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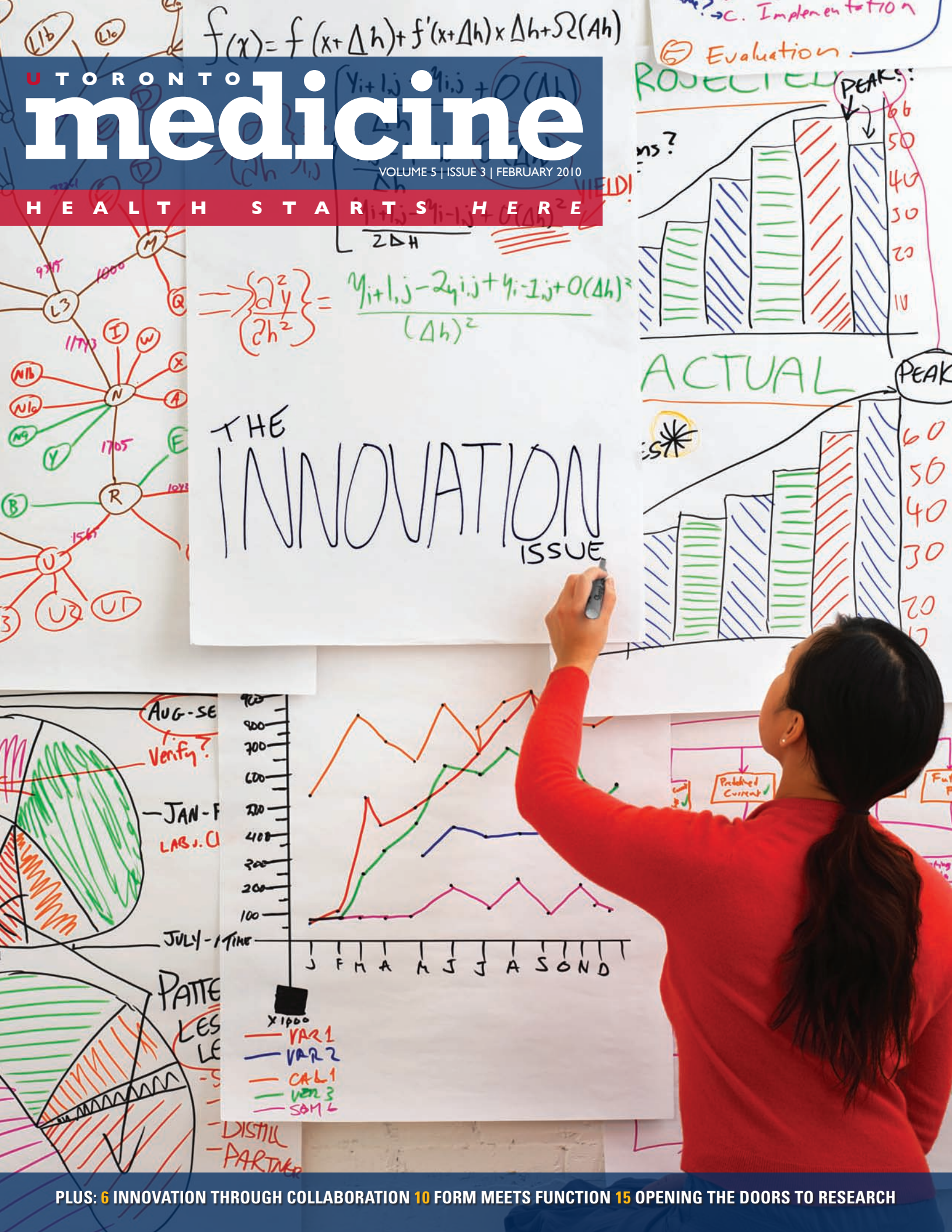
HEALTH STARTS HERE



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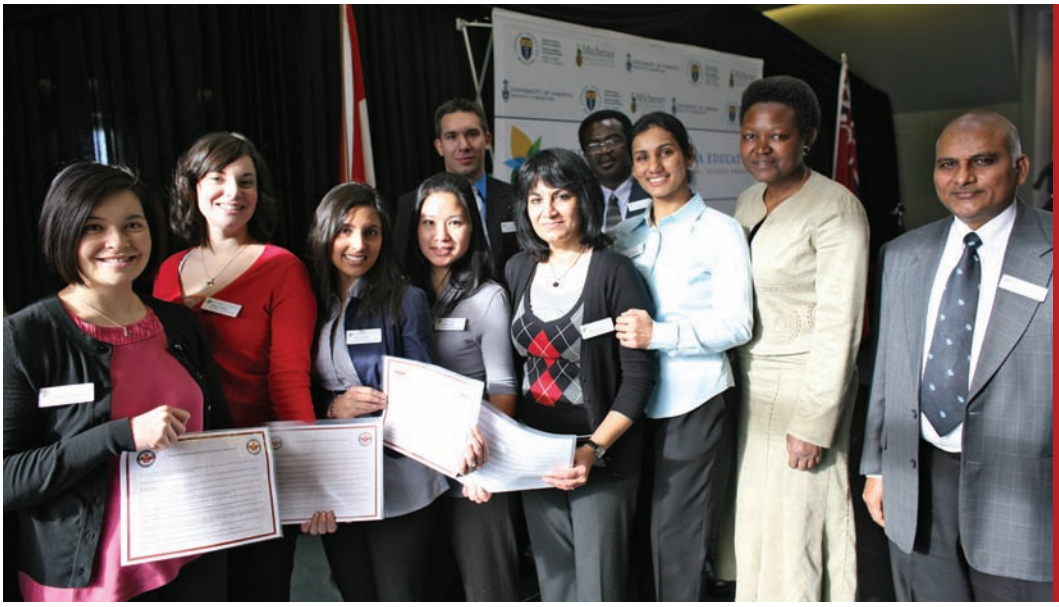


Physician Assistant Program Takes Off

Students from the inaugural class of the Bachelor of Science Physician Assistant (BScPA) program display their Code of Ethics at a January event welcoming them to U of T . The program is a partnership between U of T's Faculty of Medicine, the Michener Institute for Applied Health Sciences and the Northern Ontario School of Medicine.

Celebrating 10 Years of Earthtones

Amy Bourns, a Family Medicine resident at Sunnybrook Health Sciences Centre, performs her own song, "C'mon In," at Earthtones, an annual fundraiser for international children's charities. Earthtones, organized by the University of Toronto Medical Society, celebrated its 10th anniversary in November and featured a dozen different acts, drawn from students and faculty alike. For more information on Earthtones and the charities it supports, visit www.torontomeds.com/earthtones.

Breaking Ground in Mississauga

With construction well underway, the Health Sciences Complex at the University of Toronto Mississauga had its official groundbreaking in October. When it opens in 2011, the complex will house the Mississauga Academy of Medicine, a partnership between the Faculty of Medicine, U of T Mississauga and Credit Valley Hospital. The Academy will welcome 54 medical students to its first-year class.

KUDOS

The Faculty of Medicine's number of award winners and grant recipients is prolific. Naturally, we cannot come close to listing every honour bestowed upon members of our Faculty, but here is a sampling of recent, notable achievements.

AXS Biomedical Animation Studio, founded by **Jason Sharpe**, **Sonya Amin** and **Eddy Xuan** – all grads of the Faculty's Biomedical Communications program – was featured in the December issue of *Esquire* magazine in its Best and Brightest feature. … **Prof. Douglas Lee** (Dept. of Medicine; University Health Network) received the 2009 Canadian Cardiovascular Society's Young Investigator Award – Clinical Science Category. … **Prof. Pauline Pariser** (Family and Community Medicine) was named 2009 Family Physician of the Year for the Toronto region by the Ontario College of Family Physicians. … **Prof. Helene Polatajko** (Occupational Science and Occupational Therapy) has been elected as a Fellow of the Canadian Academy of Health Sciences. … **Prof. Peter Singer** (Dept. of Medicine; University Health Network) has been elected as a member of the Academy of Sciences for the Developing World in the Medical and Health Sciences category. … **Prof. Michael G. Fehlings** (Dept. of Surgery; University Health Network) received the North American Spine Society's 2009 Leon Wiltse Award for excellence in leadership and/or clinical research in spine care. He also won the 2009 Olivecrona Award from the Karolinska Institute

PHOTOGRAPHY: TOP: JOHNNY GUATTO ; BOTTOM: RAAGEEN KANJEE

Y NEWS

Recognizing Our Students

Students and donors alike came together last fall at the Faculty of Medicine's Annual Scholarship Reception. Pictured here are (left to right) Tharini Sivasubramaniyam (Ontario Graduate Scholarship – Faculty of Medicine); Linda Sun (Walter F. Watkins Scholarship); Parnian Arjmad (The Government of Ontario/Aventis Pasteur Graduate Scholarship in Science and Technology); and Rose Patten, donor and former Chair of Governing Council at U of T.

New Hospital Partners

The Faculty of Medicine has two new community-affiliated hospitals. Markham-Stouffville Hospital in Markham and Ontario Shores Centre for Mental Health Sciences in Whitby recently became community affiliates. The Faculty now works with 19 community-affiliated hospitals and sites, along with its 10 fully-affiliated hospitals.

in Stockholm. … **Prof. Paul G. Walfish** (Dept. of Medicine; Mount Sinai Hospital) has been elected to the Fellowship in the Canadian Academy of Health Sciences. He also received the 2009 John B. Stanbury Thyroid Pathophysiology Award from the American Thyroid Association. … **Prof. Mark Silverberg** (Dept. of Medicine; Mount Sinai Hospital) is the winner of the Canadian Association of Gastroenterology Young Investigator Award for 2010. … **Prof. Susan Abbey** (Dept. of Psychiatry; University Health Network) received the 2009 Prix d'excellence from the Royal College of Physicians and Surgeons of Canada. … **Prof. Murray Urowitz** (Dept. of Medicine; University Health Network) received the Evelyn Hess Award for body of work from the Lupus Foundation of America. … **Prof. Bernard Zinman** (Dept. of Medicine; Mount Sinai Hospital) received the Canadian Diabetes Association Lifetime Achievement Award. … Seven members of the Faculty of Medicine were honoured with the Order of Canada last year. **George Beaton** (Professor Emeritus, Dept. of Nutritional Sciences) and **Prof. James Orbinski** (Dalla Lana School of Public Health) were inducted as Officers, the Order's second-highest ranking. Four others were inducted as Members: **Prof. Roderick McInnes** (Dept. of Paediatrics; Hospital for Sick Children); **Prof. Marvin Tile** (Dept. of Surgery; Sunnybrook HSC); **Prof. Bernard Goldman** (Dept. of Surgery; Sunnybrook HSC); **Adjunct Prof. Jeffrey Lozon** (Dept. of Health Policy, Management and Evaluation); and **Prof. Patrick Gullane** (Chair, Department of Otolaryngology – Head and Neck Surgery; University Health Network). Prof. Gullane has also been awarded an Honorary Fellowship of the Royal College of Surgeons of England. … **Prof. Frances Chung** (Dept. of Anaesthesia; University Health Network) received the 2008 Distinguished Service Award from the Society for Ambulatory Anesthesia. … **Prof. Wayne Johnston** (Dept. of Surgery; University Health Network) received the Lifetime Achievement Award from the Society for Vascular Surgery. … **Prof. Ron Laxer** (Dept. of Paediatrics; Hospital for Sick Children) received the Distinguished Clinical Scholar Award from the American College of Rheumatology. … **Prof. Norman Rosenblum** (Paediatrics; Hospital for Sick Children) received the 2009 Paediatric Academic Leadership-Clinician Investigator Award from the Paediatric Chairs of Canada. … **Prof. Mladen Vranic** (Dept. of Physiology; University Health Network) and **Dr. John Challis** (Professor Emeritus, Dept. of Physiology) have been elected Fellows to the Canadian Academy of Health Sciences. … **Prof. Min Zhuo** (Dept. of Physiology) and **Prof. Andres Lozano** (Dept. of Surgery; University Health Network) have been named Fellows of the Royal Society of Canada. … **Prof. Allan S. Kaplan** (Dept. of Psychiatry; University Health Network) received the Canadian Psychiatric Association's J.M. Gleghorn Award for Excellence in Leadership and Clinical Research. … **Prof. David J.A. Jenkins** (Depts. of Medicine and Nutritional Sciences; St. Michael's Hospital) has been named a U of T University Professor. … **Prof. Wendy Levinson** (Chair, Dept. of Medicine; Sunnybrook HSC) received the Robert J. Glaser Award, the highest honour from the Society of General Internal Medicine. … **Prof. Arnold Noyek** (Dalla Lana School of Public Health) was inducted as a Senior Fellow of Ashoka Canada.

PHOTOGRAPH: GREG TJERKEMA

PHOTOGRAPH: MARGARET MULLIGAN

Innovation is more than just invention. It can encompass the many steps on the road to a major discovery. Or it can be a matter of tweaking an idea, using a novel application of a concept, or changing the way we think about doing something.

And how we measure its value is not just scientific breakthrough, but often social progress.

"I see invention as the creation of a new entity, and innovation as being much broader and having a wider application or impact on society. Innovation moves society forward," says Paul Young, Vice President, Research, at the University of Toronto. He cites the invention of the 'computer' and how it has transformed everything in society through innovative thinking. "Diabetes management, for example, has been revolutionized through the adaptation of the computer into something called an 'insulin pump'."

Young says the University of Toronto's Faculty of Medicine demonstrates innovation through discoveries such as stem cells and insulin, and through practical examples such as drug delivery technology, stem cell technology, regenerative medicine, and medical diagnostics.

"The word 'innovation' encompasses not just the technological but social and cultural innovation and great ideas, and it can include more efficient or cost-effective ways to do something, a new business process, for instance," says Young.

"In research, when we ask, 'is this an innovative idea or approach?', the stress is on something that's new and leads to something positive or better," explains Peter Lewis, the former Vice-Dean, Research and International Relations at the Faculty of Medicine. "There's a novel aspect to innovation, but there's usually also an improvement of some kind, such as increased productivity, greater efficacy, or a therapeutic effect."

But assessing the value of innovation takes time, says Lewis. "Measuring the worth of innovation is something one has to do retrospectively, maybe years later. You have to look at where you were before the innovation and where you are because of it," he says.

"These advances are not linear or predictable, because innovation and discovery are often unexpected and serendipitous," says Howard Lipshitz, Chair of the Department of Molecular Genetics at the Faculty of Medicine and the Associate Director of the Donnelly Centre for Cellular and Biomolecular Research. "But those who track the history of advances in health care and treatment invariably trace these back to unexpected basic discoveries."

His own research points to the unpredictable nature of innovation, Lipshitz says. "My lab and our collaborators have been able to identify and measure all of the RNAs in early fruit fly embryos and to track changes in these RNA populations," he explains. "It turns out that these kinds of changes occur in all animals and we guess that they can be controlled by the same machinery. If so, then our discoveries may turn out to be relevant for disease diagnosis and human health."

Lewis refers to breakthroughs such as polymerase chain reaction, inducible pluripotent stem cells and DNA sequencing as examples of innovations that have led to new practices. "In the health sciences, technological advances almost always allow you to do an experiment or approach that you couldn't do before."

So, can an institution nurture innovative thinking?

"Yes," says Young. "At U of T, that includes encouraging basic, curiosity-driven research and applied research and creating centres where interdisciplinary thinking and research can blossom." He cites the Donnelly Centre as one example. "These types of centres create physical spaces where scholars and scientists are almost forced to bump into each other, compare ideas, build on each other's ideas, and work collaboratively."

Lewis says one role of the Faculty of Medicine is to nurture such collaborations, "and bring together different scientists with ideas that might fit together. We've realized where our strengths are in our faculty members, and encourage them in every way, by providing seed money, space, and necessary infrastructure. Our motivation is to see them succeed." ■

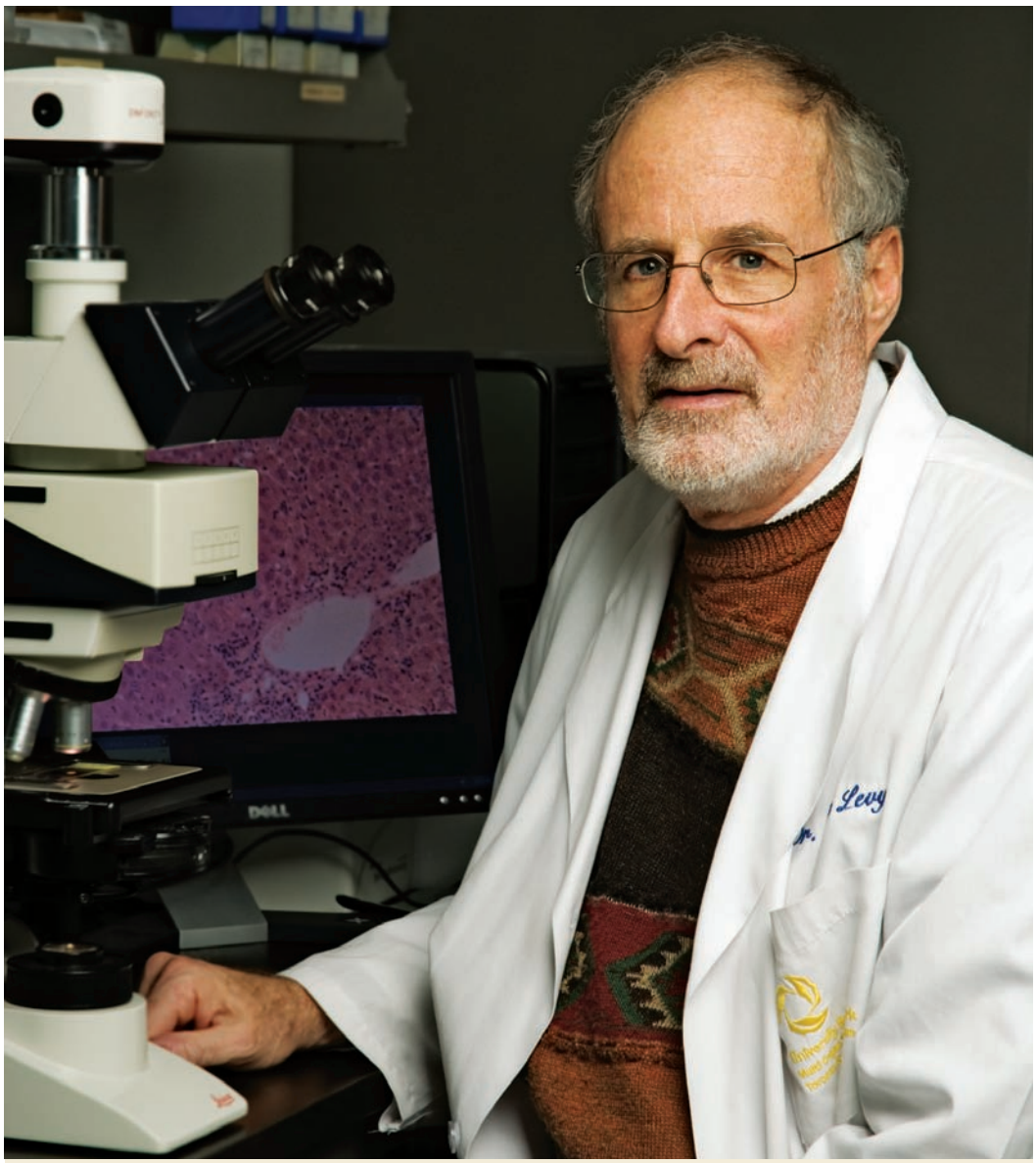
VIP

Gary Levy

Director,
University of Toronto
Transplant Institute

By Angela Pirisi

One area that we're highly focused on is doing studies to improve organ function so we can expand the use of donor organs. Currently, only 15 to 30 per cent of donor organs that we are offered are usable. So we're trying to repair donor organs using molecular approaches (e.g. shutting off inflammation) in an attempt to double or triple the use of donor organs. Our second research focus is to try to produce a state of tolerance, that is, organ transplantation without the need for immunosuppression. To this end we are using molecular approaches, such as gene profiling or identification of specific proteins, to gain understanding of the mechanisms that allow tolerance to occur. Once we have identified predictive gene signatures, hopefully in the next few years, we will be able to reduce or do away with immunosuppressive drugs in many more patients. In the short term, until we can master these immunological-modulating techniques, our most important challenge and top priority will be to increase the organ supply by all possible means, including education of the public and government, and improving donor organ function, which will expand the donor pool of organs, allowing us to help patients who require solid organ transplantation. M



EDUCATION BSc and MD, University of Toronto; FRCP(C) Internal Medicine; FRCP(Gastro)
HONOURS William Goldie Prize in Medicine (1983, 1988); Department of Medicine Research Award (1996); Canadian Liver Foundation Commemorative Medal for the Queen's Jubilee (2002)
EMPLOYMENT Joined the University of Toronto in 1981, and became a full Professor in the Department of Medicine in 1990. He is currently Medical Director of the Multi-Organ Transplant Program, University Health Network (UHN); Director of the University of Toronto Transplant Institute

CLAIM TO FAME He founded and directed UHN's Liver Transplant Unit in 1987, and the Multi-Organ Transplant Unit in 1991. The program now performs more than 400 solid organ transplants a year, including kidney, liver, lung, heart, intestine and pancreas. He has conducted research on immune-mediated mechanisms of organ injury, and discovered three key molecules (fgl2, fibroleukin, tissue factor) involved in the pathogenesis of viral hepatitis, allo and xenograft rejection.

PHOTOGRAPH: J. MICHAEL LA FOND

Innovation Through Collaboration

No innovator works alone. And the most innovative of all collaborate not only within their institutions, but also with others across the country and around the world. Here are four members of the Faculty of Medicine who embody that collaborative spirit. By Niamh McGarry

ALED EDWARDS, PhD

Banbury Professor of Medical Research
Banting and Best Department of Medical Research
Director and CEO,
Structural Genomics Consortium

For Aled Edwards, science is the gift that keeps on giving—or it can be if researchers move to a more open, sharing style of publication and collaboration.

Edwards is the Toronto-based head of the Structural Genomics Consortium (SGC), a public-private partnership engaged in pre-competitive research to facilitate the discovery of new medicines. Approximately 230 scientists work collaboratively in SGC laboratories at the Universities of Oxford and Toronto and Karolinska Institutet, Stockholm.

The SGC's primary mandate is to determine the three-dimensional structures of proteins of medical relevance—potential drug targets—and place them in public databases without restriction. Its current scientific programs are focused on developing research tools (small molecule inhibitors and renewable antibodies) to proteins implicated in chromatin biology and epigenetic regulation.

Unlike most academic and all commercial organizations, all SGC-derived reagents —substances used to bring about chemical reactions—are made available immediately and without restriction on use. The SGC science is assessed quarterly by its public/private funders, which include pharmaceutical companies (such as GlaxoSmithKline, Merck and Novartis) and Swedish and Canadian scientific and funding agencies (including the Canada Foundation for Innovation, the Canadian Institutes for Health Research and Genome Canada).

The work of the SGC and its academic and industry collaborators is motivated by a paradox in modern drug discovery research. More money than ever is being invested by the public and private sector into biomedical research, but fewer drugs are being successfully developed.

"The problem with drug discovery is simple—our understanding of human physiology and pharmacology is poor. Generating knowledge that is kept confidential does nothing to enhance this understanding," Edwards says. "One of our aims is to

convince the research world that when they generate new knowledge in this area, they should donate the results to the public domain, to the creative commons. Our own policy on intellectual property says that we will promptly put our results in the public domain and will not agree to file for patent protection on any of our research outputs. We insist that our collaborators sign up to this as well."

By putting a lot of the fundamental information into the public domain without patents, the SGC and its collaborators enable the collective brains around the world to think about the problem, rather than having the information fragmented, "where only the people who are in the know or who have signed some legal agreement can think about it," Edwards says.

"In fact, a change in research practice is occurring in front of our noses, and we are in many ways driving that change," he says. "For example, we are engaged in collaborations in which large pharmaceutical companies are generating new chemicals with us and agreeing to place them into the public domain. Even two years ago, this would have been unheard of."

This increased openness benefits everyone, he adds. "When more medicines are developed, industry becomes more profitable. More effective medicines translate into less burden on the healthcare system. Everybody wins."

The message seems to be getting through.

"We have been called a 'trusted intermediary,'" Edwards says. "In this guise, our role is to mediate interactions between the public and private sectors, and provide a forum and a mechanism to allow for open release of data. Our 'no patent' policy assures all our collaborators that we will never benefit monetarily from their ideas."

Indeed, there are an increasing number of management papers written about the open access research model the SGC has developed. They describe it as an innovative, societal way of promoting future drug discovery. "I see it as a model that suits the Canadian collaborative style well", Edwards says. "And it is within these types of research partnerships that Canadian scientists might just make their greatest contributions to drug discovery."

DAVID JAFFRAY, PhD

Head of Radiation Physics,
Princess Margaret Hospital
Professor in the Departments of Radiation Oncology and Medical Biophysics, University of Toronto, the Institute of Biomaterials and Biomedical Engineering (IBBME)
Holds the Fidani Chair in Radiation Therapy Physics

Professor David Jaffray attributes his hands-on approach to innovation to growing up as a farm kid in rural Alberta. He learned that "if it's broken, you fix it yourself"—an approach to life that has earned the physicist a reputation for pushing the boundaries of technology and invention in the field of radiation therapy.

Jaffray is best known for the development of cone beam computed tomography, or image-guided radiation treatment, which transformed how radiation therapy is carried out worldwide. The imaging system integrates with the radiation treatment system to allow therapists to see inside patients at the time of therapy. This facilitates more precise delivery of radiation therapeutic doses and has become the global standard for treating patients over the past decade. Up to half of all cancer patients receive radiotherapy at some time during their treatment process.

"The biggest clinical impact will probably be on the lung. Lung lesions are hard to hit because they are moving and there is a lot of potential for error; the lung can be in one spot when you design treatment and another spot when you treat," Jaffray explains. An image-guided system means therapy can be applied in a consistent, standardized manner and the full therapeutic dose targeted just at malignant cells, rather than aiming at a larger area and potentially damaging normal tissue.

Last July, he received a major $5.5 million Canada Foundation for Innovation (CFI) grant for a new project entitled "Robotic Positioning for Image-Guided Surgery and Radiation Therapy". Jaffray will build two translational research environments that use intra-operative and robotic systems for localized and minimally invasive radiation therapy. The funding also allows his research to go to the next level of imaging quality through the use of magnetic resonance imaging (MRI) technology.

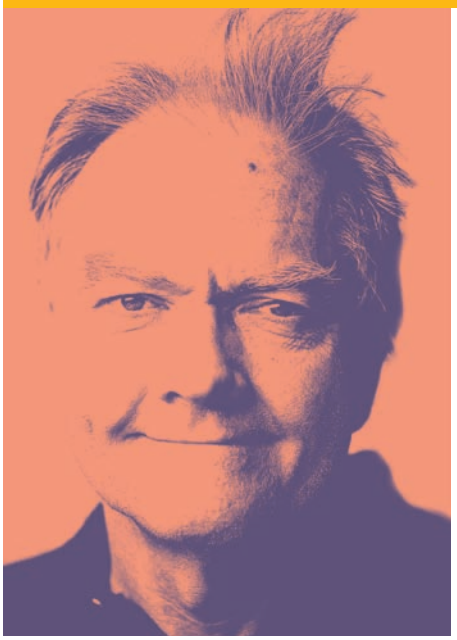
PHOTOGRAPH: PHOTOGRAPHICS @ UHN

As the Head of Radiation Physics at Princess Margaret Hospital, Jaffray straddles the gap between innovations in physics, engineering, and their application to cancer treatment. Not one who believes in the big, blockbuster drug cure, Jaffray suggests the future lies with using technology to advance therapies and, in so doing, improve patient outcome.

"I'm very happy when we advance by one per cent—so long as we do that every year," he says. "Technology impacts every part of our life and is evolving at a remarkable rate. Health care should be benefiting from those innovations. That's only going to happen if we start to become technology experts, people who can really bend the knee of technology to improve the health of individuals and improve the healthcare system itself in terms of efficiency and patient-centred care."

He envisages the harnessing of current technologies to create new medical tools, such as tiny robots (nanotechnology) that reduce the toxicity of treatments so patients can go home the next day; surgical displays to identify which cells should be removed; smart phones to monitor how a patient's hip replacement is progressing; internet links between patients and relatives allowing them keep in touch.

The answer may be to focus academic brain power on the problems clinicians see today. On a local level, Jaffray is working to do just that by encouraging stronger links between his hospital and the domains of engineering, physics, science and mathematics at the University of Toronto.



PHOTOGRAPH: GEORGE WHITESIDE

DEREK VAN DER KOOY, PhD

Professor
Department of Medical Biophysics
Department of Molecular Genetics
Terrence Donnelly Centre for Cellular and Biomolecular Research

Professor Derek van der Kooy shares 11th floor lab space in the Donnelly Centre for Cellular and Biomedical Research with two other stem cell research groups. The arrangement allows for daily exchange of ideas and technologies and exemplifies the type of collaboration regularly taking place on a larger scale across Toronto, Ontario and Canada-wide in this area.

Indeed, van der Kooy credits a "chance" collaboration 15 years ago between his group and researchers in Calgary for discoveries that could lead to improved treatment for diabetes and some types of blindness.

The Alberta-based scientists led by Sam Weiss had found interesting cells in the adult brain that seemed to have the properties of a stem cell. "Using our expertise in developmental biology and anatomy in combination with assays developed by the Calgary group, we found out together where this cell was located and characterized, in quite a lot of detail, its normal behaviour in the adult brain," explains van der Kooy.

The work on brain stem cells began a long-term collaboration between the two laboratories and later with other research groups across Canada that ultimately led to van der Kooy's discovering stem cells in other tissues, including the eye and the pancreas.

Canada—and Toronto in particular—plays a prominent role internationally in stem cell research, dating back to the discovery of stem cells by James Till and Ernest McCulloch in the early 1960s. Students who trained with Till and McCulloch now populate Toronto teaching hospitals and research institutes with stem cell biologists, creating a critical mass of expertise that makes the Toronto community highly productive and world-renowned.

Through the Toronto Stem Cell Initiative (TSCI) and the Canada-wide Stem Cell Network (SCN), researchers not only share ideas and research projects but also apply for group funding, such as the recently-awarded $25 million Canadian Foundation for Innovation award made to a Toronto-led coalition. This interaction has "changed the way research can be done," says van der Kooy. "It has benefited all of our research. We all bring different expertise and the combination of this expertise can provide answers to questions we couldn't even approach before.

"I've started to work on tissues I would never have thought about earlier. Now I'm working on the pancreas stem cell partially because of talking to people who are interested in stem cells in other systems and seeing that some of the techniques and expertise we used previously in the nervous system can be applied elsewhere."

Five years ago, van der Kooy and collaborating researchers identified a single cell in the pancreas capable of creating insulin-producing beta cells, a discovery that eventually may

lead to a much more effective treatment for diabetes. His laboratory also discovered stem cells in the retina in both human and mice adult eyes, a finding he describes as "a first step towards imagining a cure for blindness".

Both projects will benefit from Japanese researcher Shinya Yamanaka's groundbreaking discovery that adult human skin cells can be reprogrammed into an embryonic cell-like state, called induced pluripotent stem cells. The combination of Yamanaka's findings with new techniques to isolate tissue-specific stem cells opens up an exciting new field of personalized regenerative medicine, says van der Kooy.

And Toronto—as Yamanaka himself pointed out when receiving a 2009 Gairdner award at U of T—remains one of the best places to be conducting research in this rapidly-evolving field.

JASON MOFFAT, PhD

Assistant Professor
Department of Molecular Genetics
Banting & Best Department of Medical Research
Terrence Donnelly Centre for Cellular and Biomolecular Research

The technology driving Jason Moffat's research is developing so quickly that even a year ago it would not have been possible.

Twelve months ago, the technology did not exist to carry out the kind of comprehensive screens for genes indicated in cancer that are now undertaken in Moffat's laboratory. His work combines ribonucleic acid interference (RNAi), a way to turn down the production of proteins, with high-content imaging to find out which proteins are critical for cell growth. It's a unique blend of technologies that Moffat says is extremely powerful and flexible. RNAi enables large-scale screens to be implemented that systematically turn down the expression of individual genes in a cell, indicating which components are necessary for a particular process, such as cell division.

Traditionally, scientists used simple model systems, such as yeast, worms or flies, because effective loss of function genetics in mammalian cells was not possible. The advent of RNAi, in combination with large genome scale libraries, dramatically changed that. Now, the same work can be done with more complex mammal cells.

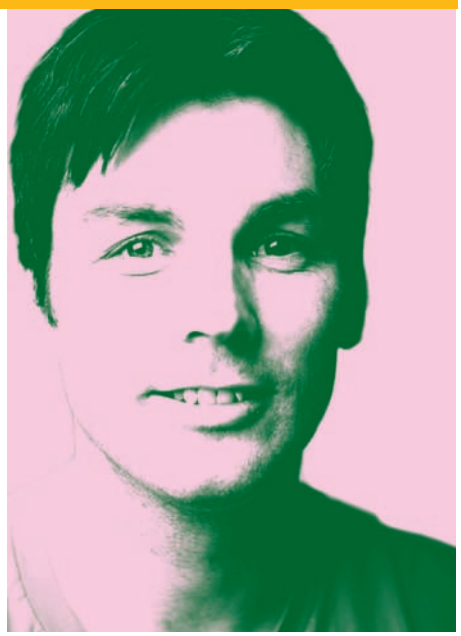
"That's really exciting from a disease perspective. We can start doing loss of function genetic screens that you could never conceive of before. It's pretty innovative!" says Moffat.

The process, which he helped develop prior to his current position at the Donnelly Centre, as a post doctoral fellow at the Whitehead Institute and Broad Institute of MIT and Harvard, is powered by a growing lentivirus-mediated library collection of short hairpin RNA (shRNA). "It was one of those technologies that took off. We didn't know how well it was going to work five years ago when we started. Now lots of people are using it." His lab is working together with the Ontario Institute for Cancer Research (OICR) to develop the libraries at the Donnelly Centre as part of the second phase of the RNAi consortium (TRC2), an international syndicate consisting of several life-sciences organizations.

Moffat's laboratory operates together with the first lentiviral-based screening platform in Canada, which assists other cancer researchers in applying RNAi technologies to their own projects. His group works in collaboration with the OICR, the Ontario Cancer Institute and other laboratories throughout the province. Interested groups are asked to commit a postdoc or graduate student to carry out the screens in collaboration with the platform.

"The plan for the next two years is to complete a number of screens that look for common essential genes amongst different cancer cell lines. We use our library in one big pool to look at a population over time and figure out which genes are essential. If you do that with different cancer cell lines, you begin to see patterns and signatures for individual cell lines and different kinds of cancer." Researchers hope that a comparison of the results to genomic information and survival information will enable researchers to hone in on genes that look like they're driving the growth of a cancer cell. In the most recent implementation of this multiplex assay, his laboratory can assess over 16,000 human or 16,000 mouse genes in a single experiment.

"It's opening up new and interesting avenues of target identification. The big picture is understanding which genes drive growth and proliferation. If we can do that, we get a good idea of which genes might be good targets for cancer." M

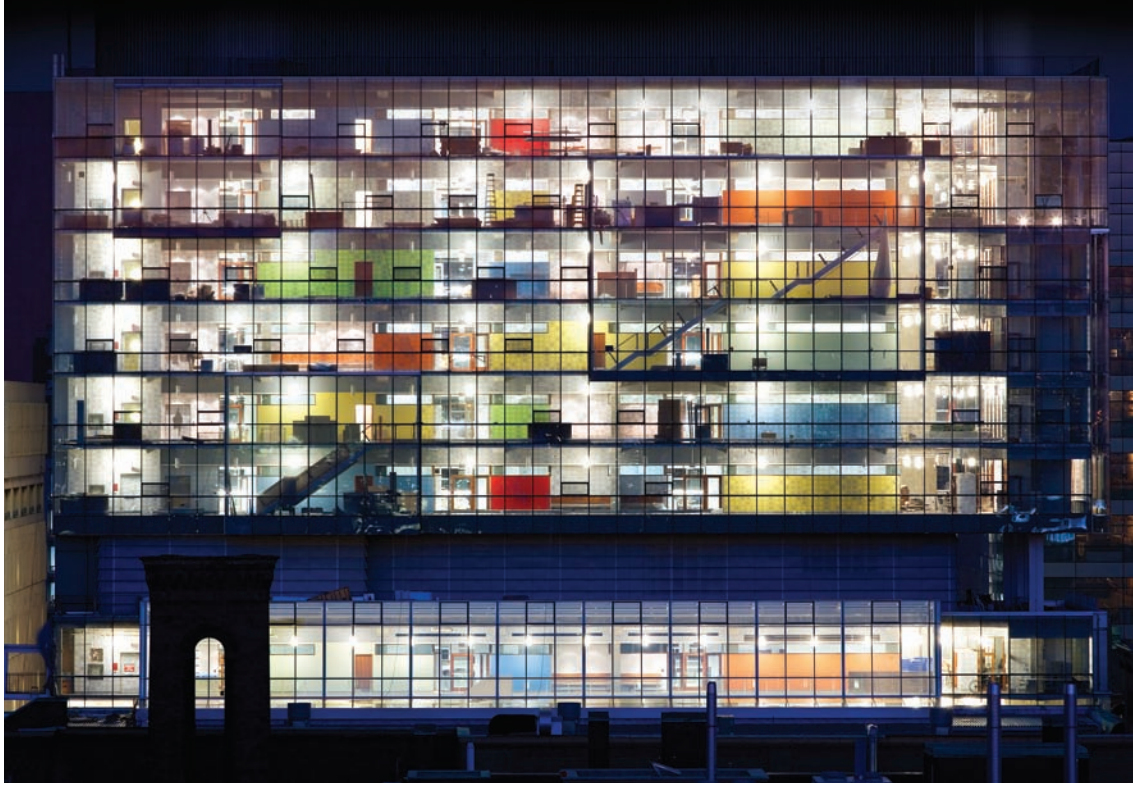


PHOTOGRAPH: GEORGE WHITESIDE

Form Meets Function

The Donnelly Centre for Cellular and Biomolecular Research provides an open, flexible and collegial environment for some of the world's best scientists

By Shibu Thomas



PHOTOGRAPH: TOM ARBAN

The building that houses the Donnelly Centre for Cellular and Biomolecular Research can be described as transparent, open and flexible. Those words would also describe the research approaches of the 32 principal investigators and the more than 400 research staff members that call the Centre home.

But was this the original objective of the team that envisioned the Donnelly Centre earlier in the decade? "Absolutely," says Dr. James Friesen, Professor Emeritus and former Chair of the Banting and Best Department of Medical Research, who is regarded, along with the late Dr. Cecil Yip, as the research visionary who helped conceptualize the Donnelly Centre and make it a reality.

"We envisaged interdisciplinary teams coming together to collaborate in an open, flexible and collegial environment," reminisces Dr. Friesen. "We heard the call of scientists who all wanted windows with natural light." The all-glass structure bears testimony to those needs.

The mandate of the Donnelly Centre is to stimulate new interactions at the interface of biology, chemistry, engineering and computer science in order to develop and apply new technologies for approaching the most challenging biological problems in the post-genomic era.

The Centre opened its doors in 2005 as a unique institute in which investigators from the Faculties of Medicine, Pharmacy, Applied Sciences & Engineering, and Arts & Science are brought together in an open, think-tank environment.

The Donnelly Centre's scientific community interacts in spectacular open-concept laboratories and meeting spaces distributed over 10 floors in a research tower that is said to symbolize the amazing potential of the post-genomic era. The laboratory floors total approximately 200,000 square feet. Each floor can accommodate three to five investigators and their teams, which include several large support rooms for shared equipment and informal meeting rooms. Laboratory benches are modular and flexible and can be readily adapted to the needs of engineers as well as computational or molecular biologists.

Today, the Donnelly Centre has rapidly become recognized as a premier international centre for post-genome biology and has solidified Canada's reputation as a leader in genomic research. The success of the Centre is evident through its ability to compete on the international scene for top researchers in high throughput mammalian cell genetics, proteomics, computational biology and functional genomics.

Prof. Igor Stagljar: "A combination of freedom, free-form thinking, and no boundaries."

Prof. Brenda Andrews, the Donnelly Centre's Director, has been successful in not only attracting top international researchers but also in joint recruitment initiatives between departments in the University that have never before been involved in co-recruitment of new faculty. Each of the new recruits, along with other researchers in the building, have started new collaborative research projects enabled in large part by the Centre's open environment.

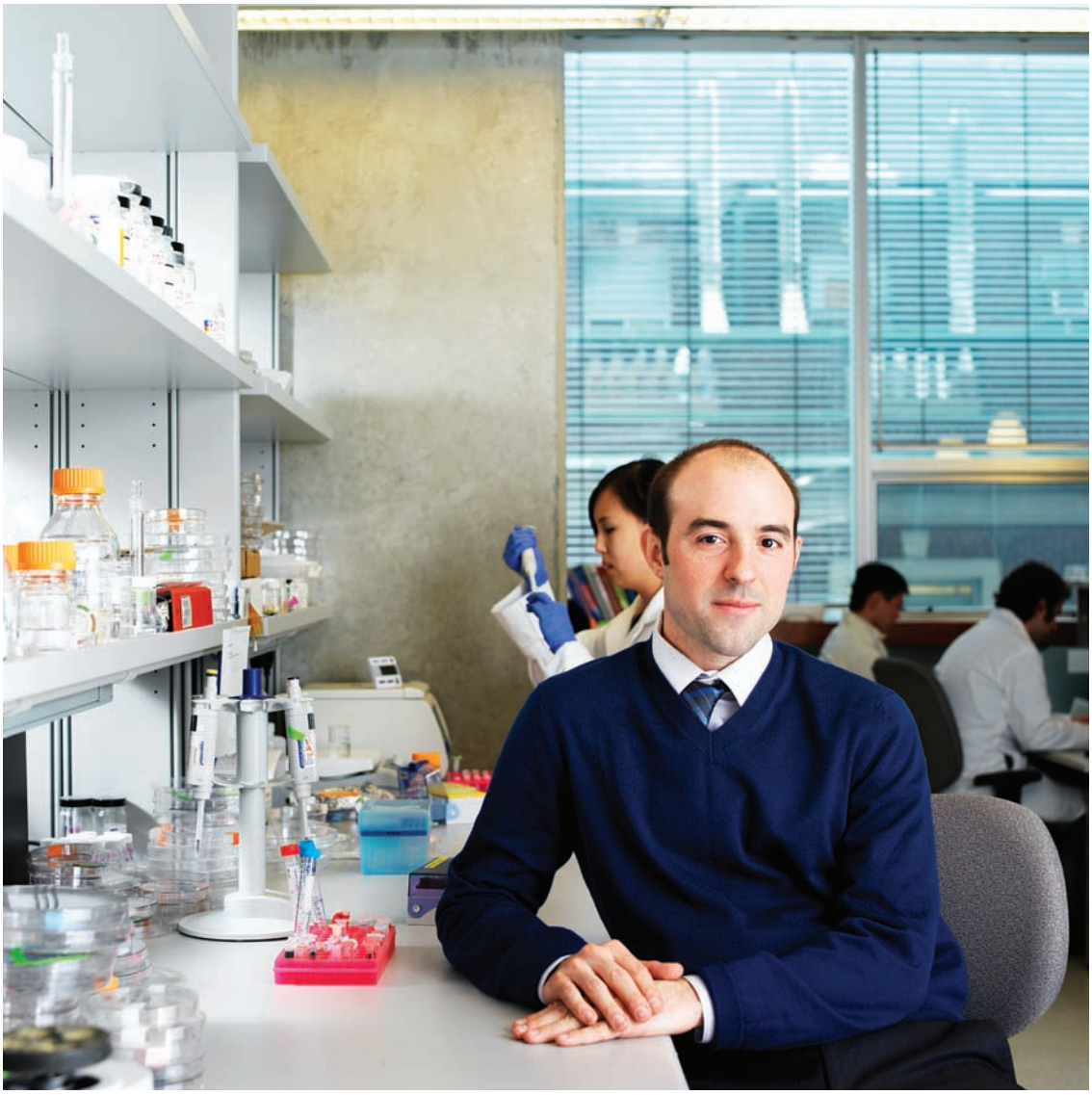
Prof. Igor Stagljar, who has his office on the 12th floor, is one of the early recruits to the Centre. Emphasis on technology development as well as the collaborative and collegial atmosphere is what attracted him. He motions towards the glass wall of the building to the expansive and unobstructed view of the skyline and the city. "I feel one with nature," he says. "It is a combination of freedom, free form thinking and of no boundaries that has such a positive impact on my work and life."

An Associate Professor in the Department of Biochemistry and the Department of Molecular Genetics, Stagljar studies how proteins interact in human cells, to understand how impaired protein-protein interactions lead to numerous human diseases such as cancer, schizophrenia, cystic fibrosis, arthritis and Parkinson's disease. Stagljar's lab has also developed a unique and internationally known test that can monitor interactions between membrane proteins, the so-called membrane yeast two-hybrid system (MYTH). The system has great potential in proteomics research.

Aaron Wheeler, Assistant Professor, Department of Chemistry, also joined the Donnelly Centre in the initial stages. When interviewing for jobs in 2005, Wheeler discovered that "interdisciplinary research" was the buzzword among many universities in North America, but he noticed that "only the University of Toronto, with its $100 million investment towards the Donnelly Centre was doing anything concrete about it." He is excited about the dynamic and informal atmosphere with the free flow of information. "It is the way of the future in research," he adds.

Wheeler is one of the developers of a technique that evaluates tiny fluid samples, sometimes referred to a "lab-on-a-chip" technology that significantly reduces the invasiveness of conventional methods for breast cancer detection. His research team was successful in analyzing hormones in blood, serum and breast tissue samples

PHOTOGRAPH: MARGARET MULLIGAN



Prof. Aaron Wheeler: "It is the way of the future in research."

PHOTOGRAPH: MARGARET MULLIGAN

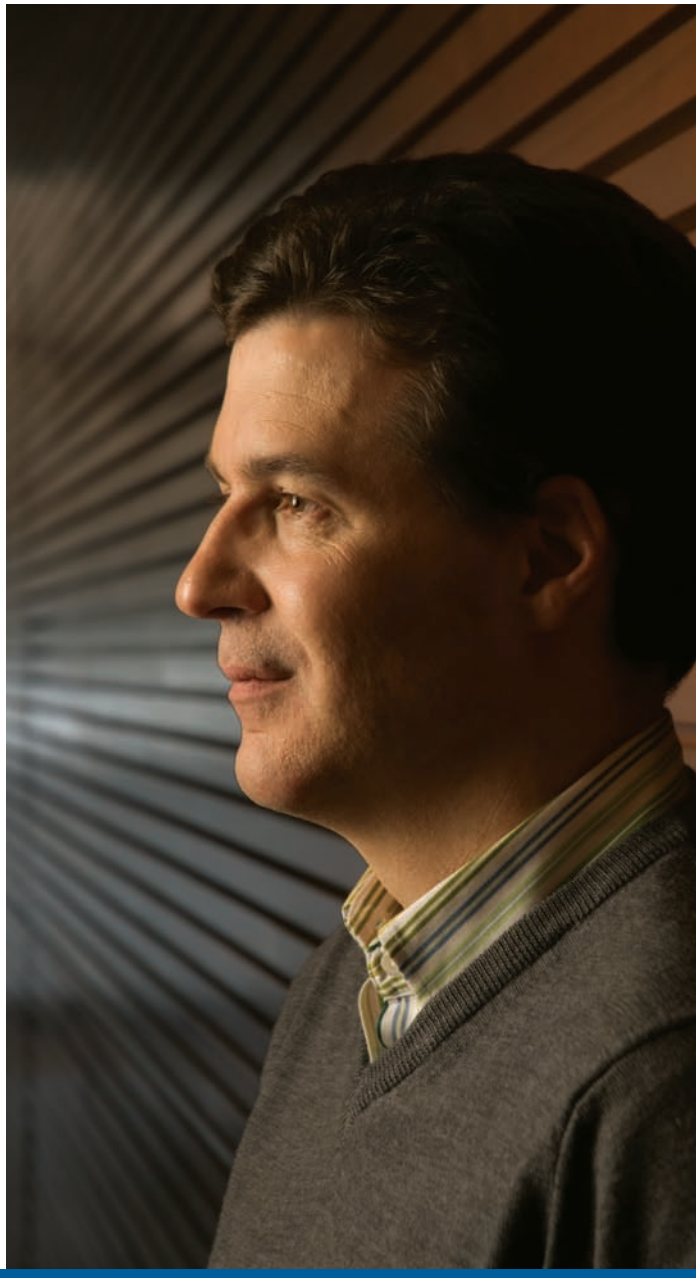
over a two-year study period. The clinical implications could be significant and investigators are developing methods to apply this technique for early detection with the hope of preventing breast cancer in individuals at higher risk.

Collaboration is a cornerstone of research at the Donnelly Centre. One example of this approach is the GenNet laboratory for automated genetics analysis. This collaborative platform combines functional genomics (the field of molecular biology that studies the vast data derived from gene projects to describe the functions and interactions of genes and proteins) and systems biology (which uses a holistic, all-inclusive and inter-disciplinary approach) to open the door to large-scale genetic network studies and network studies involving heterologous genes (in which a protein is experimentally put into a cell that normally does not make that protein, for example, human disease genes expressed in yeast). In addition to determining the roles of individual genes, genetic network analysis enables the study of cells as a complex network of biochemical factors. Understanding genetic networks will also provide researchers with novel drug targets, sensitive diagnostics for individualized therapy, and early indicators of toxic drug effects.

Another collaborative Donnelly Centre project is the establishment of the Toronto Centre for Phenogenomics. This state-of-the-art research facility is a collaboration between Mount Sinai Hospital, The Hospital for Sick Children, Saint Michael's Hospital and the University Health Network. The centre combines phenotypic profiling (based on any observable characteristic or trait of an organism) and chemical genomics (the study of genomic responses to chemical compounds). High-throughput phenotypic profiling is a high-content screening platform that allows a researcher to quickly conduct millions of biochemical, genetic or pharmacological tests. Through this process, one can rapidly identify active compounds, antibodies or genes which modulate a particular bimolecular pathway. The results of these experiments provide starting points for drug design and for understanding the interaction or role of a particular biochemical process in biology.

Dr. Friesen looks forward to seeing more results from this method of organizing research. But he has no doubts about the value of bringing people together in a collaborative, interdisciplinary environment. It allows people to "discuss, disseminate … stir things up a bit!"

IN PROFILE: STEPHEN SCHERER



As a leading genomic researcher, Prof. Stephen Scherer is by definition an innovator, exploring the multitude of diagnostic and therapeutic possibilities waiting to be revealed within the human genome. Scherer is Director of the McLaughlin Centre for Molecular Medicine (MCMM) and holder of the GlaxoSmithKline-CIHR Endowed Chair in Genetics and Genomics at The Hospital for Sick Children and University of Toronto. In 2004, his team co-discovered global gene copy number variation (CNV) and has since shown that CNV is the most abundant type of variation of human DNA. His group has also found CNV to contribute to the etiology of autism. His MCMM-supported Database of Genomic Variants facilitates hundreds of thousands of diagnoses each year.

It's a big topic, but how would you characterize the way innovation has served you in your work?

You need to always be thinking outside the proverbial box and consistently questioning dogma. Data that do not fit the norm are often the data you want to spend your most time considering. Notwithstanding all of this, innovation only comes—and comes to fruition—through hard work. An idea or discovery only becomes an innovation when you make it useful.

Given the rapid advances in technology, particularly in health care, is there tension between exploring the investigative opportunities newly available to you versus sticking to techniques or avenues of research with some proven record of success?

Hypothesis-driven research ruled for 50 years, but with the advent of genome sciences there has been a shift to a more "enlightened" process for developing hypotheses. That is, to use genomic (or global) datasets to first inform and then within that context contemplate previously unseen hypotheses. Having access to the latest technologies will give you the most complete data to draw from. I also think the term "basic" research is used too loosely. There can be outstanding "basic" research into "applied" problems and this is particularly relevant in biomedical research.

In the learning environment, how do you encourage students to engage in innovative thinking?

I don't give my powerpoint presentations out to students. I encourage them to listen to my lectures and take the notes they feel are most relevant, those things they find interesting, details that might help them think about how they might solve a problem. I also like to include some science history in my lectures. Knowledge of history can often help predict the future. Ultimately, the most important message in class lectures is to make sure the students learn the fundamentals. It's no good knowing how to use a particular database if you don't understand the strengths and weaknesses of the data within it.

To what do you attribute your own approach to research? Was it something you learned in the lab, or was it shaped by experiences or mentors outside the lab?

I'm a big believer in the Malcolm Gladwell's 10,000 hours to success rule and I suppose I've practiced this all my life. It started with my parents and then it just became what I expected myself to do. I remember my father telling me, "The early bird gets the worm." You need to put in your time starting at the bottom and working your way up. That way you know the system better than anyone else and you also know how lucky you are when you get to the top. These are the kind of people I most enjoy working with and always try to build my team around. Lastly, getting some hard knocks early builds character.

Look in your crystal ball. What do you imagine your lab will be working on in 10 years time?

I would be foolish to answer the question as posed. With the advent of information and genome technologies in science, you are stretching it to even look five years into the future. I do think in five years we will have the technologies in place to offer parents the ability to have their newborn's genome sequenced before they take their baby home. Medical schools, doctors, scientists, hospitals, governments and parents need to start thinking about this seriously. All of us, and in particular the younger generations, love information. And genetic information is the ultimate form of it in that it can tell us something about our past, present and future. So I suppose I'll continue to be a decoder of genome information, five years and probably a decade from now. ■

PHOTOGRAPH: J. MICHAEL LA FOND

Child's Play

Two U of T researchers take to the ice to better understand the brain

By Shibu Thomas

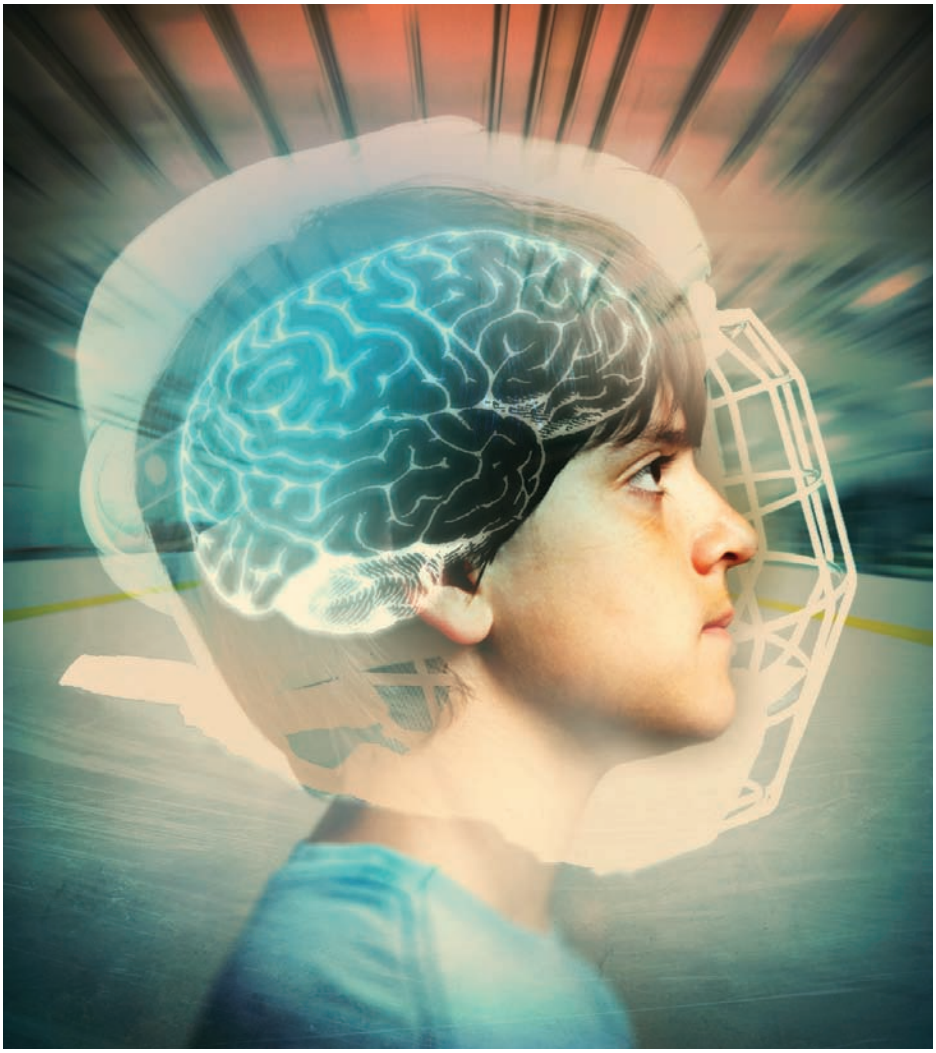


ILLUSTRATION: PAUL WATSON

The next step in understanding how the brain works could come from a minor hockey rink. That's the goal of Nick Reed and Steph Green, both registered occupational therapists at the University of Toronto's BrainFit Lab and PhD students at U of T's Graduate Department of Rehabilitation Science.

Reed and Green are seeking to understand the incidence and effects of head injury in minor hockey. Their research monitors nine minor hockey teams (six boys' and three girls' teams) ranging from ages nine to 12. At intervals throughout the season, the players undergo tests such as brain games, physical activities and functional magnetic resonance imaging (or fMRI, which looks at the brain's activity during a cognitive task such as a brain game). An exciting new technology called Head Impact Telemetry System (HITS) now incorporates helmets fitted with accelerometers, which allow realtime data to be collected while in play.

The BrainFit research program, which is supervised by Dr. Michelle Keightley, an assistant professor in the Department of Occupational Science and Occupational Therapy and a clinical neuropsychologist, could revolutionize the study of the development of the brain and its effects based on age and gender. "Our multi-disciplinary, collaborative and all-inclusive approach to this research has made this rewarding on many levels," says Green.

"Competitive sports has been, and continues to be, such a vital part of my life," says Reed. "My clinical and research interest in studying the cognitive function and performance in youth athletes following concussion and their safe return to meaningful activities are part of my way of giving back to the game." An athlete and coach himself, Reed started playing lacrosse when he was five. He's competed at all levels of the game and was even drafted for the professional National Lacrosse League. He's been coaching minor lacrosse for nine years. Reed feels that his B.Kinesiology (Hons.) from McMaster University and MScOT from U of T give him an ideal springboard to launch into this exciting field.

Green completed her HBSc with a double major in Neuroscience and Biological Sciences and then went on to receive her MScOT, both from the University of Toronto. Her study involves using fMRI to learn about the neural and clinical implications of sports-related concussion in children and youth.

In spite of a taxing workload, which includes clinical, research and teaching assignments, both Reed and Green can be found rink-side and interacting with parents, teachers as well as the media. They take seriously the need to educate the public about concussion and appear at as many events as they can, including one at the Hockey Hall of Fame, to spread the word.

The BrainFit Lab is supported by grants from the Ontario Neurotrauma Foundation, Canadian Institutes of Health Research and Children's Rehabilitation Research Network. While initially started as a three-year program, based on funding, researchers at the lab plan to continue to add new participants and to follow existing participants into the next phase. You can learn more about the BrainFit Lab by visiting their web site, www.brainfitlab.com.

Opening the Doors to Research

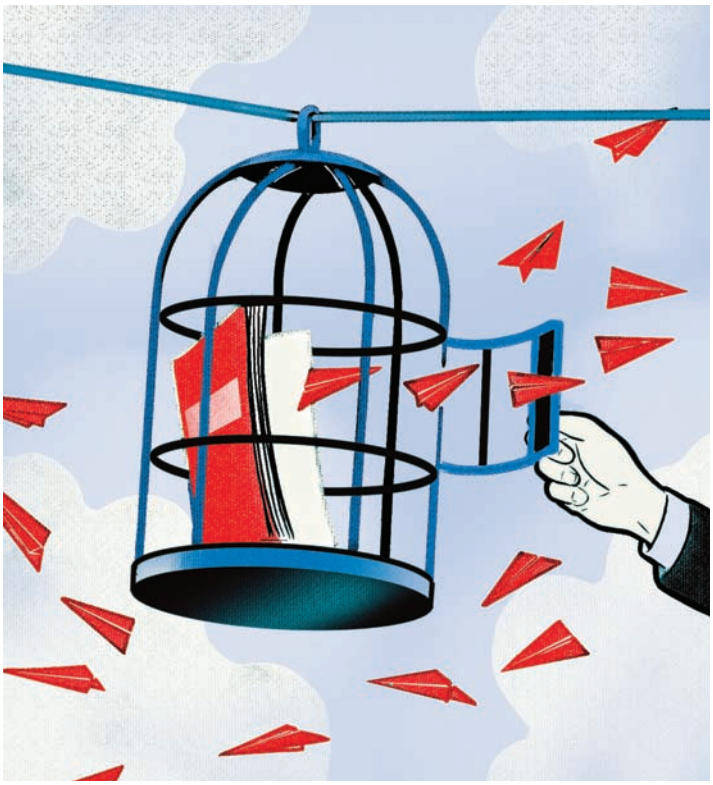
Open Access is changing the way we learn about research discoveries

By Niamh McGarry

James Till, the University of Toronto Emeritus Professor of Medical Biophysics best known for demonstrating—with Ernest McCulloch, Emeritus Professor of Medicine—the existence of stem cells, is the type of high-profile researcher best served by the traditional system of peer-review publishing.

Yet he is one of the strongest advocates for the alternative open access (OA) movement that is gaining momentum in the research world.

"In biomedical science, open resources like PubMed (a biomedical search engine from the U.S. National Library of Medicine) and GenBank (a collection of all the publicly available nucleotide sequences and their protein translations) have helped researchers to understand and appreciate the benefits of OA. There has also been increasing recognition that OA has the potential to foster collaborations in multidisciplinary areas, including collaborations of the kind needed to accelerate the translation of new knowledge into innovative practical applications," according to Till.



Making research both free and easy to access is more efficient and equitable, he believes. "Much research is published in a wide variety of expensive journals that may not be easily accessible, especially to people who do not have access to a first-rate university library." This includes researchers and scholars at less affluent institutions, as well as practitioners, policy makers, educators, students, innovators, entrepreneurs, members of the media and the public. The traditional publishing model often results in articles being submitted to several journals, and peer-reviewed repeatedly, before final acceptance—an inefficient and often lengthy process. Till believes that, because of its inherent inefficiency, the current system for quality-filtration of research publications is unsustainable in its present form, and that new approaches are needed.

Research carried out by U of T Professor Gunther Eysenbach (Department of Health Policy, Management and Evaluation and a senior scientist at the University Health Network) found three main advantages to making medical research openly accessible: faster uptake within a discipline, measureable by citations; increased knowledge transfer to other disciplines; and increased information transfer to other end users who would not normally read scientific journals, including policy makers, physicians and patients. Many funding agencies worldwide have started to see these advantages, and are introducing policies that encourage open access to research results they have supported.

The increasing number of open access journals means OA publishing is now a more viable option for researchers, says Eysenbach. *The Directory of Open Access Journals* (DOAJ), operating as a one-stop-shop to quality-controlled, open access journals, currently lists 4,434 scientific and scholarly publications. Developed and maintained since 2003 by Sweden's Lund University Libraries, it gets over eight million hits a month.

Self-archiving is another way researchers are making their work accessible. A free copy of a peer-reviewed research journal, conference article or thesis is deposited on the Internet either in an open archive or in an institutional repository. T-Space is U of T's faculty space to showcase and preserve scholarly work.

Eysenbach founded the first peer-reviewed open access journal in medical informatics 10 years ago. *The Journal of Medical Internet Research* is now the top-ranked journal in its discipline—quite an achievement for a low budget, open access publication. It uses a standard OA journal business model in which the author is charged a processing fee to publish. Additional revenues come from voluntary membership (offering extras such as PDF file access) and limited advertising.

Eysenbach is also a founding member of the new Open Access Scholarly Publishers Association (OASPA) set up to develop best practices in the field and counter quality control concerns. Increasingly, traditional publishing houses are also engaging in OA activities. "Over the next 10 to 20 years, being openly accessible is going to be the standard and everything else will be the exception," he predicts.

Ultimately, Till and Eysenbach agree, the new generation of researcher who has grown up using the Internet and its resources will continue to demand and drive continued expansion of the open access movement. M

ILLUSTRATION: JASON SCHNEIDER

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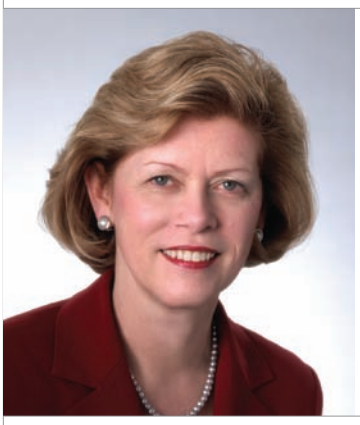

Better Ways, Valued Things

PROF. CATHARINE WHITESIDE
Dean, Faculty of Medicine, Vice-Provost, Relations with Health Care Institutions

As our economy has begun the challenging process of transformation, there has been much discussion of the value of innovation, but the concept behind it is certainly not new to our research community in Toronto.

Innovations as groundbreaking as the discovery of insulin, the identification of cancer stem cells or the conceptualization of policies that have shaped improved health services, can trace their genesis to our campus and to our affiliated hospitals and research institutes.

In the federal government's June 2009 report *Mobilizing Science and Technology to Canada's Advantage*, the word innovation is used some 56 times within the 52 page document. But what does innovation really mean?

The Council of Canadian Academies' has described it as "new or better ways of doing *valued* things" (emphasis is theirs). Health care endures as a priority for the majority of Canadians, so there can be no question that the research and education we undertake in the Faculty of Medicine and at our partner hospitals are valued. And in the pages of this issue of *UToronto Medicine*, we have focused on people and activities dedicated to finding new and better ways of achieving innovative outcomes.

The federal government's 2009 update on the implementation of their Science & Technology strategy asserts, "successful economies will be those that create a knowledge advantage by supporting research. The jobs of the future will be increasingly dependent on science and technology, and attracting those jobs requires long-term vision and a favourable environment for investment in research and development."

Many groundbreaking innovations can trace their genesis to our campus and to our affiliated hospitals and research institutes

We believe that, in creating new knowledge and in applying that new knowledge, our contributions will not only improve the health of Canadians but will have impact on the health of individuals globally. Innovation is also an important driver in creating prosperity and modernizing our economy, and it is doubly gratifying to know our impact is acknowledged and valued by our partners in the private and public sector—as well as by the public in general—in playing such a pivotal, transformative role. M

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