

OTTAWA HEALTH RESEARCH INSTITUTE

ANNUAL REPORT 2007 - 2008



RESEARCH SAVING LIVES AND PROVIDING HOPE

- › MAKING HEART SURGERY SAFER
- › PROMISING NEW STEM CELL THERAPY
- › BALANCING THE RISKS OF BLOOD THINNERS
- › BREAKTHROUGH IN MUSCLE REGENERATION
- › REACHING OUT TO OSTEOPOROSIS PATIENTS
- › FIGHTING CANCER WITH VIRUSES
- › PREVENTING CARDIOVASCULAR DISEASE

Embarking on a new era of health research

As the research arm of The Ottawa Hospital and an affiliated institute of the University of Ottawa, the Ottawa Health Research Institute (OHRI) is at the crucial intersection of health care, research and education. Our goal is to conduct world-class research that improves the health of patients at The Ottawa Hospital and beyond, but we also have a key role in recruiting top health care providers to

to take this opportunity to paint a broader picture of the OHRI today, and where we see ourselves in the next five to 10 years.

OHRI has become one of the top hospital research institutes in Canada

Since it was formed in 2001, the OHRI has grown to become one of the top hospital-based research institutes in Canada. Our hospital, The Ottawa Hospital, now serves more patients than any other in the country and is a leader in providing innovative world-class care.

The OHRI is organized into six research programs focused on cancer, chronic disease, clinical epidemiology, neuroscience, regenerative medicine and vision. At the core of these programs are 104 scientists, all of whom are also professors at the University of Ottawa and many of whom are practicing clinicians at The Ottawa Hospital. We also provide support to about 300 clinicians who conduct research on a part-time basis. We have 225,000 square feet of dedicated basic and clinical research space at the Hospital's Civic, General and Riverside Campuses.



The OHRI is governed by a 17-member Board of Directors led by Jacquelin Holzman (right). Dr. Duncan Stewart (left) is the CEO and Scientific Director of OHRI and also the Vice President of Research at The Ottawa Hospital and a Professor of Medicine at the University of Ottawa.

Ottawa, training the next generation of researchers, and partnering with public and private sector organizations to ensure that the benefits of our research are realized by Canadians.

This year we've achieved unprecedented success in these goals. We completed the largest heart surgery clinical trial ever and the results changed practice around the world, virtually overnight. We've developed novel therapies that are showing promise in early clinical trials and providing hope to thousands. We've appointed four outstanding new scientists, trained 400 students and post-doctoral fellows and filed 22 patents. We've also brought in \$77M worth of external grants and contracts and secured highly prestigious, "once-in-a-generation" funding through the Canada Foundation for Innovation's Research Hospital Fund.

We share these successes with The Ottawa Hospital and the University of Ottawa, and of course with all of the generous donors who have supported our work through The Ottawa Hospital Foundation. With continued support, we believe we can reach even greater heights in the coming years and make Ottawa a leading international city for health research. While our latest research successes are described in more detail later in this report, we would like

OHRI in 2007/2008

- 104 scientists
- 374 trainees
- 304 clinical investigators
- 571 staff
- 783 active grants, contracts and salary awards
- 633 clinical trials
- 22 patents filed
- 225,000 square feet of research space
- 488 publications

The OHRI has been able to grow over the last few years, thanks to our success in securing external, peer-reviewed grants from agencies such as the Canadian Institutes of Health Research (CIHR), the Canada Foundation for Innovation (CFI) and the Ontario Ministry of Research and Innovation (MRI). In the Summer 2007 CIHR competition, for example, we were awarded an amazing 19 research grants, more than any other research institute in Canada. We've also received major CFI grants to build state-of-

Health research *A message from the Board Chair and CEO*

the-art facilities such as the Sprott Centre for Stem Cell Research and the Kidney Research Centre. Twelve of our scientists hold prestigious Canada Research Chairs and another 25 hold other external salary awards and chairs.

As our grant success has grown, so has our national and international recognition. Our scientists currently lead highly-esteemed organizations such as the Canadian Stem Cell Network, the International Consortium of Stem Cell Networks, the Canadian Stroke Network, the Canadian Oncolytic Virus Consortium, the Canadian Cochrane Network and Centre and the International Regulome Consortium.

Most importantly, we've achieved unique success in translating our discoveries into new therapies and better health care. We're developing viruses that selectively destroy cancer cells, stem cell therapies for heart and lung disease, bio-engineered corneas for debilitating blindness and clinical decision rules to streamline care throughout the hospital. Research is progressing quickly and discoveries made today have the potential to transform care and save lives in the near future.

New funding will make Ottawa a leading city for translational research

Our success in translational research has inspired us to do even more. The vast majority of discoveries still never make it into the real world, but we believe we can change this, if we provide our researchers with the tools and support they need.

Two major new research grants have put us well on our way to making this vision a reality. Both were awarded this year through CFI's highly-competitive Research Hospital Fund Competition.

"Research is progressing quickly and discoveries made today have the potential to transform care and save lives in the near future."

The first grant, called TIMEx ("Translation of Innovation into Medical Excellence") is worth \$32M and is by far the largest grant ever awarded for health research in Ottawa. The proposal was developed by OHRI, in partnership with The Ottawa Hospital, the Children's Hospital of Eastern

Ontario, the University of Ottawa Heart Institute and the University of Ottawa. Of 39 applications submitted, just eight were selected by the international scientific review panel.



"Once-in-a-generation" funding from the Canada Foundation for Innovation will support the construction of new research facilities for cancer, regenerative medicine, vision, neuroscience and clinical research.

The OHRI was also successful in a related CFI / CIHR competition designed specifically for clinical research. Our proposal, called Knowledge Translation (KT) Canada, was ranked #1 in the competition. It will provide \$12M for a national OHRI-led KT network, with funds to be shared among several hospitals.

Together, these two grants will support four main construction projects at our General Campus (see figure above) and more than 200 pieces of new equipment. High throughput screening systems will accelerate the development of new therapies and specialized laboratories will allow researchers to manufacture these therapies for early-stage clinical trials. Increased training and support will help researchers design clinical studies, get approval to test new drugs and develop partnerships to ensure that Canadians reap the health and economic benefits of research.

OHRI is thus embarking on a new era of health research. Our successes this year have created tremendous momentum and we hope that this report will inspire you to share in our excitement.

Dr. Duncan Stewart

CEO and Scientific Director, Ottawa Health Research Institute
Vice-President, Research, The Ottawa Hospital
Professor of Medicine, University of Ottawa

Jacquelin Holzman

Board Chair, Ottawa Health Research Institute

Research saving lives and provi

Making heart surgery safer

What is the best way to prevent bleeding during heart surgery? A clinical trial led by Dr. Dean Fergusson and Dr. Paul Hébert recently provided a surprising answer to this question. In the largest heart surgery trial ever conducted, they compared three routinely-used anti-bleeding drugs and found that the most popular drug, aprotinin, actually increased the rate of death. Although all three drugs had



A research study led by Dr. Dean Fergusson (left) and Dr. Paul Hébert (right) has changed heart surgery around the world and saved thousands of lives.

been tested in patients before, this was the first major study to compare them head-to-head. The results were published in the *New England Journal of Medicine* and they generated a great deal of attention because aprotinin was widely considered to be the most effective drug, and it was also much more expensive. The study has led to a world-wide change in standard heart surgery practice and has been touted as an example of the importance of independent, investigator-driven clinical research. It was funded by the Canadian Institutes of Health Research.

Promising new stem cell therapy

Dr. Duncan Stewart, a world-leader in stem cell research, has set his sights on developing a treatment for Acute Respiratory Distress Syndrome (ARDS), a major killer in the intensive care unit. The condition involves severe inflammation in the lungs and affects patients with many types of infection (including sepsis), as well as those with traumatic injuries. No effective treatment exists. Dr. Stewart and his team have developed a novel therapeutic approach involving bone marrow stem cells engineered to express a gene called angiopoietin 1. In a mouse model of ARDS, they found that this therapy was able to reduce inflammation in the lung and stimulate regeneration and repair

of damaged tissue. After further laboratory studies, they hope to test this promising therapy in patients. The study was published in *PLoS Medicine* and funded by NSERC, the Heart and Stroke Foundation of Canada and Northern Therapeutics, a company founded by Dr. Stewart.

Groundbreaking cancer trial

Cancer patients in Ottawa have access to the most advanced therapies available, thanks to clinical trials led by oncologists at The Ottawa Hospital Cancer Centre. One example involves cetuximab, a drug that blocks growth-promoting molecules on the surface of cancer cells. Ottawa oncologist Dr. Derek Jonker was the lead on a major international clinical trial of this drug in colorectal cancer patients. The results showed that patients who received the drug survived 23 per cent longer, with significant improvements in quality of life. Further research may help better predict which patients are most likely to respond, thus leading to even greater success rates. The study was funded by the National Cancer Institute of Canada, ImClone Systems and Bristol-Myers Squibb and published in the *New England Journal of Medicine*.

A new window into Parkinson's

A universal feature of Parkinson's disease is the presence of inclusions, or aggregates of a protein called alpha-synuclein in certain nerve cells in the brain. Dr. Michael Schlossmacher recently co-discovered a key molecular switch called GATA-2 that turns on the production of alpha-synuclein. The discovery opens a unique window into Parkinson's disease and provides a potential target for developing new therapies. Genetic evidence suggests that reducing alpha-synuclein levels by just 20 to 40 per cent could have a big impact on patients. The Schlossmacher team is now trying to define how the switch works and looking for molecules that may be able to adjust it. The discovery was published in *Proceedings of the National Academy of Sciences* and funded by the National Institutes of Health and the Michael J. Fox Foundation.

Balancing the risks of blood thinners

A world-first research study led by Dr. Marc Rodger has identified a simple rule that may allow hundreds of thousands of women to stop taking blood thinning pills such as warfarin. The study examined 646 people with unexplained blood clots in the legs, arms and lungs (called unprovoked venous thromboembolism). These clots affect up to 2.5 per cent of people in their lifetime and are a major cause of death. Once the initial blood clot is treated, warfarin is prescribed to reduce the risk of further clotting. Currently, many patients take warfarin for the rest of their lives, despite the fact that drug has serious side effects,

ding hope

Success stories from a remarkable year

such as increased risk of bleeding. Dr. Rodger's study is the first to identify a group of patients (women with four clinical characteristics) who had a very low risk of blood clot recurrence and therefore may be able to safely stop taking warfarin after six months. If the results are confirmed in further studies and this rule becomes widely used, it could help prevent many cases of major bleeding and death and also reduce the large health care costs associated with chronic warfarin therapy. The study was funded by the Canadian Institutes of Health Research and published in the *Canadian Medical Association Journal*.

Regenerating muscle

Dr. Michael Rudnicki has made exciting progress in understanding muscle stem cells and developing regenerative therapies for diseases such as muscular dystrophy. Over the last 15 years, several research groups around the world have attempted to treat muscular dystrophy through muscle stem cell transplantation, but the therapy hasn't worked well yet because the stem cells die quickly after transplant. Dr. Rudnicki's group recently showed that a modified type of stem cell that lacks the "MyoD" gene survives longer and gives rise to more muscle cells after transplantation in mice compared to unmodified cells. Further research is needed before a therapy will be ready for testing in people, but the results have generated great hope and excitement. The study was published in *Proceedings of the National Academy of Sciences* and funded by the Canadian Institutes of Health Research, the National Institutes of Health and the Muscular Dystrophy Association.

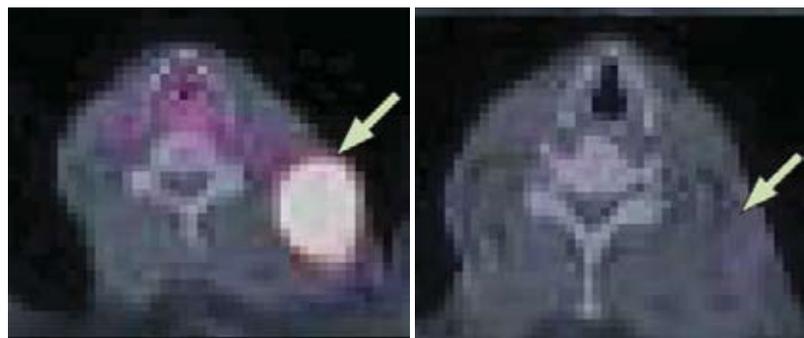
Reaching out to osteoporosis patients

While much of medical research focuses on developing and testing new treatments, an equally important area of research focuses on making sure that effective treatments are actually used. A perfect example is osteoporosis drugs to prevent fractures. These drugs have been proven highly effective, yet few women with fractures take them. To address the issue, Drs. Ann Cranney, Jeremy Grimshaw and Ian Graham designed a pamphlet and reminder letter targeted at both patients and family physicians and tested it in 270 women who had a recent wrist fracture. The patients who received pamphlets were three times more likely to receive recommended treatments. This study was funded by the Canadian Institutes of Health Research and published in the journal *Osteoporosis International*.

Fighting cancer with viruses

Ottawa is leading the development of "oncolytic" viruses that infect and destroy many types of cancer without the usual side effects associated with chemotherapy and ra-

diation. The oncolytic virus team includes Drs. John Bell and Harry Atkins from OHRI, as well as Dr. David Stojdl from CHEO. They recently formed a company with colleagues in the US (Jennerex Biotherapeutics) to help bring these viruses into the clinic more quickly. An early-stage international clinical trial in 14 terminal liver cancer patients generated attention around the world this year: 70 per cent of the patients responded to the virus and half survived for at least double their life expectancy, with



A liver tumour that metastasized to a patient's neck (bright spot, indicated by arrow in PET-CT scan) is destroyed after treatment with an oncolytic virus.

some still alive today. The study was published in *Lancet Oncology* and was selected first out of more than 1,000 submissions for presentation at the Society of Gene Therapy Annual Meeting. Clinical trials are expected to begin in Canada soon.

Preventing cardiovascular disease

Cardiovascular disease is the number one killer in Canada and high cholesterol is a major risk factor. Drs. Michel Chrétien, Ajoy Basak, Majambu Mbikay and Janice Mayne are doing pioneering research on a gene that may hold the key to lowering cholesterol. Called PCSK9, the gene is a member of a family of enzymes called proprotein convertases, which were co-discovered by Dr. Chrétien in the 1990s. Research has shown that many people have mutations in the PCSK9 gene, and depending on the mutation, these people may have either very low or very high cholesterol. The group has developed a number of small molecules and peptides that can inhibit the function of PCSK9 in cell culture. They may eventually be tested as new cholesterol lowering drugs in humans. This work was funded by the Canadian Institutes of Health Research and published in *FEBS Journal*, *BBRC* and *Lipids in Health and Disease*.

For full references, funding sources and researcher profiles see the online version of this report at www.ohri.ca/annualreport/0708.

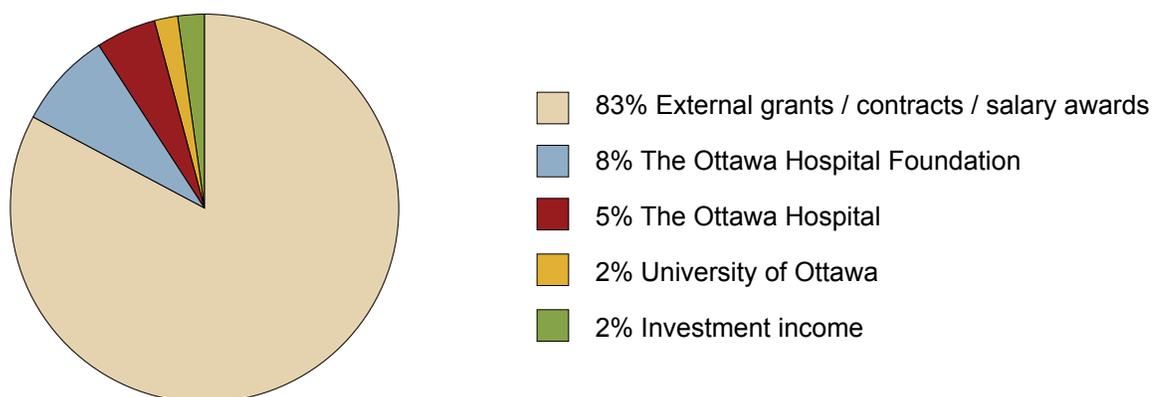
Board of Directors

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.

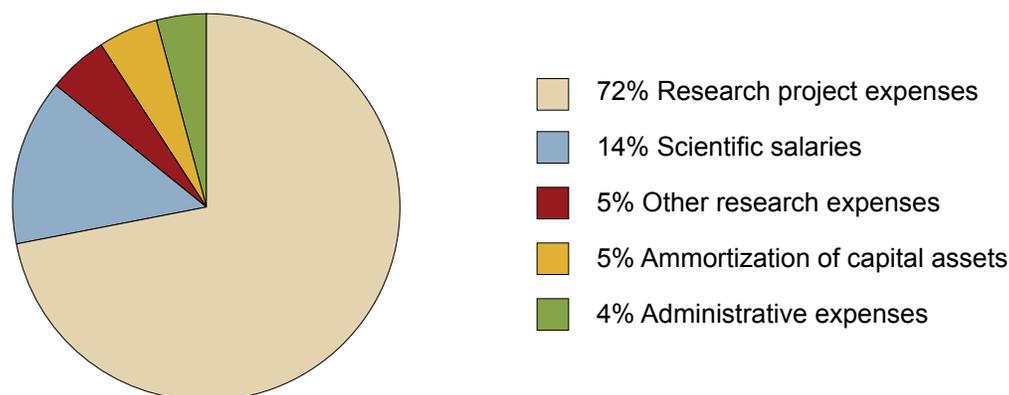
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Financial Summary*

Revenue distribution (\$92.2 M)



Expenditure distribution (\$92.8 M)



*For full financial statements see www.ohri.ca/annualreport/0708.