare diseases, oncology)
- **Molecular targeting** (rare diseases, oncology, diabetes and metabolic diseases, regenerative medicine and transplantation)
- **Personalized medicine** (type 2 diabetes, oncology)
- **Biomechanics**
- **Biomaterials**



+ than 90 active inventors

16 active business agreements

*The CHUM and the CRCHUM attach utmost importance to the protection of privacy, the confidentiality of data and access to data. For more information, visit the CITADEL management framework on our website.

YOUNG RESEARCHERS MAKING STRIDES

GUT MICROBIOTA, ALLIES IN THE FIGHT AGAINST CANCER

A SURVEYOR AND TRAILBLAZER WHO JOURNEYS INTO LITTLE-EXPLORED SCIENTIFIC REALMS, MERIEM MESSAOUDENE IS A TRAVELLER AT HEART WITH A PASSION FOR GEOGRAPHY THAT HAS TAKEN HER FROM ONE CONTINENT TO ANOTHER. AS SHE MADE HER WAY ON HER TRAVELS, SHE HAS GLEANED WISDOM HERE AND THERE AND HAS BEEN ABLE TO RELY ON A FEW COMPASSES—OF THE HUMAN TYPE.

To travel far, you need to be prepared as best as possible. This postdoctoral fellow readied herself by learning from the world's leading immuno-oncology experts such as Dr. Laurence Zitvogel. Having completed a bachelor's degree in immunology and biochemistry in Algeria, the young woman took a road less travelled and went to Paris, France. There, she completed her master's degree and PhD before joining Dr. Zitvogel at the Gustave Roussy Institute of Oncology.

"Laurence is still a true mentor for me. I was lucky to do my first postdoctoral fellowship under her supervision. She's passionate about her work on gut microbiota and cancer, for which she has received international recognition," she explained.

While with the team in Paris, she met a young doctor and researcher, Dr. Bertrand Routy. Together, they would go on to establish the immunotherapy and oncomicrobiome laboratory at the CHUM Research Centre.

AWAKENING THE IMMUNE SYSTEM

In 2018, thanks to a publication in Science, the saga of these two scientists got off to a bright start. At the time, they showed that gut microbiota, which harbours billions of bacteria, influenced the efficacy of immunotherapy treatments, which awakened the immune system so that it could fight off cancer.

“From the outset, we wanted to develop that research theme and go further to improve the treatments offered to patients, their survival and their quality of life.”

In January 2018, full of ambitious energy, she and Dr. Routy launched their laboratory on the 12th floor of the Research Centre.

Today, 12 people make up the team that aims is to transform a “bad” microbiome into a healthy one to thwart cancer’s plans. Several approaches are possible: reducing the dysbiosis caused by antibiotics, playing with diet and offering prebiotics or probiotics to increase the efficacy of the immunotherapy.

A BERRY FROM BRAZIL AS BACKUP

For a year, their team has even been trying to determine whether a fecal transplant modifying gut microbiota could increase the efficacy of immunotherapy targeting metastatic melanoma or non-small-cell lung cancer. Their objective is to increase the life expectancy of cancer patients.

It’s a first in Canada that will make it possible to identify “good” bacteria to increase the efficacy of immunotherapy.

> *Simultaneously, in early 2022, we also showed for the first time in mice that castalagin, a polyphenol from the Amazonian camu camu berry, acts as a prebiotic, modifies the gut microbiome and improves the response to immunotherapy.*

The Amazonian fruit was already known for its protective effects against obesity and diabetes. It is now known for its anti-cancer benefits, even for immunotherapy-resistant cancers. At least on an animal model.

These promising results pave the way for clinical trials that will use castalagin to complement drugs called immune checkpoint inhibitors in cancer patients.

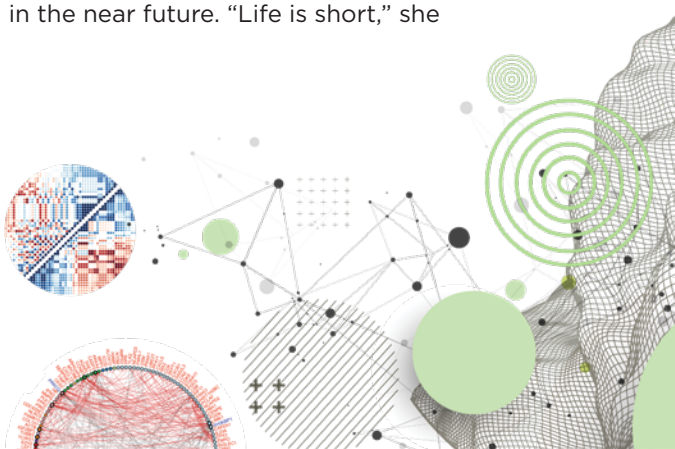
FROM PEAK TO PEAK

Meriem Messaoudene sees herself working a few more years at the Research Centre—long enough to see the results of her research implemented in clinical settings.

“I believe that we would not have made such swift progress if we had not been supported from the outset by the CRCHUM, whether by management or by the people working in the core facilities. In this regard, the exceptional expertise of the animal facility staff allowed us to establish germ-free mice essential for the continuation of our projects.”

In June, the researcher went to Vienna to present her work to the Seerave Foundation, a philanthropic organization that will provide funding for two years so that she can continue her research on castalagin to better understand its impact on bacteria.

Even though she is still as passionate as ever about her research projects, travelling for pleasure is still important to her. She is planning to scale Mt. Kilimanjaro in Africa in the near future. “Life is short,” she reminds us.



SHINGO NAKAJIMA

MUCH MORE THAN A MATTER OF WEIGHT

WITH A WISTFUL, DEADPAN LOOK ON HIS FACE SHINGO NAKAJIMA TELLS OUT OF THE BLUE: HE COULD HAVE PICTURED HIMSELF AS A VETERINARIAN. IN JAPAN. THIS DREAM OF A YOUNG BOY GROWING UP IN TOKYO TOOK A TURN ALONG THE WAY AND CROSSED PATHS WITH THAT OF STEPHANIE FULTON, A RESEARCHER IN THE CARDIOMETABOLIC RESEARCH THEME.

He has been part of her team since October 2019, exploring the neurobiology of food intake, obesity and mood disorders. A one-way ticket from Japan to Quebec that wasn't obvious at the start.

This research area has interested the young researcher since earning his PhD in nutrition at Hokkaido University. At Tokyo's *National Center of Neurology and Psychiatry,* he pursued postdoctoral research for over three years, focusing on the interactions between the brain and nutrients.

The impetus to leave his country came in the form of a grant from the *Japan Society for the Promotion of Science*. This financial assistance encourages the best young scientists in Japan to conduct research at a foreign research institution.

And off to Montreal he went!

THE BRAIN HAS ITS MOODS

"In Stephanie's laboratory, I study how diet modifies mood and behaviours. For example, we can observe behaviours of anxiety and depression in our obese mouse models," he explained.

In obese individuals, the risk of depression and anxiety are higher than in the general population. These mental health problems are the result of a combination of factors: poor diet, lack of physical activity and an accumulation of fat cells. But obesity alone cannot lead to these anxiety- and depression-related behaviours. Far from it!

At the end of 2021, Shingo Nakajima and Stephanie Fulton noted in a scientific journal that metabolic dysfunction, including inflammation and resistance to insulin or leptin, the hormone controlling appetite, are key elements in the manifestation of anxious-depressive disorders in these individuals.

> *The excessive consumption of saturated fats, such as palm oil and sugar, promotes the appearance of these metabolic changes. In the brain, this type of rich diet causes enough inflammation to modify the neural circuits responsible for controlling mood, motivation and emotions."*

THE LINK BETWEEN NUTRITION AND MENTAL HEALTH

Anxious-depressive disorders in obese individuals are in fact more related to these types of metabolic deficiencies than to body weight itself, in men as well as in women.

For Shingo Nakajima, the goal is clear: make the connection between metabolism and mental health.

"Diet isn't a drug used on an ad hoc basis to stop a disease. In contrast, it's a vital pillar in maintaining the good physical and mental health of human beings for the long term."

With his research, he hopes to pave the way for new therapies by identifying how motivation and anxiety- and depression-related behaviours can be influenced by nutrition and hormones. Because, yes, in the equation, sex is a significant variable.

THE GENDER DIFFERENCE

Notable differences have been observed between female and male mice, particularly in recent basic research work conducted in Stephanie Fulton's laboratory.

In psychiatric research, the use of female animal models is still limited. However, the incidence of depression and anxiety disorders is clearly higher in women than men.

The researcher and her team have been exploring this under-researched area: understanding neurometabolic mechanisms specific to women.

As this new era of research begins, Shingo Nakajima will take an alternate route. Not that he regrets his decision to come to the CHUM Research Centre—he has liked everything about it.

But at the end of his postdoctoral training in 2023, he will return to Japan with his family and settle there as a researcher and professor. As to achieving his childhood dream, a return to his native land may be the inspiration he needs. Who knows?

From all different backgrounds

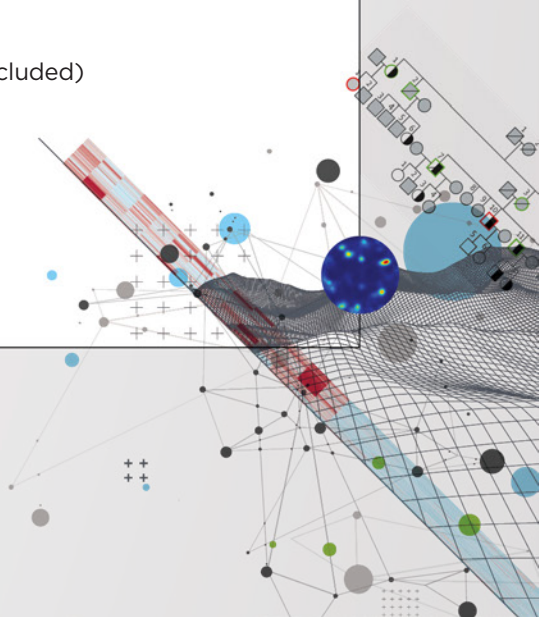
— + than 20 languages spoken at the CRCHUM (French and English included)

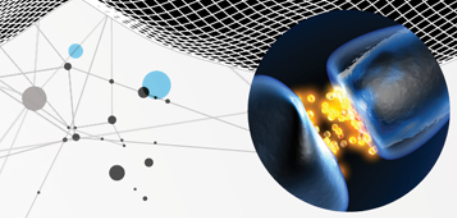
— + than 35% of the people in the CRCHUM community were born outside the country

Women well represented

— About 60% of graduate students are women

— Nearly 50% of postdoctoral fellows are women





ANA CARMENA MORATALLA

MULTIPLE SCLEROSIS, A SILENT DISEASE

TO HEAR HER KEENLY RECALLING HER LIFE AS A YOUNG RESEARCHER TODAY, IT'S HARD TO THINK THAT ANA CARMENA MORATALLA FIRST SET FOOT IN MONTREAL IN 2015, NOT SPEAKING A WORD OF FRENCH. HOWEVER, SHE BROUGHT WITH HER A MASTER'S DEGREE IN NEUROSCIENCE FROM THE UNIVERSIDAD AUTÓNOMA DE MADRID AND THE INTUITION THAT SHE WOULD THRIVE AT THE CHUM RESEARCH CENTRE.

Back in Spain, she had had a glimpse of what awaited her on the other side of the Atlantic by looking through a virtual window. Nathalie Arbour, the manager of the Neuroscience Research Theme, was on the other side of that window, waiting for her.

"I talked remotely with Nathalie to discuss a doctoral position that she had posted on a European website. I liked the topic a great deal and she allowed me to meet her team. She was inviting me into her laboratory!" she recalls.

An unusual type of recruitment for this Old World native, as possibilities for doctoral studies are very limited in Spain.

The call was too strong. A new chapter of her life would start in Montreal. For more than six years now, Ana Carmena Moratalla has been working on the 9th floor of the Research Centre, occasionally gazing out at the view of Old Port, looking at her adopted city and thinking about the journey she has taken.

A DISEASE STILL NOT UNDERSTOOD

In the laboratory, she studies the interactions between the immune system and the central nervous system in multiple sclerosis.

In Canada, more than 90,000 people live with this disease, which causes debilitating vision, memory, balance and mobility problems. That's more than the number of Canadians with HIV. But it's rarely talked about.

Scientists know that immune system dysregulation incites T lymphocytes, white blood cells responsible for activating the body's defence system against infections, to attack healthy nervous tissue in the body, whether in the brain or spinal cord.

In plain English, the disease targets myelin, a protective sheath surrounding nerve fibres, causing inflammation and leading to the deterioration of this substance essential to the transmission of nerve impulses.

COMPLEX MECHANISMS

To stop the progression of this autoimmune disease one day, Arbour and her team are tracking, in the immensity of the brain, the molecules responsible for it.

Ana Carmena Moratalla, who recently obtained her PhD, is part of this scientific saga.

In 2021, using tissues from patients who died of multiple sclerosis, she succeeded in showing that the level of an altered protein, known as ULBP4, is high in their brains, which contributes, through different mechanisms, to general inflammation. Ultimately, this protein could be a therapeutic target.

"We are still in the discovery phase. We now have to validate our published data obtained using human samples in mice models. We will then be able to see if we have a real impact on the disease."

This approach sets them apart on the research scene in Canada. In Nathalie Arbour's laboratory, scientists always begin their research with observations made on patients or their tissues before validating them in animal models.

"I'm very satisfied with this discovery. Nathalie is, too. It wasn't an easy project, but it was worthwhile if we can develop a therapy. Helping patients is the goal of our research!"

A WELCOMING ENVIRONMENT

At the Research Centre, the young researcher has enjoyed collaborating closely with the core research teams of Dr. Catherine Larochelle and Dr. Alexandre Prat, not to mention being able to count on the support of the neurologists in the CHUM's multiple sclerosis clinic—Dr. Marc Girard and Dr. Pierre Duquette—and on the quality and abundance of the biobank samples.

Thanks to a grant from the Multiple Sclerosis Society of Canada, Ana Carmena Moratalla has not only benefitted from scientific training with other research laboratories in Canada, but has also met patients.

> *« Conversing with them, listening to their needs and understanding how they see our research is very enriching. These invaluable human contacts allow us to feel that we can really help improve their lives. »*

Today, the young woman would like to try her hand at research in another environment: industry. The opportunities in Montreal are numerous, as are her contacts.

And, "the reputation of the Research Centre and the technical expertise I have gained at the cytometry and cellular imaging core facilities thanks to the Research Centre staff are additional advantages when it comes to being recruited."

Does she miss her native Spain? Sometimes, but the Hispanic community is never very far. She just has to open the door of the laboratory next door to reconnect with her roots. Like Ana Carmena Moratalla, the CHUM Research Centre is multilingual.

AUGUSTINE FERT

HIV, AN OBVIOUS CHOICE

LIVING IN MONTREAL? A COMBINATION OF CIRCUMSTANCES. STUDYING HIV? A KEEN INTEREST SINCE HIGH SCHOOL. FOR AUGUSTINE FERT, THE DESIRE TO HELP OTHERS IS IN HER DNA. THIS QUALITY OF EMPATHY IS CONSISTENT WITH THE RESEARCH WORK THAT SHE'S CONDUCTING AS PART OF THE TEAM LED BY PETRONELA ANCUTA, A RESEARCHER IN THE IMMUNOPATHOLOGY RESEARCH THEME.

Augustine Fert has the humility of a long-distance runner. The finish line is far off, but the runner sees every kilometre as a small victory. And so it has been with Fert's academic career—from an advanced vocational training certificate in medical biology analysis to a master's degree in genetics and cellular biology at the University of Lyon in France and on to doctoral studies.

Now in the last year of her PhD program, the young researcher, who specializes in virology, sometimes feels she's run a real marathon. The life of a PhD student requires a lot of endurance and resilience.

At the CRCHUM, where virology is a booming area of research, she found her place.

TH17 IN THE LINE OF SIGHT

Antiretroviral therapy has helped improve the health of HIV-positive individuals, but they are at greater risk of developing complications related to the chronicity of inflammation, such as cardiovascular diseases.

These health problems are mainly due to the viral reservoirs in which HIV persists and to the constant activation of the immune system.

"I am trying to understand why Th17 lymphocytes, pro-inflammatory cells, are more permissive to HIV than other types of lymphocytes."

Petronela Ancuta's team showed in previous work that, in the immune battle, these cells are among the first victims of HIV. Their loss creates a breach in the integrity of the gut mucosal barrier and leads to systemic inflammation.

"My goal is really to reduce chronic inflammation in people with HIV. To do so, I am working more specifically on the metabolic aspect of Th17, which is very sensitive, particularly to glucose metabolism."

Fert is working with metformin, a drug used to treat type 2 diabetes (a comorbidity of HIV) that is well tolerated and already approved by the FDA. It also delays cell aging, one of the side effects of the disease.

"By using metformin, we hope to reduce HIV activity in Th17s and thus reduce their metabolism. The use of metformin could help reduce the chronic inflammation seen in people with HIV receiving combination antiretroviral therapy and improve their quality of life."

THE IMPORTANCE OF THE COMMUNITY

Before studying HIV at the Research Centre, Fert wasn't aware of the difficult reality of living with the disease. For her, as for a lot of people, it was controlled by combination antiretroviral therapy.

Thanks to the involvement of Petronela Ancuta and Nicolas Chomont, a researcher at the Research Centre, through CanCURE, the Canadian HIV cure research consortium, Augustine Fert and her colleagues have the opportunity to regularly meet with people with HIV.

> *« Talking to them makes you realize that they take a lot of drugs to control the side effects caused by the combination antiretroviral therapy, not to mention the depression that sometimes results from it. »*

It's also an opportunity to talk in plain terms about our basic research projects and gauge their interest in the research work underway.

"We're lucky in Montreal: the HIV community is very involved in research and access to human samples is fairly easy. With my project, I can see that my work could have an impact in the more or less short term on the lives of the people I've met."

A FUTURE WAITING TO BE WRITTEN

"The facilities are incredible here. All the research is concentrated in the same place. For me, access to the metabolomics and cytometry core facilities, and especially the expertise of the facility managers, is a distinct advantage compared to other institutions."

She hopes to be a research associate in a few years.

"A research associate is an important reference person in a university laboratory. I like supervising interns, transmitting my knowledge and continuing to carry out laboratory manipulations. It's a source of tranquility for me."

Until then, she hopes to do a postdoctoral fellowship in industry, either in Europe or North America, to be exposed to other ways of doing research.

Since writing her childhood poem about germs, Fert has managed to make her way to the world of research. Where will her next step take her?

RADIOMICS TO PREDICT THE RISKS OF RELAPSE

AT THE AGE OF FIVE, MARION TONNEAU KNEW THAT SHE WOULD BECOME A PEDIATRICIAN. AS A YOUNG GIRL, SHE WAS ALREADY TAKING CARE OF HER FAMILY MEMBERS BY PRESCRIBING SMARTIES, NEATLY STOWED AWAY IN HER DOCTOR'S KIT. THE CANDIES HAVE SINCE BEEN REPLACED AND THE LITTLE GIRL BECAME A DOCTOR WHO IS NOW PASSIONATE ABOUT ARTIFICIAL INTELLIGENCE.

Dr. Tonneau could have completed her medical specialty in Lille, France. But her desire to break out of her comfort zone brought her to Montreal, a city that she had discovered in July 2017 during an anaesthesia clerkship at Hôpital Notre-Dame.

This time she came with a fellowship from the Nuovo-Soldati Foundation for young medical researchers carrying out cancer research. Currently a radiation oncology resident, she first set foot in the Research Centre in February 2021 at the height of the COVID-19 lockdown. But that didn't spoil her positive outlook.

Today, she works with Dr. Houda Bahig's team on a project involving artificial intelligence and pulmonary radiotherapy, which, in 2022, received funding over three years from the Canadian Institutes of Health Research.

A STORY OF IMAGING AND BIG DATA

In recent years, medical imaging has undergone an unprecedented revolution: radiomics. Its goal is to better characterize tumours through the large-scale analysis, extraction and mining of data from images taken during regular imaging tests.

The idea here is to succeed in detecting, in the images, information the naked eye is unable to see, which is therefore inaccessible to doctors.

"Thanks to radiomics, I hope to predict the risk of local relapse in patients with localized non-small-cell cancer, i.e. patients not presenting metastases and whose lymph nodes are not involved."

These patients will have previously been treated by stereotactic radiotherapy, a treatment that consists of aiming, with extreme precision, a multitude of very small, high-energy radiation beams towards the area needing to be treated.

On paper, her project seems simple. The reality is another matter.

AN ENORMOUS AMOUNT OF PREPARATION

To succeed in establishing a radiomic signature, you have to design and train a prediction algorithm to analyze tumour images taken by a scanner and automatically extract biological information of relevance to the medical team.

“In our case, we work with a clinical database of 1,000 patients treated at the CHUM. To begin, we extracted from medical files all the radiotherapy planning scans taken prior to treatment. These scans are used to configure the machine to deliver the right dose of radiation at the right locations while minimizing toxicity.”

When undergoing stereotactic radiotherapy for lung cancer, patients benefit from a “4D scan,” during which they breathe normally so that the position of the tumour to treat can be determined based on the respiratory cycle.

“We’ll use these “4D scans,” already annotated by the clinicians, to extract the radiomic features of the tumour to predict risks of relapse. A “4D scan” is made up of about 10 images per patient. With 1,000 patients, that makes a large quantity of data to analyze!”

LETTING THE DATA TALK

Once the analytical phase has been completed, Dr. Tonneau and her colleagues will associate the radiomic features with the known clinical data of each patient to define their prediction algorithm.

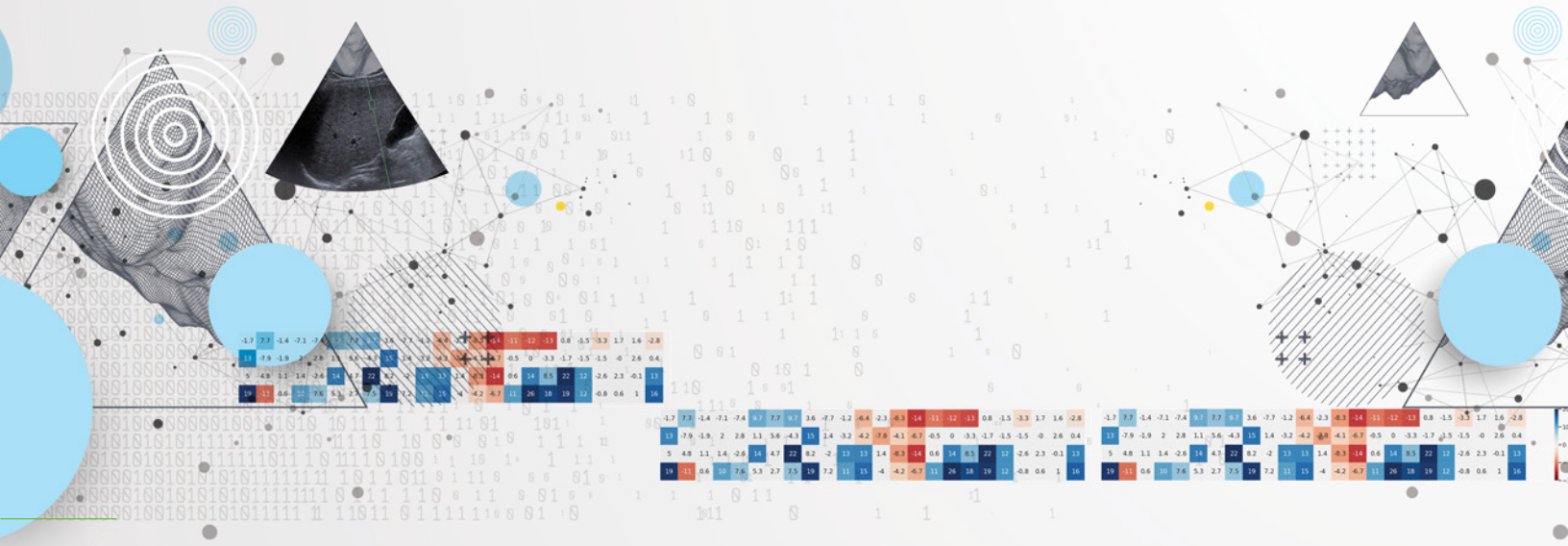
“Because we work retrospectively, we already know what patient has relapsed or not and at what point in time. Now, the idea is to test our predictive model on an independent cohort in another hospital.”

In a few years, the young researcher hopes to be able to determine the profile of a patient at risk of relapse, modify the therapeutic strategy accordingly and optimize treatments.

Working in radiomics, an emerging sector of artificial intelligence, is a source of daily motivation for her, someone who knew nothing about it before coming to Montreal.

> *« I’ve loved working here. My experience at the Research Centre confirmed my desire to pursue a career as a clinician and researcher. I find it very intellectually stimulating. »*

Before pouring herself heart and soul into this adventure, Dr. Tonneau must complete her residency in Lille, which means another two years in France. She would like to continue the project as a France-Quebec collaboration and possibly return to Montreal one day.



ANNIE PELEKANAKIS

THE HIDDEN SIDE OF CANNABIS USE

STUDYING AT UNIVERSITY OPENS UP A RANGE OF SOMETIMES UNEXPECTED POSSIBILITIES. ANNIE PELEKANAKIS WANTED TO BECOME A DOCTOR. AFTER EARNING HER BACHELOR'S DEGREE IN PHYSIOLOGY, SHE CHANGED HER CAREER GOALS. SHE CHOSE THE AREA OF PUBLIC HEALTH WITH ONE CERTAINTY IN MIND: SHE PREFERRED TO WORK IN PUBLIC HEALTH PREVENTION RATHER THAN PRESCRIBING PILLS.

After completing her master's degree in public health at the University of Montreal, co-directed by researchers Jennifer O'Loughlin and Isabelle Doré from the Innovation Hub, Pelekanakis went on to pursue doctoral studies, focusing on the connections between substance use and mental health.

Under the supervision of Marie-Pierre Sylvestre, another researcher from the CHUM Research Centre, she will approach this component by interviewing the NDIT (Nicotine Dependence in Teens) cohort, established between 1999 and 2000 by Jennifer O'Loughlin.

A total of nearly 1,300 young adults, recruited at the age of 12 or 13 between 1999 and 2000 in 10 Montreal-area high schools, make up the sample. For more than 20 years, these people have been questioned at regular intervals about their use of cannabis, alcohol and cigarettes.

A DATA COLLECTION UNDERTAKING UNIQUE IN CANADA

"For the last two years, our questionnaire has been available online. It's easier for the participants. During this data collection cycle that I'm involved in, we are focusing on the cannabis aspect."

Up to now, no study has collected such information—let alone among the Canadian population. The NDIT cohort is rather unique in the world.

"The main goal is to determine the reasons that young adults use cannabis and to identify the risk factors. It's worth mentioning that the scientific literature has focused a lot more on teens."

After 20 years, an average of 800 participants respond to each new questionnaire. Pelekanakis hopes that this will be the case again this time. It will allow them to, among other things, continue other longitudinal studies started a few years ago.

> *"We also want to study how cannabis use is related to anxiety and depression disorders and sleep problems. There is really a desire to understand how they will manage their symptoms.*

NOT IMPACTED BY THE PANDEMIC

With Marie-Pierre Sylvestre and Jennifer O'Loughlin, the young researcher has had a chance to get a peek at the scope of a longitudinal study conducted with the NDIT cohort.

Before and during the pandemic, the two researchers focused on differences in frequency of use of psychoactive substances, including alcohol, cannabis and nicotine (both regular and e-cigarettes) in young adults between the ages of 24 and 33.

Recent scientific literature considers this group as being most affected by anxiety and psychological distress.

Up to now, no study had collected such data, let alone among the Canadian population.

In their work published in *The Lancet Regional Health — Americas*, they showed that the weekly or daily use of psychoactive substances was fairly stable.

These results are quite different from certain messages in the media that helped convey the idea that, during a pandemic, social isolation, financial problems and psychological distress cause a dramatic rise in the use of psychoactive substances.

BETTER PROTECTING MENTAL HEALTH

Even though the collection of current data interests her, she admits that she loves analyzing it.

"I'm passionate about exploring data and understanding what it has to say. Playing an active role in collecting information allows me to take a more nuanced approach when interpreting the data. The two go hand in hand," she says.

Inherent in her research project is the desire to be able to identify interventions to put in place or develop to counter the growing mental health problems among young people, notably anxiety and depression. This could be done by programs offered in schools, for example.

> *I believe that we have an important advisory role to play in prevention with organizations such as the Ministry of Health.*

The idea of recommending best practices and transmitting knowledge based on science comes up frequently in our discussion with Pelekanakis, who would one day like to be a university researcher—in Canada or elsewhere.

DID YOU SAY CORE FACILITIES?

BENJAMIN PÉANT

TOMORROW'S LABORATORIES TODAY

HAVE YOU EVER HEARD OF A LAB-ON-A-CHIP? IF NOT, RUN OVER AND HAVE A CHAT WITH BENJAMIN PÉANT, THE MANAGER OF THE CHUM RESEARCH CENTRE'S MICROFLUIDICS CORE FACILITY SINCE 2019. DURING HIS LUNCH BREAK, CHANCES ARE YOU'LL FIND HIM WITH HIS NOSE IN A BOOK ON THE MILITARY HISTORY OF THE NAPOLEONIC ERA. THE MAN IS CRAZY ABOUT HISTORY—AND BIOLOGY!

Even though his first choice as a teen was the field of archaeology, a high school biology teacher's enthusiasm for his subject quickly had Péant setting his sights in another direction. Of course, he doesn't dig below the surface of the earth in search of clues from the past; instead, he probes the strata of living organisms at a microscopic level.

His first research work was conducted while a student in the master's program in molecular and cellular biology in Lyon, France. After that, he attended Laval University for his PhD in molecular microbiology.

In 2004, Péant joined the research group of Dr. Fred Saad and Anne-Marie Mes-Masson for his postdoctoral fellowship in molecular oncology. At the time, he worked mainly on prostate cancer. He has been a research associate with this group since 2008, working simultaneously for the past four years on miniaturized laboratories of the future in the Microfluidics Core Facility.

A LAB IN THE PALM OF YOUR HAND

Today, microfluidics devices or labs-on-a-chip, developed at the Research Centre, allow scientists to test, observe and predict the effects of treatments on patient tumour samples in a controlled environment. This method also reduces the quantity of reagents used and analysis time. The future!

> *Our devices are made of flexible polymer parts that are biocompatible and gas permeable, which allow us to grow three-dimensional biological structures ex vivo, notably micro-dissected tumours.*

Unique in the world, the technology for this microdissection and the device were developed and refined over a period of ten years by Anne-Marie Mes-Masson's team, which Benjamin Péant belongs to, in partnership with Thomas Gervais, a professor at Polytechnique and CRCHUM researcher.

Using the biopsy of a tumour from a patient, scientists cut between 500 and 600 spheres, 300 microns in diameter, which will be grown in the microfluidic devices and exposed to different treatment or culture conditions.

The potential advantage is that, by preserving the tumour's microenvironment and architecture, as well as the cell composition of the original tissue, it would be possible to better predict the patient's response to a treatment than current cell culture methods.

A COMPLEMENTARY TRIO

Two biologists, Jennifer Kendall-Dupont and Benjamin Péant, and a medical engineering specialist, Amélie St-Georges-Robillard, work together in the core facility, offering several custom services.

"In basic research, we can determine, for example, what the reaction of cells will be to different substances. The 3D models that we offer research teams, more complex than 2D models, allow researchers to better understand what is going on in the tumour microenvironment and monitor the response to given stimuli."

For companies or even university customers, the team offers a more translational approach: characterization of the response to new molecules on mouse or human samples.

''We are currently working on validating a preclinical tool for ovarian cancer. Our goal is to test the response to therapies before patients even begin their treatments. By identifying resistance to certain treatments beyond a reasonable doubt, this tool could guide doctors in their treatment choices."

A FLEXIBLE CORE FACILITY

Thanks to their engineering component and equipment, the team is able to customize their labs-on-a-chip to each customer's need, even though it has earned its stripes working on oncology projects.

The trio recently developed devices to grow pancreatic islets for Dr. Poitout's laboratory.

"Our view is really to democratize knowledge about this emerging technology and to further this knowledge to improve health care and, ultimately, patients' lives. We have therefore trained teams in Montreal, the United States and France in our microdissection technique."

For Benjamin Péant, belonging to the core facility's team has allowed him to discover the Research Centre from a different angle.

"After serving briefly on the Institutional Animal Protection Committee, I have been a member of the Quality Assurance Committee for a few months. I really appreciate the collaborative, family atmosphere at the Centre. It's a healthy and very competitive environment to work in."

UNIQUE HUMAN EXPERTISE

IF UNIVERSITÉ DE MONTRÉAL WERE LOOKING FOR A SPOKESPERSON AMONG ITS GRADUATES, THEY COULD ASK KHALIL BOUYAKDAN. THE MAN HAS THE INSTITUTION ENGRAVED IN HIS HEART. HE SPENT HIS ENTIRE UNIVERSITY CAREER THERE BEFORE BECOMING THE MANAGER OF THE METABOLIC PHENOTYPING CORE FACILITY AT THE CHUM RESEARCH CENTRE IN 2018.

Arriving from Lebanon with his parents at the age of four, this scientist has had a smooth academic trajectory in Montreal, including a bachelor's in biochemistry and a master's on the embryonic development of the brain at the CHU Sainte-Justine. For his PhD, he focused on metabolism and the hypothalamus in the laboratory of Thierry Alquier, a researcher and the manager of the Cardiometabolic Research Theme.

Together, they showed for the first time in mice that the protein ACBP directly influences neurons, allowing rodents and humans to maintain a healthy weight. In fact, no matter how much we exercise and eat a balanced diet, weight control has more to do with your brain than you think!

The two men have worked together since. Khalil Bouyakdan manages the core facility, while his former thesis director is his scientific advisor.

ANALYZING METABOLISM

"Understanding metabolism and its failings is the goal of the Metabolic Phenotyping Core Facility. The phenotype is all the observable characteristics of an individual or animal. It's what the genes express," he explained.

In this field, most tests were developed for humans and then adapted to rodents – most often mice – in order to conduct basic research studies on metabolic diseases.

For example, research teams study mice and want to understand why they become obese or are resistant to obesity.

''In their search for explanations, they come to us to measure in rodents, among other things, glucose metabolism and insulin tolerance, to calculate energy expenditure as a function of oxygen consumption, to determine the source used to generate this energy and to monitor weight progression, internal temperature and movements in real time."

These days, Bouyakdan, like many funding bodies, encourages the research teams to include female mice in their metabolic studies. The fact of having only males skews results: estrogens are known to have beneficial effects on metabolism.

AN OUTSTANDING CORE FACILITY

But what sets this core facility of the Research Centre apart from those of other institutions isn't the specialized equipment, which is rather standard.

"It's all about human expertise. Our two animal health technicians, Mélanie Éthier and Grace Fergusson, have extraordinary skills and exceptional dexterity, especially for specialized surgeries and advanced tests. Their fifteen years of experience has led to the high demand for our services."

The two women began in the laboratory of Dr. Vincent Poitout, now Director of Research at the CHUM and a researcher, gaining the knowledge needed to isolate pancreatic islets, for example. Dr. Poitout is among their many customers at the CHUM Research Centre.

For the needs of a local team, Bouyakdan's team recently "pushed" a metabolic test further by adding a radioactive glucose tracer. It allows researchers to see the liver's production of glucose and determine what tissue picks up the glucose and in what quantity.

In addition to the members of his team, he can count on the collaboration of the two veterinarians from the animal facility, Hélène Héon and Maryse Boulay, as well as their colleagues on the Institutional Animal Protection Committee.

A TRANSMITTER OF SCIENCE

Because of the core facility's excellent reputation, Khalil Bouyakdan receives requests from universities in Quebec and Canada, occasionally from private companies, and internationally for projects carried out with teams from the Research Centre.

"Outside the Research Centre, our visibility is due in large part to the fact that our contributions are mentioned in the 'Acknowledgements' section of articles and that we are sometimes included in the list of authors," explained the scientist, still just as enthusiastic after five years in his position. A gracious nod to the research teams.

> *« Our goal is to do good science and to facilitate research on diabetes and obesity, among others, and to let the public reap the benefits. »*

In that respect, Khalil Bouyakdan has the power to change things, one study after another.

APRIL 2021

Dr. Michaël Chassé is appointed Associate Scientific Director, Data Science, at the CRCHUM

JUNE 2021

Five researchers receive grants totalling nearly $950,000 from the Natural Sciences and Engineering Research Council of Canada

Sophie Petropoulos becomes the Canada Research Chair in Functional Genomics of Reproduction and Development

Hugo Bouchard receives the Canada Research Chair on Emerging Applications of Spectral Computed Tomography

MAY 2021

Twelve researchers receive career awards from the Fonds de recherche du Québec – Santé (FRQS) for a total of $2.3 million dollars

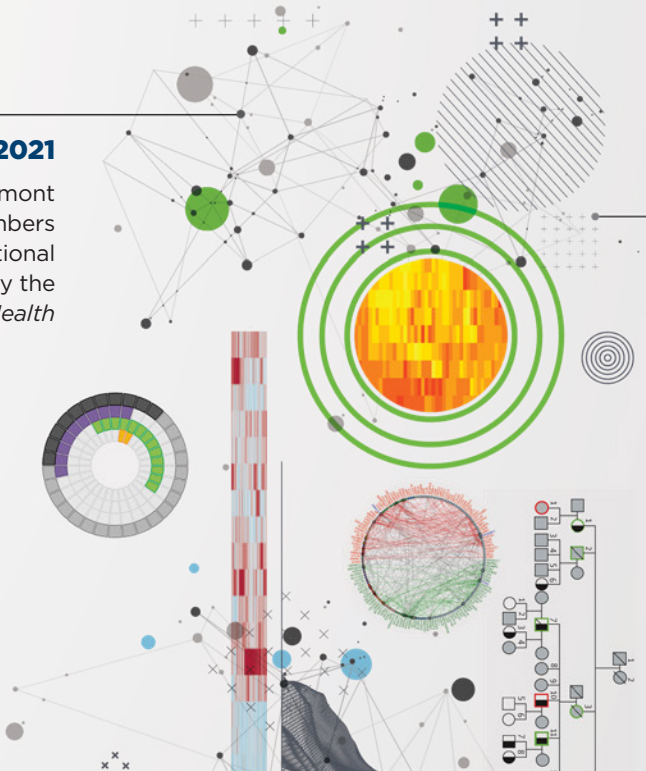
JULY 2021

Eight research teams receive more than $5.5M in funding from the Canadian Institutes of Health Research (CIHR)

Nadia Sourial receives a grant from the IMPULSION program—Support for the economic recovery (FRQS) for her socio-geriatric telemedicine project

2021-2022 HIGHLIGHTS

Here is a summary of the major achievements of our research teams that marked 2021-2022. The CHUM Research Centre is now home to 38 active research chairs, including two new Canada Research Chairs.



AUGUST 2021

HIV research: Nicolas Chomont and Andrés Finzi are full members of two of the 10 international consortia funded by the *National Institutes of Health*

SEPTEMBER 2021

Aude Motulsky is appointed Deputy Director of the University of Montreal's Digital Health Consortium

Researcher Guy Rutter, a world leading expert in type 2 diabetes, joins the CRCHUM from Imperial College London (United Kingdom)

OCTOBER 2021

Dr. Bertrand Routy and his team receive $1M in funding from the Weston Family Foundation for their project combining cancer immunotherapy and the microbiome

NOVEMBER 2021

Speech given by Fabiola Gianotti, Director General of the European Organization for Nuclear Research (CERN), at the 12th Scientific Day

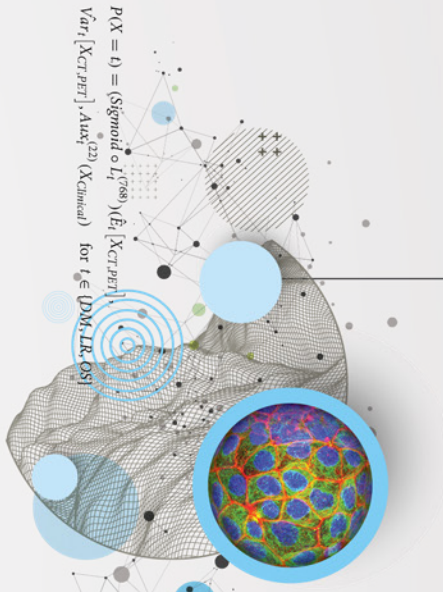
JANUARY2022

The CRCHUM bestows its 2021 Awards of Excellence. Awardees: Nathalie Grandvaux (Contribution to the Institution's Operations), Dr. Bertrand Routy (Young Researcher), Dr. Cécile Tremblay (Career), and a collective of 13 researchers for their work on COVID-19 (Scientific Contribution of the Year)

Dr. Gilles Soulez becomes the new manager of the CRCHUM's Imaging and Engineering Research Theme

Nathalie Grandvaux receives the Recognition Award (teaching staff) from the Dean of the Université de Montréal's Faculty of Medicine

Dr. Antoine Boivin receives the renewal of his Canada Research Chair in Patients and Public Partnership



FEBRUARY 2022

Alex Parker and his team receive $1.6M million from the Weston Family Foundation to conduct further research into the microbiome and amyotrophic lateral sclerosis

11 research teams receive $5.7M in Canadian Institutes of Health Research grants

Lise Gauvin receives the Paul-Lupien and Jean-Davignon Founders' Award (Quebec Society of Lipidology, Nutrition and Metabolism)

MARCH 2022

Health and Artificial Intelligence: Drs. Michaël Chassé and An Tang, as well as Nadia Larichi of Polytechnique Montréal, receive $1.2M in funding from IVADO

PhD student Stephanie Coronado-Montoya (Dr. Didier Jutras-Aswad's laboratory) obtains a science communication grant from the Fonds de recherche du Québec

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