Ottawa Hospital Research Institute
OHRI IRHO
Institut de recherche de l'Hôpital d'Ottawa

THREE BIG IDEAS

that could change the world

And the OHRI researchers who are leading the charge

Ottawa Hospital Research Institute
Annual Report 2008 - 2009

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Message from the CEO

Dr. Duncan Stewart leads the OHRI while running a regenerative medicine laboratory and treating patients with heart and lung disorders.

Over the course of a single year, it may appear that scientific progress happens in very small steps, but it's all about very big ideas.

This year, our annual report explores some of the biggest ideas in health science today – ideas about stem cells as a source of regeneration, blood vessels as a stealth cause of disease and ways to do clinical research differently. These ideas are truly changing the world, and scientists at the Ottawa Hospital Research Institute (OHRI) are leading the way. While many big ideas drive our work, there is one common theme behind them all: the desire to help people live longer and healthier lives.

Research at OHRI has already helped many people, and our potential to do more has never been greater. This year, we began treating patients in a world-first clinical trial of a cancer-fighting virus and we're about to start another world-first trial of an engineered stem cell therapy for heart attack. But developing new therapies is just one part of the battle – we're also comparing different approaches to prevent, diagnose and treat disease, and making sure the results of research are actually applied in the clinic. Finally, we're investigating the molecular basis of health and disease, to provide the foundations for the next generation of medicine.

The impact of OHRI research is felt around the world, but the benefits to the local community are magnified. Each year, our clinical trials provide thousands of patients at The Ottawa Hospital with innovative health options, and our strong research program helps the Hospital attract the best clinicians. As an affiliated institute of the University of Ottawa, we also provide training opportunities to more than 400 students and postdoctoral fellows each year. And our research is also helping to create the next generation of industries and jobs, with more than seven companies started by OHRI scientists and dozens of partnerships with other local companies. In the current climate of economic uncertainty, this last contribution could not be more important.

Of course, the economic uncertainty has also had an impact on OHRI, as it has on all organizations that rely on endowments and donations. Fortunately, we were able to cover our shortfall this year using surpluses from previous years, and although next year will be tight, our long term plan should allow for growth with stability.

Moving forward, OHRI is well-positioned to expand its role as a leading Canadian hospital research institute. We were one of the few hospitals in the country to receive a prestigious research infrastructure grant from

the Canada Foundation for Innovation last year, and this grant will ensure that we have some of the best research facilities in the world. Our scientists have also been successful in obtaining external funding for their own research programs, and we have received crucial support from many generous donors to The Ottawa Hospital Foundation.

I would like to conclude by thanking everyone who believes in big ideas and in OHRI's role in the future of health research, from our many donors and research volunteers, to our scientists, staff, students, board members and partners. We are delighted to share this report with you.

Dr. Duncan J. Stewart
CEO and Scientific Director, Ottawa Hospital Research Institute
Vice-President, Research, The Ottawa Hospital
Professor of Medicine, University of Ottawa

Message from the Board Chair

As the Board Chair of the Ottawa Hospital Research Institute (OHRI), I often have the pleasure of greeting community leaders, government officials and business people when they come to visit the Institute. As these people walk through the laboratories and clinics and meet our scientists and students, they often comment on how it all seems a bit like science fiction: sequencing genes, regenerating body parts and harnessing viruses against cancer. And the scientists themselves often say that just 10 years ago, much of what they are doing today would have seemed like science fiction to them as well. That's how quickly health research is advancing. It is tremendously exciting to be involved in this process.

As you'll read in the pages of this report, researchers at OHRI are full of "big ideas" and they are leading the world in many areas of biomedical and clinical research. On behalf of the Board of Directors, I would like to express our deepest respect and gratitude for the scientists, students and staff who believe in their ideas enough to work very long hours and overcome countless challenges to try to improve this world for the rest of us.

I would also like to take this opportunity to thank the Members of our Board of Directors, especially the 11 other external Members who volunteer their time to provide independent oversight and guidance to the Institute. These people lead very busy lives, but somehow always manage to find time to help. Their experience in business, law, governance and commercialization is crucial to the Institute's success.

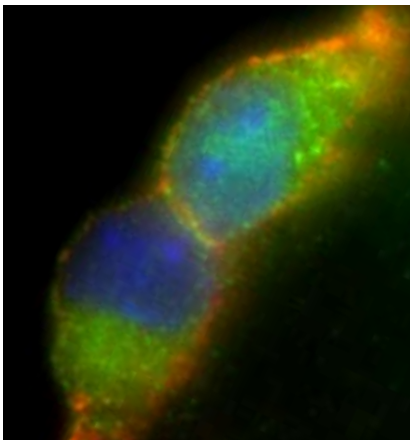
Biotech entrepreneur Ken Newport has chaired the OHRI Board since April 2008.

Before closing, I would like to say that despite this being a challenging year financially for all hospital-based research institutes, including this one, I believe that OHRI has all the ingredients for long term success: dedicated and productive researchers, committed volunteers, inspired leadership and an incredibly generous community. With all these pieces in place, the future is bright.

Ken Newport
Chair, Board of Directors, Ottawa Hospital Research Institute

Idea #1

Renovating the body:
harnessing the potential of stem cells



Stem cells are responsible for renewing and regenerating the body's tissues throughout life. Muscle stem cells such as those above are crucial in building new muscle fibres. Photo courtesy of Fabien Le Grand.

The concept of the stem cell is one of the most powerful in all of medicine, providing an elegant model to explain how the body develops and heals itself, while also fuelling dreams of growing new organs and staying young and healthy forever.

Today, stem cells are so pervasive in popular culture that one almost needs to step back a bit to appreciate how novel the concept was when it was first proposed nearly 50 years ago. At the time, a lot of what we knew about human cells came from cancer cells, which could easily be grown in the laboratory. When a cancer cell divided in the lab, it produced another identical cancer cell. But researchers knew that there must be more to it, because many types of non-cancerous cells, from muscle cells to red blood cells, could not divide at all, and yet somehow the body keeps producing them throughout life.

The answer came in the 1960s, when Canadian scientists Drs. Ernest McCulloch and James Till discovered a master cell in bone marrow that could give rise to many types of blood cells, while also producing more identical master cells. In effect, this "stem cell" acted like a reservoir that could regenerate all the components of blood.

Today we know that stem cells are at the root of the development of every organ in the human body, and many adult tissues contain stem cells that are active throughout life. But can these cells be harnessed to rebuild the heart after a heart attack? Restore vision to the blind? Reconnect a broken a spinal cord?

These big questions are what drive people at the Sprott Centre for Stem Cell Research, which opened at the Ottawa Hospital Research Institute in 2006. The Centre is led by Dr. Michael Rudnicki, who is also a Professor in the University of Ottawa's Faculty of Medicine, Canada Research Chair in Molecular Genetics and Scientific Director of Canada's Stem Cell Network.

"Stem cells definitely have the potential to give rise to all the tissues in the human body, but getting them to grow whole organs on command in a lab dish is a pretty tall order," says Dr. Rudnicki. "I think that in the short term, the bigger potential will be in new drugs that stimulate the stem cells that already exist inside our bodies, or the slightly more specialized progenitor cells they give rise to."

Some of these drugs already exist. For example, erythropoietin is a drug that stimulates red blood cell progenitors to produce more red blood cells, and it has been used to treat anemia for many years.

Dr. Rudnicki envisions similar drugs to stimulate stem and progenitor cells in the muscle, brain, heart and other organs. And his team is making impressive progress. This year, they discovered a molecular trick to make muscle stem cells produce 20 per cent more muscle. Across the hall, his colleague Dr. Lynn Megeney has discovered a compound that does the same thing for heart muscle. They are now working to develop these compounds into drugs for people with heart and muscle wasting diseases.

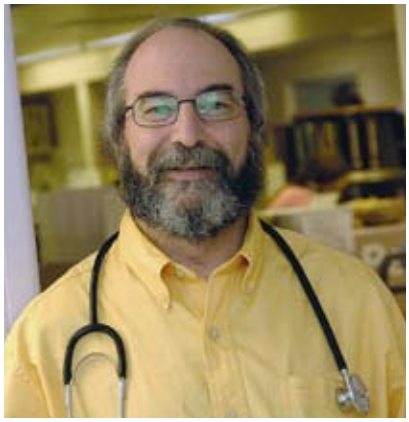
Another hot area of stem cell research is in finding ways to turn normal cells into stem cells. While much attention has focused on using these cells for transplantation, Dr. Rudnicki thinks there is even more potential in using these cells to screen new drugs in the lab.

"Stem cells are very rare and difficult to extract from the body, but if we can generate them in large quantities from normal, easily accessible cells, we'll be able to develop and test drugs that stimulate stem cells much more quickly," he says.

Dr. Rudnicki is careful not to downplay the potential of stem cell transplantation, however. In fact, he says stem cell transplantation is the field's greatest success story so far, with bone marrow stem cells being used to treat leukemia for nearly 50 years. The most common application is for people who have had strong chemotherapy that damages the immune system. A bone marrow stem cell transplant can plant the seeds of a new immune system in these people.

According to bone marrow transplant specialist Dr. Harry Atkins, we have had a lot of success with these cells, but we are still just at the cusp of

Dr. Michael Rudnicki (right) leads the OHRI's Sprott Centre for Stem Cell Research and Regenerative Medicine Program. Graduate student Vince Punch is pictures at left.



Dr. Harry Atkins is involved in a number of clinical trials of stem cell-based therapies.

understanding their potential.

"When we first started using blood and bone marrow stem cells in the clinic, we really didn't understand how they worked, but in the last decade, we've discovered that they may be much more powerful and flexible than we once thought, and we've started using them in totally novel ways," he says.

These new ways include experimental therapies for autoimmune diseases, heart disease, lung disease and stroke, all of which are being developed and tested by OHRI researchers.

Dr. Atkins, for example, leads a clinical trial with neurologist Dr. Mark Freedman that is testing bone marrow stem cell transplantation as a treatment for severe cases of multiple sclerosis. This disease is thought to be an autoimmune disease, in which the patient's own immune system targets and destroys brain tissue. The transplant is used to regenerate a new immune system in these patients, after their existing immune system is destroyed with strong chemotherapy. More than 20 patients have been treated in the last seven years and so far, none has experienced a relapse, and some have regained abilities they thought were lost forever.

Another example comes from the lab of Dr. Duncan Stewart, the CEO and Scientific Director of OHRI. Dr. Stewart has developed and tested the world's first engineered cell therapy for pulmonary hypertension and he just received funding to begin a similar trial in heart attack patients. Both therapies involve extracting stem-like cells from the blood of patients, engineering them to be more powerful in the laboratory, and then injecting them back into the body, where they can help repair and regenerate damaged tissue.

As Medical Director of the OHRI's Regenerative Medicine Program, Dr. Atkins' job is to facilitate this kind of bench-to-bedside research, and he thinks we're close to getting the formula right.

"We've got basic scientists with very strong molecular expertise working alongside physicians and surgeons who understand clinical problems and can help translate discoveries into new treatments," he says. "We also have exceptionally talented students and staff working with us in world class facilities. The sky is the limit."

And as to the question of whether or not we'll be able to use stem cells to regenerate every organ in the human body? According to Dr. Rudnicki, that's beside the point.

"Whatever the answer ends up being, there is no doubt that stem cells and regeneration will play a key role in the medical therapies of the

future, and the idea of the stem cell has already transformed the world and how we think about health and disease," he says.

Idea #2
You're only as healthy as your blood vessels

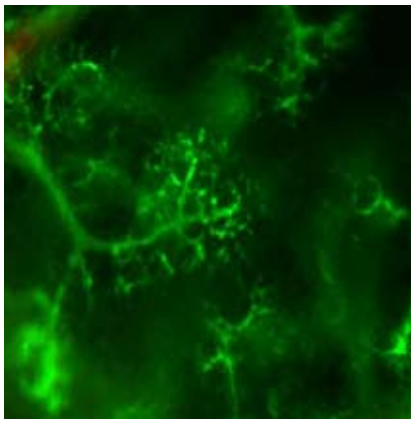
Dr. Antoine Hakim used to start every lecture with a shocker: "Every 10 minutes, someone in Canada suffers a stroke," he would say. As the Scientific Director of the Canadian Stroke Network, founder of the Heart and Stroke Foundation Centre for Stroke Recovery, Director of Neuroscience at OHRI and Head of Neurology at the University of Ottawa, Dr. Hakim gave a lot of lectures like this.

Then a few years ago, the speech became even more shocking: "For every stroke that we know about," he would say, "there are ten more covert strokes that we can't even detect - in effect a stroke a minute!"

While the "classical" strokes are caused by blockages in the large arteries that feed the brain, covert or "micro-strokes" are caused by abnormalities of the smallest blood vessels, which may be just one fiftieth the thickness of a human hair. As we age and as our blood vessels become less healthy and flexible, these abnormalities occur more frequently. And although we may not notice micro-strokes when they occur, increasing evidence suggests that they could play a significant role in the gradual decline in brain function that has traditionally been associated with old age.

This concept goes well beyond stroke – just think about the tens of thousands of kilometers of blood vessels that link every organ in our body and consider this revolutionary idea: that wear and tear on these vital highways throughout life accounts for most cases of chronic disease, including kidney disease, eye disease, diabetes, heart disease and lung disease. Indeed, researchers have found evidence that blood vessel abnormalities occur in all these organs as we age, and they seem to be linked to the development of disease.

OHRI CEO Dr. Duncan Stewart has championed a very similar idea as the root cause of pulmonary hypertension, a rare but lethal lung disease that preferentially affects young women. Unlike the chronic diseases of aging, this condition has a strong genetic component. The Stewart lab has shown that the recently identified "pulmonary hypertension gene" plays an



Increasing evidence suggests that blood vessels (such as those shown above) may be at the root of some of the most common chronic diseases that affect the heart, brain, kidney, lung and eye. Photo courtesy of Yupu Deng and Dominique Yelle.

Dr. Rhian Touyz is developing a new laboratory to study blood vessels in patients with a variety of chronic diseases.

important role in protecting the cells that line blood vessels from damage. He has pioneered the concept that mutations in this gene cause the tiny blood vessels in the lung to degenerate, and this is what causes pulmonary hypertension in people with the genetic form of this disease. Moreover, he has developed a revolutionary stem cell therapy to regenerate these vessels. The therapy is already being tested in clinical trials and is receiving international attention.

Dr. Rhian Touyz is another big proponent of the concept of blood vessels as a root cause of disease. Dr. Touyz is a Senior Scientist in OHRI's Kidney Research Centre, a physician at The Ottawa Hospital's Hypertension Clinic (for people with high blood pressure) and a Professor at the University of Ottawa. She has devoted her career to understanding how abnormalities in blood vessels contribute to hypertension and various chronic diseases and she is now setting up an innovative new laboratory to investigate this.

"The new facility will allow us to investigate blood vessels in exquisite detail, both in patients and in the lab," she says. "We will be able to non-invasively study the structure and function of blood vessels in people with conditions such as kidney disease, heart disease, diabetes and obesity, and then we will be able to isolate blood vessels from these same people and study them in the lab, to correlate what we are seeing in the clinic with what is happening at the gene, molecular and cellular levels. This will help us carry out very powerful experiments that will provide clear evidence about the role of blood vessels in chronic diseases."

The equipment for the new lab is being funded by the Canada Foundation for Innovation, as part of OHRI's "Translation of Innovation into Medical Excellence" project, which was awarded $32M in the peer-reviewed Research Hospital Fund competition. The equipment will be available to researchers in all areas of OHRI, as well as to those based at the University of Ottawa, the University of Ottawa Heart Institute and CHEO (all of whom were partners in the grant).

According to Dr. Touyz, this multi-disciplinary, collaborative approach is key to the success of the emerging field of vascular health.

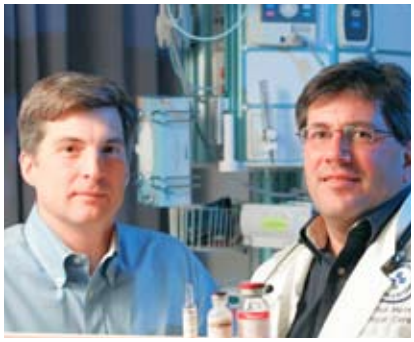
"Medical departments are often organized by organ, and this separation may be one reason why it has taken us so long to appreciate the common role of blood vessels in diseases that affect different organs," she says. "But attitudes are changing at the same time as techniques are becoming much more advanced, so I think we're now in a position to move the field forward quite rapidly. This is especially important now that we're seeing more and more children and adolescents with hypertension and cardiovascular disease, and it is predicted that for the first time ever, this may cause the current generation to have a shorter lifespan than their parents."

"We can reduce our risks by eating better and exercising more," adds Dr. Touyz, who also holds the Canada Research Chair in Hypertension. "But I also believe that this new coordinated approach to vascular health research has a crucial role to play in improving health for this generation and the next."

Idea #3

High impact clinical research:

getting more bang for the health care buck



Dr. Dean Fergusson (left) and Dr. Paul Hébert (right) led a large clinical trial that has made heart surgery safer around the world.

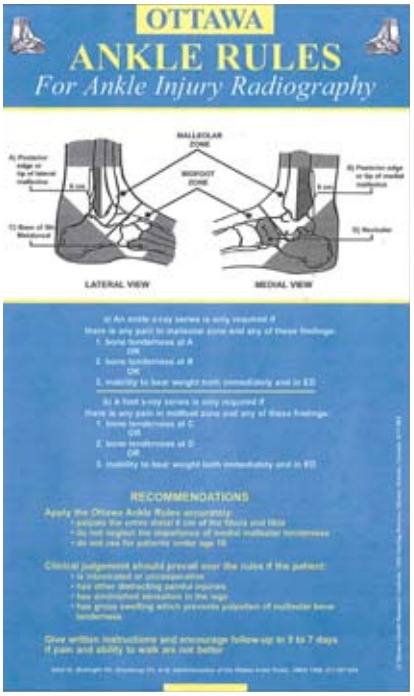
As in many parts of the world, health care spending in Canada has risen dramatically in recent years – in fact, it has nearly doubled over the last 30 years, even accounting for inflation and population growth. Despite the considerable increase in health care expenditures, research suggests that 30 to 40 per cent of patients do not receive the most effective health treatments and 20 to 25 per cent receive obsolete or harmful treatments.

Disturbing statistics such as these have fuelled debates around the world about how to provide better and more cost-effective health care. In Canada, some physician groups have called for more private sector involvement, while in the US, President Obama has embarked on a major campaign for public health insurance.

People are passionate on all sides of this issue, but one idea has been gaining increasing momentum: the idea that we need more research to understand how to provide better health care for less money. The goal is laudable, but it raises many questions, such as, 'What kind of research should we be doing?', 'What evidence is there that it will actually make a difference?' and 'If it's so simple, why haven't we done it already?'

According to Dr. Dean Fergusson, the crucial issue is that we need to do more of the "right kind" of clinical research to really have an impact. Dr. Fergusson is the Acting Director of OHRI's Clinical Epidemiology Program and an Associate Professor of Medicine at the University of Ottawa.

"We need to do much larger studies that compare different treatments using meaningful outcomes in a diverse group of patients," he says. "These studies are difficult and they require a large investment of money and time, but they provide much more valuable information than small studies that simply compare one drug against a placebo, and try to



The Ottawa Ankle Rules help emergency physicians evaluate ankle injuries more efficiently.

make conclusions based on short-term outcomes."

A good example is the BART clinical trial, which Dr. Fergusson designed and led along with OHRI critical care researcher Dr. Paul Hébert. This study compared three different drugs that were commonly used to prevent bleeding during high risk heart surgery. All had been proven effective compared to placebo, but BART was the first rigorous trial to compare them head-to-head and it showed that people who received one drug, aprotinin, were actually 50 per cent more likely to die. Aprotinin also cost 10 times more than the other two drugs. Based on these results, marketing of aprotinin was suspended around the world, resulting in safer surgery for patients as well as significant cost savings for hospitals.

There are many other examples of this kind of practice-changing research at OHRI, in areas ranging from thrombosis to asthma to emergency medicine to cancer. In a number of cases, OHRI researchers have also developed their findings into "clinical decision rules", that help clinicians use research results to efficiently diagnose and treat medical problems. Dr. Ian Stiell, for example, has developed a simple checklist-type rule that can determine which patients are likely to have a broken ankle and should be given an x-ray, and which simply have a sprain. The rule is used around the world and is internationally referred to as the "Ottawa Ankle Rule". Over the last decade, OHRI researchers have developed similar internationally recognized rules that have improved detection and management of blood clots, head injuries and other conditions.

"There are many inspiring examples of clinical research making a difference, but there are still thousands of questions that have not yet been addressed," says Dr. Fergusson.

Some claim that much of the problem lies in the approval process for new drugs, which only requires that a drug be proven safe and effective compared with a placebo. Industry generally does not fund studies that compare competing treatments.

Research funding agencies in Canada and the US are paying attention to the problem however, and taking steps to remedy it. The US Congress recently approved $1.1B in new spending on "comparative effectiveness research". And the Canadian Institutes of Health Research (CIHR) has begun funding more large clinical trials, including head-to-head drug comparisons. CIHR has also funded a number of special "knowledge translation" projects to help get research results into practice (one of these, called KT Canada, is led by Dr. Jeremy Grimshaw at OHRI).

Hospitals and research institutes are also taking up the challenge. OHRI's Methods Centre, which is led by Dr. Fergusson, is a leading example.

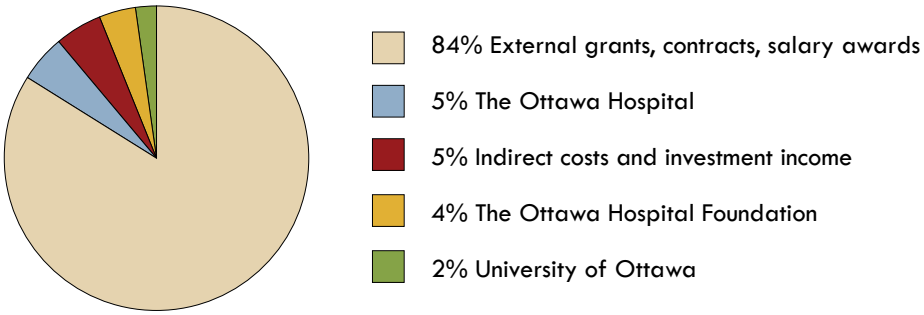
The Centre coaches clinicians in designing clinical studies that will have maximum impact. Dr. Phil Wells, OHRI's Director of Clinical Research, also organizes a highly successful week-long course every year that attracts investigators from across Ontario and beyond who want to hone their clinical research skills.

OHRI, The Ottawa Hospital and the University of Ottawa have also partnered to bring a satellite of the Institute for Clinical Evaluative Sciences to Ottawa. Called ICES-uOttawa, the centre will give local researchers access to the most comprehensive health databases in the province. There is also potential to link these data with encrypted patient records from The Ottawa Hospital Data Warehouse, providing a powerful approach to study health before, during and after a hospital visit.

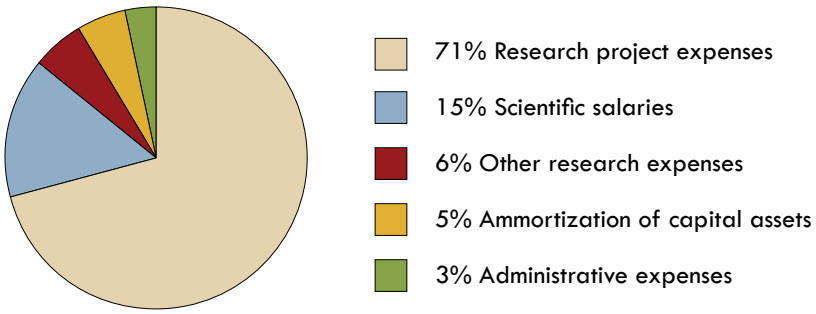
"With world-class clinical researchers in Ottawa and a lot of unique resources, I think we are very well positioned to play a lead role in this next generation of high impact clinical research," says Dr. Fergusson. "There is nothing more exciting than knowing that you have the power to improve health for thousands of people and there are many researchers at OHRI who feel the same way."

Financial summary*

Revenue distribution ($87.7 M)



Expenditure distribution ($91.0 M)



*Full financial statements will be available at www.ohri.ca/corporate/annualreports.asp.

Top 10 sources of peer-reviewed funding

1. Canadian Institutes of Health Research ($20 M)
2. Heart and Stroke Foundation of Ontario ($4.8 M)
3. Ontario Institute for Cancer Research ($2.1 M)
4. National Cancer Institute of Canada ($1.9 M)
5. Ontario Ministry of Health and Long-term Care ($1.6 M)
6. Canada Research Chairs Secretariat ($1.5 M)
7. Genome Canada ($1.3 M)
8. Multiple Sclerosis Society of Canada ($0.8 M)
9. Canadian Blood Services ($0.6 M)
10. Natural Sciences & Engineering Research Council of Canada ($0.6 M)

OHRI quick facts

People
- 103 scientists
- 344 investigators
- 443 trainees
- 692 staff

Research publications
- 818 in 2008

Research projects
- 857 grants, contracts and salary awards
- 617 clinical trials

Commercialization
- 5-10 patents per year
- Seven startup companies overall

Facilities
- 225,000 sq. ft. of basic and clinical research space at The Ottawa Hospital's Civic, General and Riverside campuses

Board of Directors

The OHRI is a not-for-profit corporation governed by a Board of Directors that includes members of the University of Ottawa, The Ottawa Hospital, The Ottawa Hospital Foundation and the community.

Chair
Ken Newport, Biotech entrepreneur

Vice Chair and Treasurer
Ian Mumford, Chief Operating Officer, Canadian Blood Services

Directors
- Dr. Jacques Bradwejn, Dean, Faculty of Medicine, University of Ottawa
- Don Hewson, President and CEO, HBS Marketing
- Jacquelin Holzman, Past Chair, Ottawa Hospital Research Institute
- Dr. Jack Kitts, President and CEO, The Ottawa Hospital
- Michael LeClair, Chair, The Ottawa Hospital Foundation
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- Lynn Pratt, Partner, Deloitte & Touche LLP
- Dr. Denis Prud'homme, Dean, Faculty of Health Sciences, University of Ottawa
- Dr. Duncan Stewart, CEO and Scientific Director, Ottawa Hospital Research Institute, Vice-President of Research, The Ottawa Hospital and Professor of Medicine, University of Ottawa
- Bashir Surani, Member of The Ottawa Hospital Board of Governors
- D. Lynne Watt, Partner, Gowling Lafleur Henderson LLP
- Shirley Westeinde, Chair, Westeinde Group of Companies
- Carole Workman, Executive Director, Canadian Association of University Business Officers

Ten selected high impact research papers

New way to enhance stem cells to stimulate muscle regeneration
Wnt7a activates the planar cell polarity pathway to drive the symmetric expansion of satellite stem cells. Le Grand F, Jones AE, Seale V, Scimè A, Rudnicki MA. Cell Stem Cell. 2009 Jun 5;4(6):535-47.

Blood clots may be early warning sign of cancer
Systematic review: the Trousseau syndrome revisited: should we screen extensively for cancer in patients with venous thromboembolism? Carrier M, Le Gal G, Wells PS, Fergusson D, Ramsay T, Rodger MA. Ann Intern Med. 2008 Sep 2;149(5):323-33.

Investigating the molecular basis of vascular disease
Redox-sensitive signaling by angiotensin II involves oxidative inactivation and blunted phosphorylation of protein tyrosine phosphatase SHP-2 in vascular smooth muscle cells from SHR. Tabet F, Schiffrin EL, Callera GE, He Y, Yao G, Ostman A, Kappert K, Tonks NK, Touyz RM. Circ Res. 2008 Jul 18;103(2):149-58.

New guideline for reporting clinical research reviews
Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. Moher D, Liberati A, Tetzlaff J, Altman DG; the PRISMA Group. Ann Intern Med. 2009 Jul 20.

New insight into egg cell division
Polar body emission requires a RhoA contractile ring and Cdc42-mediated membrane protrusion. Zhang X, Ma C, Miller AL, Katbi HA, Bement WM, Liu XJ. Dev Cell. 2008 Sep;15(3):386-400.

Surprising finding about asthma overdiagnosis
Overdiagnosis of asthma in obese and nonobese adults. Aaron SD, Vandemheen KL, Boulet LP, McIvor RA, Fitzgerald JM, Hernandez P, Lemiere C, Sharma S, Field SK, Alvarez GG, Dales RE, Doucette S, Fergusson D; Canadian Respiratory Clinical Research Consortium. CMAJ. 2008 Nov 18;179(11):1121-31.

Discovery of pathway that regulates stem cells in the eye
Progenitor cell proliferation in the retina is dependent on Notch-independent Sonic hedgehog/Hes1 activity. Wall DS, Mears AJ, McNeill B, Mazerolle C, Thurig S, Wang Y, Kageyama R, Wallace VA. J Cell Biol. 2009 Jan 12;184(1):101-12.

Benefits of exercise during prostate cancer therapy
Randomized controlled trial of resistance or aerobic exercise in men receiving radiation therapy for prostate cancer. Segal RJ, Reid RD, Courneya KS, Sigal RJ, Kenny GP, Prud'Homme DG, Malone SC, Wells GA, Scott CG, Slovinec D'Angelo ME. J Clin Oncol. 2009 Jan 20;27(3):344-51.

Deciphering how brain cells talk to each other
Human Freud-2/CC2D1B: a novel repressor of postsynaptic serotonin-1A receptor expression. Hadjighassem MR, Austin MC, Szewczyk B, Daigle M, Stockmeier CA, Albert PR. Biol Psychiatry. 2009 Aug 1;66(3):214-22.

Possible new target for cancer therapy
Regulation of glioblastoma cell invasion by PKC iota and RhoB. Baldwin RM, Parolin DA, Lorimer IA. Oncogene. 2008 Jun 5;27(25):3587-95.