Resounding Approval

Sunnybrook Research Institute’s success rate soars above national average

By Alisa Kim

Scientists at Sunnybrook Research Institute (SRI) had a stellar showing in the Fall 2017 Project Grant competition held by the Canadian Institutes of Health Research (CIHR).

The national funding agency approved 15 projects led by SRI researchers, for a total investment of $11.8 million. At 26%, SRI’s success rate was well above the national average success rate of 15%. More than 3,400 grant applications were submitted, making it the second largest competition in CIHR’s history.

“Once again, our scientists have shown the critical importance of the questions they are asking. Getting research funding is a formidable task, with the number of worthy proposals far exceeding the money available. These results speak not only to the excellence of our faculty, but to their hard work and determination,” says Dr. Michael Julius, vice-president of research at SRI and Sunnybrook.

Among those who were successful is Dr. David Goertz, a scientist in Physical Sciences, who was awarded a five-year grant worth $776,475. He along with SRI scientists Drs. Kullervo Hynynen, Bob Kerbel and Meaghan O’Reilly are studying how to enhance cancer immunotherapy using ultrasound-stimulated bubbles. Goertz and colleagues have shown that focused ultrasound paired with microbubbles can improve the tumour-killing effects of an immune-checkpoint inhibitor. They will use liver tumours to investigate the mechanism of how this happens, and how best to exploit and control this effect.

Dr. Eileen Rakovitch was awarded a four-year grant worth $910,352 in the Fall 2017 CIHR Project Grant competition. She will study how gene expression in women with ductal carcinoma in situ can be used to predict response to radiotherapy. [Photo: Nation Wong]
Dr. JoAnne McLaurin, a senior scientist in Biological Sciences, says she was "ecstatic" to learn of her success and looks forward to being able to concentrate on "science, the projects and papers again" after an intense period of grant-writing. She will receive $933,300 over five years. She is working with SRI neuroscientists Drs. Carol Schuurmans and Bojana Stefanovic to examine a treatment strategy for Alzheimer’s disease that aims to balance the neuronal network through the conversion of astrocytes into inhibitory neurons. In people with Alzheimer’s disease and in rodent models of the disease inhibitory neurons are dysfunctional and ultimately lost.

“The premise of my grant is to form new neurons from glial cells in the memory centre of a preclinical model of Alzheimer’s disease,” says McLaurin. She notes that several cognitive processes, including working memory, depend on an intact inhibitory network. This approach to balancing excitatory and inhibitory activity could prove to be superior to the use of drugs and stem cells to replace inhibitory neurons, which can have severe side effects.

Dr. Eileen Rakovich, a clinician-scientist in the Odette Cancer Research Program, was awarded a four-year grant worth $910,352. Her project is titled “DCIS-Precise: a genomics-driven model for predicting DCIS response to radiation.” She is looking at how gene expression in women with a type of breast cancer called ductal carcinoma in situ (DCIS) can be used to predict response to radiation therapy. The goal is to develop genomic biomarkers that predict the benefit of radiotherapy in women with DCIS. Such biomarkers would help to reduce unnecessary treatment in women with a low risk of disease recurrence. They would also serve to identify those with aggressive DCIS who will benefit from radiation, and those with radiation-resistant disease who will need other interventions to lower their future risk of breast cancer.

Dr. Bojana Stefanovic, a senior scientist in Physical Sciences, is the recipient of a five-year grant worth $918,000. Her project titled “Modulating peri-ischemic neuronal hyperexcitability” was ranked second of 38 applications in her committee. “We were exhilarated to learn of the results,” says Stefanovic. Using preclinical models of stroke she will study the peri-infarct zone, the damaged but potentially recoverable brain region surrounding the site of a stroke. With her colleagues she will modulate the activity of these neurons and monitor their function in the hours after a stroke, with an ultimate aim of enhancing recovery.

Two proposals by SRI scientists earned top marks by review panels. Dr. Astrid Guttmann, an associate scientist in Evaluative Clinical Sciences, submitted a grant that ranked first among 57 applications in her committee. She will receive $585,224 over four years for her work, which seeks to optimize Canada’s health care for refugees. Dr. Baiju Shah, a scientist in Evaluative Clinical Sciences, was awarded $392,256 over three years. His project, which will evaluate the impact of improved access to drugs on the care, outcomes and costs of type 2 diabetes, ranked first of 51 proposals in his committee.

Nine other SRI scientists were awarded funding in the Project Grant competition:

Dr. Greg Czarnota, director of the Odette Cancer Research Program and senior scientist in Physical Sciences, was awarded a one-year bridge grant worth $100,000 to study the use of quantitative ultrasound for a priori breast cancer chemotherapy response prediction.

Dr. Stephen Frennes, a clinician-scientist in the Schulich Heart Research Program, will receive a one-year grant of $611,999 to conduct a randomized trial comparing the clinical outcome of single versus multiple arterial grafts.

Dr. Jean Gariépy, a senior scientist in Physical Sciences, was awarded $860,625 over five years. The grant supports the discovery and development of agents that block the VISTA receptor, an immune checkpoint on T cells, toward restoring antitumor immunity.

Dr. Paul Karanicolos, a clinician-scientist in the Odette Cancer Research Program, will receive $1,832,175 over five years to lead a randomized controlled trial that will evaluate whether tranexamic acid reduces perioperative blood transfusion in patients undergoing liver resection.

Dr. Patricia Lee, a clinician-researcher in urogynecology at Sunnybrook, was awarded $481,950 over three years to conduct a randomized controlled trial on laser treatment for stress urinary incontinence.

Dr. Greg Stanisz, a senior scientist in Physical Sciences, will receive $650,250 over five years. He will study saturation transfer MRI as a biomarker of tumour response to radiotherapy in patients with glioblastoma multiforme.

Dr. Cari Whyne, director of the Holland Musculoskeletal Research Program and senior scientist in Physical Sciences, was awarded $966,960 over four years. With SRI clinician-scientist Dr. Albert Yee, who is co-principal investigator on the grant, she will analyze changes to bone quality after cancer treatment, in particular, the impact of multimodal treatment on the skeletal stability of the metastatic spine.

Dr. Graham Wright, director of the Schulich Heart Research Program and senior scientist in Physical Sciences, will receive $791,775 over five years for his work on MR-guided management of occlusive peripheral arterial disease.

Dr. Burton Yang, a senior scientist in Biological Sciences, was awarded $990,675 over five years to study the role of circ-Itga9 in cardiac remodelling.

All told, the agency approved 512 research grants and an additional 33 bridge grants, for a total commitment of $372 million. In order to fund more projects, CIHR applied an across-the-board reduction of 23.5% to the budgets of funded applications. The average grant is $720,534 over a nearly four and half-year period.
News @ SRI

More Tricouncil Grants

Dr. David Spaner, a senior scientist in the Odette Cancer Research Program, received funding from the Canadian Institutes of Health Research (CIHR) through the Joint Canada-Israel Health Research Program. The award is worth almost $1.2 million. It will support his research into understanding the role of type 1 interferon in resistance to cancer immunotherapy.

Dr. Amy Yu, an associate scientist in the Hurvitz Brain Sciences Research Program, was awarded a Catalyst grant from CIHR worth $200,000 over two years. She will develop a stroke-specific comorbidity index to predict mortality and disability in a population-based study.

A handful of SRI scientists were awarded Discovery grants from the Natural Sciences and Engineering Research Council of Canada. The term of the award is five years.

Dr. Christine Démoré, a scientist in Physical Sciences, was awarded $145,000 to develop miniature ultrasound probes for diagnostic imaging in the esophagus.

Dr. Simon Graham, a senior scientist in Physical Sciences, will receive $280,000 for his work on robust correction for the effects of head motion on functional MRI of brain activity.

Dr. Angus Lau, a scientist in Physical Sciences, was awarded $105,000 for the development of MRI-guided radiotherapy.

Dr. Carol Schuurmans, a scientist in Biological Sciences and the Dixon Family Chair in Ophthalmology, was awarded $200,000 for her research into the molecular mechanisms that control Muller glia activation in the retina.

Dr. Walter Swardfager, a scientist in Evaluative Clinical Sciences, will receive $115,000 to study human circannual metabolic biorhythms.

Diverse Support for Cancer Research

Dr. Bob Kerbel, a senior scientist in Biological Sciences, was awarded a grant worth £189,132 ($289,635 CAD) from Worldwide Cancer Research. He will use the funds to develop a new antivascular therapy approach that treats metastatic cancer by targeting vessel co-option.

Dr. Greg Stanisz, a senior scientist in Physical Sciences, also received a Discovery grant. He is using prostate tumours with different degrees of aggressiveness and sensitivities to radiation treatment to test whether MRI techniques developed in his lab can predict treatment response.

Dr. Arun Seth, a senior scientist in Biological Sciences, was awarded a one-year grant from the Ontario Molecular Pathology Research Network. He will receive $34,800 to look for markers predictive of progestin therapy response in conditions that affect the lining of the uterus, including endometrial atypical hyperplasia, which can progress to cancer, and low-grade endometrioid adenocarcinoma.

Two cancer researchers at SRI were awarded 2017 Movember Discovery Grants from Prostate Cancer Canada.

Dr. Stanley Liu, a scientist in Biological Sciences, will receive $200,000 over two years to analyze combined genetic and protein changes that appear in cancer recurrence after radiation. The aim is to identify key changes that can serve as biomarkers that will help identify patients who have prostate cancer that is more likely to recur after radiation treatment.

And That’s Not All

Dr. Benjamin Goldstein, a senior scientist in the Hurvitz Brain Sciences Research Program, received a grant-in-aid from the Heart and Stroke Foundation worth $300,000 over three years. The award will support his work on integrating markers of neurocognition and inflammation with retinal vascular photography in adolescents at increased risk for cardiovascular disease.

Dr. Jessica Widdifield, a scientist in the Holland Musculoskeletal Research Program, was awarded a Young Investigator operating grant worth $300,000 from the Arthritis Society. The funds will support her research into the use of rheumatology electronic medical records to evaluate and optimize care and management of arthritis.
Tool Kit: DISCO DAD3240 High-Precision Dicing Saw

Sunnybrook Research Institute (SRI) is the birthplace of some of the most advanced ultrasound imaging equipment on the market. With the recent purchase of the DISCO DAD3240 semi-automatic dicing saw its position as a leading technological hub is further pronounced.

The high-speed, high-precision saw was acquired via Dr. Christine Démoré, scientist in Physical Sciences and the Odette Cancer Research Program at SRI. “Our number-one application of the dicing saw is to make the fine-scale active piezoelectric layers for micro-ultrasound probes,” Démoré says. Her research in capturing high-resolution ultrasound images of the esophagus, achieved by fabricating miniature ultrasound probes with the transducers cut by the dicing saw, is a central example of this.

The machine is an upgrade from the DISCO DAD3220, which has served the SRI community for more than 10 years, and was frequently used to capacity. Although the previous-generation saw is still functional and can continue to be used, the new system adds much-needed dicing capacity and new capability. Users can exercise more precision over a larger workpiece; they can work with wafers or workpieces that are up to eight inches in diameter, as opposed to the previous version’s maximum of six; they can automatically control the water flow, which cools the blade and removes cutting debris; and can more easily cut through thick or layered material with less damage due to the higher power spindle.

Aside from the esophageal project, Démoré says the machine has a wide range of applications. “Where the pathology is too deep to be imaged with current micro-ultrasound imaging probes, but a small endoscope, or even a large needle could be positioned near the tissue of interest, the dicing saw can be used to make a miniature, high-resolution ultrasound probe that fits in the endoscope.”

Démoré’s group isn’t the only one enjoying the advantages of the new machine. The labs of Drs. Brian Courtney, Stuart Foster, Kullervo Hynynen and Meaghan O’Reilly are also frequent users. “Although my group uses it for making ultrasound imaging devices, which generate an acoustic pulse and then detect reflections from tissues to visualize organs and diagnose disease, other groups use it for therapeutic ultrasound devices to generate high-intensity ultrasound beams to treat diseases,” Démoré says.

The dicing saw is operated by graduate students and research assistants, and is used almost every day. Housed in SRI’s device development lab, it was delivered in October 2017 and operational by mid-November 2017. — Matthew Pariselli

Investing in Image-Guided Therapy Research

The Ontario Ministry of Research, Innovation and Science awarded three senior scientists in Physical Sciences grants through the Ontario Research Fund-Research Infrastructure program. These awards match investments made by the Canada Foundation for Innovation into image-guided therapeutics research.

**Dr. Greg Czarnota**, director of the Odette Cancer Research Program, will receive $3.3 million to lead a project looking at combined MRI-linear accelerator ultrasound therapy instrumentation.

**Dr. Kullervo Hynynen**, director of Physical Sciences, was awarded $2.5 million to research advanced neurotherapeutics involving MRI-guided transcranial focused ultrasound.

**Drs. Christine Démoré and Stuart Foster**, scientists in Physical Sciences, are part of a team that was awarded $6.6 million from the Terry Fox Research Institute. The researchers are using nanoparticles with photoacoustic imaging for cancer therapy guidance. The aim is to be able to destroy tumours without damaging normal tissue.

**Dr. Graham Wright**, director of the Schulich Heart Research Program, was awarded $869,131 to expand preclinical research into cardiovascular interventions.
We Are SRI

CV: Dr. Colleen Bailey

Bio Basics: A scientist in Physical Sciences and the Odette Cancer Research Program at Sunnybrook Research Institute (SRI). Completed her undergraduate degree at the University of Guelph, PhD at the University of Toronto and a postdoctoral fellowship at University College London in London, U.K. Born in Trenton, Ont. Joined SRI in July 2017, and has lived in Toronto since then.

What is your research focus?

I look at MRI methods to monitor cancer therapy. At the Odette Cancer Centre they have a lot of new developments in radiation therapy, and I’m trying to come up with ways we can monitor patients to predict who’s responding to therapy and who’s not. Then we can adjust treatment based on what we see, hopefully.

You were here as a student from 2006 to 2012. What's it like being here now as an appointed scientist?

It’s good. It’s interesting because I still know quite a few people, but there are new faces, too. Now, I’m more on the management side, so trying to deal with grants and things like that, and getting my own program organized. PhD programs are good here because they’re pretty independent, but this is on another level.

Why did you choose to study cancer treatment?

There’s just so much to do. I guess you can say that about a lot of diseases, though. I actually started my PhD on a stroke project, but then a scientist here, Dr. Greg Czarnota, was trying to measure cell death with ultrasound, and I guess he thought, ‘Let’s see what we can do with MRI.’ I did some measurements for him, and then that led into my whole PhD project. There’s so much you can look at with cancer treatment.

What are you working on at the moment?

We just started this, so it’s quite early, but we had a collaborator come in November from Sweden, Dr. Filip Szczepankiewicz, who has a new sequence on the MRI scanner. MRI scanners come with standard sequences, but you can write your own to try to do different things. He’s helping us set up this sequence that’s intended to look at diffusion MRI at a much smaller scale than the standard sequence does it. We’re hoping to see microscopic changes that you can’t see with the standard sequence.

How do you like to unwind?

I play Frisbee. Actually, that started with a team I was on at Sunnybrook. I also like to knit.

You’re shipped to a desert island and you can bring only one movie and one album. What do you bring?

I would probably bring The Princess Bride [laughs] and The Hard and the Easy, by Great Big Sea.

For a longer transcript visit sunnybrook.ca/research.

Behind the Scenes With Benoit Chambaron

Bio basics: Manager, comparative research, Sunnybrook Research Institute. [Comparative research is essential to the progress of human medicine. Researchers must study animal models when there is no complete alternative and to comply with government regulations. Animals allow us to study disease processes so we can understand those processes better and develop ways to stop or prevent them.] Previously worked at the Research Institute of the McGill University Health Centre. Completed his MBA and bachelor of business administration at the Université du Québec à Montréal. Born in France and immigrated to Canada at age eight. Joined SRI in June 2016.

What attracted you to SRI?

My mom was being treated here at the Odette Cancer Centre. I was back and forth for her treatment, so I knew the hospital a little bit. I heard about the opening and it was exactly what I was doing in Montreal. I thought it would be nice to expand my [work] experience.

What is a typical day for you?

At 7 a.m. we have a team meeting. There are 16 staff in total. We go through everything that needs to be done for the day and assign tasks. We try to plan ahead for the next few days so we can assist the researchers. We assist with [procedures] and writing their protocols. We meet with them to see what their next project is to ensure they have the right space and equipment, and to see if people need to be trained.

We start early to have the room free for the investigators to do their work. We do the husbandry of the animals (feeding, giving water and doing a daily health check) as early as possible so that by the time the researchers come in—I’d say the peak time is 10 a.m.—we’ve done the first check.

I do a walk-around once a day to talk to the researchers to see if everything is okay. Usually when I don’t hear anything, that means things are good. [Laughs.]

What are the challenges?

Building issues. We have such harsh weather—from super hot to very cold. That’s very demanding on the heating, ventilation and air conditioning. We have to be as proactive as possible to limit the variation of temperature in the rooms. Also because research is such a large group, there are a lot of projects. It’s quite a challenge to be on top of all the different protocols.

What do you like to do outside work?

I travel a lot. Because my family’s in Europe, I go to Europe a few times a year. As long as I have a long weekend, I try to go away.

For a longer transcript visit sunnybrook.ca/research.
Trainees’ Post: for Students and Postdocs

Confronting a PhD defence date: Miho Tanaka shares her feelings as she prepares for the big day

Unlike hair colour and nose shape, perseverance isn’t an attribute normally mentioned on the subject of hereditary traits. Ask Miho Tanaka what she’s inherited from her family, however, and it's among the first words she utters.

Born and raised in Osaka, Japan, Tanaka grew up in what she calls “a working class” family. Her father, uncle and grandfather began academic endeavours but were forced to abandon them when funds ran dry. Determined to become the first in her family to achieve a PhD, she immigrated to Canada on her own. In January 2011, she landed a position in the lab of Sunnybrook Research Institute (SRI) senior scientist Dr. James Carlyle, studying natural killer cells and their function as a defence against cancer. “In the immune system there are different cell types. It’s almost like a battlefield, where there are different parts at work—a sniper has a different role than a medic. I look at a specific cell type called natural killer cells and its role in the battle against cancer,” she says.

It’s a function she has evaluated closely and one she will unpack when she defends her thesis in spring 2018. Despite hurdles along her academic course, including failed exams and periods of deep self-doubt, Tanaka has indeed persevered and can see the light at the end of the PhD tunnel. Here, she shares with Matthew Pariselli the challenges she encountered during her thesis, what her source of motivation is and what she wishes she did more of throughout the process.

Why did you decide to come to Canada?

I always wanted to get out of Japan. It’s such a unique country with a unique culture, but I wanted to know different points of view. Canada was a place my family talked about immigrating to, but we never did. I heard that Canada was inclusive, there was beautiful nature and the people were nice.

How would you describe your experience of acclimation?

It was tough. The transit system, the people, how people communicate, it was all very different. Relevant to my PhD, the biggest difference was the education system. In Asia, education is very one-way. You sit down, memorize things and write them out; that’s it. The first exam I had here was essay-based. I was given an idea, and I had to plan experiments to prove a hypothesis. I struggled with that and actually failed the course. Also, in labs, the supervision style is very different. In Japan, it’s very hands-on. The PI [principal investigator] takes care of your progress. Here, the approach is mostly hands-off. You have to take initiative. That’s not something I had. A lot of students who receive most of their education in Asia don’t have that.

What fuels your drive?

My family. It’s in my family’s blood to never give up. My grandparents and parents made an effort to put my generation in school. My sister was the first one to go to grad school; she has an MBA. I’ll be the first to get a PhD. I want to give back to my parents who sacrificed so much. I have four nephews and one niece, and I want to be a role model for them. It’s easier to do something if you have someone in your own family who’s done it, someone to look up to.

How do you feel as your defence date draws near?

I’m excited and proud. I know toward the end it’ll be really tough, but I like challenges. When I overcome it it’ll feel really good, so I’m excited for that reason.

I’m proud because it hasn’t been easy, but I’ve managed. Two years into my PhD I did an oral defence about my work and I failed. That was my biggest struggle. It’ll be a similar process this time, but there will be more pressure because I’ll be finishing up. I’m not too nervous because I’ve worked so hard over the years and gained confidence. Two years ago, I was at the edge of quitting. I had to take time to think about things, but I decided to stay, face my PhD and pour all of my energy into it. It was tough, but I found my passion again, and for that I’m proud.

What have you learned since you began your PhD that you wish you knew earlier?

That talking about my work with my peers is really important. This teaches you a lot every day and makes you see a point you may not have seen. I wish I’d done it in the first few years. I was not confident or comfortable talking about my project, but speaking with my lab mates when they asked about the work would have been great. It would have been especially helpful when I was feeling discouraged. I also wish I reached out to female senior scientists, professors or PIs—women who could understand the experience. That’s something I’d recommend to other students. Learn from my mistake.
Applause
Recognizing the scientific and scholarly achievements of SRI faculty and trainees

Dr. David Gladstone, a scientist in the Hurvitz Brain Sciences Research Program, was awarded a Mid-Career Investigator award from the Heart and Stroke Foundation. The award, worth $80,000 per year for four years, supports his research into improving prediction and prevention of cardioembolic stroke.

Dr. Kullervo Hynynen, director of Physical Sciences, was named a Fellow of the IEEE (Institute of Electrical and Electronics Engineers) for contributions to image-guided therapeutic focused ultrasound. The prestigious honour is conferred to no more than 0.1% of the total IEEE voting membership.

Dr. Moira Kapral, an affiliate scientist in the Hurvitz Brain Sciences Research Program, also received a Mid-Career Investigator award from the Heart and Stroke Foundation. The award supports her research into stroke health services.

Dr. Laurence Klotz, a clinician-scientist in the Odette Cancer Research Program, was presented with the Dean's Lifetime Achievement Award from the University of Toronto Faculty of Medicine. It recognizes alumni who have made outstanding contributions to research, teaching, clinical care, administration or public service.

Dr. Graham Wright, director of the Schulich Heart Research Program, secured a renewal of his Tier 1 Canada Research Chair in Imaging for Cardiovascular Therapeutics. The award is worth $1.4 million over seven years. It will support his research on the use of MRI to assess cardiovascular disease and to guide interventions in the heart.

Dr. Martin Yaffe, a senior scientist in Physical Sciences, was awarded the 2017 Edmond Odette Prize for Innovation and Technology in Cancer Care. The award celebrates his contributions to medical imaging research. His innovative work in digital mammography helped to set this technique as the new diagnostic standard in North America.

Kudos to our Trainees

Abdikarim Abdullahi, a PhD student supervised by senior scientist in Biological Sciences Dr. Marc Jeschke, is first author of a paper that was published in Endocrine Reviews. The paper, "Taming the Flames: Targeting White Adipose Tissue Browning in Hypermetabolic Conditions," was selected as the cover article of the December 2017 issue.

Dr. Oscar Aguilar, who did his PhD in the lab of Dr. James Carlyle, senior scientist in Biological Sciences, has taken up a postdoc in the lab of Dr. Lewis Lanier at the University of California, San Francisco.

Graduate students of Dr. Krista Lanctôt, a senior scientist in the Hurvitz Brain Sciences Research Program, were recognized by the Alzheimer’s Drug Discovery Foundation. Myuri Ruthirakuhana, a PhD student, and Parco Chan, a master’s student, each won a 2018 Young Investigator Award from the organization.

Dr. Aaron Prodeus, whose PhD was supervised by senior scientist in Physical Sciences Dr. Jean Gariépy, successfully defended his thesis. Dr. Trisha Roy, whose PhD was co-supervised by Dr. Graham Wright, director of the Schulich Heart Research Program, and Dr. Andrew Dueck, a clinician-scientist at SRI, also successfully defended her doctoral dissertation.
Abdikarim Abdullahi, a PhD student in the lab of SRI senior scientist in Biological Sciences Dr. Marc Jeschke, is first author of a paper that was published in *Endocrine Reviews*. The paper, “Taming the Flames: Targeting White Adipose Tissue Browning in Hypermetabolic Conditions” was selected as the cover article of the December 2017 issue. Inset: the cover image: a brown fat cell surrounded by capillaries. [Photo: Nation Wong]