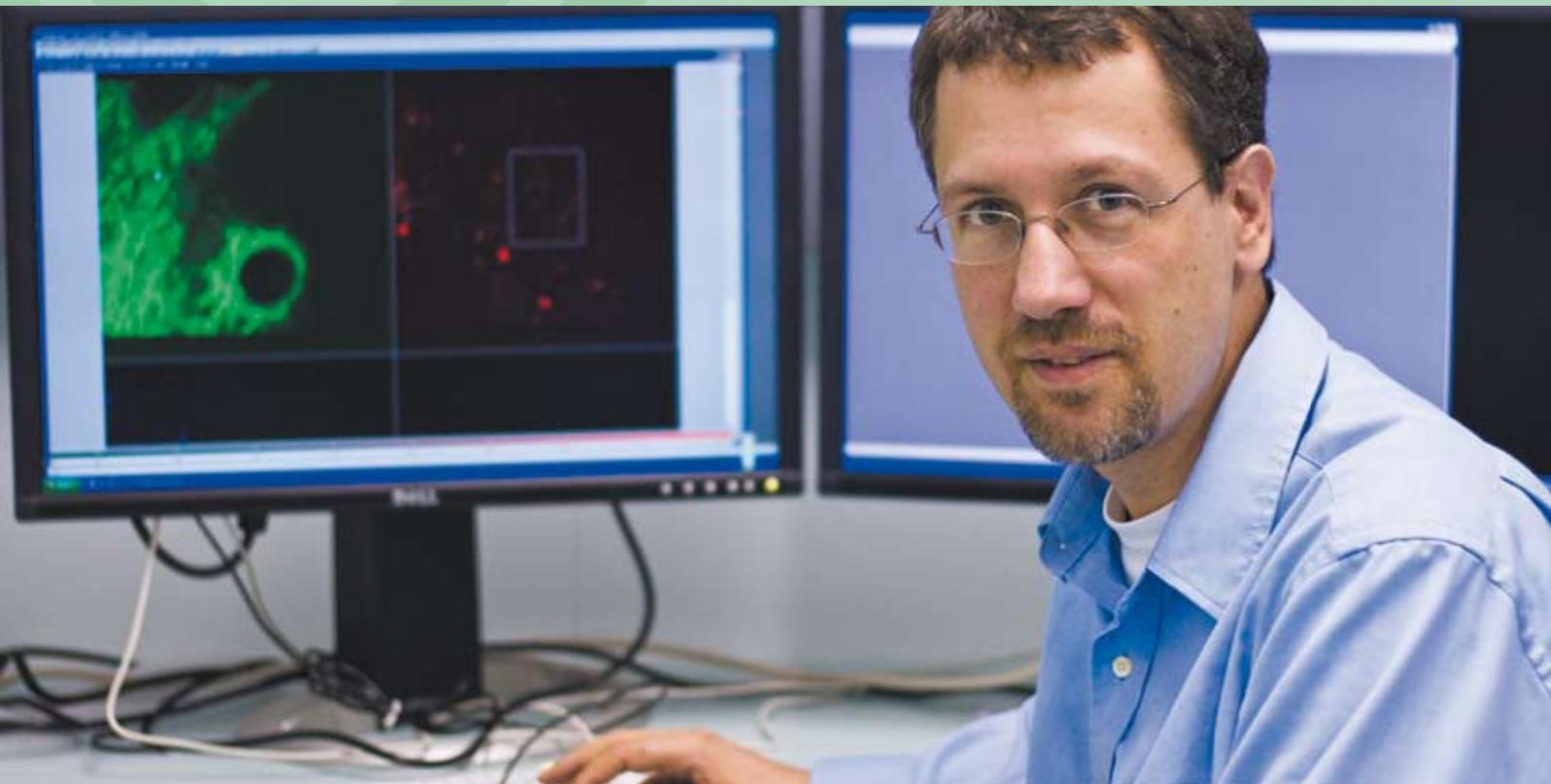


LuminesCent



Professor Wolfgang Weninger.

Note from the Editor

Happy New Year and welcome to the first edition of *LuminesCent* for 2009.

Late 2008 was a flurry of activity at the Centenary Institute, with several prominent scientific publications. You can read about two of these recent discoveries by Professor Wolfgang Weninger (p1) and Professor John Rasko (p6) in this edition.

The researcher profile on page 4 features Dr Ammira Hadi Al-Shabeeb and outlines her journey from university in war-torn Iraq to Centenary Research Officer. A fascinating journey.

A special Thank You Day event held in November was a huge success – thanks to you, our generous supporters who sent in messages (p2).

After a short break for the holiday season, Centenary scientists have been back in the laboratories, gearing up for a productive year. I look forward to sharing the news from the Institute with you throughout 2009.

Erin Sharp, Editor

Scientists film inner workings of the immune system

Forget what's number one at the box office. The most exciting new film features the intricate workings of the body, filmed by Centenary scientists using ground-breaking technology.

For the first time in Australia, we have filmed an immune cell becoming infected by a parasite and followed the infection as it begins to spread throughout the body.

Professor Wolfgang Weninger, head of the Immune Imaging program, says the discovery (published in *PLoS Pathogens*) was made possible using high powered multi-photon microscopy which allows living cells to be viewed and filmed in real time – something that was impossible until recently.

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Scientists film inner workings of the immune system continued

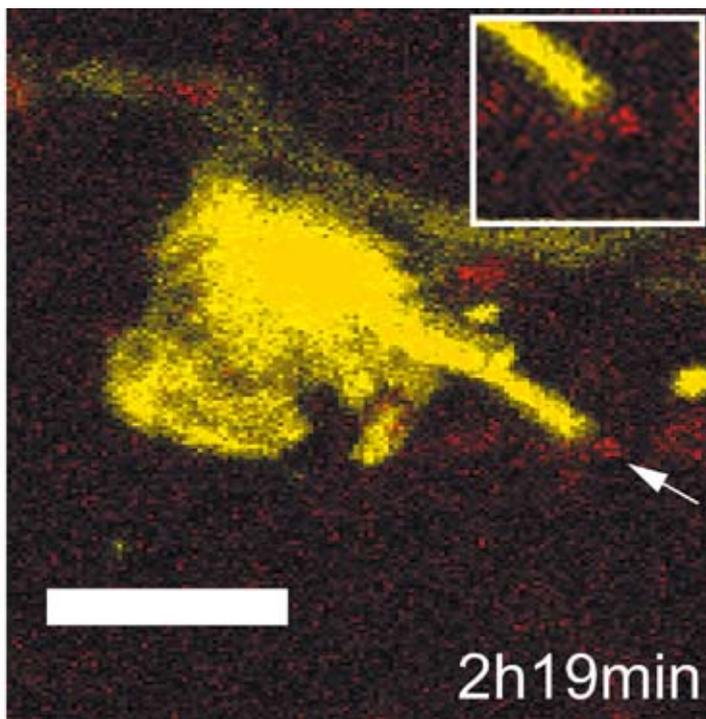
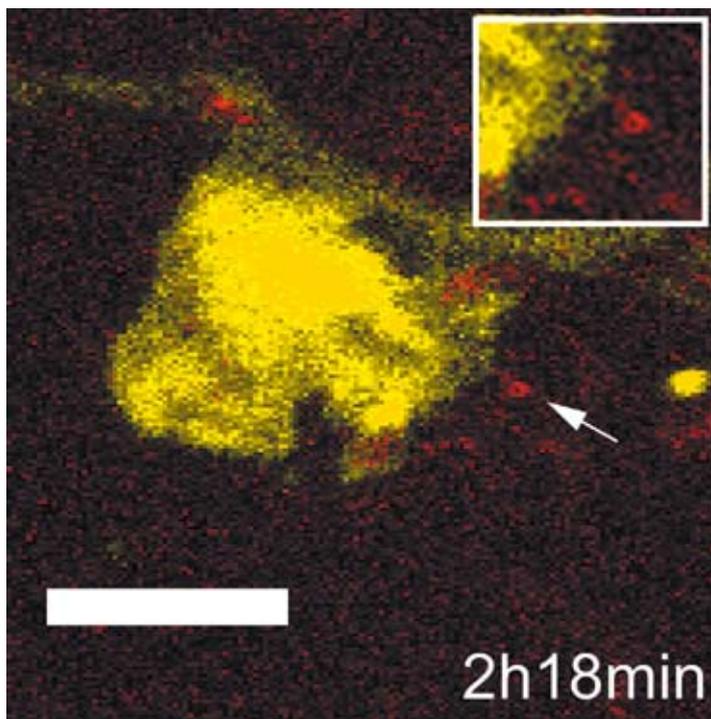
"Using multi-photon microscopy, we studied dendritic cells in the skin. Under normal conditions we found the cells in the epidermis (top layer) were static, whereas in the dermis (second layer) they were very active, moving around as though seeking out pathogens," explains Professor Weninger. "Once we established this, it was fascinating to introduce the Leishmania infection and watch as the parasite was picked up by the cells and the process by which it began to spread throughout the body."

Leishmaniasis (pronounced leash-ma-nigh-a-sis) affects up to 12 million people in parts of Africa, the Middle East and South America. The disease causes skin sores and can affect internal organs such as the spleen, liver and bone marrow. If left untreated, it can be fatal.

The ability to visually follow a pathogen on its journey through the immune cells provides critical insight for future vaccine design.

"We now have a general idea of how pathogens are recognised by the immune system and which cells are involved," Professor Weninger says. "This means we can look at identifying the molecules responsible for the uptake of Leishmania infection and these molecules could become vaccine targets. Additionally, we can investigate the immune responses of other infections which could lead to better vaccines."

"On the other side of the story, scientists can now visualise the pathway of current vaccines in the immune system, providing greater understanding and the potential for refining current interventions against disease."



Dendritic cells (yellow) are infected by the Leishmania infection (red) as it starts to spread throughout the body.

Centenary supporters say thanks!



Signal Transduction Research Assistant, Dominik Kaczorowski, and Vascular Biology PhD student, Jennifer Young, read the inspirational messages from Centenary supporters.

In November, the Centenary Institute celebrated Thank You Day – an opportunity to acknowledge dedicated medical researchers for their commitment to life-saving research.

Executive Director Professor Mathew Vadas unveiled hundreds of thank you notes to Centenary scientists written by you, our supporters, at a special afternoon tea attended by all staff.

"The cards are a wonderful example of why we do what we do," Professor Vadas told the Centenary team. "While you work long and hard at

the laboratory bench, it is important to remember that the work you are doing is immensely valued by the community and will go a long way to helping all Australians live longer, healthier lives."

The well-wishes from the community were much appreciated by the Centenary researchers.

"We are all really blown away by the level of support these cards represent. It means a great deal and will help motivate us as we pursue projects that may take a life's work to complete," said PhD student Jennifer Young from the Vascular Biology laboratory.

Deciphering the body's healing secrets



Healthy blood vessels play a key role in the prevention and treatment of diseases such as cardiovascular disease and diabetes.

Endothelial cells line the blood vessels and are critical to the regulation of blood vessel growth and function.

Researchers at the Centenary Institute have discovered a mechanism that helps control the development of endothelial cells.

Professor Jenny Gamble, Head of the Vascular Biology program at Centenary, says the process by which endothelial progenitor cells (EPCs) change to mature endothelial cells is an important but little understood control.

"If endothelial cell lining is injured or damaged, for example during wound healing, an organ transplant or heart attack, the EPC leave the bone marrow, circulate in the blood and home to the site of the injury where they continue to repair and are induced to become mature cells," she explains.

Publishing in the journal *Blood*, Professor Gamble and her team found that this process, called differentiation, is partly controlled by the enzyme sphingosine kinase-1.

"We found that high levels of SK-1 keep the cells as EPCs whereas a decrease in the amount of SK-1 allows the cell to differentiate to functionally mature endothelial cells."

By understanding these fundamental tools the body uses to heal itself, there is potential to manipulate this process to create new treatments.

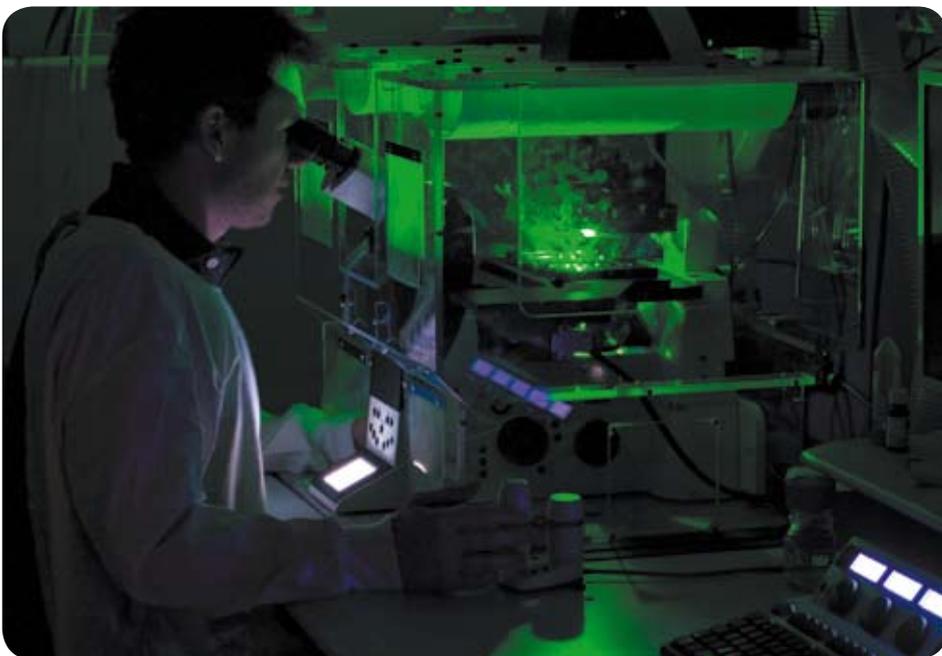
For example, the vascular complications of diabetes are attributed, in part, to the decreased numbers and function of EPCs.

Additionally, stents are used extensively for the treatment of cardiovascular disease. However they can often be problematic because of a lack of good endothelial cell coverage.

Increased understanding of the process of differentiation may allow SK-1 to be manipulated to drive this process and therefore improve treatments of these diseases in the future.

Centenary scientists rewarded for their dedication to cutting-edge research

Centenary Institute researchers performed extremely well in recent funding announcements, being awarded \$9 million for research projects dedicated to cancer, cardiovascular and infectious diseases.



"The Centenary Institute is committed to ground-breaking research to help all Australians live longer, healthier lives. But without funding we would not be able to pursue our research agenda," said Centenary's Executive Director, Professor Mathew Vadas.

"The quality of Centenary's research programs is highlighted by the outstanding 50% strike rate for funding from the National Health and Medical Research Council announced in late 2008. This is almost double the national average of 26%."

Centenary researchers were also successful in gaining funding from the Australian Research Council, Clive and Vera Ramaciotti Foundation, RT Hall Trust, Sylvia and Charles Viertel Foundation, Cancer Institute NSW, Cancer Council, GlaxoSmithKline Australia, Heart Foundation, Rebecca L Cooper Foundation, University of Sydney and the Alcohol and Health Research Grant Scheme.

"With funding awarded on a peer-reviewed basis, I believe the high level of funding confirms we are heading in the right direction at the Centenary," Professor Vadas added. "It is very encouraging that Centenary Institute researchers and their projects are held in such high esteem among the broader scientific community."

Researcher Profile

One of the personal qualities essential for a successful research scientist is persistence. Dr Ammira Hadi Al-Shabeeb has demonstrated it in abundance.

Ammira started her PhD in cancer research (brain tumours) at the Al-Nahrain University in Baghdad, Iraq in 2000. She was collecting her samples and starting genetic analysis when war broke out in 2003.

Explosions and gun fire were a constant part of her life in Baghdad, but when describing the time Ammira focuses on the impact on her research:

"It was quite a stressful time," she explains. "I was very worried about my research – the university had shut down. There was no electricity – so no fridges or freezers for my samples. It was dangerous to go outside, but I really wanted to continue my work so I moved my samples from the university to the hospital where they had a generator."

Once the university re-opened many of the staff were too scared to return to work. But Ammira went back, even taking a small generator from her home to the lab, determined to finish her research. And finish she did. Ammira was awarded her PhD in 2005 with the highest mark in her year.

Where to after you were awarded your PhD?

I was working in the Pathology Department in the Faculty of Medicine and felt I had the ability to continue my research outside of Iraq. I started applying for positions and was offered three – one in Jordan, one in Munich and one in Sydney. The position in Munich was a good one, but I had always dreamt of coming to Australia.

So I accepted the position at Sydney University and Westmead Hospital. Then I had to find funding. The Islamic Development Bank in Saudi Arabia offer scholarships to Muslim students all around the world and I was very lucky to receive one of these. I was the only female in my year to get a scholarship!

Then I had to apply for my Australian visa... I couldn't apply in Baghdad as the only



consulates are in the Green Zone where Iraqis cannot go. So I travelled to Jordan to submit my application. I then had a long six-month wait to hear. The day they called and said my visa had been issued, I was jumping up and down, I was so excited.

So you took up your position at Sydney Uni and Westmead Hospital. How did you come to work at Centenary?

While working at Westmead, I had been travelling in each week to attend the science seminar series at Centenary and thought it would be a great place to work. When I saw the position advertised for the Cancer Drug Resistance program, I decided to apply – and was so happy to be accepted.

What is your area of work at Centenary?

I am working on drug resistance in multiple myeloma – a particularly nasty blood cancer. The lab recently discovered a particular molecular marker that can predict response or non-response of multiple myeloma patients to a new drug, a proteasome inhibitor called Velcade. We are now investigating if similar markers

can predict treatment response in other proteasome inhibitors. By understanding these mechanisms, it may allow for the development of better, more targeted treatments for cancer patients.

Why did you choose a career in medical research?

I love a challenge! I have never taken the easy path and have always pushed myself further. Research is very challenging but I find it very rewarding, especially the prospect of helping to improve the health of people around the world.

And finally, who has had the biggest influence on your career to date?

My mother. It is quite hard to do everything I have done, especially as a woman in Iraq. My mother has always supported me and is so proud of me. She never told me not to follow my dreams, even though she knew they would take me out of Baghdad. She wanted me to be successful. From a career perspective, my supervisors throughout my studies and research have been instrumental in getting me to where I am today. Their support and encouragement has been very important.

LAUNCHING THE CENTENARY INSTITUTE FOUNDATION

The Centenary Foundation was launched at Government House on 28 October. Deputy Prime Minister, The Hon Julia Gillard MP was guest of honour. Ms Gillard spoke movingly about the vital role medical research plays in ensuring the health of Australians and encouraged those present to support the Centenary Institute.



Foundation Chairman, Neil Lawrence, Centenary Institute Executive Director Professor Mathew Vadas, Deputy Prime Minister, The Hon Julia Gillard MP, and Centenary Chairman, The Hon Michael Egan launch the Foundation.

The Centenary Institute is in an exciting growth phase, having grown to 170 staff in the past year. The Foundation, chaired by Neil Lawrence, Executive Creative Director of the STW Group, aims to support this growth by securing funds and pro bono assistance from philanthropic and corporate sources.

There are three ways you can become involved:

1. Become a Friend of the Foundation

As a Friend of the Foundation, you will be helping our researchers find new diagnostics, treatments and cures for the diseases that impact us most – cancer, cardiovascular and infectious diseases.

In return, we will dedicate a Seat of Knowledge in our lecture theatre with an inscription of your choice and you will be invited to exclusive events with noted scientists from Australia and around the world.

Foundation membership is offered for donations of \$1,000 or more.

2. Help establish the Foundation Fellowship

The Fellowship will fund one scientist for up to five years post PhD, working in either cancer, cardiovascular or infectious disease research at Centenary Institute. This prestigious Fellowship is designed to attract brilliant young scientists back from overseas or interstate.

Funds needed: \$125,000 per year for five years.

3. Contact Sally Castle at the Centenary Institute on 1800 677 977 with your fundraising ideas.



Professor Barbara Fazekas de St Groth (right) explains her immune system research to guests at the launch.



Dr Bernadette Saunders (right), from the Centenary Institute's tuberculosis research program, mingles with guests.



CENTENARY WELCOMES

The Centenary Institute is pleased to welcome Joseph Carrozzi to the Board of Governors. Mr Carrozzi is a National Managing Partner at leading accounting firm PricewaterhouseCoopers. He is responsible for managing the firm's relationships with some of the largest organisations in Australia, both ASX100 listed companies and also a number of major multi-nationals operating in Australia. On a personal level, Mr Carrozzi is married with three teenage children.

Kidney function discovery sheds light on genetic complexity of disease

Centenary Institute researchers have demonstrated that in order to find a cure for cancer, haemophilia and other diseases, researchers need to be looking for complex, interacting genetic factors.

The study, published in the *Journal of Clinical Investigation*, has exposed a greater level of genetic complexity for diseases than was originally thought.

The researchers looked at two disorders of kidney function – iminoglycinuria and hyperglycinuria. These disorders, first described 50 years ago, are conditions where large amounts of individual amino acids (the building blocks of proteins in our body) are wasted by the kidney.

Professor Rasko, Head of Centenary's Gene and Stem Cell Therapy program said they have now unravelled the genetic explanation by showing that not one,

but up to four different pumps present in the kidney determine whether or not this particular abnormality occurs.

Professor Rasko explains: "From the point of view of understanding complex diseases in humans, it suggests we need to integrate much greater levels of complex genetic information to reach a clear understanding."

Professor Rasko says these findings provide a foundation to improve our understanding of common human diseases, and greater potential to develop effective gene therapies to reduce the impact of diseases on patients.

"Gene therapies, whereby cells can be modified and then re-introduced into the body without the genetic mutations that cause illness, provide enormous potential to help cure diseases including haemophilia, cancer and cardiovascular disease," Professor Rasko explains.

"A crucial ingredient of successfully developing gene therapies is a thorough understanding of all the genetic factors at play in disease. This discovery takes us one step closer to understanding the complex factors at work in these serious diseases."



Professor John Rasko, Cynthia Ng, Jessica Vanslambrouk and Dr Charles Bailey have discovered complex, interacting factors at play in genetic disease.

Young Winemaker of the Year Awards

On November 1 The Wine Society hosted their annual Young Winemaker of the Year Awards.

The night was a dazzling success with Ben Haines from Mitchelton

Wines in Victoria named The Wine Society's 2008 Young Winemaker of the Year.

The Centenary Institute raised over \$7,500 from our silent auction

and lucky dip on the night. Many thanks to the Wine Society and their guests for their generous support.

The Wine Society has also confirmed the Centenary Institute as one of their three payroll giving charities. Thank you.

AWARDS AND ACHIEVEMENTS



Professor Chris Semsarian

Congratulations to Chris Semsarian, Head of the Centenary Institute's Agnes Ginges Molecular Cardiology laboratory, who has been awarded full Professorship by the University of Sydney.

Professor Semsarian leads a team of 12 scientists researching the causes, new treatments and possible cures for genetic heart disorders with a particular focus on sudden cardiac death in the young. In 2008, Professor Semsarian published a major breakthrough in the cause of chronic heart failure – linking a double gene mutation with significantly increased risk of disease.

Congratulations to Dr Jeff Holst, one of the Centenary Institute's up-and-coming young researchers, who has been awarded the inaugural Discovery Award for his research into the immune system. The award – for an early career scientist whose discovery has already demonstrated its importance or impact – is part of Research Australia's Thank You Day program for 2008.

The Centenary Institute's Executive Director, Professor Mathew Vadas, was recently awarded Life Membership of the Australian Cancer Research Foundation (ACRF) for his outstanding services as Chairman and member of the ACRF's Medical Research Advisory Committee (MRAC).

Professor Vadas was appointed to the ACRF MRAC in 1997 and then to the position of MRAC Chairman in 2003. He served in the Chairman's position for five years before stepping down from the role at the end of 2007 and continued to serve as a committee member in 2008.



Australian Cancer Research Foundation Chairman, Tom Dery, presents Professor Mathew Vadas with his Life Membership.



Dr Jeff Holst was awarded the inaugural Discovery Award for his research into the immune system.

While undertaking in-depth studies at the prestigious St Jude Children's Research Hospital in the USA, Dr Holst discovered a key mechanism that controls 'negative selection', which can lead to autoimmunity. This finding, published in *Nature Immunology* in 2008, will allow further investigation of autoimmune diseases with the potential to develop improved diagnostics and treatments.

Dr Holst continues his research in the Gene and Stem Cell Therapy Program at the Centenary Institute and has turned his focus to cancer.

Message from the Director

I am continuing to be amazed at the rapidity of the growth of Centenary Institute. This year we will have a touch more than 200 staff and researchers in our building – almost a doubling in two years.



This remarkable growth has come from a very significant success with grants both at the national and international level – which in turn reflects well on the excellence of our research. I am also pleased to report that our Institute has one of the highest citations per paper in Australia, a strong independent measure of the esteem of our scientists.

In addition to internal growth, Centenary has and continues to contribute strongly to the development of the campus: in particular we were involved in an successful application (through the Higher Education Endowment Fund) for \$95m for a new building to be built adjacent to Centenary by the University of Sydney – the Centre for Obesity, Diabetes and Cardiovascular Disease.

We also are keen supporters of building our cancer research prowess through a

mutually synergistic arrangement with the Sydney Cancer Centre and to supporting the conglomeration of Institutes and the Royal Prince Alfred Hospital in forging a body to make all our work more effective and prominent.

Your support has been essential through the last two years. It gives great comfort to all of us to know that the community is interested in our work, appreciates our responsible and ethical approach to research and supports our endeavour with donations large or small.

Times are tough, but difficult circumstances often bring out the best in people. We shall make your support count.



Professor Mathew Vadas

How your donations are used

Simply put, every dollar donated to the Centenary Institute helps us to fund ground breaking research into the causes, treatment and possible cures for cancer, cardiovascular and infectious diseases.

Your donations are used to:

- recruit and retain the best medical research scientists and to buy their supplies;
- buy state of the art equipment that allows new techniques to be pursued and research project times to be reduced; and
- help our scientists travel to conferences to build new global collaborations and ensure that the discoveries made at Centenary are shared with research colleagues.

How do we know we're doing good science?

The Centenary Institute is committed to conducting world class research that will help people in Australia and around the world to live longer, healthier lives. We also understand that unless you can measure the impact you're having, a goal like that mightn't mean much.

Here are some of the measures we use to test the value of our work to the community.

Publications

When a discovery is made by a team of scientists it is submitted for publication in a peer reviewed journal. If it is deemed to have a valuable contribution to the global body of knowledge in that field then it is published. In 2008, Centenary published 81 articles in peer reviewed journals.

These published articles are referenced by other researchers when publishing their work. One measure of the impact that a published finding has had on its field is the number of times it is quoted in other journal articles. In a recent comparison against 16

other Australian medical research institutes, using the measure of average citations per paper, the Centenary Institute ranked second.

Grants

The peer review process for medical research grants ensures that only the most promising science receives funding and that duplication of research is avoided. In 2009, the Centenary Institute received \$9.2M in peer reviewed funding from granting bodies.

Last year Australia wide one in four grant applications were funded by the National Health and Medical Research Council. Our success rate was one in two, double the national average.

Collaborations

By collaborating with colleagues in other Institutes, scientists at the Centenary Institute are able to harness the best and brightest minds to help solve the big questions in their field. In 2008, Centenary Institute was engaged in over 65 collaborative research projects in Australia and around the world.

