



WINTER 2011/2012

IN THIS ISSUE

5

Doors Open to New Biomedical Imaging Research Suite

- 4 TOOL KIT
- 6 TRAINEES' POST
- 7 APPLAUSE

A Glimpse of Tomorrow's Medicine

Research day celebrates the promise of image-guided therapies

By Alisa Kim

On November 10, 2011, researchers, trainees and staff gathered for the second annual Centre for Research in Image-Guided Therapeutics (CeRIGT) Research Day at Sunnybrook Research Institute (SRI).

The event showcased the science of CeRIGT, a \$160-million centre that will add more than 150,000 square feet of research facilities to SRI. Here, scientists and their teams will create tools to detect and diagnose disease sooner and more accurately, invent technologies to treat disease minimally invasively, and develop biological and drug therapies tailored to the individual.

Dr. Barry McLellan, president and CEO of Sunnybrook, opened the day by recounting milestones in establishing CeRIGT. So far, these include the building of the magnetic resonance imaging (MRI)-guided high-intensity focused ultrasound surgery suite, the biomarker imaging research lab and the biomedical imaging research suite. He congratulated all involved in CeRIGT on the "hat trick," and invited everyone to the launch of the suite later that day.

Next, **Dr. Michael Julius**, vice-president of research at Sunnybrook, welcomed attendees and commended them for their role in fulfilling SRI's mandate of translating research into clinical impact. "The care on which we rely doesn't come out of thin air;



Dr. Ferenc Jolesz, professor of radiology at Brigham and Women's Hospital and Harvard Medical School, gave the keynote lecture

it rests squarely on your shoulders, your dedication, your calling. Today's treatments are yesterday's discoveries," he said.

Julius noted that in addition to the \$74 million investment from the federal government through the Canada Foundation for Innovation, the centre would not exist without the backing of the hospital's senior leadership and Board of Directors. "Sunnybrook Research Institute is a part of Sunnybrook Health Sciences Centre, and one cannot separate the successes of one from the successes of the other," he said.

Continued on page 2

Where's the Research?

Two weeks after the October 6 provincial election, Premier Dalton McGuinty reorganized his cabinet. At the same time, he renamed the Ministry of Research and Innovation the Ministry of Economic Development and Innovation (MEDI), thus giving the ministry a research-free moniker. Brad Duguid is the first minister of MEDI.

One of the first actions of the new ministry was to cancel rounds 6 and 7 of the Ontario Research Fund-Research Excellence fund. Proposal development for round 6 was well underway, having been launched in the summer. Scientists at SRI had submitted the required notices of intent; full proposals were due January 27.

Money from the ORF-RE has been diverted to set up the Southwestern Ontario Development Fund and to make the Eastern Ontario Development Fund permanent. The funds—each worth \$80 million over four years—are focused on regional economic stimulation and job creation.

Additional funding for these new funds comes from cancelling the Clinical Trials Fellowship Program, and by reallocating funding that had been earmarked for business support loans.

The ministry is retaining the Ontario Research Fund-Research Infrastructure and the Early Researcher Awards funds.

Continued from page 1

Dr. Ferenc Jolesz, codirector of the National Center for Image Guided Therapy at Brigham and Women's Hospital (BWH) in Boston, gave the keynote lecture. Jolesz described his hospital's Advanced Multimodality Image Guided Operating suite (AMIGO), a medical and surgical research environment that allows multidisciplinary teams to treat patients using intraoperative, multimodality imaging without the patient or medical team ever leaving the operating room.

In AMIGO, one imaging modality offsets the weakness of another. Thus, X-ray and ultrasound, which produce images in real time, are combined with cross-sectional digital imaging systems like computed tomography (CT), MRI and positron emission tomography, which provide better definition. An exciting clinical application of AMIGO is molecular image-guided therapy through optical imaging and mass spectrometry. The improved sensitivity and specificity of images obtained from these probes provide greater definition of tumour margins, enabling clinicians to remove or destroy cancerous tissue more thoroughly.

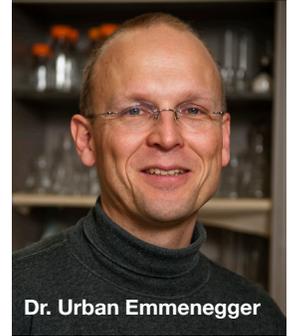
Following this, SRI researchers gave talks on how advances in imaging can more effectively detect and treat cancer, and diseases of the musculoskeletal system, heart and brain.

From the Odette Cancer Research Program, **Dr. Anne Martel** a senior scientist in physical sciences at SRI, spoke on the use of dynamic contrast enhanced-MRI to assess the therapeutic

Funded: Cancer Researchers

Two scientists at Sunnybrook Research Institute have each been awarded operating grants worth \$60,000 per year for two years from the Cancer Research Society.

Dr. Urban Emmenegger, a scientist in biological sciences and an oncologist at the Odette Cancer Centre, will use the funds to study autophagy, a cellular response that can enable cell survival or cell death, as a complementary therapeutic target in antivasular tumour therapy.



Dr. Arun Seth, a senior scientist in biological sciences, is a co-investigator on a study that aims to identify the regulator of telomerase and its possible role in controlling telomerase expression in cancer cells. The lead investigator is Dr. Mario Chevrette from the Research Institute of McGill University Health Centre.

Prostate Cancer Canada also awarded **Emmenegger** an operating grant worth \$60,000 per year for two years. He will use the funds for his research on autophagy modulation to overcome resistance to systemic prostate cancer therapy.

Cancer Care Ontario has awarded **Dr. Greg Czarnota**, director of the Odette Cancer Research Program and a scientist in physical sciences, a Cancer Imaging Network of Ontario research grant worth \$70,000 over two years. Czarnota will use the funds to study the combination of ultrasound and optical methods for personalizing care in locally advanced breast cancer.

response of tumours. **Dr. Martin Yaffe**, also a senior scientist in physical sciences and head of SRI's biomarker imaging research lab, discussed his work on quantitative pathology in cancer research and care.

Martel and Yaffe, along with other scientists and clinician-scientists at Sunnybrook, will work together in the treatment planning, analysis and evaluation facility. Here, work in image registration and analysis techniques will provide insight into the molecular nature of disease, and guide the development of new, targeted therapies.

The event also featured the unveiling of the biomedical imaging research suite. McLellan noted that the state-of-the-art facility, which enables researchers to do preclinical and clinical studies using MRI, CT and focused ultrasound, has already fostered scientific collaboration and partnerships with industry.

Attendees made their way to S wing for a cake-cutting and a tour of the suite by lab members from various research groups who demonstrated how the equipment is being used. (For more on the launch of the biomedical imaging research suite, see page 5.)

The day concluded with remarks from **Dr. Kullervo Hynynen**, director of the physical sciences platform at SRI and the project lead of CeRIGT. Hynynen looked ahead to next year's CeRIGT Research Day and the completion of the whole centre, set for April 2012. "Then we'll just need to fill the space," he said.

The Canada Foundation for Innovation, the country's largest funding agency for research infrastructure, has awarded grants to two Sunnybrook Research Institute (SRI) scientists through its Leaders Opportunity Fund (LOF).

The LOF awards are matched dollar for dollar by Ontario's Ministry of Economic Development and Innovation (formerly the Ministry of Research and Innovation). Both programs invest in infrastructure to attract the world's leading researchers to Canadian institutions and enable them to do cutting-edge work.

Dr. Jean Gariépy, a senior scientist in physical sciences, was awarded a \$400,000 LOF grant, which was matched by the province, to develop biomolecules that can perform diagnostic and therapeutic functions. He will use the funds to purchase state-of-the-art equipment that will allow him to create and analyze the ligand binding and functional properties of these biomolecules.



Dr. Jean Gariépy

"The equipment will include peptide synthesizers, and peptide and protein purification equipment, as well as instruments to characterize binding events. It will be housed in the molecular targeting and therapeutic laboratory [part of the Centre for Research in Image-Guided Therapeutics] on M7," said Gariépy.

Dr. Samira Mubareka, a scientist in biological sciences who studies microbiology and infectious diseases, was also awarded a LOF grant. She received \$102,921, which was matched by the province, to develop preclinical models of the transmission and pathophysiology of the influenza virus. She will use the funds to buy supplies for her preclinical research, as well as equipment to study how the virus is spread and the reverse genetics rescue process.



Dr. Samira Mubareka

The following SRI scientists are previous LOF recipients who have received matching grants through the Ontario Research Fund—Research Infrastructure program:

Dr. Marc Jeschke, a senior scientist in the Trauma, Emergency & Critical Care Research Program and director of the Ross Tilley Burn Centre at Sunnybrook, was awarded \$400,000 to purchase an imaging system that will further his research on stress-induced diabetes caused by burns.

Dr. Jonathan Rast, a scientist in biological sciences, is studying how genes operate in the immune response of the purple sea urchin, whose immune system bears similarities to our own. He was awarded \$117,435 to purchase microscopy equipment so that he can observe how cells behave in response to an immune reaction. He will also buy equipment that will allow him to view how genes turn on and off during an immune response.

Dr. Bojana Stefanovic, a scientist in physical sciences, is studying the link between brain function and the vascular state. She was awarded \$251,151 to buy a two-photon fluorescence scanning laser microscope that will allow her to study how fine blood vessels in the brain support abnormal activity in preclinical models of Alzheimer's disease.

Sunnybrook Ranked Among Top Five Research Hospitals in Canada

Sunnybrook Research Institute has ranked fifth in *Canada's Top 40 Research Hospitals List 2011*, by Research Infosource Inc., a national firm that provides research and development data for businesses and universities.

The list, published in a supplement on Canada's innovation leaders, rates hospitals by total research income in 2010, which includes all internal and external, government and nongovernment sources. Sunnybrook's standing was based on its 2010 research income of \$106 million. This figure is a 26% increase from 2009—the highest year-over-year growth among the top five research hospitals.

Total research income of Canada's top 40 research hospitals was \$2.1 billion in 2010, highlighting the crucial role hospitals play in Canada's research sector and overall economy.

As Research Infosource noted, the top six research hospitals, each of which conducts more than \$100 million in research annually, are "research powerhouses," operating above the scale of 34 of the top 50 universities in the country.

Sunnybrook Research Institute is the research enterprise of Sunnybrook Health Sciences Centre. Of the top five from the list, it is the only general hospital in Ontario with a single research institute. University Health Network and Hamilton Health Sciences, ranked first and second, respectively; each has three affiliated research institutes. Toronto's Hospital for Sick Children and McGill University Health Centre ranked third and fourth, respectively.

The supplement also featured an editorial written by the vice-president of research at Sunnybrook, **Dr. Michael Julius**. In "Getting Down to Business," he asked if taxpayers are getting the best bang for their dollar when it comes to health care—and concluded that they are not, but they could do, if Canada dedicates itself to the task.

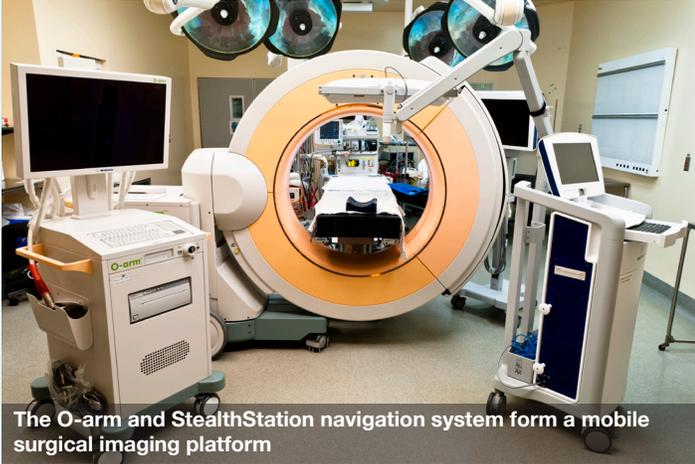
Breast Cancer Screening: Worth It?

In November, the Canadian Task Force on Preventive Health Care published new breast cancer screening guidelines for women not at high-risk. They recommended that women aged under 50 years not get annual mammograms. This suggestion sparked controversy across the country.

Dr. Martin Yaffe, a senior scientist in physical sciences at SRI, weighed in during several interviews with the media, and in an editorial published in *The Globe and Mail*. His verdict? Annual screening mammograms for women starting at age 40 are absolutely worth it. As he notes in the editorial, "mammography screening works and saves lives."

Go to www.sunnybrook.ca/research to read the full commentary.

Tool Kit: O-Arm Surgical Imaging System



The O-arm's donut-shaped CT scanner gantry (a movable frame that contains the X-ray tube and detectors) allows for simple, low-radiation, 2-D fluoroscopic images or full 3-D reconstructions in standard and high-definition resolution. The system's digital flat-panel detector provides a large field of view, resulting in precise images of a patient's skeletal anatomy.

The system, worth \$1.6 million, is part of the preclinical testing facility within SRI's Centre for Research in Image-Guided Therapeutics. Whyne will use the equipment in her research on photodynamic therapy for cancer that has spread to the spine. The therapy combines a light-sensitive drug with a locally applied light delivered via a laser fibre inside a small tube called a cannula. When the drug is taken up in the tumour and a light from the laser is turned on, the cancerous cells die.

"The O-arm allows us to visualize exactly where that cannula is placed, so we can ensure optimal treatment delivery intraoperatively," says Whyne.

Currently located in the hospital's musculoskeletal operating room on the second floor of M wing, the system will eventually be housed in the preclinical testing facility in S wing, set for completion next spring.

The purchase of the O-arm surgical imaging system was made possible by a \$57-million infrastructure grant from the Canada Foundation for Innovation through its Research Hospital Fund.

Sunnybrook Research Institute (SRI) has acquired a Medtronic O-arm and StealthStation surgical navigation system to develop minimally invasive procedures for musculoskeletal surgical applications. Together, they form a mobile surgical imaging platform for use in spine, orthopaedic and trauma-related surgeries.

"The O-arm, used in combination with the Stealth navigation system, allows us to navigate surgeries in real time based on intraoperative, conebeam CT [computed tomography] scans," says **Dr. Cari Whyne**, director of the Holland Musculoskeletal Research Program at SRI.

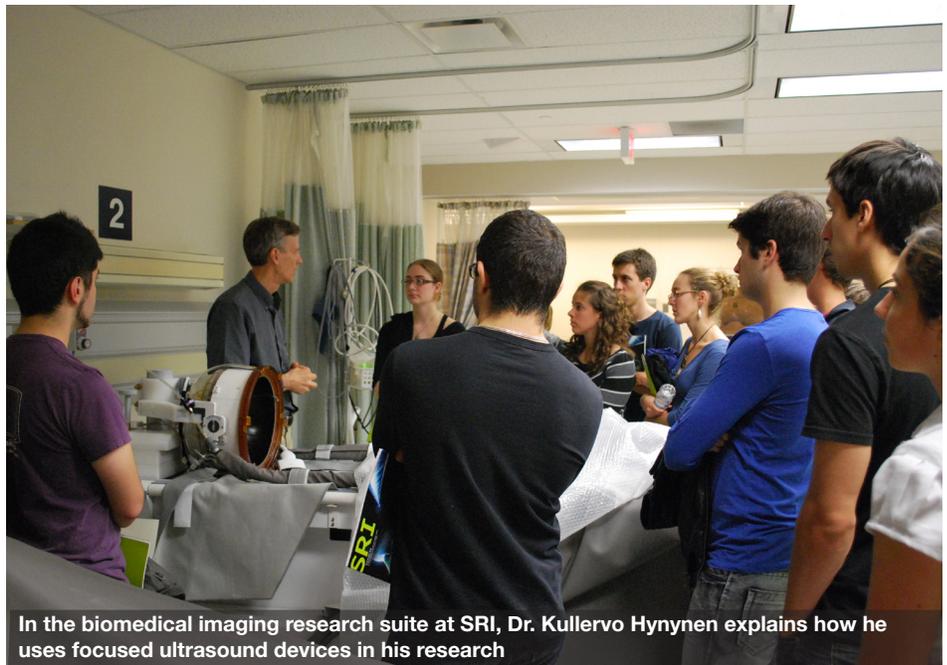
CV will return with the next edition of *Nexus*, published in spring 2012. It will reflect the recent changes to SRI's structure, in which all researchers at SRI will have a home in one of biological sciences, evaluative clinical sciences or physical sciences.

Not Your Average Road Trip

A group of undergraduate students in biomedical engineering from École Polytechnique de Montréal used their reading week to visit Sunnybrook Research Institute (SRI) and explore career options in research.

The group of 15 students were in Toronto from October 11 to 13, 2011. The tour of SRI was the last stop on their itinerary, which included visits to the Institute of Biomaterials and Biomedical Engineering at the University of Toronto, and some biomedical companies in the city's west end.

Dr. Kullervo Hynynen, director of physical sciences at SRI, gave the students a tour of the biomedical imaging research suite on the ground floor of S wing. He described his research and showed the students state-of-the-art equipment, including magnetic resonance imaging systems, a computed tomography scanner and focused ultrasound devices. For the full story, visit www.sunnybrook.ca/research.



Doors Open to New Biomedical Imaging Research Suite

Leading-edge facility will advance work in image-guided therapeutics and technology development

Sunnybrook Research Institute (SRI) celebrated the opening of its biomedical imaging research suite on November 10, 2011. The event was part of SRI's second annual research day for the Centre for Research in Image-Guided Therapeutics (CeRIGT).

The biomedical imaging research suite is a core facility of CeRIGT in which teams of scientists and clinician-scientists are conducting studies using computed tomography (CT), magnetic resonance imaging (MRI) and focused ultrasound. Their aim is to develop and optimize noninvasive imaging methods for brain, cardiac, cancer and musculoskeletal applications.

Devices in the facility are a Toshiba Aquilion ONE dynamic-volume, whole-body CT scanner with a 320-row detector; an InSightec ExAblate 4000 brain system; a Bruker 7T MRI system; a GE 1.5T Signa MRI system; a GE 3T long-bore, whole-body, research MRI system; and a C13 dynamic nuclear polarization (DNP) polarizer for MR metabolic imaging. Sunnybrook Research Institute is one of only two institutions in Canada to have a hyperpolarizer system.

As part of the celebration, guests enjoyed a cake reception and a tour of the facility. For the full story and more photos from the event, visit www.sunnybrook.ca/research.



Dr. Alison Burgess, a research associate in Hynynen's focused ultrasound lab, describes how the InSightec ExAblate brain system could one day be used to treat stroke patients



Dr. Rajiv Chopra, a scientist in physical sciences, demonstrates MRI-guided interventions for oncology



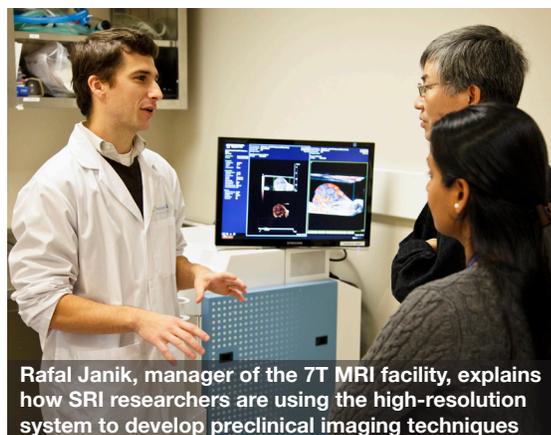
Research engineer Bonny Biswas and Dr. Graham Wright, director of the Schulich Heart Research Program, look at a visualization of an MR-guided electrophysiology intervention



L to R: Dr. Kullervo Hynynen, director of physical sciences; Dr. Michael Julius, vice-president, research; Dr. Ferenc Jolesz, professor of radiology at Brigham and Women's Hospital and Harvard Medical School; and Drs. Greg Stanisz, Simon Graham and Graham Wright, all from physical sciences



Dr. Charles Cunningham, a scientist in physical sciences, demonstrates disease characterization with the C13 DNP polarizer for MR metabolic imaging



Rafal Janik, manager of the 7T MRI facility, explains how SRI researchers are using the high-resolution system to develop preclinical imaging techniques

Trainees' Post

For Students and Postdocs

Failed experiments: staying motivated when it feels like your research is going nowhere

It happens to so many graduate students: hitting the dreaded wall.

"It's a rite of passage. You haven't done a graduate degree unless you've overcome challenges," says **Dr. John Hudson**, a post-doctoral fellow in the lab of **Dr. Peter Burns**, a senior scientist in physical sciences at Sunnybrook Research Institute (SRI).

After graduating with an engineering degree from McMaster University, Hudson began his PhD in medical biophysics at the University of Toronto in 2004. Burns, who is chair of the department, was his supervisor. His project was on the use of ultrasound and ultrasound contrast agents to measure blood flow. As his research progressed, Hudson found himself in unfamiliar territory doing biology and working with preclinical models.

In spite of a steep learning curve and failed experiments, Hudson persevered. It paid off—he successfully defended his thesis last February. He's now working with clinicians from Sunnybrook's Odette Cancer Centre to monitor changes in tumour blood flow in response to antiangiogenic therapy.

Here, he tells **Alisa Kim** about the obstacles he encountered in his research and how he stayed sane through it all.



Dr. John Hudson is a postdoctoral fellow in the lab of Dr. Peter Burns at Sunnybrook Research Institute

When did you start having difficulties with your research?

It happened all throughout. Projects never work the first time you do an experiment. Sometimes the challenges are minor and it takes a bit of extra work. I ran into a roadblock that took about a year to resolve.

What happened?

I was trying to get an ex vivo kidney model to work to use as a perfusion phantom to validate my perfusion model. It sounded easy to do, but it became extremely complicated because as soon as you take an organ out of a living animal, the organ starts to die, and the vascular properties change. It just didn't work. This was right in the middle of my PhD. It was the crucial experiment to my project. I was getting help from everyone I could find. I was downtown talking to transplant surgeons, and in the operating room trying to learn how to handle this material. Eventually we abandoned it and went an entirely different way to validate the model, and that worked within two months. Sometimes you need to know when to call it quits.

How did you deal with the frustration?

I just kept plugging away, kept trying. There comes a point where you have to stop and try to approach the problem from different angles. In graduate school, you're trained to be independent, but it's important to accept other ideas and opinions. Sometimes you have your head down trying to fix something, and all it takes is someone who hasn't seen your problem before to say, 'Have you tried this . . . ?' or 'Your machine is unplugged.' I tried to engage other people who might have had some inspiration.

Did your supervisor help you troubleshoot the problem or offer any helpful insights?

My particular problem was something we both didn't have much experience in. I had a [thesis] committee as well—**Dr. Graham Wright** [director of the Schulich Heart Research Program at SRI] and Dr. Alex Vitkin, from Princess Margaret Hospital. We all brainstormed, and they encouraged me to keep trying to solve it on my own. But they were instrumental in helping me determine to stop. I invested so much time and energy into [this] one thing that it was really hard to stop. They were there to give guidance and make sure I graduated. They were the ones to put their foot down and say, 'Okay, John; let's try to solve this some other way.'

What were some things that helped you stay motivated?

I think it's really important to have a distraction. My big thing is competitive sailing. I've sailed double-handed dinghies down on the lake. It's the best thing ever. Having some side projects that you find interesting that aren't necessarily related to what you're doing [also helped].

What advice do you have for other graduate students who feel stuck in their research?

What really helped me was knowing that I wasn't the only one having problems, that everyone else wasn't just breezing through this. You tend to be an island when your head is stuck in a problem. Knowing this is a common experience in graduate school and that people make it through helped me keep going. I thought, 'You'll make it through, too—eventually.'

Applause

Dr. Sandra Black Irma M. Parhad Award for Excellence 2011



The Consortium of Canadian Centres for Clinical Cognitive Research presented **Dr. Sandra Black**, director of the Brain Sciences Research Program at Sunnybrook Research Institute, with the Irma M. Parhad Award for Excellence 2011 at the Canadian Conference on Dementia held October 27 to 29, 2011, in Montreal.

The award is presented annually to an individual who makes outstanding contributions to the field and leads the way to better understanding in the treatment of patients living with cognitive disorders. Black is the Brill Chair in Neurology at the University of Toronto. She leads the Sunnybrook site of the Heart and Stroke Foundation Centre for Stroke Recovery.

Alzheimer Society Rewards Scientist

The Alzheimer Society of Canada has awarded **Dr. Krista Lanctôt**, a senior scientist in the Brain Sciences Research Program, a Quality of Life research grant worth \$144,182. Lanctôt will use the funds to conduct a discontinuation trial of cholinesterase inhibitors for severe Alzheimer's disease in a long-term care setting.

A Hearty Success

The sixth annual Schulich Heart Program Research Day was held on November 23, 2011 at Sunnybrook Research Institute (SRI). The event attracted researchers, clinician-scientists, staff and students from inside and outside SRI, and focused on state-of-the-art cardiovascular disease management.

The day was divided into three sessions: cardiovascular imaging, outcomes assessment and analysis, and new surgical and interventional methods. Guest speakers were Dr. Chris Buller from St. Michael's Hospital and Dr. Elliot McVeigh from Johns Hopkins University School of Medicine.

Dr. Jack Tu, a cardiologist and senior scientist in evaluative clinical sciences, delivered a keynote lecture on ethnicity and cardiovascular disease in Ontario. He also summarized research on global rates of heart disease and the risk factors associated with different ethnic groups.

Dr. Graham Wright, director of the Schulich Heart Research Program, summarized the work of SRI cardiac researchers. Wright and his team are using magnetic resonance imaging to characterize preclinical models of heart conditions for use in designing diagnostic and therapeutic studies. He also co-leads a Canadian Institutes of Health Research team that is studying occlusive vascular disease.

Dr. Bradley Strauss, chief of the Schulich Heart Program and senior scientist in biological sciences, presented results from a multisite Phase 1 clinical trial evaluating different dose levels of collagenase, an enzyme-based therapy he developed to treat patients with chronically blocked arteries. In the study, Strauss used a microcatheter to inject collagenase into blocked arteries to soften plaque buildup and allow for stenting the next day. Twenty male patients participated in the study, which was a collaboration between Sunnybrook and St. Michael's Hospital. Strauss reported a 75% success rate in crossing and stenting 15 of the 20 patients.

For the full story, go to www.sunnybrook.ca/research.

It's a Girl!

Congratulations to first-time parents Ewelina and Jarek Maliszewski on the birth of their healthy baby girl.

Julia Rose Maliszewski was born on October 24, 2011 at Sunnybrook's Women & Babies birthing facility. She weighed seven pounds, 12 ounces.

Ewelina Maliszewski is a PhD student in the lab of **Dr. Isabelle Aubert**, a senior scientist in the Brain Sciences Research Program at Sunnybrook Research Institute.



Jarek and Ewelina Maliszewski with their baby girl Julia Rose

Symposium Highlights Cancer Research

On November 14 and 15, 2011 the Odette Cancer Research Program at Sunnybrook Research Institute hosted the Canadian Institutes of Health Research symposium on novel cancer therapies and innovations in treatment monitoring at Sunnybrook's Vaughan Estate.

The two-day event focused on quantitative imaging methods such as ultrasound and optical imaging, and how these can be used to measure cell death. The aim of the symposium was to bring together experts in cancer research and expand the roles of ultrasound and optical methods clinically.

CIHR Funds Study by SRI Scientist

The Canadian Institutes of Health Research has awarded **Dr. Don Redelmeier**, director of the evaluative clinical sciences platform at Sunnybrook Research Institute, a one-year catalyst grant. Redelmeier will receive \$100,000 in support of the STORK study (Symptomatic Thrombosis and Occlusions following Reproductive Kindling) to determine if reproductive clinical interventions increase the risk for premature cardiovascular disease in women.

WHAT'S ON

February 3

Informed Consent Workshop: Writing, Obtaining and Documenting

Clinical Studies Resource Centre

9:30 a.m.–1:00 p.m.

Sunnybrook Health Sciences Centre, C1 03

February 13–14

10th Annual Imaging Network Ontario Symposium

University of Toronto Residence

89 Chestnut Street Residence

“Best wishes for a safe and happy holiday, and a healthy and prosperous new year!”

— Dr. Michael Julius, vice-president, research

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Photography: Eleni Kanavas and Doug Nicholson

Nexus is published by the office of communications, Sunnybrook Research Institute: www.sunnybrook.ca/research.

We welcome your suggestions. Please send them to Eleni Kanavas at eleni.kanavas@sri.utoronto.ca.



Dr. Michael Julius, vice-president, research, and staff from research administration raise a toast to a successful year at Sunnybrook Research Institute at the annual holiday celebration