



# RISING TO THE CHALLENGE

## ANNUAL REPORT 04-05

Ottawa Health Research Institute

**OHRI**



**IRSO**

Institut de recherche en santé d'Ottawa

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## LEADERSHIP THROUGH PARTNERSHIP: WORKING TOGETHER TO SET US APART

### A MESSAGE FROM THE CHIEF EXECUTIVE OFFICER AND THE CHAIR OF THE BOARD OF DIRECTORS

The Ottawa Health Research Institute (OHRI) was established in 2001 as the research arm of The Ottawa Hospital, through the merger of the former research institutes at the Hospital's Civic and General campuses. In partnership with the Hospital and the University of Ottawa, the OHRI has grown rapidly to become one of Canada's largest and most important research institutes. With state-of-the-art research facilities and a workforce of almost 300 scientists and clinical investigators, the Institute also houses the work of more than 250 graduate students and research fellows, and over 500 support staff.

A key indicator of our success is our peer-reviewed grant funding, which rose from approximately \$9.4 million in 1996 to \$30 million at the time of the merger. It will reach nearly \$54 million during 2005-06.

Our scientists are at the leading edge of their fields and are making discoveries that lead to prevention, diagnosis or innovative therapy for a range of important diseases including cancer, diabetes, heart disease, kidney failure, vision loss, multiple sclerosis, stroke, Parkinson's disease and infectious diseases including AIDS. We also lead the way in translating medical knowledge into improved health care, including the development of clinical decision rules that will help both physicians and patients make important decisions based on the best available evidence.

Our ability to carry out research is made possible only through our partnerships with The Ottawa Hospital and the University of Ottawa. Many OHRI physician-scientists carry out clinical work in The Ottawa Hospital, and this immediate, day-to-day connection makes clinical trials of new therapies easier to plan and deliver. Other physicians team with scientists doing basic research, accelerating the discovery and development of therapies that may help millions of people.

Our partnership with the University of Ottawa is critical for training the next generation of researchers. All OHRI scientists have appointments at the University of Ottawa, either in the Faculty of Medicine or the Faculty of Health Sciences. This means that students can study with faculty members who are working in the most advanced areas of health research. In return, the OHRI gains access to the best and brightest of these students, who bring ideas, talent and energy to the research enterprise.

The Institute is governed by a board of directors that includes members from the hospital, the university and the community. Several board committees assist with financial management, government relations and the commercialization of results.

Financial support for the Institute comes from both the hospital and the university, as well as from the community through the Ottawa Hospital Foundation. In fact, the Foundation is in the middle of a \$100 million campaign, of which 40 percent is earmarked for OHRI research. Additional support comes from the community through the Ottawa Regional Cancer Foundation.



We would like to conclude by thanking our loyal and dedicated scientific and support staff as well as our trainees who have shown a determined commitment to the vision of the OHRI. We also wish to thank the patients of The Ottawa Hospital, who have so willingly joined forces with us to advance the frontiers of medical science.

**Ms. Jacquelin Holzman, Chair  
and Dr. Ronald Worton,  
Chief Executive Officer and  
Scientific Director**



## TESTIMONIAL: MAKING A DIFFERENCE, ONE LIFE AT A TIME

Multiple sclerosis (MS) is a disease that damages the central nervous system. Its symptoms vary from person to person, but can include excruciating fatigue, an inability to walk and slurred speech. It is believed to be a disorder of the immune system and there is no known cure.

But there may be new hope for MS sufferers in the therapy being used by physician scientists Dr. Mark Freedman, Director of the Multiple Sclerosis Research Unit, and Dr. Harry Atkins, a hematologist studying stem-cell therapies for autoimmune diseases. This innovative treatment uses chemotherapy to eliminate the patient's defective immune system, then restores it through a transplant of the patient's own stem cells.

Jennifer Molson of Ottawa knows at first hand what this therapy can achieve. First diagnosed with multiple sclerosis at age 21, she was facing severe disability only five years later.



“Until early 1996, I was healthy and active, but that May my left hand went numb and didn't get better. My family doctor referred me to a neurologist, and in July I was diagnosed with the relapsing-remitting form of MS. The doctors thought Dr. Freedman was the best person to look after me, so they transferred me to his clinic.

During the next five years I had multiple relapses and by February 2001, I had developed the secondary-progressive form of MS, which is very bad—sometimes I could barely stand up. Then Dr. Freedman told me about the stem cell transplant study. Although I knew the procedure carried a risk of death, I knew what my future would be like if I didn't do something, so I decided to go ahead with it.

Dr. Atkins was my doctor for the actual transplant therapy that I had in July 2002. It was probably another year and a half to two years before I really started to feel better. But now, in mid-2005, I think the past four to five months have been the best I've had since the summer of 2000. I'm driving again, I no longer need a cane to walk, I have more stamina and I've gone back to work part-time.

I know the therapy is intended to keep you from getting worse, but for me, it has actually reversed the course of the disease. Dr. Freedman and Dr. Atkins are my heroes and I would like to thank them and all the people who have made and continue to make this research possible. ”

**Jennifer Molson, Ottawa**



# NEW FRONTIERS: GROUND-BREAKING DISCOVERIES HERE AT HOME

## Antidepressants and suicide attempts

A group of OHRI investigators, led by Dr. Dean Fergusson, OHRI Scientist and Associate Professor in the University of Ottawa's Faculty of Medicine, has found that a particular class of antidepressants contributes to a significantly increased risk of suicide attempts.

The group based its study on an exhaustive review of published, randomized, controlled trials of selective serotonin reuptake inhibitors (SSRIs). The study noted a more than twofold increase in the likelihood of suicide attempts for patients receiving SSRIs, compared with placebo or therapeutic interventions other than tricyclic antidepressants, another class of drugs.

Although small, the incremental risk remains a very important population issue because of the widespread use of SSRIs. While other studies have suggested a possible link, this review identifies a very real correlation and is the most elaborate and comprehensive research to date.

## Gene research into mental retardation

About 10 years ago, Dr. David Picketts discovered a gene that was altered in patients with a severe form of mental retardation. The research, conducted while Dr. Picketts was a research fellow at Oxford University, was hailed as one of the most important discoveries in mental retardation. The natural question at the time was "What is the next step?"

Fast forward to today. Dr. Picketts, now a Senior Scientist at the OHRI and an Associate Professor at the University of Ottawa, has successfully taken the research to the next stage by developing a strain of mice with a genetic alteration in the same gene that causes the human disease. This opens the way to a better understanding of how mutations cause mental retardation. It also provides animals for testing new therapeutic approaches.

## Muscular dystrophy puzzle solved

About 20 years ago, neurologists discovered that glucocorticoids, traditionally used to treat inflammations, had beneficial effects on children suffering from muscular dystrophy. Glucocorticoids continue to be the only effective treatment against this incurable condition, yet no one knew until recently how or why the drugs work, thereby diminishing the likelihood of improving their effectiveness.

That mystery has now been solved. OHRI Senior Scientist Dr. Lynn Megeny and Dr. Bernard Jasmin, a Professor and Chair of the Department of Cellular and Molecular Medicine at the University of Ottawa, have discovered that glucocorticoid treatment alleviates the symptoms of muscular dystrophy by countering the devastating effects of a specific biochemical pathway in muscle fibres. By finally understanding why and how the drugs work, Drs. Megeny and Jasmin now hope to improve the treatment by developing other drugs that target this pathway and reduce or avoid some of the negative side effects.

## Stem cells and muscle regeneration

Stem cells are found in many tissues of the body. In bone marrow, for example, stem cells provide a steady stream of specialized red and white blood cells to replace those that have completed their jobs and have been removed from the bloodstream. In muscle, they repair or regenerate muscle fibres damaged by trauma or disease.

The potential to harness transplanted stem cells to enhance tissue repair and regeneration for a vast array of diseases is just beginning to be realized.

Our progress depends greatly on our ability to control the development of these cells. Discovering the molecules that control stem-cell behaviour is a central theme of the OHRI's new Centre for Stem Cell and Gene Therapy, led by OHRI Senior Scientist and University of Ottawa Professor Dr. Michael Rudnicki.

About two years ago, Dr. Rudnicki and his team showed that mice lacking a molecule called Pax7 were unable to make muscle,

Dr. Ronald Worton, OHRI CEO, has expressed considerable excitement over this discovery. His research team discovered the defective gene in children with Duchenne muscular dystrophy 20 years ago and he has spearheaded the creation of the OHRI's Stem Cell Centre in anticipation of the day when stem cells will be used to regenerate muscle in affected children.

demonstrating that Pax7 was necessary for repairing muscle tissue. Now the team has shown that introducing Pax7 into stem cells that do not normally make muscle forces those cells to do exactly that.

In simple terms, Dr. Rudnicki and his team have discovered how to control the process by which stem cells develop new muscle. This inspires tremendous hope for the fight against diseases such as muscular dystrophy, in which the muscle undergoes significant degeneration as a result of a defective gene.





## START HERE A TRAINING GROUND FOR FUTURE ACHIEVEMENT:

# OUR FUTURE IN THEIR HANDS

With 171 graduate students, 82 postdoctoral fellows and 30 honour, undergraduate and high-school students, the OHRI is developing into one of the most advanced hospital-based research and teaching institutes in Canada. Such an environment not only provides fertile ground for innovative research, but it also attracts some of the best students.

“We truly appreciate the contributions that excellent students and post-doctoral fellows make in our labs,” says Dr. Jay Baltz, Senior Scientist and Associate Director responsible for training at the OHRI. “Trainees bring a high level of intellectual curiosity, creative thinking and youthful energy to a research group and are, therefore, a vital component of research at the OHRI. Recognizing their value to the organization, the OHRI has committed to providing the best possible research environment to enhance the learning experience. Our goal is to produce graduates who can compete with the top students from the best universities in the world. I think we are succeeding.”

Dr. Patrick Seale agrees. A doctoral student in the OHRI's Molecular Medicine Program from 1998 to 2004 and now a postdoctoral fellow at Harvard University, Dr. Seale's observations about the OHRI illuminate the excellence of the Institute's training:

“All the resources of the OHRI were important for me as a student, but I'd especially single out its enormous technical resources—the equipment is phenomenal and you have everything you need on site. That makes doing experiments a lot more convenient and much more fruitful.

Moreover, the research being done at the OHRI is world class, the equal of work being carried out anywhere. It's being presented at international meetings and is being published in peer-reviewed journals of the highest quality.

There's also the atmosphere. The collaborations at the OHRI are very good and the atmosphere within the Molecular Medicine Program, where I was working, was very collegial. There was extensive interaction with other research groups and everything was very open in terms of discussing and sharing our research.

So I think I can safely say that my aspiration to pursue an academic science career was fostered and encouraged by my experience at the OHRI and by its senior scientists. I feel that having the freedom to pursue the research that interests one is crucially important and working at an academic institute such as the OHRI has certainly reinforced my convictions in that regard.”

**Dr. Patrick Seale, Harvard University**



# HONOURING SUCCESS: RECOGNIZING OUR VERY BEST

## AWARDS AND RECOGNITIONS

OHRI scientists, investigators and management have won numerous awards and recognitions for the quality and importance of their work. The examples below are just a few of many.

- **DR. SHAWN AARON**  
*Premier's Research Excellence Award, 2004; University of Ottawa Faculty of Medicine's Young Professor Award, 2003*
- **DR. ROGER BROUGHTON**  
*J. David Grimes Career Achievement Award, 2004*
- **DR. DENNIS BULMAN**  
*Robert H. Haynes Young Scientist Award, Genetics Society of Canada, 2004*
- **DR. MICHEL CHRÉTIEN**  
*2004 Chevalier de l'Ordre de la Légion d'honneur de la République de France, for collaboration between French and Canadian scientists.*
- **DR. ANTOINE HAKIM**  
*Ottawa Life Sciences Council Career Achievement Award, 2004*
- **MR. ROBERT HANLON, OHRI CHIEF OPERATING OFFICER**  
*Ottawa Life Sciences Council Entrepreneur of the Year, 2004*
- **DR. DAVID PARK**  
*University of Ottawa Young Researcher Award, 2003*
- **DR. IAN STIELL**  
*Order of the International Federation for Emergency Medicine, 2004*
- **DR. PHILIP WELLS**  
*OHRI Researcher of the Year Award, 2004*
- **DR. RONALD WORTON, OHRI CHIEF EXECUTIVE OFFICER**  
*Honorary Fellow of the Royal College of Physicians and Surgeons of Canada, 2004*

## CANADA RESEARCH CHAIRS

In 2000, the Government of Canada allocated \$900 million to establish 2,000 research professorships—Canada Research Chairs—in universities across the country.

Chair holders advance the frontiers of knowledge in their fields, not only through their own work, but also by teaching and supervising students and by coordinating the work of other researchers.

### Tier One

- **DR. JEREMY M. GRIMSHAW**  
Health Knowledge Transfer and Uptake
- **DR. ANNETTE O'CONNOR**  
Health Care Consumer Decision Support
- **DR. MICHAEL RUDNICKI**  
Molecular Genetics
- **DR. RHIAN TOUYZ**  
Hypertension

### Tier Two

- **DR. MIGUEL ANDRADE**  
Bioinformatics
- **DR. MARJORIE BRAND**  
Regulation of Gene Expression



- **DR. JEFFREY DILWORTH**  
Epigenetic Regulation of Transcription
- **DR. ALAN MEARS**  
Genetics of the Eye
- **DR. KAVEH SHOJANIA**  
Patient Safety
- **DR. PHILIP S. WELLS**  
Thrombosis

### Endowed Chairs

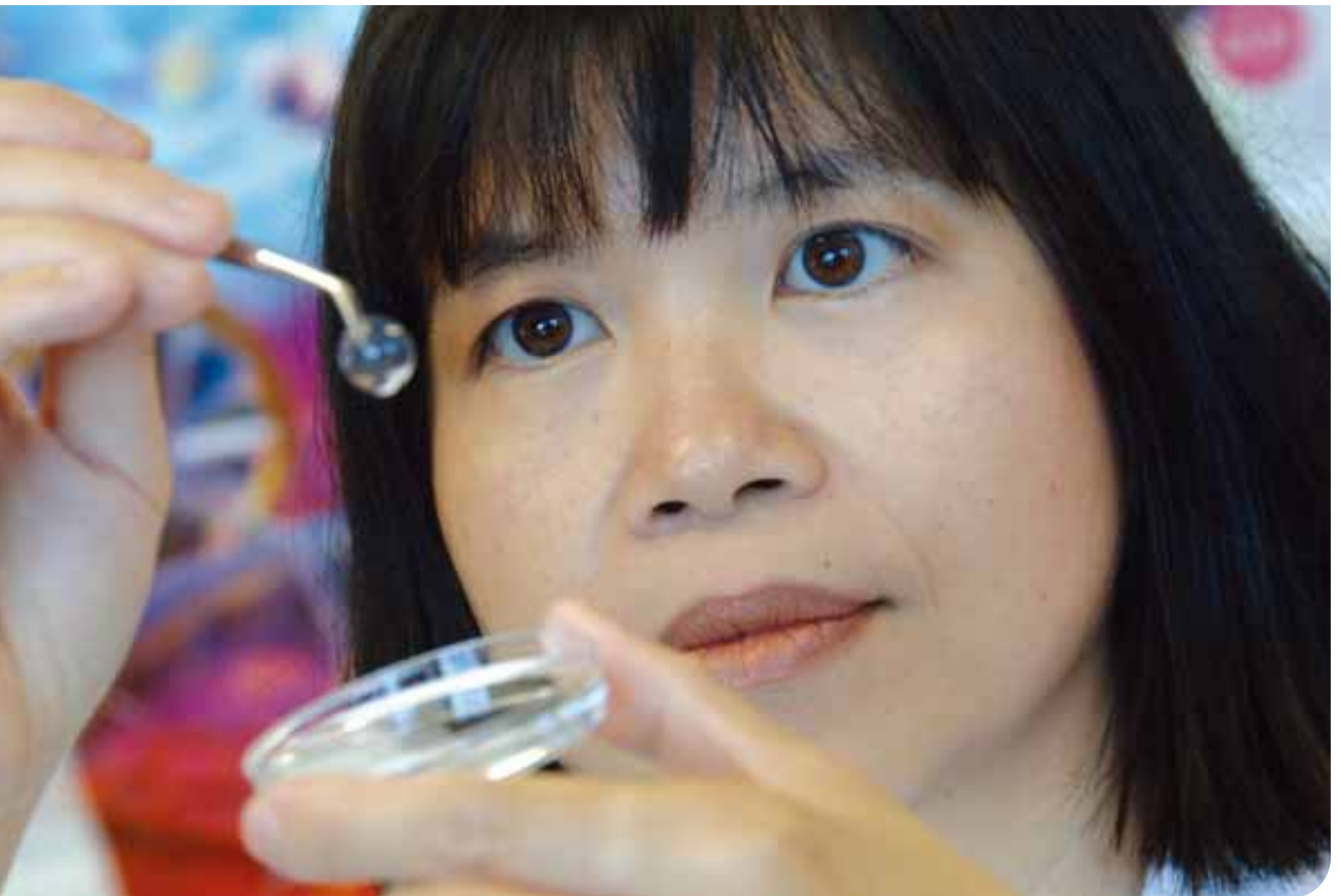
- **DR. REJEAN MUNGER**  
The Clifford, Gladys and Lorna J. Wood Chair for Vision Research
- **DR. CATHY TSILFIDIS**  
The Donald and Joy Maclaren Chair for Vision Research
- **DR. LEO RENAUD**  
The David Grimes Research Chair in Neuroscience
- **DR. RONALD WORTON**  
The Evelyne and Rowell Laishley Chair

# SHARING VICTORIES: WORKING TOGETHER IS LEADERSHIP AT ITS FINEST

Canadian researchers are extremely willing to both share their findings with each other and work with colleagues around the world to advance medical knowledge. The OHRI, as many of its research projects demonstrate, is a leader in this open, collegial environment.

In early 2004, for example, OHRI researchers began a collaboration with two Canadian pharmaceutical companies to carry out the first Canadian-led clinical trial of an HIV vaccine. The vaccine, which comprises components provided by the companies involved, may allow HIV sufferers to reduce their intake of the toxic drugs that cause damaging side effects. Led by the OHRI's Dr. Jonathan Angel, an infectious disease specialist studying immune-based therapies, the trial involves 20 Ottawa patients as part of an international study that groups together 40 other such clinical trials.

In a broader context, the OHRI participated in an internationally attended meeting hosted by the Canadian Institutes of Health Research in October 2004. The result of the meeting was *The Ottawa Statement*, published in the *British Medical Journal* in early 2005. This statement establishes the principles of registering clinical trials so clinicians, researchers, patients and the public will have access to information about such trials and their results.





Also on the international front, several OHRI scientists and investigators are involved in research projects that span institutions around the globe:

- Dr. Ben Tsang is working in a number of collaborations with institutes in Asia on studies of reproductive technologies.
- Dr. Mark Walker and Dr. Shi-Wu Wen are both involved in obstetrics and maternity studies with researchers in China.
- Dr. Michael Rudnicki is heading the International Regulome Consortium. In collaboration with France, the United Kingdom, Singapore, Australia and the Netherlands, this impressive team of scientists is working to identify the proteins that regulate gene expression and their role in both normal and diseased tissue.
- Dr. Philip Wells and Dr. Marc Rodger are working with a number of other countries in a series of collaborations. Dr. Rodger is leading a study to determine the role that low-molecular-weight heparin

plays in preventing complications in pregnancy. Another collaborative endeavour is aimed at developing a tool to predict patients at risk of developing recurrent venous thromboembolism.

As well as being deeply involved in these collaborations, OHRI scientists are providing the leadership for two Networks of Centres of Excellence. The Stem Cell Network, previously led by OHRI Chief Executive Officer Dr. Ronald Worton, is now directed by OHRI Senior Scientist Dr. Michael Rudnicki. Senior Scientist Dr. Antoine Hakim is at the helm of the Canadian Stroke Network.

It is through such far-flung partnerships that OHRI scientists gain access to leading-edge medical research being done abroad and are able to share their own findings with their peers around the globe. Such openness contributes enormously to the development of new clinical applications that will help people who are ill.





## **BENCH TO BEDSIDE AND BACK**

# **REAL-WORLD RESULTS**

The OHRI's research focuses on the understanding, prevention, diagnosis and treatment of disease. One goal is to develop and test new therapies for patient care. Because OHRI scientists work in a combined clinical and research environment, they have unique opportunities for observing patients' responses to treatment and for using this information to further refine their therapies. As a result, the benefits of research can be applied more quickly and patient care is further improved.



## Keeping new mothers healthy

Among the research teams at the OHRI is the nationally recognized Obstetrics and Maternal Newborn Investigations (OMNI) group. This group is led by Dr. Mark Walker, a Scientist in the Clinical Epidemiology Program, an Assistant Professor of Obstetrics and Gynecology at the University of Ottawa and a physician in the Division of Maternal-Fetal Medicine at The Ottawa Hospital. OMNI specializes in perinatal epidemiology, the study of disease in babies and their mothers from just before birth until just afterward.

One important OMNI study reveals that mothers who are carrying twins or triplets are four times more likely to have heart attacks than mothers carrying single babies. Such mothers are also at greater risk of suffering from high blood pressure or from blood clots in the legs or lungs. This new knowledge will help improve the prenatal and post-natal care of mothers who are expecting multiple births.

## Improving children's health through prenatal research

In the same area of research but on a much larger scale, Dr. Walker has begun a long-term study of pregnancy involving 8,000 mothers and babies. Projected to last for decades, the research will investigate how the conditions of a baby's prenatal development affect the health of the child and the adult he or she becomes. The OHRI scientists conducting the study expect that its results will help them understand a wide range of problems such as complications in pregnancy, childhood obesity, developmental delays and, ultimately, diseases of adolescence and adulthood.

## Helping people breathe

The negative health effects of obesity are numerous and well known. What hasn't been so obvious, however, is the impact of excess weight on breathing.

Through a study of 58 obese women, an OHRI team led by Dr. Shawn Aaron, who is also an Associate Professor in the University of Ottawa's Faculty of Medicine, has cast considerable light on this problem and its implications.

The patients, of whom 41 percent were thought to suffer from asthma, were put on a strict weight-loss program and lost an average of 44 pounds each. This brought about a sharp improvement in their breathing and their capacity for exercise. As a result, the researchers are pursuing the study to find out whether obesity may sometimes cause a misdiagnosis of asthma when the disease is not, in fact, present—a critical concern since an accurate diagnosis is essential to choosing the best therapy for the patient.

## Treating cancer with viral infections

In May 2004, the Terry Fox Foundation awarded \$2 million to the OHRI to support research into how viruses might be used to fight cancer. The research team is headed by Dr. John Bell, and the funding supports a major collaborative research effort with other scientists who are carrying out similar work elsewhere in Canada.



The viruses under investigation, called oncolytic viruses, have a unique ability: they infect tumour cells and kill them. The OHRI team is working with a particular type of oncolytic virus that, in one study, eliminated late-stage lung cancer in 100 percent of the animals treated with the virus. In the test tube, the virus is effective against 75 to 80 percent of the cancers tested—an important factor, since there are so many different types of cancer.

Better yet, oncolytic viruses affect only tumours, leaving normal, healthy tissue untouched. This means that virus-based cancer therapies might be much less unpleasant and dangerous for the patient than current radiation and chemotherapy treatments. Human trials of the virus therapy have not yet begun, but Dr. Bell expects that they are not far off.

## Improving survival after cardiac arrest

If a person suffers a cardiac arrest outside a hospital—which happens to more than 25,000 Canadians every year—the chances of survival are much greater if there's a bystander who knows how to perform cardiopulmonary resuscitation, or CPR.

This is the conclusion of a 10-year study carried out by a team under the leadership of Dr. Ian Stiell, OHRI Senior Scientist and Acting Chair of Emergency Medicine at the University of Ottawa. The key finding of the study, which used data from 17 Ontario cities, shows that the chance of survival is 3.7 times greater if the victim gets immediate CPR from a bystander. This emphasizes the need for increased government initiatives that will train many more Canadians in CPR, especially in families where genetic or environmental factors increase the risk of a cardiac arrest.





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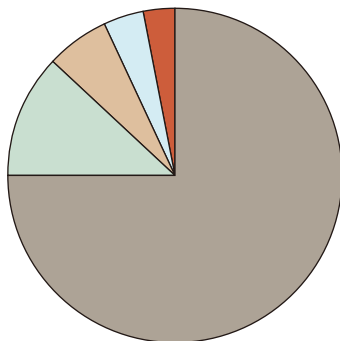
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## 2004–2005 FINANCIAL STATEMENTS

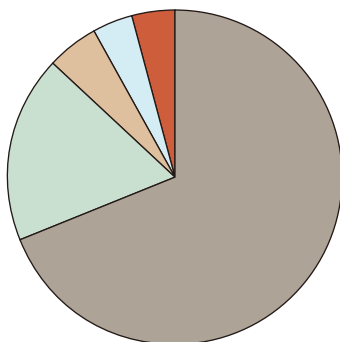
### Revenue Distribution



Total revenue: \$65.8 million

- 75% External grants/contracts/salary awards
- 12% The Ottawa Hospital Foundation
- 6% The Ottawa Hospital
- 4% University of Ottawa
- 3% Investment income

### Expenditure Distribution



Total expenditures: \$65.9 million

- 69% Research project expenses
- 18% Scientific salaries
- 5% Other research expenses
- 4% Amortization of capital assets
- 4% Administrative expenses

For more information, please visit our website at [www.ohri.ca](http://www.ohri.ca)