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#### Our Mission

The relief of pain and suffering and the promotion of well-being, through an understanding of the fundamental mechanisms of cardiovascular biology in health and disease.

#### Whoweare

Founded in 1994, the Victor Chang Cardiac Research Institute is an independent research facility that is committed to excellence in research, training and the rapid translation of discoveries into new diagnostic, preventative and therapeutic regimens for people with or at risk of heart disease. The Institute is dedicated to the memory of cardiac surgeon Victor Chang and his passionate belief in the power of discovery.

Our team of over 150 full-time staff work across five Research Divisions – Cardiac Physiology & Transplantation, Developmental & Stem Cell Biology, Molecular Cardiology & Biophysics, Molecular Genetics and Structural & Computational Biology.

# 2011 marked 20 years since the tragic passing of Dr Victor Changac.

Victor may no longer be with us, but his legacy remains.

It's in our 130 scientists, working every day to push back the boundaries of the unknown; to discover something life changing for millions of Australians and people around the world.

This legacy is perhaps his greatest achievement. It's the source of our inspiration and drives us towards our future.

It's a legacy of excellence, for the benefit of everyone, everywhere.

Victor Chang Cardiac Research Institute 2011 Annual Report

#### Mary Aikenhead Ministries

#### **Board Committees**

#### Finance

Chair, Mr John Kean OAM

#### Appeals

Chair, Mrs Louise Di Francesco

#### Media & Communications

Chair, Ms Jill Margo AM

#### Scientific Advisory Committee

#### Chief Operating Officer

Mrs Carla Northam (until April)
Ms Dianne Kitcher (from October)

#### **Fund Development**

Ms Jan Savage Media and Communications

#### Administration

Finance

Human Resources Information Technology Policy

**Essential Services** 

Core Facilities

#### Affiliations

University of NSW St Vincent's Health Australia

#### **Executive Director**

Cardiac Research Institu

**Board of Directors** 

Chairman, Mr Steven Lowy AM

Professor Robert Graham AO

#### **Deputy Directors**

Professor Richard Harvey Professor Jamie Vandenberg

#### Molecular Cardiology and Biophysics

Division Head, Professor Robert Graham AO

#### Developmental and Stem Cell Biology

Division Head, Professor Richard Harvey

#### Cardiac Physiology and Transplantation

Division Head, Professor Michael Feneley

#### Structural and Computational Biology

Acting Division Head, Dr Daniela Stock

#### Molecular Genetics

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Acting Division Head, Dr Catherine Suter Victor Chang Cardiac Research Institute Annual Report 2011

#### Trustees' Foreword

It is now two years since the Trustees of Mary Aikenhead Ministries took up their responsibilities for the governance of the Education, Health, Research and Welfare ministries which were the result of 172 years of service to the Church and the Australian community by the Sisters of Charity.

In addition to their engagement with the many stewardship activities involving the Colleges, Hospitals and Research Institutes, 2011 has been significant for the Trustees for two reasons:

Firstly, on 5 March 2011, the Trustees met with representatives of the Holy See in Rome to discuss the inaugural report of Mary Aikenhead Ministries. This meeting was very constructive and affirming, and was followed up with a very complimentary letter from the Vatican, acknowledging the success of the governance transfer and the importance that the Trustees have placed on leadership development for these vital works of the Church.

Secondly, in July the Trustees hosted the second annual Mary Aikenhead Ministries Conference which was attended by a large number of the leaders from across our ministries. The theme of the Conference was "The Heart of our Mission" and some very gifted speakers reminded us of the reason "why it is that we do what we do" – namely a commitment to the gospel imperative of service to God's people in the tradition of Mary Aikenhead as passed down to us by the Sisters of Charity.

The Trustees of Mary Aikenhead Ministries would like to congratulate both Steven Lowy and Bob Graham on the continued success and contribution of the Victor Chang Cardiac Research Institute to the health and research communities. The Trustees are also very grateful to the people of great commitment and ability who continue to contribute so much to ensure that the Institute continues to excel.

On behalf of the Trustees of Mary Aikenhead Ministries, I am pleased to commend to you the 2011 Annual Report of Victor Chang Cardiac Research Institute.



David Robinson

Chairman, Trustees of Mary Aikenhead Ministries



#### The Mary Aikenhead Ministries Trustees

Mary Aikenhead Ministries was established by the Holy See as a Public Juridical Person at the request of the Congregation of the Religious Sisters of Charity of Australia to succeed to, and to carry on and expand, various health and aged care, education and welfare ministries conducted by the Sisters of Charity.

The Victor Chang Cardiac Research Institute Limited is a Research Ministry within Mary Aikenhead Ministries, which operates in accordance with the Canonical Statutes approved by the Holy See. Mary Aikenhead Ministries also assumes an Australian civil identity under Australian law as the Trustees of Marv Aikenhead Ministries. The Trustees operate pursuant to the Constitution of Trustees of Mary Aikenhead Ministries. In 2011, the Trustees included Mr Richard Harpham, Mr David Robinson, Sr Linda Ferrington, Professor Gabrielle McMullen, Ms Rowena McNally, Dr Tessa Ho and Sr Elizabeth Dodds.



Victor Chang Cardiac Research Institute Annual Report 2011 Victor Chang Cardiac Research Institute Annual Report 2011

#### **Our Story**

A pioneering surgeon, researcher and humanitarian, Dr Victor Chang founded the National Heart Transplant Program at St Vincent's Hospital in 1984 and spearheaded the Heart of St Vincent's Appeal in 1990.

This Appeal raised much-needed funds for a Cardiac Transplant Ward and Cardiac Diagnostic Unit at St Vincent's - and created the impetus for establishing the Victor Chang Cardiac Research Institute after his untimely death in 1991.

#### Establishment

The new Institute was opened in St Vincent's Hospital, Sydney on 14 February 1994, thanks to generous donations from the late Kerry Packer AC; the Federal Government; and the Australian public.

The Institute was incorporated as an independent research facility on 27 February 1995. In 1996 new premises in the Garvan Building were opened by the late Diana, Princess of Wales.

#### Independence

The Institute was soon outgrowing these premises and funds were raised to build a state-of-the-art research facility nearby.

Through contributions from the NSW and Australian Federal Governments, the Lowy and Packer families, The Atlantic Philanthropies, the National Australia Bank, ANZ Bank, Citigroup and many others, the \$80 million Lowy Packer Building was formally opened by HRH Crown Princess Mary of Denmark in September 2008.

As part of the opening ceremonies, Her Royal Highness unveiled a life-sized sculpture of Dr Victor Chang that was kindly designed and donated by sculptress Ms Linda Klarfeld. The statue takes pride-of-place in the forecourt of 'his' new building.

#### Working for a bright future

In Australia, more than 40,000 people die of cardiovascular diseases each year, with 10,000 succumbing to heart failure. Heart failure remains the most common cause of hospital admission for people aged over 65, although it can affect anyone regardless of age or gender.

Through heart surgery, Dr Victor Chang was able to save hundreds of lives, but he knew that research could save thousands.

In his memory, the five research divisions and their laboratories work with a single vision – to reduce the incidence, severity and impact of heart diseases, particularly those causing muscle diseases, which directly affect the heart's ability to pump sufficient blood for the body's needs and can result in the most severe forms of heart failure. Our research programs address vital contemporary issues – including heart development and congenital heart disease, inherited heart diseases, the potential application of adult stem cell technologies in cardiovascular care, cardiac arrhythmias, and how heart function is regulated in response to stresses like high blood pressure and ageing.

Through heart surgery, Dr Victor Chang was able to save hundreds of lives, but he knew that research could save thousands.

St Vincent's Hospital 1962 final

Ms Fiona Coote, Mrs Ann Chang and Diana, Princess of Wales, at the opening of the Institute in 1996.

Dr Victor Chang and colleague, Dr Mark Shanahan.

HRH Crown Princess Mary of Denmark in 2005, prior to the



Victor Chang Cardiac Research Institute Annual Report 2011 7 Victor Chang Cardiac Research Institute Annual Report 2011

As a highly accomplished surgeon, humanitarian and skilled campaigner, Dr Victor Chang was a pioneer in the modern era of heart transplantation.

His achievements include the development of Australia's National Heart Transplant Program at St Vincent's hospital, which has since performed more than 1500 successful heart, heart-lung, and single lung transplants since 1984. He also saw the incredible value of research – playing a key role in development of an artificial heart valve and, in later years, an artificial heart assist device.

Victor Chang (Yam Him)
was born in Shanghai to
Australian-born Chinese
parents in 1936. He came to
Australia in 1953 as a student
at the Christian Brothers
College, Lewisham. In 1962
he graduated from Sydney
University with a Bachelor
of Medicine, Bachelor of
Surgery, becoming an intern
and later a registrar in
cardiothoracic surgery at
St Vincent's Hospital.

Travelling overseas to extend his skills, Dr Chang attained a Fellowship in Surgery from the English and American College of Surgeons and returned to St Vincent's Hospital in 1972, where he worked with the renowned Dr Harry Windsor and Dr Mark Shanahan, who had performed Australia's first heart transplant at St Vincent's Hospital in 1968.

During the 1980's Dr Chang lectured extensively in China, Hong Kong, Indonesia, Singapore and Malaysia. He also founded the Australasian-China Medical Education and Scientific Research Foundation, which sponsored South-East Asian doctors, nurses and students to work in Australia to develop improved skills and quality-of-care to take back to their home countries.

At the same time, he helped teams from St Vincent's travel to China, Singapore and Indonesia where they shared their medical, surgical, nursing, hospital administration and audiovisual expertise.

In 1986 Dr Chang was awarded Australia's highest recognition, a Companion of the Order of Australia (AC), while the University of New South Wales awarded him its highest degree of MD (Honoris Causa) for "scholarly achievement and humanitarian endeavour".

Victor Chang died in tragic circumstances in Sydney on 4 July 1991. He was an honorary Professor of Surgery to the Chinese Academy of Medical Science in Peking; an honorary Professor of Surgery to Shanghai Medical School; official adviser on cardiac surgery development in Indonesia; and a member of the Australia China Council. In 2000, Dr Victor Chang

In 2000, Dr Victor Chang was named Australian of the Century by the people of Australia.

# Victor Chang Ac (1936 – 1991)



#### Chairman's Report

Milestones are important in our lives. They serve to mark the most significant events and provide an opportunity for us to reflect on our life's journey – the progress made, as well as the disappointments and setbacks.

Milestones are also important for institutions like ours. The 4th of July 2011 marked the 20th anniversary of the passing of Victor Chang, the skilled and compassionate heart surgeon whose name and vision lives on at the Victor Chang Cardiac Research Institute.

At the time, his death touched the entire nation in a profound way. In a way that has rarely, if ever, been repeated.

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That such a man, whose mission was to save lives, could have his own life taken so callously, so needlessly, left all of us numb and bewildered.

In life, Victor was an exceptionally talented, inspiring individual. The skill of his own hands, and his knowledge and research, saved countless lives but in death he continues to inspire. When the Institute was established in 1994 all of us involved were committed to ensuring that his legacy remained secure and that we could go on saving lives in his name.

When we review the past year, it is clear that the hard work and commitment shown since 1994 is paying dividends.

Heart disease remains Australia's number one killer, but real progress is being made through the efforts of the Institute's research team and the vast number of

In life, Victor was an exceptionally talented individual. In death, he continues to inspire.



people in the community who support their work in so many different ways. Progress can be seen on all fronts.

We can be proud to have recruited and supported some of the best and brightest minds not only from Australia but from around the world. We can be proud to have published this year alone over 68 papers in journals of the highest calibre, including Nature, Cell and Science.

The Institute has contributed to the knowledge of the international scientific community and continues to make discoveries that will help save more lives in future.

Another important measure of the Institute's performance that I am pleased to report is its success this year in securing highly competitive, peer-reviewed research grants. We received a total of \$6 million in new National Health and Medical Research Council Grants and Fellowships over the next three to five years and \$650,000 in new grants from the National Heart Foundation and other foundations and trusts.

Although the Institute had budgeted for a loss of \$2.4 million in 2011. I am pleased to report that through disciplined cost management, and success in grant outcomes and fundraising, this was kept to \$1.3 million, which is \$1.1 million better than expected.

This strong fiscal performance reflects the efforts of all our Board teams, in particular the Finance and Appeals the Institute continues to face a significant challenge to year, a diverse range of reduce the gap between what it receives in grants and its operating costs.

In 2011, total grant funding was a record \$12.5 million while operating costs were more than \$18 million. Our efforts to make up this shortfall of \$5.5m every year highlights the importance of fundraising and promoting our work to donors and supporters throughout the community. This is fundamental to the success and sustainability of the organisation.

To that end, we had a recordbreaking year at the annual "Heart-to-Heart Ball" held in August. More than 800 friends and supporters of the Institute attended and we raised almost \$1 million. The guest-of-honour was the Premier of NSW, the Hon Barry O'Farrell, who spoke about the contribution medical research, and the Victor Chang Cardiac Research Institute in particular, makes to the wellbeing of the community and its impact on the economy of the State.

This event is not only an important fundraising initiative but serves to promote the work of the Institute throughout the community and recruit ever more supporters – our Friends – to our cause.

I am pleased to note that during the year Marcus Chang, youngest son of Victor Chang, was named as an Ambassador of the Institute. In this role he works closely with the staff of the Institute to secure funding and promote the work of our researchers.

Another outstanding example of promoting the work of the Institute is embodied in the Victor Chang Awards for Committees. As in past years, Excellence in Cardiovascular Journalism. In its second entries arrived from across Australia, representing both regional and metropolitan media. These featured stories that have touched and informed the nation and the awards recognise the role that the media plays in raising awareness about heart disease.

> At the "Heart-to-Heart Ball" I spoke about my admiration for the research team at the Institute, led by Professor Bob Graham, who in 2011 was honoured by election to Life Membership of the NSW Division of the Heart Foundation of Australia.

Our researchers are brilliant individuals, at the top of their profession and they undertake their work diligently and without the adulation that others in the community enjoy.

I would like to take this opportunity to acknowledge the ongoing support and advice provided by my fellow board members, the Trustees of the Mary Aikenhead Ministries, Board Member, Sr Anthea Groves and Appeals Committee Member, Sr Clare Nolan, as well as all of the Sisters of Charity, who continue to support and inspire us.

I'd also like to acknowledge the tireless work and leadership of the Board Committees including John Kean and the Finance Committee, Louise Di Francesco and the Appeals Committee, and Jill Margo and the Media and Communications Committee all of whom ably help steer the Institute in our ongoing fundraising challenges.

During the year, we farewelled a long-standing board member, John McGuigan, who served as Chair of the Appeals Committee from 1996 to 2010. We thank John for his dedicated service to the Institute and welcome new board member. Ryan Stokes, who brings considerable corporate experience and knowledge to the board.

Already, Ryan has made a major impact by playing a pivotal role together with James Packer in expanding the reach of the Institute to Western Australia.

Throughout this annual report you will find outstanding examples of research and discoveries that remind us that progress is being made in the quest to better understand why heart disease continues to exact such a toll on society.

Without the support of everyone involved in the Institute - the board, staff and our wider group of friends and supporters in the community – there would be no such progress.

I look forward to the year ahead and trust that I will be able to report to you next year on yet more progress as we continue to build on and honour Victor Chang's legacy.



Chairman

As our Chairman, Mr Steven Lowy noted, 2011 marked twenty years since the tragic passing of Dr Victor Chang. I was fortunate to have worked with Victor for one year in 1974. As a senior house officer Heart transplantation was at the time, I distinctly recall his warm outgoing persona, his commitment to his patients, his ability to inspire confidence in his patients despite their illness, and his collegiality towards us, his junior colleagues.

Although the first heart transplant had already been performed at St Vincent's hospital by Harry Windsor and Mark Shanahan in 1968, only one year after Christian Barnard's first anywhere in the world, success was short-lived. Not through a lack of technical expertise, but because we lacked drugs to allow sufficient immunosuppression for the heart to function immediately

after transplantation. Drugs and the ability to biopsy heart tissue to determine if the heart was being rejected were only developed in the late 1970s and early 1980s. discontinued during this period – a dark period indeed, as we had a potentially powerful tool, but no way to really harness it.

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When appropriate immunosuppressive drugs finally became available, Victor pioneered their use to establish heart transplantation as a remarkably durable and effective treatment for people with severe heart failure - a treatment that has now saved countless thousands of lives. But this took much more than the availability of suitable immunosuppressive drugs. It took someone with Victor's drive, tenacity, commitment and courage, as well as political acumen and persuasion, to garner the support of the Government to establish Australia's, and one of the world's first and most successful heart transplant programs. So it is timely that we remember Victor's achievements and vision, his pioneering surgical efforts

# How far have we come in 20 years?



and his caring of not only his patients, but also the families of those who lost a loved one and yet unselfishly agree to the use of the heart to help others in need.

In the 20 years since Victor's passing, much progress has been made possible by research conducted by the Victor Chang Cardiac Research Institute and our colleagues at St Vincent's Hospital.

Such progress includes the clinical application of betablocking drugs to show that they actually save lives in patients with heart failure. Pioneering work from our own by Professor Ann Keogh and Peter Macdonald shows that they even benefit patients with very severe heart failure a very radical concept at the time. Beta-blockers have also been shown to optimise heart function before all types of heart surgery, and in so doing can markedly improve outcomes.

Other advances include

new treatments for atrial fibrillation (AF) – a severe and common heart rhythm disturbance, for which 20 years ago there were only poorly effective drug treatments and the prospect of life-long blood thinner treatment to prevent a stroke. These new treatments include the use of radioablation therapy that has been guided by developmental biology discoveries from our own Deputy Director, Professor Richard Harvey. More recently, surgical approaches to limit clot formation in patients with AF have been used, and a major advance in diagnosing patients at risk of clot formation that was pioneered by Professor Diane Fatkin and Michael Feneley.

20 years ago, statins – drugs for treating high cholesterol had only just been developed and their benefits had not been demonstrated in large clinical trials. This was shown in the late 1990s in a landmark study published in the New England Journal of Medicine, with our own Professor Terry Campbell as one of the investigators involved. Since that time statins have become frontline treatment for high cholesterol and their widespread use has saved countless thousands of lives.

Another important cardiovascular condition is pulmonary hypertension a condition in which narrowing of the pulmonary arteries that provide blood to the lungs causes the right heart to fail. Until very recently, there have been absolutely no treatments for this condition and it inevitably led to severe heart failure and death at a young age. Due to work, spearheaded by Ann Keogh, SVH is now the largest centre in Australia treating this condition and several very effective treatments are now in common use for this condition – again advances that have saved or prolonged countless lives.

I could go on – robotic cardiac surgery, pacemakers for heart failure, closure of a hole-in-the-heart and replacement of diseased heart valves using devices applied via a tube in the leg rather than by invasive openheart surgery, and a major new way of prolonging donor hearts from the time they are taken from a donor until they are implanted into the sick patient – are all advances that have been developed over the past 20 years, and are all advances that have involved significant input from researchers at the Victor Chang Cardiac Research Institute and St Vincent's Hospital.

So what has happened over the last year? In 2011 the Institute published 68 papers, the enormous support of including many in the world's leading journals. We also had a very solid year in terms of the grants we have been awarded, as Steven noted. In addition, six of our trainees successfully completed and were awarded PhD degrees from the University of New South Wales for work carried out at the Institute.

In 2011, the Institute again held a major symposium featuring 15 international and local speakers including the 2008 Nobel Laureate, Professor Martin Chalfie, who who chairs our Appeals gave the 2011 Princesses' Lecture. This year we were honoured to have our Board Member Professor Les Field. introduce the Princesses' Lecturer and our Minister for Health and Medical Research. the Hon. Jillian Skinner, opened the symposium, which highlighted groundbreaking research spanning from discovery to clinical translation.

Finally, the Institute was also

active in its out-reach to the community, with 120 Year 11 students recognised for their excellence in science by receiving a Victor Chang School Science Award. This is the eighth year we have given these awards with more and more schools being added each year. It was also the first full year in operation for the Victor Chang 'Health Check Booth', which carries out vital cardiovascular tests, including blood pressure, glucose and cholesterol. Over a third of participants tested in the booth in 2011 were referred to their GP for immediate follow-up, showing just how valuable this initiative is to our community.

Of course none of this would have been possible without our Board, our Appeals Committee and our many Friends – the good people who supported us throughout the year, either directly or in-kind, and of course the fantastic efforts of our faculty, staff and trainees.

In particular, I'd like to thank the monumental efforts of our Chairman, Steven Lowy, as well as all our Board, including John Kean, who heads our Finance Committee, Louise Di Francesco, Committee and all of the members of her Appeals Committee, and Jill Margo, who heads our Media and Communications Committee In addition, I'd like to take this opportunity to thank the Trustees of the Mary Aikenhead Ministry, Mrs Ann Chang and all of the Chang Family for their continued support, the University of New South Wales for their continued collegiality, St Vincent's Hospital that so ably cares for the patients that are the reason for our being, and last but by no means least, the Sisters of Charity, who as always continued to inspire us in 2011.

Professor Robert M Graham AO, FAA, MBBS (Hons), MD, FRACP, FACP, FAHA **Executive Director** 

#### **Board of Directors**

The successful operations of the Victor Chang Cardiac Research Institute are heavily reliant on the dedication, commitment and vision provided by the Board of Directors and subsidiary committees.

# Our vision, our driving force

#### Mr Steven Lowy AM, B.Com (Hons), Chairman

Mr Lowy joined the Victor Chang Board as an inaugural member in 1995 and became Chairman in 2008. He currently serves as Co-Chief Executive Officer of the Westfield Group. Mr Lowy holds a Bachelor of Commerce (Honours) degree from the University of NSW. Prior to joining Westfield in 1987, he worked in investment banking in the US. Mr Lowy is President of the Board of Trustees of the Art Gallery of New South Wales. He is a director of the Lowy Institute for International Policy, a member of the Prime Minister's Business-Government Advisory Group on National Security, and Chairman of the Board of Management for the Associate Degree of Policing Practice NSW (ADPP). Mr Lowy is a Life Governor of the Victor Chang Cardiac Research Institute. In addition to his role as Chairman of the Board, he is a member of the Institute's Finance Committee.

#### Professor Robert M Graham AO, FAA, MBBS (Hons), MD, FRACP,

FACP, FAHA Professor Graham is Executive Director of the Victor Chang Cardiac Research Institute, and a member of its Finance, Appeals, and Media and Communications Committees. He is the Des Renford Professor of Medicine, and Professor of Biotechnology and Biomolecular Science, University of NSW, and vProfessor (adjunct) of Physiology and Biophysics, Case Western Reserve University School of Medicine, Cleveland, Ohio. He is a Fellow, Australian Academy of Science (AAS) and foreign member, Royal Danish Academy of Sciences and Letters. He is a member of the American Association for Clinical Research, the American Society of Clinical Investigation and the American Heart Association, and a Life Member. Heart Foundation of Australia. He is also a member of the Research Committee. National Health & Medical Research Council.

Mr David Craig BEC, FCA, CTFP Mr Craig joined the Victor Chang Board in 2007 and is a member of the Institute's Finance Committee, Since 2006 he has been the Chief Financial Officer of the Commonwealth Bank of Australia. He is responsible for the overall financial frameworks of the bank, incorporating the areas of finance, audit, security, property, procurement and investor relations. Mr Craig has over 30 years of experience in financial management, strategy, mergers and acquisitions. His previous roles included: Chief Financial Officer for Australand; Global Transition Finance Leader for IBM Business Consulting Service; Global Chief Financial Officer of PwC Consulting, and Chief Operations Officer and for 15 years Senior Audit Partner of PricewaterhouseCoopers Australasia. Mr Craig has also served as a director of Australian Gas Light Company.

Mr Craig is a Bachelor of Economics, a Fellow of The Institute of Chartered Accountants in Australia and a member of the Australian Institute of Company Directors. He is also a director of the Financial Executives

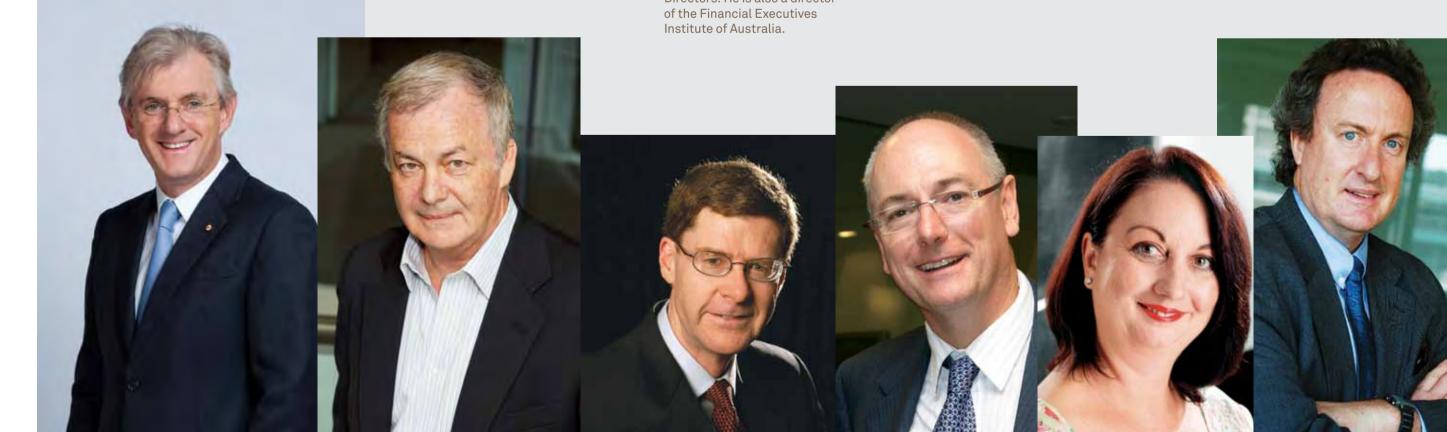
#### Mr Chum Darvall BA, F FIN, FAICD Mrs Louise Di Francesco

Mr Darvall joined the Victor Mrs Di Francesco joined Chang Board in 2008, and the Victor Chang Board in is a member of its Finance 2010 and is the Chair of its Committee. He was Chief Appeals Committee. Executive Officer, Deutsche Mrs Di Francesco has worked Bank Australia and New in the media industry for Zealand, from July 2002 to more than 30 years, initially March 2011. He is now nonas a journalist, and for the executive Vice Chairman past 22 years, in media and of Deutsche Bank. Prior to corporate communications. this he worked in a variety She is a specialist in all of roles across the banking areas of corporate media industry including: Director of management, public relations, scientific papers and 4 text Treasury and Head of Global issues management and crisis Markets at Deutsche Bank management, and has worked and positions in the financial on campaigns for AAPT, CeBIT, markets division of Westpac. Mercedes Australian Fashion Mr Darvall's current Board Week, Alterian, Carbon Planet, memberships include: Wilson Australand, Lend Lease, HTM, the Financial Markets Multiplex, Colliers, Landcom Foundation for Children, and James Fairfax. Macquarie University Council Mrs Di Francesco is a board and Major Performing Arts member of National not-for-Board of the Australia Council. profit organisation, Fitted for Work.

#### Professor Leslie Field AM, FAA. DSc, PhD, BSc

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Professor Field joined the Victor Chang Board in 2009. He was appointed to his current position as Deputy Vice-Chancellor (Research) at the University of NSW in 2005. His main areas of research are organometallic chemistry, catalysis and NMR spectroscopy. He is the author of more than 200 books. He is the recipient of the Rennie Medal (1983): The Edgeworth David Medal (1986); The Organic Chemistry Medal (1992); the Centenary of Federation Medal (2003) and the RACI Leighton Medal (2010). He was elected as a Fellow of the Australia Academy of Science in 1996 and appointed as a Member of the Order of Australia in 2011 for his services to Chemistry and to Higher Education.



#### Mrs Barbara Ell

Mrs Ell has been a Victor Chang Board member since 2001 and is a Life Governor of the Institute. She is a member of the Institute's Appeals Committee and is the Chair of the Victor Chang Day Organising Committee. Mrs Ell was born in Auckland. New Zealand and educated at St Mary's College prior to her nursing training at Auckland Hospital. She then continued her nursing career at Merriwa District Hospital, After marrying, Barbara moved to Sydney, where she raised her three children, Justine, Sara and Robert. In addition to serving on the Victor Chang Appeals Committee, Barbara is widely recognised for her leadership in philanthropy and charity work.

#### Mr Angelos Frangopoulos BA(COMM), MAICD, JP

Mr Frangopoulos joined the Victor Chang Board in 2009 and is a member of its Media and Communications Committee. He is the Chief Executive Officer of Australian News Channel Pty Ltd, the owner and operator of Skv News Australia and Sky News New Zealand. Before joining Australian News Channel, he held positions at British Sky Broadcasting, the Nine Network and Prime Television. Mr Frangopoulos is the Chairman of the Australia Day Council of NSW, a member of the Charles Sturt University Council, a member of the Advisory Board of Macquarie University's Centre for Media History, and a Director of the Australian Subscription Television and Radio Association.

#### Sr Anthea Groves RSC. OAM, RN LHA Dip. of Nursing Administration

Sr Anthea Groves has been a member of the Victor Chang Board since 2003. She is a member of the congregation of the Sisters of Charity and is Patient Liaison Officer at St Vincent's Hospital Sydney. Sr Anthea is a Director of the Sisters of Charity Foundation.

#### Mr John Kean OAM, FCA, FAICD

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Mr Kean has been a member of the Victor Chang Board since 2003, is a Life Member of the Institute and is the Chair of the Institute's Finance Committee. He is Executive Chairman of Pinpoint Pty Limited. He also acts as an Independent Business Advisor and holds directorships in various businesses involved in marketing, finance, education, primary production, property and healthcare. In addition to serving as a director of the Victor Chang Institute, he was an inaugural member of its Appeals Committee.

#### Ms Jill Margo AM, BA (Hons)

Ms Margo joined the Victor Chang Board in 2008 and is the Chair of the Institute's Media and Communications Committee. She is a medical journalist on The Australian Financial Review. She has won numerous international and national media awards. including two Walkleys and a Churchill Fellowship. Since 2000, she has been a member of working parties charged with developing clinical and consumer guidelines for the management of prostate cancer. In 2006, Ms Margo was awarded an Order of Australia for services to journalism and cancer. She holds a BA (Honours) in English literature, and is a best-selling author and biographer.

#### Mr John McGuigan LLB

Mr McGuigan jointed the Victor Chang Board in 2004. He is a co-founder of Hunter Bay Partners, a private investment company with investments in the Energy and Food sectors and is Chairman of White Industries. He has both an accounting

and legal background. Mr McGuigan has served on the boards of a number of and maintains an active involvement in charitable and civic organisations. In addition to serving as a Director of the Victor Chang Institute Board, Mr McGuigan was Chair of its Appeals Committee from 2004 until 2010. Mr McGuigan retired from the Board in 2011.

#### Mr Rvan Stokes BCom

Mr Stokes joined the Victor Chang Board in 2011. He is Chief Executive Director of Australian Capital Equity Ltd (ACE) and Executive Officer of Seven Group Holdings (SGH).

Mr Stokes is also a Director of WesTrac, CMH, Yahoo!7, and Iron Ore Holdings, an alternate Director of Seven West Media and Chairman of Vividwireless. He is also public and private companies, a Director of the Australian Strategic Policy Institute Council, Perth International Arts Festival and the Australian Institute of Management, WA.

#### Dr Gary Weiss LLB (Hons), LLM, JSD

Dr Weiss joined the Victor Chang Board in 2009 and is a member of its Finance Committee. He holds the degrees of LL.B (Hons) and LL.M (with dist.), as well as a Doctor of Juridical Science (JSD) from Cornell University, New York. Dr Weiss is Chairman of Coats plc and Secure Parking Pty Ltd, an **Executive Director of** Ariadne Australia Limited and a Director of several other organisations, including Premier Investments Limited, Ridley Corporation Ltd and The Centre for Independent Studies.



Victor Chang Cardiac Research Institute Annual Report 2011

#### **Our Committees**

All of our hard working committee members are volunteers; they are the lifeblood of our organisation.

#### Appeals Committee

The Appeals Committee consists of a group of volunteers and staff who are responsible for the Institute's fundraising events, aimed at raising the vital funds needed by the Institute to conduct its groundbreaking research.

The Committee has as its core an ethos of friendraising over fundraising, because if you don't have friends, you can't raise funds!

#### Members

Mrs Louise Di Francesco, Chair Mrs Ann Chang Mr Marcus Chang Mrs Bernie Connolly Mr Alan Crouch Mrs Barbara Ell Ms Linda Duncombe Mr Errol Goldberg Professor Robert Graham Mr Cameron Irving

Ms Dianne Kitcher Mr Ross Koscharsky

Mr Das Menon

Sr Clare Nolan Mrs Antoinette Ogilvie Mr Michael Renford

Mr Robert Ryan

Ms Jan Savage

Mr John Shim

Ms Ruth Zukerman

#### Finance Committee

The Finance Committee is responsible for the oversight of finances for the Board of Directors. The Committee oversees the audit of the Institute's accounts, investment management, management remuneration, and also sets finance policy for management to follow.

#### Members

Mr John Kean, Chair Mr David Craig

Mr Chum Darvall

Professor Robert Graham Ms Dianne Kitcher

Mr Steven Lowy

Mr Kiran Narsey

Ms Jan Savage

Dr Gary Weiss

#### Media and Communications Committee

The Media & Communications committee is responsible for the overall strategic direction of media and communications activities at the Institute. The committee meets bi-monthly and seeks to bring new ideas in traditional and emerging media platforms to promote the work of the Institute.

#### Members

Ms Jill Margo, Chair Mrs Louise Di Francesco Mr Angelos Frangopoulos Professor Robert Graham Ms Dianne Kitcher Ms Jan Savage Ms Anna Dear

#### Victor Chang Day Organising Committee

This committee is responsible for organising the Institute's major annual fundraising event, the Victor Chang Day Gala Ball.

#### Members

Mrs Barbara Ell, Chair Ms Eliana De Sousa Professor Robert Graham Mr Cameron Irving Mrs Ann Chang Mr Ken Laing Mrs Michelle Parker Ms Ruth Zukerman Ms Emma Quick

Mrs Diana Ritchie Ms Jan Savage

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#### Scientific Advisory Board

The Scientific Advisory Board comprises six internationallyrenowned scientists, who carry out an exhaustive evaluation of the Institute's research programs every five years, to ensure the Institute remains at the cutting edge of cardiovascular knowledge generation and continues to produce research of a worldclass standard.

#### Members

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#### **Professor Doug Hilton**

Chair, Director Walter and Eliza Hall Institute. Australia

#### **Emeritus Professor** John Chalmers

Senior Director and Head, Professorial Unit. The George Institute for International Health and University of Sydney, Australia

#### Professor Witold Filipowicz

Professor of Biochemistry, Friedrich Miescher Institute for Biomedical Research (FMI), Switzerland

#### Professor Lily Jan

Jack and DeLoris Lange Professor of Physiology and Biophysics, University of California, USA

#### Professor Janet Rossant

Chief of Research, The Hospital for Sick Children, Canada

#### Professor Stephen Vatner

Chairman, Department of Cell Biology and Molecular Medicine, New Jersey Medical School, USA

#### Faculty Review Committee

The Faculty Review Committee comprises eminent scientists from local research organisations who evaluate individual faculty members every five years in order to evaluate their productivity, promote the development of goals and expectations, foster and support faculty development and mentorship, and guide junior faculty in career advancement.

#### Members

#### Professor John Shine

Chair, Professor of Medicine and Professor of Molecular Biology, The University of New South Wales, Group Leader Neural Stem Cells, Garvan Institute of Medical Research

#### **Professor Peter Gunning**

Head, Oncology Research Unit in the School of Medical Sciences, The University of New South Wales

#### Professor John Rasko

Professor of Medicine, Central Clinical School, The University of Sydney and Centenary Institute of Cancer Medicine & Cell Biology

#### Professor Phil Robinson

Head, Cell Signalling Unit, Children's Medical Research Institute. Westmead

#### Committee on Appointments and Promotions

The Committee on Appointments and Promotions meets on an ad hoc basis to evaluate potential candidates for faculty positions within the Institute.

#### Members

#### Professor Robert Graham

Chair, Executive Director, Victor Chang Cardiac Research Institute

#### Professor Terry Campbell

Senior Associate Dean, The University of **New South Wales** 

#### Professor David Celermajer

Scandrett Professor of Cardiology, Central Clinical School, The University of Sydney and Heart Research Institute

#### Professor Richard Harvey

Deputy Director, Victor Chang Cardiac Research Institute

#### Professor Doug Hilton

Director, The Walter and Eliza Hall Institute

#### Professor Levon Khachigian

Centre for Vascular Research, The University of **New South Wales** 

#### Professor Charles Mackay

Department of Immunology. Monash University, Melbourne

#### Professor John Mattick

Executive Director, The Garvan Institute of Medical Research

#### Professor Jamie Vandenberg

Deputy Director, Victor Chang Cardiac Research Institute

#### Intellectual Property and Commercialisation Committee

The Intellectual Property and Commercialisation Committee (IPCC) is responsible for advising the Institute on its research commercialisation activities. The Institute has also appointed consultants TM Ventures to assist with linking our research to industry and forming new collaborations.

#### Members

#### Professor Robert Graham

Chair. Executive Director. Victor Chang Cardiac Research Institute.

#### Ms Britt Granath

Senior Policy Officer, Victor Chang Cardiac Research Institute.

#### Ms Dianne Kitcher

COO, Victor Chang Cardiac Research Institute.

#### **Dr Trevor Davies**

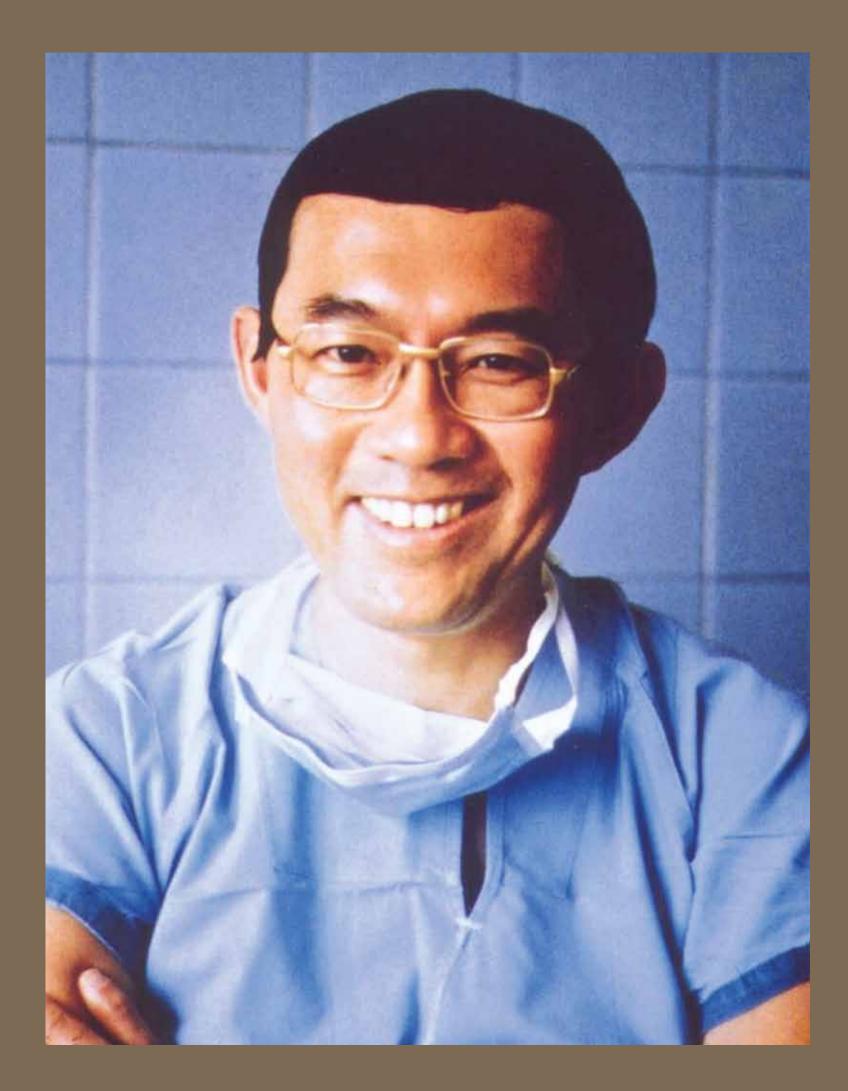
Partner, Allens Patent & Trade Mark Attorneys.

#### Professor Joan Dawes

Senior Consultant, Pestat Ltd; and Innovation Dynamics Consulting Group.

#### Ms Mary Sawyell

Senior Associate. Baker McKenzie.



Victor Chang Cardiac Research Institute Annual Report 201'

#### Days in the life of Victor Chang By Michael F O'Rourke

July 4 2011, marked 20 years since the tragic passing of Dr Victor Chang, a medical pioneer who touched the hearts of many. Passionate about research, his tragic death led to the establishment of the Victor Chang Cardiac Research Institute. Professor Michael O'Rourke, Laboratory Head in the Cardiac Physiology & Transplantation Division at the Victor Chang Institute, set out a pen portrait of Victor — the man with whom he shared a professional life at St Vincent's Hospital from 1972-1991, and who came to be a very close friend.

'Enthusiasm personified' was Victor Chang. Enthusiasm, sensitivity and a great sense of humour.

When Victor arrived in 1972, as a cardiac surgeon, what a difference he made. I was Director of the Coronary Care (CCU) Ward and with other staff, introduced counterpulsation for heart support in desperately ill patients, transferred from other hospitals. Our staff were all aware of Victor's judgement and his "people skills" were overwhelming. As other Australian hospitals developed their own counterpulsation programs, Coronary Care Unit (CCU) work lessened and Victor became the master of coronary artery bypass surgery.

So what was a typical day with Victor? It depended where you were. In Sydney he was in the operating theatre, or in the wards, alone or with one or two house staff. Sometimes he was in his room, where his door was always open, happy to be interrupted, but engaged in spirited discussion on the phone about a new project — recommencing the heart transplant program, designing a new heart valve, organising a new tour, or speaking to other enthusiasts about new or old (but always fast) cars. Any surgical challenge he wanted to know about early, and his response was immediate. His friends and colleagues always had their passports available, because Victor loved to share the challenge.

## Enthusiasm, sensitivity and a great sense of humour

Victor and the Cameron Wing operating team, St Vincent's Hospital.



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# In between journeys abroad, Victor was accomplishing much at home.

Memories of Victor come flooding back, the first from 30 years ago. Victor's team of cardiologist, anaesthetist, perfusionist, scrub nurses, ITU nurses and educational nurses, arrived in Shanghai to an old military airport and were 'received' by a galaxy of smiling faces, many familiar from previous visits to Sydney, all in Mao suits. On a rare officers' quarters, Victor told and customs, which became increasingly outrageous. He managed to clear the area with the tale of a great delicacy of monkey brain, served so fresh that there was no room for the guests' feet under the table. We only recovered no more, and relaxed on a distance, and the red moon above. Nights at banquets with etiquette tight, returning a toast and offering a toast, human interaction warm in old dilapidated buildings.

Victor introduced his group to the beauties of China and to historical figures like Tau Shou Chi, our first host who had survived the Cultural Revolution and the Great Leap Forward, and who answered our questions frankly about his attention on Chou En Lai and Mao Tse Tung

Chou En Lai and Mao Tse Tung. In China, later in Indonesia, Victor paired our group during the day for hospital work, and we met for meals at night. In Jakarta, Victor announced a special evening at the Presidential Palace where we gathered to hear the Minister for Health thank the national cardiac centre and for "rehabilitating" the relationship between Indonesia and Australia at the same time. On that sultry night in Jakarta under a hazy moon, we celebrated operated on, no deaths and the last on counterpulsation following surgery.

How had Victor achieved all this? Competence, sensitivity, reliability, enthusiasm and hard work.

Victor was accomplishing much at home. He wished to recommence the transplant program at St Vincent's that Harry Windsor and Mark Shanahan had with government support. The NSW Government appointed a committee of eminent doctors and scientists to advise. There amongst politicians and his patrons, raising money and gaining support for St Vincent's involvement. And Kerry Packer was on his side, with an airplane

available to fetch donor hearts – an arrangement that continued for at least a decade.

There was action in the air on that hot December day. Royal Prince Alfred Hospital (RPAH) were about to do their first transplant, and had a patient – a young woman with post-partum cardiomyopathy. decided that the patient RPAH to St Vincent's. The O'Rourke family were about to go on Christmas Holidays. The car was loaded. Victor insisted that I join the posse. Armed with stethoscope and trying to remember the group into foreign territory. We proceeded to the cardiac ward at that hospital where my old boss, Dick Richards in fresh white coat and upright stance, and the hospita matron met us at the bedside summarised the case and file which Victor accepted. I took out my symbol of the profession, which Dick had forward with the patient only in my sight. I greeted her, placed the stethoscope queue had gathered behind me. Ambulance officers were waiting outside. The press were not to be seen. Nurse Rosina joined the patient in the ambulance, and we left for Darlinghurst.

Victor had triumphed, again. He maintained his dignified stance in his departure from RPAH, and in his later detailed discussion with the patient. It was a big day and time for the O'Rourkes to take a holiday. Victor was just beginning.

From: Bob Graham To: All Staff

Date: Monday July 4, 2011

Time: 11.53am

#### Dear all

As many of you know, today marks the 20th anniversary of the tragic passing of Dr Victor Chang.

Today is a chance for us, as an Institute, to honour the life and achievements of Dr Chang, and also to look forward to the future, inspired by all that Chang stood for.

Yesterday, we announced Marcus Chang, Victor's youngest son, as a new Ambassador to the Institute.

Marcus Chang, along with Fiona Coote, Australia's first female and Victor Chang's youngest heart transplant recipient, Australia's Got Talent winner Mark Vincent and myself, answered questions from the media about Victor Chang at a press conference here at the Institute.

Today, on the actual anniversary of Victor's passing, is a chance for us to look towards the future, with Marcus stepping up to help us with our ongoing challenges — to firstly raise awareness about heart disease in our community, and secondly, to help us in our quest to secure funding and donations.

We look forward to having Marcus on board with us, and are extremely grateful for his bravery in speaking publicly and his commitment to the Institute.

I was fortunate to have worked with Victor Chang for a year – for many of you who didn't know Victor, he was a surgeon who filled you full of confidence. He was larger than life, gregarious, outgoing. And he was a leader in cardiothoracic surgery and heart transplantation. But perhaps his most impressive attribute was his humanity and caring for both his patients and the families of heart donors, whose loved ones had died. Although not trained as a researcher, he made many important contributions at the translational level and worked hard to increase research funding.

You should all be extremely proud of the work that you are doing here, every day, that honours the memory of this remarkable man.

#### Cheers,

#### Bob Graham

Robert M. Graham AO, FAA, MD | Executive Director, Victor Chang Cardiac Research Institute; Des Renford Professor of Medicine, UNSW From left: Victor Chang and Fiona Coote,

Fiona Coote and Marcus Chang, at the Victor Chang Heart to Heart Ball 2011.



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## Research Divisions



Developmental & Stem Cell Biology Division

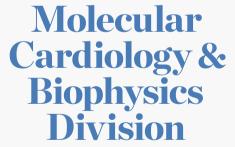
Discovery in Focus
Dunwoodie Laboratory
Harvey Laboratory

Cardiac Physiology & Transplantation Division



### Molecular Genetics Division

Discovery in Focus Suter Laboratory



Discovery in Focus Vandenberg Laboratory Fatkin Laboratory



# Structural & Computational Biology Division

Discovery in Focus Stock Laboratory 24

#### Feneley Laboratory

The Cardiovascular Mechanics Research Program, headed by Professor Feneley, has developed sophisticated approaches to directly measuring heart muscle contractility. His laboratory is broad-based; performing studies extending from the isolated heart muscle cell (or cardiac myocytes) to integrated physiological experiments, to cardiac

transplantation and myocardial preservation, to clinical research in patients with dilated cardiomyopathies and other causes of heart failure.

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Of particular interest to the program are geneticallyengineered animal models of human heart diseases. By isolating heart cells from these models and then investigating their contractile function, a detailed understanding can be obtained into the mechanisms whereby specific genes and the proteins they encode can alter heart contractile function. Using the same isolated cardiac cells as well as intact animal, the group is also able to investigate how important factors, such as blood pressure, hormones and aging, can affect contractility of the individual heart cells or the intact organ.

#### Macdonald Laboratory

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Heart transplantation is by far the most effective treatment for patients with advanced heart disease. Its application is currently limited to only a small percentage of people who could benefit, due to the scarcity of suitable donor organs. Peter Macdonald's research group is working on novel methods of donor management and donor heart preservation with the aim of being able to extend this lifesaving treatment to a larger number of Australians.

In 2011, the Macdonald laboratory received a JT Reid Foundation Grant to purchase a Transmedics Organ Care System to facilitate a study of resuscitating hearts from DCD donors, or donors from cardiac death. They also published a systematic review and a meta-analysis of thyroid hormone administration to brain-dead potential organ donors, in the journal Critical Care Medicine.

In 2011, Professor Macdonald commenced a two year term as President of the Transplantation Society of Australia and New Zealand.

#### Keogh Laboratory

Professor Anne Keogh's research group focuses on pulmonary arterial hypertension, heart transplantation, immunosuppression and left heart failure. Through their research, they aim to find the best tailored therapies for individual patients with Class-I-IV heart failure, including drug therapy, synchronised pacing and ventricular assist devices.

For Pulmonary Hypertenstion (PH), the group works with the broadest range of drugs available in Australia, including Ambrisentan, Sildenafil, Prostacyclin, Iloprost, and Treprostinil.

In place now is a comprehensive management system for dealing with pulmonary hypertension from any cause, with Pulmonary thromboendarterectomy now having been performed successfully by Professor Keogh's group for over 18 months.

#### O'Rourke Laboratory

The aim of Professor Michael O'Rourke's research group is to understand the principles underlying pulsatile blood flow in the circulation, and its application to human aging and disease. In the process. they aim to understand the secrets of how the heart and circulation have adapted to each other in young humans and all animals.

In 2011, a number of highlights included publication of McDonald's Blood Flow in Arteries, 6th edition (edited by Professor O'Rourke), 50 years after the first edition in 1960, as well as validation of a mechanistic theory on the ill effects of aortic stiffening with age on the brain, and the progression of a method for destiffening the aged aorta.

#### Muller Laboratory

Under the leadership of Associate Professor David Muller, this program investigates new treatments to prevent, treat and reverse coronary artery disease and prevent heart attacks, particularly in patients who have received a heart transplant.

# Cardiac Physiology & Transplantation Division

Improving heart transplants Saving more lives



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#### Harvey Laboratory

The heart is a muscular pump under complex electrical and hormonal control, and it must continue to beat and respond flawlessly to the many demands of life. The Harvey laboratory investigates both the origins of the heart, as well as how this may go wrong in children with structural heart disease. The laboratory also investigates how the heart maintains itself after wear and tear, injury or infection through the action of stem cells. The heart arises from a small group of naive cells in the embryo

that form a muscular tube and begin to beat. A process of tissue specialisation and growth lead to the adult structure. Understanding the genes and molecular pathways that shape the heart is the focus of the laboratory that works at the molecular, cellular and whole organ levels. Many of the processes of the developing heart are also used again by stem cells in the adult heart and understanding these processes will most certainly give clues to how we might coax the heart to regenerate after severe injuries such as heart attack.

The group's biggest highlight of 2011 was a publication in the prestigious journal, Cell Stem Cell, describing a new population of stem cells in the adult heart and that they arise within the naive progenitor fields of the embryo. The group also described the action of one of the genes that functions in the early developing heart as a "decision-maker", setting the size of the heart and its trajectory of specialisation into muscles and vessels. This was published in the Journal of Cell Biology.

#### **Dunwoodie Laboratory**

Around 3 per cent of all babies are born with a birth defect. Defects of the heart are the most common form of birth defect representing a third of the total. Despite the fact that congenital heart disease (CHD) is so common, in around 80 per cent of cases, the cause is unknown. The Dunwoodie Laboratory's research aims to identify the causes of CHD and other birth defects, with It is clear that gene alterations and environmental factors are the main contributors to birth defects.

In 2011, amongst a number of highlights, the group published research in the international journal Human Molecular Genetics, after discovering a new group of genes that could be defects in children. They found that as well as genes that are active in the heart as it forms, genes not directly involved in the development of the heart may also cause a congenital heart defect. The research could help identify a far greater range of causes for CHD and underpin better treatment for patients.

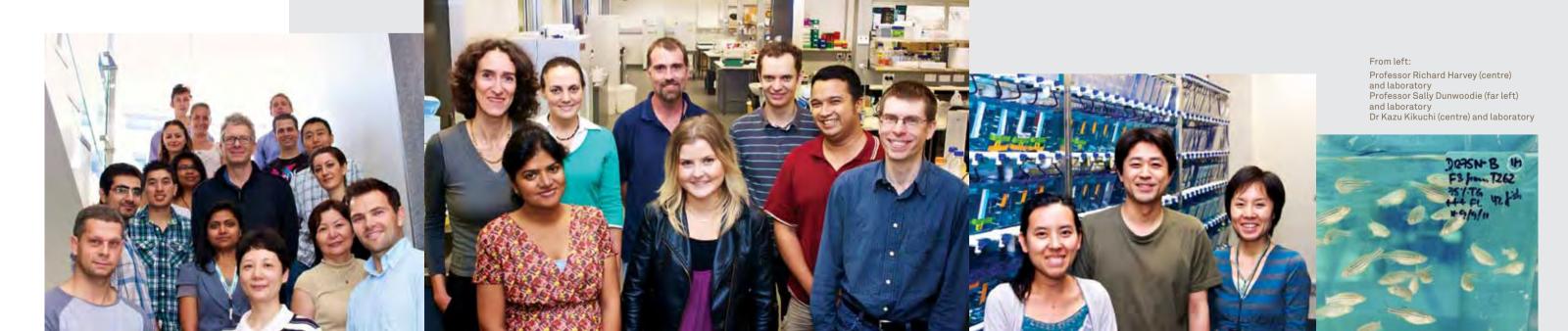
Amongst other highlights, the awarding of the degree, Doctor of Philosophy (PhD) to Stanley Artap who worked in the Dunwoodie laboratory for 5 years, was significant. Dr Artap, conducted research into the role of the Cited2 gene in causing defects in embryonic development, and now takes up a prestigious postdoctoral position at the Harvard Medical School in the USA.

#### Kikuchi Laboratory

An exciting new addition to the Victor Chang Cardiac Research Institute in 2011 was a research program under the leadership of Dr Kazu Kikuchi, who moved responsible for causing heart to Sydney after postdoctoral training in the US. In the human heart, damaged heart muscle is replaced by scar tissue, instead of undergoing regeneration. This significantly reduces cardiac function and increases susceptibility to heart failure. Unlike mammals and indeed humans, zebrafish fully regenerate heart muscle after injury. Dr Kikuchi's group studies the molecular and cellular regulations of heart muscle regeneration in zebrafish, with a long-term objective of providing novel insights into how regeneration might be enhanced in the human heart.

# **Developmental** & Stem Cell **Biology Division**

What can we learn from the beginnings of life?



Annual Report 2011

"The need for greater knowledge into what causes and ideally what can treat and cure childhood heart disease has never been greater."

#### Sally Dunwoodie

Head of Embryology Laboratory

#### **Discovery in Focus**

# Shedding new light on congenital heart defects.

**Dunwoodie Laboratory** 

Sally Dunwoodie was promoted to full Professor in 2011. A significant achievement, as the first female faculty member at Victor Chang to have done so. As Head of the Embryology Laboratory, she also led a team of researchers to some important discoveries in 2011, publishing papers in journals of the highest international distinction.

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In 2011, Sally and her group discovered a new group of genes that could be responsible for causing heart defects in children, which affect more than 2000 babies born each year in Australia.

They found that as well as genes that are active in the heart as it forms, genes not directly involved in the development of the heart may also cause a congenital heart defect. Their findings were reported in the prestigious international journal Human Molecular Genetics.

In Australia, heart disease is the leading cause of childhood death, accounting for 30 per cent of deaths in children under five.

Heart disease in children can range from a relatively simple hole in the heart, to a highly complex range of conditions that can either cause the developing baby to die in the womb, or can severely affect the heart's rhythm and blood flow.

Professor Dunwoodie says the discovery could help identify a far greater range of causes for congenital heart defects (CHD), underpinning better treatment for patients and improving genetic counselling for families. "Cures for heart disease in children are rare. A number of surgical techniques are available to improve quality of life for kids with heart disease, but in many cases this involves massive and repeated surgery on tiny babies. So early intervention and genetic testing to see if family members are likely to have a baby with a heart defect, are where the real differences are going to be made."

It is estimated up to 20 per cent of heart defects are linked to specific gene abnormalities, but for the remaining 80 per cent, the cause is largely unknown.

"Up until now, scientists around the world have identified gene abnormalities, or mutations, in a number of cases of CHD, by looking at those genes that are active in the heart as it's developing — the logical place one would search.

"What our research shows, is that we now must widen that search, to include genes that are active outside the heart as it forms, elsewhere in the embryo, because they may also impact on the heart's formation," continued Professor Dunwoodie.

There are currently up to 32,000 adult survivors in Australia who were born with CHD, with their offspring having a much greater risk of developing heart disease at birth. The number of adult survivors of childhood heart disease is increasing steadily at a rate of 5 per cent per year.

"The need for greater knowledge into what causes, and ideally what can treat and cure childhood heart disease, has never been greater," concluded Professor Dunwoodie.



#### Richard Harvey

Deputy Director and Head of the Developmental and Stem Cell Biology Division

**Discovery in Focus** 

# On the cutting edge of stem cell research.

Annual Report 2011

Harvey Laboratory

Professor Richard Harvey, Deputy Director of the Victor Chang Cardiac Research Institute, and Head of the Developmental and Stem Cell Biology Division, is what one might call an international 'superstar' in the world of developmental biology.

Amongst a number of world first discoveries, such as identifying one of the most important genes that cause birth defects in babies, in 2011 his group identified a new population of adult stem cells in the heart. The research, published in the prestigious international journal Cell Stem Cell, could pave the way to advancing the development of new regeneration and repair therapies for people who have suffered heart attack or heart failure; the leading cause of death in Australia.

Heart disease claimed the in 2009, killing one Australian every 23 minutes.

The findings come following reports in scientific literature and news media that stem cells harvested from human hearts during surgery show promise for reversing heart attack damage.

Professor Harvey says the findings, which used the mouse as a model system, are hugely promising.

"The first part of our study was actually the discovery and characterisation of a new population of multi-potent, adult stem cells that live in the heart – that is, stem cells that are extremely powerful in dividing, and responding to their native environment to form whatever tissue is needed for repair.

"The fact that this new group lives of over 22,500 Australians of cells are multi-potent, and of cells are very high up in highly specific to the heart, gives us great hope that when can generate a number of we translate these cells into the human setting, they will work well at regenerating and repairing a broken heart – or a heart that has suffered injury through heart attack or heart failure."

> This is the first time this new population of stem cells has been formally described, and its origins clearly defined.

Regeneration therapies involve 'waking up' resident stem cells and stimulating them to migrate to the site of injury in the organ or tissue itself. This differs from cell therapies in which stem cells are extracted from the heart and grown in a tissue culture dish before being directly injected or infused into the damaged area.

"We believe this population the stem cell hierarchy, and progenitor cells that would exist in a healthy heart, ready for action. This could bode very well for regeneration therapies that are just beginning to be trialed around the world with other populations of stem cells," added Professor Harvey.



#### Graham Laboratory

Professor Robert Graham's laboratory studies adrenergic receptor structure and function, and their regulation of heart contractility – these are proteins on the surface of many cells, including heart muscle cells, that respond to the stress hormones. adrenaline and noradrenaline. Activation of these receptors during times of stress, the so-called "fight or flight response", is critical for our survival. Nonetheless. excessive stimulation of

these receptors can cause abnormal heart rhythms, high blood pressure and excessive thickening of heart muscle. In 2011, the group reported on the detailed structural analysis of these and other cell surface receptors, which revealed for the first time that the ability of these protein structures to fold themselves correctly, which is required for their proper functioning, is energetically determined work reported in the international journal, Journal of Structural Biology.

In an additional paper published in the prestigious journal, Cardiovascular Research, the group reported the discovery of a novel pathway inside the cell that couples one particular type of adrenergic receptor to its ability to increase heart muscle cell contractility. Another major focus of the

Graham laboratory, is the use of stem cells and the activation of the innate regenerative ability of heart muscle cells, to promote repair of the heart injured by such diseases as a heart attack. In collaboration with colleagues in the US (Professor Husain), the Graham laboratory has identified a protein, the c-kit tyrosine kinase receptor, that is responsible for heart muscle cells losing their ability to regenerate soon after birth. Inactivating this receptor may thus allow our hearts to repair themselves properly after injury, just as our livers can.

#### Fatkin Laboratory

Associate Professor Diane Fatkin's laboratory investigates the role of gene mutations in two common heart diseases, dilated cardiomyopathy and atrial fibrillation.

Dilated cardiomyopathies (dilated = enlarged, cardio = heart, myo = muscle, and pathy = disease) are conditions that primarily affect heart muscle leading to enlargement or dilatation of the heart. When the heart enlarges, its pumping action becomes weaker and less blood is pumped around the body. Atrial fibrillation is a type of heart beat irregularity where the heart beats both fast and abnormally.

The Fatkin Laboratory has made significant progress this year by discovering that early signs of familial dilated cardiomyopathy may be detected by echocardiographic screening. In particular, enlargement of the left ventricle (one of the heart chambers) in asymptomatic family members can indicate an increased risk of progressing to dilated cardiomyopathy within a 5-year period. To start to address the

question of how dilated cardiomyopathy may be prevented in these family members, the group studied a mouse model and found that administration of the beta-blocker drug, carvedilol, from an early age effectively reduced disease development. Preliminary findings in a pilot clinical trial using carvedilol in asymptomatic family members with left ventricular enlargement show promising results for beneficial effects in humans. This study was the first to look at any type of treatment for asymptomatic relatives in familial dilated cardiomyopathy. The ultimate aim of these studies is to identify family members at risk of developing the disease and to act at an early stage so that dilated caridiomyopathy is prevented.

#### Vandenberg Laboratory

The efficient pumping of blood by the heart depends on the carefully coordinated spread of electrical impulses through every cell in the heart. If this process becomes disordered, even in just one part of the heart, it will no longer pump blood efficiently and may even stop altogether. The aim of the work in the Mark Cowley Lidwill Research Program in Cardiac Electrophysiology, led by

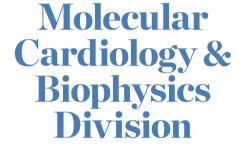
Professor Jamie Vandenberg. is to investigate situations where these electrical impulses become disordered, and to understand the causes of such conditions.

In 2011, Professor Vandenberg group published a landmark paper in the journal, Nature Structural and Molecular Biology, describing the operation of the 'gates' that effectively open and close the hERG K+ channel, a protein important for regulating the rhythm of the heartbeat. They also developed a Graphics Processor Unit (GPU) for modelling the spread of electrical signals in anatomically accurate models of the heart.

In 2011, Adam Hill was promoted to Group Leader and founded the Computational Cardiology Research Group within the Mark Cowley Lidwill program in cardiac electrophysiology. His research uses novel computational and experimental tools to help us understand why, when and in whom cardiac rhythm disturbances occur. In the past year his work has helped understand the function of ion channels – the molecular machines that underlay cardiac electrical waveform. He has also developed new computational algorithms to facilitate tissue and organ level simulations of the heart that are being used to help understand and predict arrhythmic outcomes in people with inherited ion channel defects.

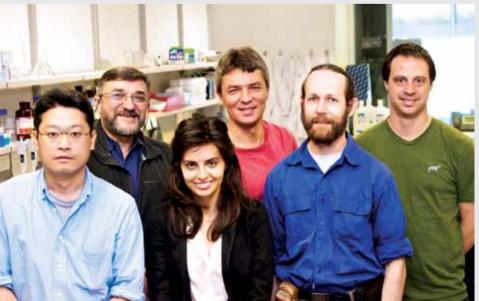
#### Martinac Laboratory

Humans and animals are able to perceive vibrations when they hear something or something touches our skin. Even our heart cells can tell when something is touching them. When the heart is beating and pumping blood. its cells feel the motion and respond by sending an electrical current throughout the heart. This electrical current is made possible by a type of protein - called an ion channel - which sits in the membrane of the cells and regulates the flow of current. An ion channel acts like a tap on a hose, opening to let ions flow through the membrane of a cell, and closing to shut off the electrical current. The Martinac laboratory studies the role and regulation of those specific ion channels that respond to mechanical forces acting on the membrane of heart cells, as they are important targets for drugs. Understanding these proteins should provide new and better means to treat diseases, such as cardiac hypertrophy, or an abnormally enlarged heart. In 2011, the Martinac lab published two feature articles on such ion channels that react to pressure in bacteria, in the internationally acclaimed Biophysical Journal. They also secured funding for a new collaborative project with a group at the Friedrich-Alexander University in Erlangen, Germany, to understand how these channels work in the heart cells in both health and disease.



How does the heart pump and flow? How do our genes affect our heartbeat?





From left: Professor Bob Graham (back centre) Professor Boris Martinac (back left) and laboratory

"In time this research should allow patients the freedom and peace of mind to take their medication without the fear of their heart suddenly stopping."

#### Jamie Vandenberg

Deputy Director and Head of the Electrophysiology Laboratory.

#### **Discovery in Focus**

# Unlocking the 'gates' on sudden cardiac death.

Vandenberg Laboratory

It's estimated around 40-50 per cent of all drugs in development will block one of the main 'channels' that carries electricity in the heart and, as a result, can cause heart rhythm problems called cardiac arrhythmias. Most sudden cardiac deaths are caused by cardiac arrhythmias. "Depending on the position

Since 1996, nine drugs have been withdrawn from the market or had their use severely restricted due to this serious side effect.

In 2011, Victor Chang scientists, led by Deputy Director Professor Jamie Vandenberg, published research that will bring us a step closer to understanding how the rhythm of the heartbeat is controlled and why many common drugs, including some antibiotics, antihistamines and antipsychotics, can cause this potentially fatal abnormal heart rhythm.

The paper, published in the prestigious journal Nature Structural and Molecular Biology, discovered a key clue as to why this happens, by understanding how the 'gates,' which effectively 'open' and 'close' the channel, operate.

of these gates, many common drugs bind, or attach themselves to these channels, blocking the ions from passing through. This causes what we call Long QT syndrome, where the length of the heart beat is longer than usual, which greatly increases the risk of arrhythmia."

The group of drugs most commonly associated with this side effect are antipsychotic drugs, taken by patients with schizophrenia and other psychiatric disorders. Patients taking these drugs are up to three times more likely to die of sudden cardiac death due to an abnormal heart rhythm.

The team studied the hERG potassium channel, an ion channel that determines how long each heart beat lasts and the channel which is most susceptible to being 'blocked' by drugs.

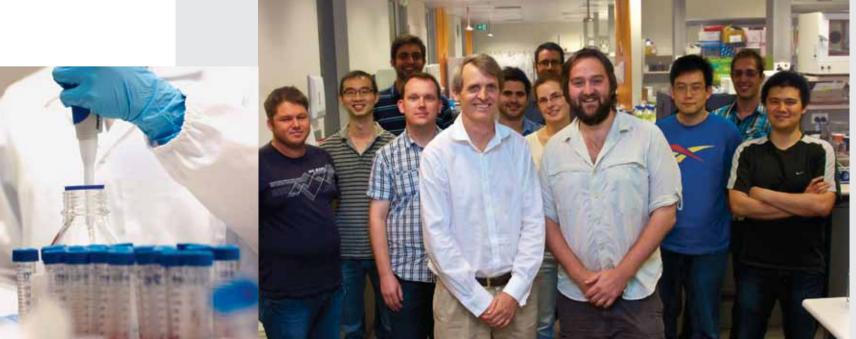
"The hERG channel is a particularly 'sticky' channel, in that most drugs will bind to it when the outer gate is closed. What we've done is to discover how these outer gates operate, in the hope that we can then design drugs more effectively to minimise the unwanted side effects," said Professor Vandenberg.

The team suspects this 'gate mechanism' will also apply to other channels that are important in the heart's electrical system, as well as those that control electrical communication in the brain.

"The biggest benefit of this research is that it should allow the better design of drugs so they no longer block these important electrical channels in the heart. In time, this should allow patients the freedom and peace of mind to take their medication without the fear of their heart suddenly stopping."







#### Diane Fatkin

Head of the Inherited Heart Diseases Laboratory

#### **Discovery in Focus**

# Putting prevention at the forefront of dilated cardiomyopathy.

**Fatkin Laboratory** 

Diane Fatkin and her team of researchers in the Inherited Heart Diseases Laboratory, set out on one of the largest cohort studies in the world into an inherited form of

Associate Professor

in 2011.

heart disease in 2000, and successfully published their results in Circulation Cardiovascular Genetics

They revealed some of the early markers for developing familial dilated cardiomyopathy (FDCM) a major risk factor for heart failure, stroke and chronic illness, and the most common cause of heart transplantation.

Dilated cardiomyopathy is a problem with the heart muscle, where the pumping action of the heart becomes weak. It's an increasing problem and its prevalence increases with age.

Gene changes that are

Victor Chang Cardiac Research Institute

inherited in families are an important cause of dilated cardiomyopathy, but there is very little known about what these genes are and how they cause impairment of heart function. Identifying the genetic causes of dilated cardiomyopathy as well as clinical markers of early disease provides a real possibility of early intervention for asymptomatic family members at risk of developing the disease in the future that is, relatives with no apparent symptoms.

The study, carried out in St Vincent's Hospital, looked at over 600 asymptomatic relatives. It is one of only a few international studies on the subject, and the second largest cohort study of its kind in the world.

Associate Professor Fatkin says through this study, preventative measures can be at the forefront of this disease.

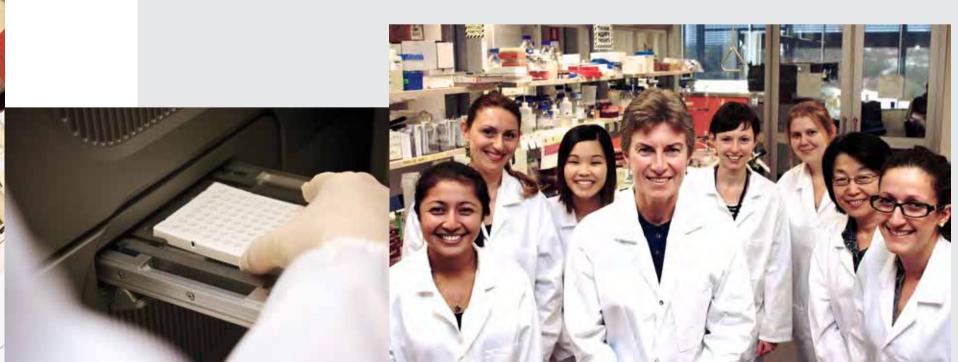
"This research will allow us to better define the high risk groups for dilated cardiomyopathy, so that we can identify those that are most likely to develop the condition, and start to look at preventative measures through garden variety screening methods.

"What it really boils down to is collaboration with clinicians at if you have a family history of dilated cardiomyopathy, you need to be screened - even if you or your relatives have no apparent symptoms. We also identified that dilation of the left ventricular chamber is an early marker, so those are the people we really need to be following up closely also.

Annual Report 2011

"We now want to carry out a larger, long-term trial in this population to find ways to prevent dilated cardiomyopathy, rather than waiting for symptomatic severe disease to develop," added Associate Professor Fatkin. "This will deliver real health benefits to families and cost benefits to the community."





Diane Fatkin (centre) and laboratory

#### Suter Laboratory

Epigenetic "marks" sit on top of our genes – like lights on a Christmas tree – dictating which genes are switched 'on' or 'off', in a given cell. Epigenetics is the process that allows our genome to create all the different cell types in our bodies. These marks are laid down as we develop in the womb, and sometimes the marks can be placed incorrectly, leading to important genes being switched on or off inappropriately. The Epigenetics Laboratory is

interested in understanding how a mother's diet during pregnancy can influence the correct setting of epigenetic marks, that may in turn influence the health of her children, and even grandchildren, in their adult life.

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In 2011, the Epigenetics laboratory published a paper in the prominent genetics journal PLoS Genetics, showing how vitamin supplementation during pregnancy causes widespread epigenetic changes in the offspring. Now the lab is investigating whether epigenetic changes might also be induced by maternal obesity and diabetes during pregnancy a highly relevant problem with our increasingly overweight population.

With the upgrade of their next-generation sequencing machine in 2011, the Suter Lab will be able to examine epigenetic marks genomewide faster and more economically than ever before.

#### Preiss Laboratory

The genes in our DNA contain a code to instruct the cell on how to produce protein molecules, which are the "workhorses" of the cell, carrying out all the functions necessary for life. How does the cell convert DNA into working proteins? The cell converts DNA into an mRNA copy and then translates this into a protein product, a process called protein translation.

The RNA Biology laboratory investigates how the cell controls protein translation from individual genes. The researchers study how tiny bits of genetic material – called microRNAs (or non-coding RNA) – bind to particular sections of our genes and block the cell from producing proteins. This works in a similar way to the controller of an assembly line, who coordinates the speed of production along the line to make sure the overall process works smoothly. In recent years, microRNAs have become a hot topic in research – it is hoped that we might someday take advantage of the microRNA system to control diseases such as cancer and heart disease that can be caused by problems in the protein production machinery.

Failure to properly regulate the translation of specific mRNAs is also linked to a growing spectrum of diseases. importance of control of The RNA Biology laboratory investigates the control of gene translation in mammalian and yeast cell culture models and employs a cooperated in several nextmix of conventional molecular biology approaches as well as cutting edge methods such as next generation gene sequencing.

In 2011, the RNA Biology laboratory published a paper demonstrating the protein translation for our understanding of the role of non-coding RNA. Dr Preiss and Dr Suter have further generation sequencingbased projects.

Dr Preiss recently accepted a position as Professor of RNA Biology at The John Curtin School of Medical Research, The Australian National University, and his laboratory now resides in Canberra.

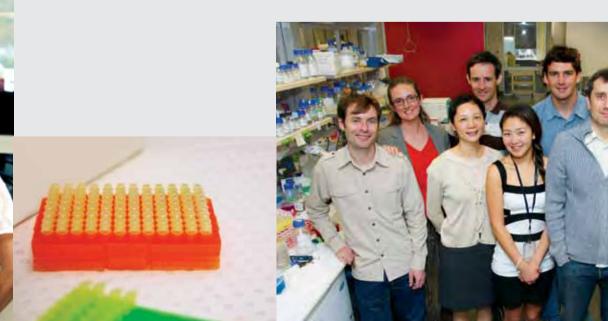
### Molecular **Genetics Division**

Like lights, genes can be switched on and off. How does this make you, you?



Dr Cath Suter (far right) and laboratory (front centre) and laboratory







"What this research tells us is that we can change or modify how our genes behave 'epigenetically'. We found differences at thousands of genes in response to a dietary change."

#### Cath Suter

Acting Head of Molecular Genetics Division

**Discovery in Focus** 

# Genetic revolution – how diet can affect our genes over many generations.

**Suter Laboratory** 

Cath Suter has carved out a name for herself as an international leader in the burgeoning field of research known as 'Epigenetics'.
Epigenetics is the study of what genes are doing, how they are behaving, which ones are switched 'on' and which are switched 'off', and is believed to determine our future susceptibility to developing disease.

In 2011, Suter's group made an important evolutionary discovery, published in PLOS Genetics, about how exposure to a certain diet over many generations, can have a long-term effect on how we are genetically programmed.

"Most of us know by now that our genes and DNA are passed on from one generation to another, however it's commonly believed that it's just pot luck as to what we're born with," said Dr Suter, who heads up the Epigenetics Laboratory in the Molecular Genetics Division of the Victor Chang Cardiac Research Institute.

"What this research tells us however, is that we can actually change or modify how our genes behave 'epigenetically'. We found differences at thousands and thousands of genes in response to a dietary change," added Dr Suter.

Using a mouse model, scientists fed their subjects a vitamin supplement that was high in folate, vitamin B12, thiamine and zinc, and were compared to two control groups; one that was fed a normal diet, and the other fed the vitamin supplement for either one generation or many generations.

They found the genetically identical mice that were exposed to the vitamin supplement had significant 'epigenetic' changes to their entire genome, and that this was magnified through generations.

The group that were fed a normal diet, had epigenetic changes that were only very subtle.

Dr Suter said the finding, which is a world-first, could explain why some populations have a greater risk of developing some types of diseases.

"To put this into context, someone living with a Western diet, compared to someone who grew up in centuries of an Asian or Eastern diet, will have largely exaggerated epigenetic differences if their parents, grandparents, greatgrandparents and beyond, all ate the divergent diet – in a human sense, this would be hundreds of years."

The research is part of a larger study that looks into how maternal nutrition can affect the future disease susceptibility of offspring.







#### Structural Biology Laboratory X-ray crystallography gives

The Structural and Computational Biology Division uses complementary approaches to biomedicine that integrate the very latest in computing and technology. Dr Daniela Stock heads the Division and her laboratory uses X-ray crystallography and other techniques to determine the structure of proteins and protein complexes at high resolution.

us very high resolution images of molecules that allow us to see the precise atomic positions of the atoms within a protein. The Stock Laboratory has recently made world first discoveries using our state-of-the-art X-ray crystallography machine that show how bacteria move through fluid and can change their paths to swim towards nutrients and away from hazards. A highlight of this year was a collaboration with Oxford University that used a technique called mass spectrometry to reveal the structure and lipid composition of ATP synthase, a critically important enzyme that provides our cells with energy. The research will help understand diseases involving ATP synthase, which can affect heart, brain and muscle function, as well as temperature regulation and ageing.

#### In 2011, Stock laboratory member Dr Lawrence Lee was promoted to a Group Leader. Lawrence now runs his own research program within the Structural and Computational Biology division, focusing on understanding the dynamics and structure of protein complexes. These are the biological machines that work constantly to keep our cells, tissues and organs functioning normally. His group has attracted the interest and expertise of leading national and international scientists in structural biology, biophysics and nanotechnology, to establish new and interdisciplinary methods to study these biological machines.

# Structural & Computational Biology Division

What secrets can we uncover from the most basic units of life?



"One of the most important discoveries in basic biological research around the world in 2011."

#### Professor Robert Graham AO

Executive Director of the Victor Chang Institute

#### **Discovery in Focus**

# A quantum leap in understanding key cell structures.

Stock Laboratory

At the Victor Chang Cardiac Research Institute, as Head of the Structural and Computational Biology Laboratory since 2006, Dr Daniela Stock's group focuses on structural biology, in particular X-ray crystallography of proteins. This technique creates very high-resolution pictures of proteins, to determine their structure, at near atomic resolution. Seeing medically important proteins at such resolution often helps to understand how they work or why they don't work, and what needs to be done to fix them, which is vital in the design of effective drugs.

Amongst a number of significant career highlights, Daniela published a paper in the prestigious journal Science in October 2011.

The study has been described as one of the most important discoveries in basic biological research around the world in 2011.

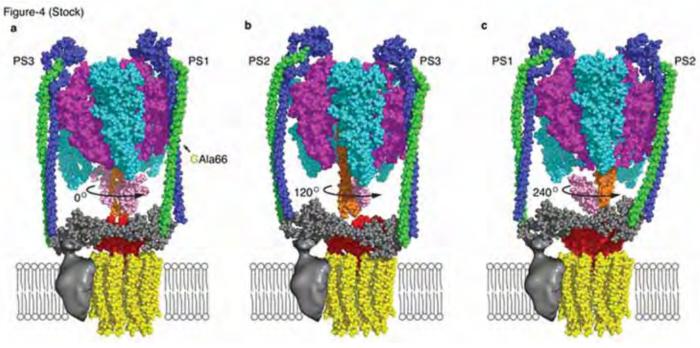
The landmark discovery provides not only new insights into the structure and function of the energy converting protein, ATP synthase, but introduces a generic new method to study the interaction of proteins with lipids and drugs in unprecedented detail.

Using high-end mass spectrometry, Dr Stock in collaboration with Dr Carol Robinson and her colleagues at Oxford University in the United Kingdom, determined for the first time how this protein interacts with the critical fatty acids that form the membrane around our cells. The research will help understand diseases involving ATP synthase, which defects in our body's energy can affect heart, brain and muscle function as well as temperature regulation and ageing.

Knowing how much lubrication is needed for ATP synthase to operate efficiently is critical to understanding how it converts the energy stored in the food we eat to provide the fuel for our cells to live and function.

"No one in the world has ever done mass-spectrometry in such a sensitive and sophisticated way before this is an incredible coup. While basic in nature, this discovery will aid enormously in the future of applied and clinical research right around the world, as well as helping us understand major diseases caused by converting machinery," said Professor Robert Graham of the research.





#### Awardees and Achievements 2011

The future is bright for our researchers, many of whom were awarded accolades of the highest honour in 2011.

Sally Dunwoodie was promoted to full Professor by the University of NSW.

Boris Martinac was awarded the Bob Robertson Medal at the BioPhysChem2011 Symposium for his major contributions to research and teaching of Biophysics in Australia. He was also selected as the Peter Lauf Lecturer at the International Congress on Hydration and Cell Volume Regulation held in Tuebingen, Germany in September, for outstanding achievements in research on mechanosensitive ion channels.

Richard Harvey was honoured by being asked to present the Basic Science Lecture at the **Annual Scientific Meeting** of the Cardiac Society of Australia and New Zealand, Perth in August.

Lawrence Lee, Stock Laboratory, and Adam Hill, Vandenberg Laboratory, were promoted to Group Leader positions for their outstanding research achievements.

Adam Hill and Kazu Kikuchi were awarded Australian Research Council (ARC) Future Fellowships and Jen Cropley, Suter Laboratory, received an ARC Discovery Early Career Researcher Award (DECRA).

Lawrence Lee, Stock Laboratory, was selected out of 160 international applicants as a New & Notable Symposium Speaker at the American Biophysical Society Annual Meeting, Baltimore, USA, in March.

Alastair Stewart, Stock Laboratory, was awarded the AAAS Program for Excellence in Science Award.

Nicola Smith, Graham Laboratory, was selected as an outstanding young researcher and communicator for which she received a 2011 NSW Young Tall Poppy Science Award.

Naisana Asli, Harvey Laboratory, was the winner of the Postdoctoral Poster Award at the Australasian Society of Stem Cell Research Meeting.

Robert Graham was honoured by election to Life Membership of the NSW Division, Heart Foundation of Australia.

#### Degrees Awarded

Six people successfully completed and were awarded PhD degrees from UNSW. including: Leah Cannon and Li Sze Yeo (Fatkin Lab), James Chong (Harvey Lab), Cheryl Li (Suter Lab), Alex Shaw (Preiss Lab), and TingWai Yiu (Graham Lab/Iismaa).

Mrs Ann Chang (2004) The Hon. Neville Wran Ac QC (2008)Past Patron

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Our voluntary Committee Members, Patrons, Life Governors,

Ambassadors, Life Members, Donors and Supporters are the

heart and soul of the Victor Chang Institute. Their dedication,

unconditional. We thank them for their generosity, enormous time and the expertise they provide so willingly and freely.

commitment and encouragement of our research is

Mr Ziggy Switkowski (2003) Mr Sam Chisholm (2003)

> ANZ Bank (2004) Citigroup (2005)

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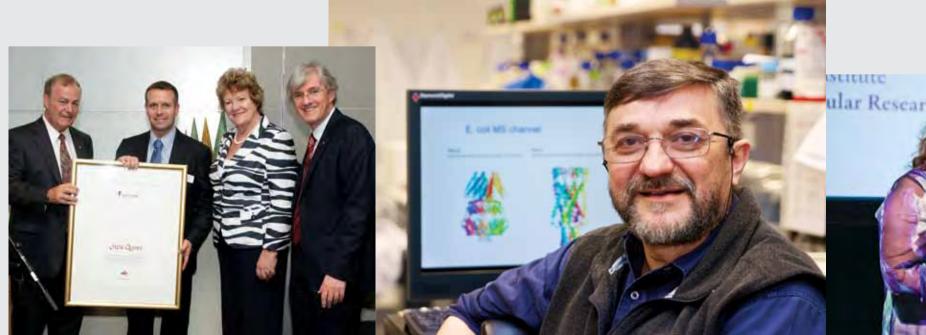
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Young Ambassador Mr Mark Vincent (2009)





Professor Robert Graham, Paceline founder Steve Quinn, the Hon. Jillian Skinner MP and Chairman Steven Lowy. Professor Boris Martinac Dr Nicola Smith receiving the 'Young Tall Poppy' award.

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#### Paul Korner Seminar Series

The Paul Korner Seminar Series are presented weekly, providing our young scientists the opportunity to present an update of their research progress and achievements.

The Series was established in 1998 to recognise the outstanding contributions of Professor Paul Korner, a pioneer of cardiovascular research in Australia.

#### David Humphreys

"A comprehensive profile of microRNAs in murine cardiomyocytes."

#### Adam Hill

"The electrical jigsaw: Putting together the pieces of Long QT syndrome."

#### Ming Li

"Manipulating cardiomyocyte (CM) terminal differentiation for CM regeneration."

#### Jennifer Cropley

"Epigenetic variation and the dietary programming of latent Hardip Patel disease risk.'

#### Siiri Iismaa

"The key to the multiple functions of Transglutaminase "Biological rotary motors -2: location, location, location."

#### Vesna Nikolova-Krstevski

"The role of Endocardial Endothelium in the development of Atrial Fibrillation."

#### Ling Gao

"Enhanced pro-survival signaling by Phosphatase Inhibition – A potential strategy for improving preservation of marginal donor hearts."

#### Romaric Bouveret

"At the heart of systems biology."

#### Matt Perry

"Unraveling the molecular mechanisms of hERG channel gating."

#### Tekashi Nomura

"Stretching MscS and MscL: The origin of mechanosensitivity in acterial mechanosensitive channels."

#### Jeff Squires

"Discovery of 5-methylcytosine sites in mRNA and noncoding RNA by next-generation sequencing."

"High-throughput sequencing: applications and outcomes."

#### Lawrence Lee

Taking high-resolution structure in vivo."

#### Danielle De Jong

"A needle in the systems biology haystack."

#### Simon Keam

"Piwi and piRNAs: A role in somatic gene silencing?"

#### Dhakshinari Hulugalle

"Computational investigation of the association between Zn2+ sites and redox active disulfides in protein structures."

#### Nicola Smith

"Unravelling the pharmacology of low affinity GPCRs: Free Fatty Acid receptors 2 & 3."

#### Alastair Stewart

"The dynamic stator stalk of A-type ATPases."

#### Sara Ballouz

"Missingness", mutants and meta-analysis: candidate disease gene prediction in the genomics age."

#### **Duncan Sparrow**

"Congenital scoliosis: getting to the heart of the problem."

#### **Evgeny Petrov**

"Studies of bacterial mechanosensitive channels under high hydrostatic pressure."

#### Alex James

"Exploring an inhibitory role for the Notch4 receptor in angiogenesis."

#### Juliane Heide

"hERG's split personality."

#### Mahdi Moradi

"Genetic complexity underpinning Atrial Septal Dysmorphology.'

#### Alexandra McCorkindale

"The Piwi/piRNA pathway: an unexpected role in potency."

#### Li Xin "The study on cardiac-specific Nkx2-5

protein complex."

#### Marion Mohl

"The a1A-adrenergic receptor mediates cardiac hypertrophy through the Gaq/PI3K/Rac1 signalling pathway."

#### Gavin Chapman

"Ligand-induced trafficking of the Notch1 Receptor."

#### Charles Cranfield

"Clustering of the mechanosensitive ion channels MscS and MscL: A FRET-FLIM study."

#### Mirana Ramialison

"Fish 'n chips and heart development."

#### Stefan Mann

"The genetic wheel of fortune - epistatic effects of potassium channel variation on Atrial Fibrillation."

#### Carly Hynes

"At the heart of the tail: 3'UTRs and iso-miRs in cardiac hypertrophy."

#### Nicole Schonrock

"Decoding the non-coding: microRNA networks surrounding Alzheimer's disease Amyloid-beta."

#### Professor Mark Febbraio

Barbara Ell Seminar Series

Head, Cellular & Molecular Metabolism Laboratory, Head of Basic Science. Division of Metabolism & Obesity at Baker IDI Heart and Diabetes Institute

"Cvtokines, inflammation and metabolic disease: the good the bad and the ugly!"

#### Professor Susan Clark

Senior Principal Research Fellow Group Leader, Epigenetic Research Laboratory, Garvan Institute Cancer program

"Mining the cancer epigenome."

#### Professor Stephen Simpson

ARC Laureate Fellow, School of Biological Sciences, The University of Sydney

"Graphic nutrition: a tale of sex, cannibalism, ageing and obesity."

#### Dr John Taylor

This Seminar Series was named after Mrs Barbara Ell, an avid

supporter of the Institute, a Life Governor and a hard working

Each month, the Institute invites a renowned Australian Scientist

to present a lecture as a part of the Barbara Ell Seminar Series.

member of both the Board and Appeals Committee.

Director, CSIRO eResearch & Computational and Simulation Sciences Computational science and the high performance computing frontier."

#### Professor Richard Lewis

Group Leader and NHMRC Research Fellow, Institute for Molecular Bioscience.University of Queensland (UQ)

"Conotoxins: novel membrane protein probes and potential therapeutics."

#### Professor Julio Licinio

Director, John Curtin School of Medical Research College of Medicine, Biology & Environment the Australian National University

"Obesity and depression: Case examples of the search for genes of major effect and genes of small effect in common and complex disorders."

#### Dr Ethan Scott

Lecturer. School of Biomedical Sciences, The University of Queensland

"The cerebellum and motor learning: Genetic and optical strategies for studying neural circuits in zebrafish."

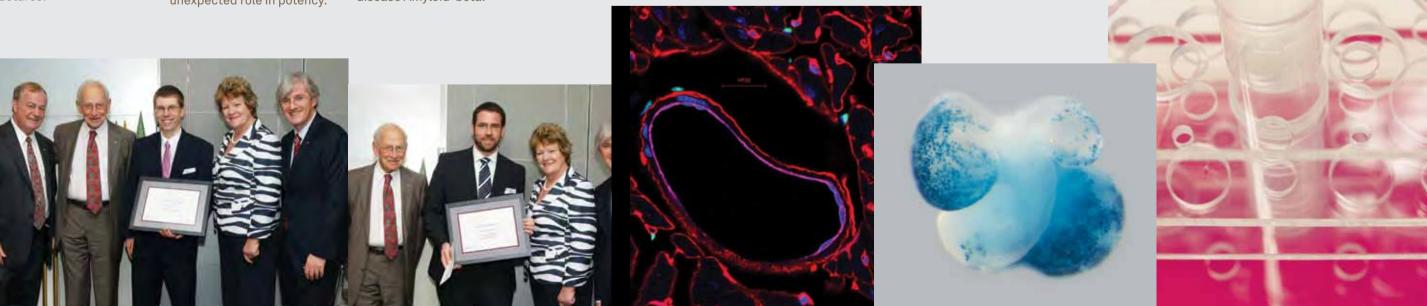
#### Dr Oliver Rackham

Head, Synthetic Biology and Drug Discovery, Western Australian Institute for Medical Research & Centre for Medical Research the University of Western Australia

"Re-engineering cellular gene expression."

#### From left: Professor Robert Graham, Professor Paul Korner, winner

Dr Duncan Sparrow, the Hon. Jillian Skinner MP and Chairman Steven Lowy. Professor Paul Korner, runner-up Dr Stefan Mann and the Hon. Jillian Skinner MP



Winner **Duncan Sparrow** 

Runner Up Charles Cranfield

People's Choice Stefan Mann

Victor Chang Cardiac Research Institute

Annual Report 2011

The Victor Chang 13th International Symposium and Princesses' Lecture in

# **A unique** coming together of brilliant minds.

conjunction with St Vincent's Hospital

In November, the winner of the 2008 Nobel Prize for Chemistry, Dr Martin Chalfie (shared with Osamu Shimomura and Roger Y. Tsien), delivered the 2011 Victor Chang Princesses' Lecture, which honours both HRH Crown Princess Mary of Denmark and the late Diana, Princess of Wales. The lecture commenced the Victor Chang Cardiac Research Institute and St Vincent's Hospital's 13th International Symposium.

Dr Martin Chalfie, from Colombia University New York, scientists talking about delivered the public lecture on his Nobel Prize winning work on the discovery and development of the Green Fluorescent Protein (GFP) and how it has helped his team study the basic mechanisms underlying cell function.

GFP, first discovered in the jellyfish, is used as a tagging tool in bioscience, as it glows bright green when exposed to light. GFP, and now other fluorescent markers, allow scientists to look at cells in animals in real time, and discover the inner workings of living organisms that were previously invisible.

"Martin Chalfie took an interesting observation and turned it into one of the most sophisticated and effective tools for imaging biological processes, from tracking the progression of bacterial infection in mammals to looking at how cancer cells spread throughout the body," said Professor Jamie Vandenberg, Victor Chang Deputy Director and symposium organiser.

Chalfie's lecture commenced three days of the world's leading clinicians and the latest in basic science, from developing new imaging techniques for the future, right through to the application of these techniques for patient care.

One of the fifteen speakers at the Symposium was Dr Kazu Kikuchi, the Victor Chang Cardiac Research Institute's most recent faculty recruit. Dr Kikuchi is one of many scientists around the world directly benefitting from the work of Martin Chalfie, in that he uses fluorescent markers to study heart muscle regeneration in zebrafish.

Victor Chang Cardiac Research Institute

Unlike humans, zebrafish can naturally restore lost heart muscle after injury. Dr Kikuchi's lab studies how cardiac regeneration is blocked or enhanced in zebrafish and how this can be used as a model for repairing damaged muscle in the human heart after heart attack or heart failure.

"Kazu Kikuchi has taken the technology that Martin Chalfie developed and is applying it to one of the most cutting edge cardiac problems of our time," added Professor Vandenberg. "This is a unique coming together of brilliant minds, and a great example of how researchers can collaborate on a problem to strengthen the future of biomedical research and clinical care right around the world."

#### **Speakers**

Ohio (US)

Brad Amos Cambridge University,

Martin Chalfie Columbia University, New York (US)

Sally Dunwoodie Victor Chang Cardiac Research Institute Diane Fatkin Victor Chang Cardiac

Research Institute Stuart Grieve Royal Prince Alfred

Hospital (Sydney) Rory Hachamovitch Cleveland Clinic,

Cameron Holloway University of Oxford (UK)

Kazu Kikuchi Victor Chang Cardiac Research Institute

James Moon Heart Hospital

(Melbourne)

Annual Report 2011

Imaging Centre London (UK) Karlheinz Peter Baker IDI

Tri Phan Garvan Institute (Sydney)

David Prior St Vincent's Hospital, University of Melbourne

Michael Roberts Princess Alexandra Hospital (Brisbane)

Christian Soeller University of Auckland (New Zealand)

Joseph Suttie University of Oxford

Liza Thomas Liverpool Hospital and University of NSW (Sydney)

#### Company Sponsors

Out thanks to the following companies who supported the Symposium

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Leading Innovation	Sigma	
Leica	Thermo Fisher	
Lift Technologies	Toshiba	
Millenium Science	United Airlines	
Miltenvi Biotec		







From left:

Jillian Skinner MP.

Professor Robert Graham and the Hon.



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2011 Publications

# In 2011, we published papers in many of the world's leading journals.

#### Primary Papers

Adji A, **O'Rourke MF**, Namasivayam M. Arterial stiffness, its assessment, prognostic value, and implications for treatment. *Am J Hypertens*. 2011; 24:5-17.

Ballouz S, Liu JY, Oti M, Gaeta B, Fatkin D, Bahlo M, Wouters MA. Analysis of genome-wide association study data using the protein knowledge base. *BMC Genetics* 2011; 12:98.

Berger J, Berger S, Jacoby AS, Wilton SD, Currie PD. Evaluation of exon-skipping strategies for Duchenne muscular dystrophy utilizing dystrophin-deficient zebrafish. *J Cell Mol Biol.* 2011; 15:2643-51.

Baumwol J, Macdonald PS, Keogh AM, Kotlyar E, Spratt P, Jansz P, Hayward CS. Right heart failure and "failure to thrive" after left ventricular assist device: Clinical predictors and outcomes. *J Heart Lung Transplant*. 2011; 30:888-95.

Bondue A, Tannler S, Chiapparo G, Chabab S, Ramialison M, Paulissen C, Beck B, Harvey RP, Blanpain C. Defining the earliest step of cardiovascular progenitor specification during embryonic stem cell differentiation. *J Cell Biol.* 2011; 192:751-65.

Caprioli A, Koyano-Nakagawa N, Iacovino M, Shi X, Ferdous A, Harvey RP, Kyba M, Olson E, Kyba M, Garry DJ. Nkx2-5 represses Gatal gene expression and modulates cellular fate of cardiac progenitors during embryogenesis. *Circulation* 2011; 123:1633-41.

Chapman G, Sparrow DB, Kremmer E, Dunwoodie SL. Notch inhibition by the ligand Delta-Like 3 defines the mechanism of abnormal vertebral segmentation in spondylocostal dysostosis. *J Hum Mol Genet*. 2011; 20:905-916. [Cover figure]

Chiu J, Tactacan CM, Tan SX, Lin RC, Wouters MA, Dawes IW. Cell cycle sensing of oxidative stress in saccharomyces cerevisiae by oxidation of a specific cysteine residue in the transcription factor swi6p. *J Biol Chem.* 2011; 286:5204 5214.

Chong JJH, Chandrakanthan V, Xaymardan M, Asli NS, Li J, Heffernan C, Menon MK, Ahmed I, Scarlett CJ, Rashidianfar A, Biben C, Zoellner H, Colvin EK, Pimander J, Biankin AV, Zhou B, Pu WT, Prall OWJ, Harvey RP. Adult cardiac MSC-like stem cells with a proepicardial origin. Cell Stem Cell 2011; 9:527-540.

Clancy JL, Wei GH, Echner N, Humphreys DT, Beilharz TH, Preiss T. mRNA isoform diversity can obscure detection of miRNAmediated control of translation. RNA 2011; 17:1025-31. Cole N, Hall T, Don EK, Berger S, Boisvert CA, Neyt C, Ericsson R, Joss J, Gurevich DB, Currie PD. Development and evolution of the muscles of the pelvic fin. *PLoS Biol.* 2011; 9:e1001168.

Costa MW, Lee S, Furtado MB, Xin L, Sparrow DB, Martinez CG, Dunwoodie SL, Kurtenbach E, Mohun T, Rosenthal N, Harvey RP. Complex SUMO-1 regulation of cardiac transcription factor Nkx2-5. PLoS One 2011; 6:e24812.

Du H, Davidson PM, Everett B, Salamonson Y, Zecchin R, Rolley JX, Newton PJ, **Macdonald PS.** Correlation between a selfadministered walk test and a standardised six minute walk test in adults. **Nurs Health Sci.** 2011; 13:114-7.

Duque G, Li W, Yeo LS, Vidal C, Fatkin D. Attenuated anabolic response to exercise in lamin A/C haploinsufficient mice. *Bone* 2011; 49:412-418.

Dweck MR, Joshi S, Murigu T, Alpendurada F, Jabbour A, Melina G, Banya W, Gulati A, Roussin I, Raza S, Prasad NA, Wage R, Quarto C, Angeloni E, Refice S, Sheppard M, Cook SA, Kilner PJ, Pennell DJ, Newby DE, Mohiaddin RH, Pepper J, Prasad SK. Midwall fibrosis is an independent predictor of mortality in patients with aortic stenosis. J Am Coll Cardiol. 2011; 58:1271-9.

Esposito G, Butler TL, Blue GM, Cole AD, Sholler GF, Kirk EP, Grossfeld P, Perryman BM, Harvey RP, Winlaw DS. Somatic mutations in NKX2-5, GATA4 and HAND1 are not a common cause of tetralogy of Fallot or hypoplastic left heart syndrome. *Am J Med Genet*. 2011; 155:2416-1421.

Fatkin D, Yeoh T, Hayward CS, Benson V, Sheu A, Richmond Z, Feneley MP, Keogh AM, Macdonald PS. Evaluation of left ventricular enlargement as a marker of early disease in familial dilated cardiomyopathy. *Circ Cardiovasc Genet*. 2011; 4:342-8.

Furtado MB, Biben C, Shiratori H, Hamada H, Harvey RP. Characterization of Pitx2c expression in the mouse heart using a reporter transgene. *Dev Dyn.* 2011; 240:195-203.

Gao L, Tsun J, Sun L, Kwan J, Watson A, Macdonald P, Hicks M. Critical role of the STAT3 pathway in the cardioprotective efficacy of zoniporide in a model of myocardial preservation - the rat isolated working heart. *Br J Pharmacol.* 2011; 162: 633-647.

Grage SL, Keleshian AM, Turdzeladze T, **Battle AR**, Tay WC, May RP, Holt SA, Contera SA, Haertlein M, Moulin M, Pal P, **Rohde PR**, Forsyth VT, Watts A, Huang KC, Ulrich AS, **Martinac B.** Bilayer-mediated clustering and functional interaction of MscL channels. *Biophys J.* 2011; 100:1252-60.

Grandos-Riveron JT, Pope M, Bu'Lock FA, Thornborough C, Eason J, Setchfield K, Kirk EP, Fatkin D, Feneley MP, Harvey RP, Brook JD. Combined mutation screening of NKX2-5, GATA4 and TBX5 in congenital heart disease: multiple heterozygosity and novel mutations. *Congenit Heart Dis.* 2011; 7:151-159.

Hayward CS, Salamonsen R, Keogh AM, Woodard J, Ayre P, Prichard R, Walker R, Kotlyar E, Macdonald PS, Jansz P, Spratt P. Effect of alteration in pump speed on pump output and left ventricular filling with continuousflow left ventricular assist device. ASAIO J. 2011; 57:495-500.

Hoyne GF, Chapman G, Sontani Y, Pursglove SE, Dunwoodie SL. A cell autonomous role for the Notch ligand Delta-like 3 in αβ T-cell development. *Immunol Cell Biol*. 2011; 89:696-705.

Jabbour A, Hayward CS, Keogh AM, Kotlyar E, McCrohon JA, England JF, Amor R, Liu X, Li XY, Zhou MD, Graham RM, Macdonald PS. Parenteral administration of recombinant human neuregulin-1 to patients with stable chronic heart failure produces favourable acute and chronic haemodynamic responses. Eur J Heart Fail. 2011; 13:83-92.

Jabbour A, Gao L, Kwan J, Watson A, Sun L, Qiu MR, Liu X, Zhou MD, Graham RM, Hicks M, Macdonald PS. A recombinant human Neuregulin-1 peptide improves preservation of the rodent heart after prolonged hypothermic storage. *Transplantation* 2011; 91:961-7. [Cover figure]

Victor Chang Cardiac Research Institute

Keogh AM, Strange G, Kotlyar E, Williams T, Kilpatrick D, Macdonald PS, Brown K, Pidoux A, Kermeen F, Steele P, Dalton B, Gabbay E. Survival after the initiation of combination therapy in patients with pulmonary arterial hypertension: an australian collaborative report. Intern Med J. 2011: 41:235-244.

53

Keogh AM, Strange G, McNeil K, Williams TJ, Gabbay E, Proudman S, Weintraub RG, Wlodarczyk J, Dalton B. The bosentan patient registry: Long-term survival in pulmonary arterial hypertension. *Intern Med J.* 2011; 41:227-234.

Kikuchi K, Gupta V, Wang J, Holdway JE, Wills AA, Fang Y, Poss KD. tcf21+ epicardial cells adopt non-myocardial fates during zebrafish heart development and regeneration. *Development* 2011; 138:2895-902.

Kikuchi K, Holdway JE, Major RJ, Blum N, Dahn RD, Begemann G, Poss KD. Retinoic acid production by endocardium and epicardium is an injury response essential for zebrafish heart regeneration. *Dev Cell* 2011; 20:397-404.

Lawlor KT, O'Keefe LV, Samaraweera SE, van Eyk CL, McLeod CJ, Maloney CA, Dang TH, Suter CM, Richards RI. Doublestranded rna is pathogenic in drosophila models of expanded repeat neurodegenerative diseases. *Hum Mol Genet*. 2011; 20:3757-3768.

Lengkeek NA, Boulos RA, McKinley AJ, Riley TV, Martinac B, Stewart SG. The synthesis of fluorescent DNA intercalator precursors through efficient multiple heck reactions Australian J. Chem. 2011; 64:316-323.

Li CCY, Cropley JE, Cowley MJ, Preiss T, Martin DIK, Suter CM. A sustained dietary change increases epigenetic variation in isogenic mice. *PloS Genet*. 2011; 7:e1001380.

Li W, Yeo LS, Vidal C, McCorquodale T, Herrmann M, Fatkin D, Duque G. Decreased bone formation and osteopenia in lamin a/c-deficient mice. *PLoS One* 2011; 6:e19313.

Liew GYH, Feneley MP, Worthley SG. Noninvasive coronary artery imaging: Current clinical applications: Cardiac Society of Australia and New Zealand Guidelines. Heart Lung Circ. 2011; 20:425-437.

Lim HS, **Subbiah RN**, Leong-Sit P, Gula LJ, Skanes AC, Yee R, Klein GJ, Krahn AD. How to diagnose the cause of sudden cardiac arrest. *Cardiol J.* 2011; 18:210-6.

Listijono DR, Watson A, Pye R, Keogh AM, Kotlyar E, Spratt P, Granger E, Dhital K, Jansz P, Macdonald PS, Hayward CS. Usefulness of extracorporeal membrane oxygenation for early cardiac allograft dysfunction. *J Heart Lung Transplant*. 2011; 30:783-9.

Lithander FE, **Keogh AM**, Killeen L. Overweight and obesity among older adults on admission to

hospital. Ir Med J. 2011; 104:87-8.

Lopes Floro K, Artap ST, Preis JI, Fatkin D, Chapman G, Furtado MB, Harvey RP, Hamada H, Sparrow DB, Dunwoodie SL. Loss of Cited2 causes congenital heart disease by perturbing left-right patterning of the body axis. Hum Mol Genet. 2011; 20:1097-110.

Marjaneh M, Kirk EP, Posch MG, Ozcelik C, Berger F, Hetzer R, Otway R, Butler TL, Blue GM, Griffiths LR, Fatkin D, Martinson JJ, Winlaw DS, Feneley MP, Harvey RP. Investigation of association between PFO complicated by cryptogenic stroke and a common variant of the cardiac transcription factor GATA4. PLoS One 2011; 6:e20711.

Martin DI, **Cropley JE, Suter CM.** Epigenetics in disease: leader or follower? *Epigenetics* 2011; 6:843-848.

Martinac B. Bacterial mechanosensitive channels as a paradigm for mechanosensory transduction. *Cell Physiol Biochem.* 2011; 28:1051-60.

Matsui Y, Eguchi K, **O'Rourke MF**, Ishikawa J, Shimada K, Kario K. Association between aldosterone induced by antihypertensive medication and arterial stiffness reduction: The J-CORE study. *Atherosclerosis* 2011; 215:184-8.

Mohl MC, Iismaa SE, Xiao XH, Friedrich O, Wagner S, Nikolova-Krstevski V, Wu J, Yu ZY, Feneley M, Fatkin D, Allen DG, Graham RM. Regulation of murine cardiac contractility by activation of {alpha}1A-adrenergic receptoroperated Ca2+ entry. Cardiovasc Res. 2011; 91:310-9.

Namasivayam M, Adji A, **O'Rourke MF.** Influence of aortic pressure wave components determined noninvasively on myocardial oxygen demand in men and women. *Hypertension* 2011; 57:193-200.

Ng CA, Hunter MJ, Perry MD, Mobli M, Ke Y, Kuchel PW, King GF, Stock D, Vandenberg JI. The N-terminal tail of hERG contains an amphipathic -helix that regulates channel deactivation. *PLoS One* 2011: 6:e16191.

Nikolova-Krstevski V, Leimena C, Xiao XH, Kesteven S, Tan JC, Yeo LS, Yu ZY, Zhang Q, Carlton A, Head S, Shanahan C, Feneley MP, Fatkin D. Nesprin-1 and actin contribute to nuclear and cytoskeletal defects in lamin A/C-deficient cardiomyopathy. *J Mol Cell Cardiol*. 2011; 760:189-206.

Olsen KC, Sapinoro RE, Kottmann RM, Kulkarni AA, **Iismaa SE**, Johnson GV, Thatcher TH, Phipps RP, Sime PJ. **Transglutaminase 2 and its role in pulmonary fibrosis.** *Am J Respir Crit Care Med.* 2011; 184:699-707.

Oti M, Ballouz S, Wouters MA. Web tools for the prioritization of candidate disease genes. *Methods Mol Biol*. 2011; 760:189-206.

O'Rourke MF, Adji A, Namasivayam M, Mok J. Arterial aging: A review of the pathophysiology and potential for pharmacological intervention. *Drugs Aging* 2011; 28:779-95.

Pelecanos R, Li J, Gongora M,

Chandrakanthan V, Scown J, Suhaimi M, Brooke G, Christensen ME, Doan T, Rice AM, Osborne GW, Grimmond SM, Harvey RP, Atkinson K, Little MH.
Comprehensive transcriptome and immunophenotype analysis of renal and cardiac MSC-like populations supports strong congruence with bone marrow MSC despite maintenance of distinct identities. Stem Cell Res. 2012: 8:58-53.

Petrov E, Rohde PR, **Martinac B.** "Flying-patch" patch-clamp study of G22E MscL mutant under high hydrostatic pressure. *Biophys. J.* 2011; 100:1635-1641.

Qian L Wythe JD, Liu J, Gartry J, Vogler G, Mohapatra B, Otway R, Hang Y, King IN, Maillet M, Zheng Y, Crawley T, Taghli-Lamallem O, Semsarian C, **Dunwoodie SL**, Winlaw D, **Harvey RP, Fatkin D**, Towbin JA, Molkentin JD, Srivastava D, Ocorr K, Bruneau BG, Bodmer R. Conserved Cdc42 interaction with tinman/Nkx2.5 via microRNA-1 in regulating heart function. *J Cell Biol*. 2011; 193:1181-96 Riek RP, Graham RM. The Elusive  $\pi$ -Helix. *J Struct Biol.* 2011; 173:153-60.

Annual Report 2011

Schonrock N, Humphreys DT, Preiss T, Gotz J. Target gene repression mediated by miRNAs miR-181c and miR-9 both of which are down-regulated by amyloidbeta. *J Mol Neurosci*. 2011; 46:324-335

Sontani Y, Chapman G, Papathanasiou P, Dunwoodie SL, Goodnow CC, Hoyne GF. Cooperation between somatic Ikaros and Notch1 mutations at the inception of T-ALL. Leuk Res. 2011; 35:1512-9.

Squires JE, Preiss T. Function and detection of 5-methylcytosine in eukaryotic RNA. *Epigenomics* 2010; 2:709-15.

Strange G, Keogh AM, Dalton B, Gabbay E. Pharmacoeconomic evidence of bosentan for pulmonary arterial hypertension. Expert Rev Pharmacoecon Outcomes Res. 2011; 11:253-263.

Strange G, Manterfield C, Miller T, Pidoux A, Brown K, Williams T, Gabbay E, **Keogh A.** Non-parenteral therapy for pulmonary arterial hypertension: a review of efficacy, tolerability and factors related to patient adherence. Clinical Medicine Insights: Therapeutics 2011; 3:113-124.

Szekely D, Vandenberg JI, Dokos S, Hill AP. An improved curvilinear gradient method for parameter optimization in complex biological models. *Med Biol Eng Comput*. 2011; 49:289-96.

Takeuchi JK, Lou X, Alexander JM, Sugizaki H, Delgado-Olguin P, Holloway AK, Mori AD, Wylie JN, Munson C, Zhu Y, Zhou Y, Yeh R-F, Henkelman RM, Harvey RP, Metzger D, Chambon P, Stainier DYR, Pollard KS, Scott, IC, Bruneau BG. Chromatin remodelling complex dosage modulates transcription factor function in heart development. Nature Commun. 2011; 2:187-198.

Tay AE, Faddy S, Lim S, Walker BD, Kuchar D, Thorburn CW, Macdonald PS, Keogh AM, Kotlyar E, Farnsworth A, Hayward CS, Jansz P, Granger E, Spratt P, Subbiah RN. Permanent pacing for late-onset atrioventricular block in patients with heart transplantation: A single center experience. Pacing Clin Electrophysiol. 2011; 34:72-75.

Tong J, Li W, Vidal C, **Yeo LS, Fatkin D,** Duque G. Lamin A/C deficiency is associated with fat infiltration of muscle and bone. *Mech Ageing Dev.* 2011; 132:552-9.

Victor Chang Cardiac Research Institute 54 Annual Report 2011

Wang DT, Hill AP, Mann SA, Tan PS, Vandenberg JI. Mapping the sequence of conformational changes underlying selectivity filter gating in the K(v)11.1 potassium channel. Nat Struct Mol Biol. 2011; 18:35-41.

Wang J, Panáková D, Kikuchi K, Holdway JE, Gemberling M, Burris JS, Singh SP, Dickson AL, Lin YF. Sabeh MK. Werdich AA. Yelon D, Macrae CA, Poss KD. The regenerative capacity of zebrafish reverses cardiac failure caused by genetic cardiomyocyte depletion. Development 2011; 138:3421-30.

Wang KC, Zhang L, McMillen IC, Botting KJ. Duffield JA. Zhang S. Suter CM, Brooks DA, Morrison JL. Fetal growth restriction and programming of heart growth and cardiac insulin-like growth factor 2 expression in the lamb. J Physiol. 2011; 589:4709-22.

Yeoh T, Hayward CS, Benson V, Sheu A, Richmond Z, Feneley MP, Keogh AM, Macdonald P, Fatkin D. A randomised, placebo-controlled trial of carvedilol in early familial dilated cardiomyopathy. Heart Lung Circ. 2011; 20:566-73.

Zhang S, Rattanatray L, McMillen IC, Suter CM, Morrison JL. Periconceptional nutrition and the early programming of a life of obesity or adversity. Prog Biophys Mol Biol. 2011; 106:307-14.

Zhou M, Morgner N, Barrera NP, Politis A, Isaacson SC, Matak-Vinković D. Murata T. Bernal RA, Stock D, Robinson CV. Mass spectrometry of intact V-type ATPases reveals bound lipids and the effects of nucleotide binding. Science 2011; 334:380-5.

Books & Book Chapters

Beilharz TH. Preiss T. Polyadenylation state microarray (PASTA) analysis. In, Castrillo JI and Oliver SG, Eds. 'Yeast Systems Biology. Methods and Protocols'. Methods in Molecular Biology (MiMB) series. Vol. 759. Chapter 9. (Series Ed: Walker JM. ISSN: 1064-3745). Humana Press. Springer, New York, Accepted 14/04/2009. Publication Date: August 17, 2011 ISBN 978-1-61779-172-7.

Beilharz TH, Humphreys DT, Preiss T. miRNA effects on mRNA closed-loop formation during translation initiation. In: Rhoads RE. ed. miMRNA Regulation Of The Translational Machinery, Progress In Molecular And Subellular Biology, vol 50. Springer-Verlag Berlin Heidelberg 2011.

Brennan K. Colony Management. In: Pease S., Saunders T.L. (eds) Advanced Protocols for Animal Transgenesis: An ISTT Manual. Springer Verlag Berlin Heidelberg. 2011 ISBN 978-3-642-20791-4.

Martinac, B. and Kloda, A. Evolutionary origin of stretch activated ion channels. In: Cardiac mechanoelectric coupling and arrhythmias, Kohl P, Sachs F and Franz, R. Editors. 2nd edition, Oxford University Press, Oxford 2011; ISBN: 978-0-19-957016-4.

Commentaries & Editorials

Davidson PM. Macdonald **PS.** Interventions for modern times: complex, collaborative, and culturally appropriate. Circ Cardiovasc Qual Outcomes 2011; 4:584-6.

Graham RM, Harvey RP. The ontogeny of cardiac regeneration. (invited commentary). Circ Res. 2011; 108:1304-5.

O'Rourke MF. Generation of accurate aortic pressure waves from calibrated upper limb pressure waveforms. Am J Hypertens. 2011; 24:1266.

Reviews

Betihavas V. Newton PJ. Du HY. Macdonald PS, Frost SA, Stewart S, Davidson PM. Australia's health care reform agenda: Implications for the nurses' role in chronic heart failure management. Aust Crit Care 2011; 24:189-197.

Fatkin D; Members of the CSANZ Cardiac Genetic Diseases Council Writing Group. Guidelines for the diagnosis and management of familial dilated cardiomyopathy. Heart Lung Circ. 2011; 20:691-3. [Invited Review]

Ingles J\*, Zodgekar P\*, Yeates L, Macciocca I, McGaughran J, Semsarian C, Fatkin D. Guidelines for genetic testing of inherited cardiac disorders. Heart Lung Circ. 2011; 20:681-7. (\*Co-first authors) [Invited Review]

lyer A, Kumarasinghe G, Hicks M, Watson A, Gao L, Doyle A, Keogh AM, Kotlyar E, Hayward CS, Dhital K, Granger E, Jansz P, Pye R, Spratt Davidson PM. An intervention to P, Macdonald PS. Primary graft failure after heart transplantation. J Transplant. 2011; 175768. [Invited Review] [Cover Figure]

Sparrow DB, Chapman G, Dunwoodie SL. The mouse notches up another success: understanding the causes of human vertebral malformation. Mamm Genome. 2011; 22:362-76.

Wouters MA, Iismaa SE, Fan SW, Haworth NL Thiol-based redox signalling: rust never sleeps. Int J Biochem Cell Biol. 2011; 43:1079-85. Letters to the Editor

Grav B. Macdonald PS. Kuchar D. Reversal of cardiomyopathy with ivabradine. Med J Aust. 2011; 41:213-214.

Lim HS, Kuchar D, Subbiah R, Walker B. Secondary r' wave in V(1) as a sign of left-sided antegrade accessory pathway conduction. Ann Noninvasive Electrocardiol. 2011; 16:407-8.

O'Rourke MF, Clubb J. Guidelines for assessment of cardiovascular disease in life insurance. J Am Coll Cardiol. 2011; 57:1570-1.

O'Rourke MF, Takazawa K. Measurement of central aortic pressure: an acceptable compromise? J Hypertens. 2011; 29:2038-9.

Study Protocol

Du HY, Newton PJ, Zecchin R, Denniss R, Salamonson Y, Everett B, Currow DC, Macdonald PS, promote physical activity and selfmanagement in people with stable chronic heart failure. The Home-Heart-Walk study: study protocol for a randomized controlled trial. Trials. 2011; 12:63.

Annual Finance Report ABN 61 068 363 235

	2011	2010
Income	\$	\$
Grants	12,498,476	11,842,464
Fundraising	2,070,769	2,268,958
Bequest	1,237,926	1,243,885
Investment income*	1,592,861	1,298,130
Other	107,114	198,128
Total Income	17,507,146	16,851,565
Operating Expenses		
Salaries and related expenses	11,453,900	10,954,504
Research consumables	2,041,799	1,989,251
Fundraising expenses*	331,681	638,907**
Depreciation	2,036,709	2,089,784
Other operational expenses	2,153,090	2,060,287
Total Expenses	18,017,179	17,732,733
Deficit before non operating expenses	-510,033	-881,168
Non Operating expenses		
Unrealised loss/(gain) on investment revaluation to market	-825,991	72,573
Net deficit	-1,336,024	-808,595

<sup>\*</sup> Fundraising expenses are funded from investment income

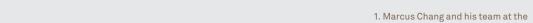
<sup>\*\*</sup> Includes the cost of 2 cars purchased on behalf of the Freshest Group which were used to fundraise for the Victor Chang Cardiac Research Institute at their Annual Ball

Victor Chang Cardiac Research Institute Annual Report 2011 Victor Chang Cardiac Research Institute Annual Report 2011

"Outstanding examples of research and discovery remind us that progress is being made in the quest to better understand heart disease... but without the support of our wider group of friends and supporters in the community, there would be no such progress."

We crowned Massimo Mele as Crabfest Champion, we danced the night away to Marcia Hines at the Heart to Heart Ball, we splashed out at the Des Renford Gala Day and cheered from the sidelines for the riders in Paceline – fundraising activities at the Chang were fun, physical and financially successful in 2011!

On behalf of researchers and staff at the Victor Chang Institute, we say thank you. This is your Institute, you are the heart of our organisation.



- 1. Marcus Chang and his team at the Westfield Golf Day, Canberra.
- 2. Young Ambassador Mark Vincent and Angel Tupai sing at the Victor Chang Heart to Heart Ball.
- 3. The starting line at the Yarra Bay
- 4. Massimo Mele is crowned 2011 'Crabfest' champion.
- 5. Professor Robert Graham at the Victor Chang Heart to Heart Ball.
- 6. Ms Amanda Keller, Ms Marcia Hines, and Mrs Kerri-Anne Kennerley at the Victor Chang Heart to Heart Ball.
- 7. Lindey Milan, John Winning, Massimo Mele and Deborah Hutton at the Victor Chang Crabfest.

# Fundraising in 2011

Because 'Discoveries Need Dollars'



The Victor Chang Health Check Booth

# A Hearty Check

Getting to know your risk factors

In 2011, almost 2000 working Australians had their blood pressure, cholesterol and blood sugar tested in the Victor Chang Health Check Booth, in its first full year of operation.

From Sydney Markets, HCF and Priceline HQ, to PricewaterhouseCoopers, Penrith City Council and Kia Motors, the Victor Chang Health Check Booth set off on its mission to get working Australians to start thinking about their heart as a health priority.

Of the nearly 2000 people tested in the Booth in 2011, 32 per cent of results were deemed sufficiently high that they were referred to their GP for immediate follow-up.

In 2012, the Booth will travel beyond borders, to far reaching parts of Australia, and help spread the word that getting to know your risk factors could save your life.

Jayne Baric, Victor Chang Health Check Booth Manager, describes why she's involved with the project.

"The risk of heart disease can be largely reduced if we get people to start thinking about their risk factors early – I think this is one of the most powerful messages we need to get out there to all Australians."

"A third of people that we tested in 2011 were referred to their GP for immediate care - knowing that the tests we are carrying out could one day save that person's life, is incredibly inspiring," added Ms Baric.

Victor Chang



One third of people tested were under 40 and there was an equal mix of gender.

> 65% did not know their glucose level

55% did not know their cholesterol level

38% did not know their blood pressure

32% were advised to visit their GP

22% had high cholesterol

14% blood

had high pressure

11% had high glucose/ blood sugar Victor Chang Awards For Excellence In Cardiovascular Journalism

Channel Seven's Sunday Night The Regional Award was Program took out the top honour in the second annual Victor Chang Awards for Excellence in Cardiovascular Journalism, announced at the Victor Chang "Heart to Heart" Ball in August.

The story, "Healing Hearts", that went to air nationally, highlighted the urgent need for Australian women to take care of their heart health. Reporter Rahni Sadler and producer Rebecca Le Tourneau received the Award on the night of the Ball.

"This was a story that epitomised everything the Victor Chang media awards are about - that is, recognising the powerful role journalists play in helping to inform and educate all Australians about heart disease and getting the message out there that heart disease continues to kill more of us every year than any other disease." said Professor Robert Graham.

presented to young journalist, Sonny Coombs, from the Yorke Peninsula Country Times (YPCT) in Kadina, South Australia, for his poignant series of articles about local girl, Hayley Spinks, whose struggles with a congenital heart condition, sadly resulted in her death.

Both Mr Coombs, and Hayley's mother Kim Thomas, attended the Ball to receive the Award at Sydney's Convention Centre, Darling Harbour.

#### Winners

#### Metropolitan Award Winner

Rebecca Le Tourneau (Producer) and Rahni Sadler (Reporter), Channel Seven Sunday Night Program (New South Wales).

#### Regional Award Winner

Sonny Coombs, Yorke Peninsula Country Times (South Australia).

#### Honourable Mention

Tyson Cottrill, NBN Television (Newcastle, NSW).

# Spreading the word on heart disease



Ms Rahni Sadler, Mr Sonny Coombs, Mr Tyson Cottrill and Ms Rebecca Le Tourneau, 2011 Media Award winners. Mr Sonny Coombs, Regional Media



#### Victor Chang School Science Awards

Year 11 students from 120 schools in the Blacktown, Wollongong, Campbelltown, Bankstown and Penrith areas, were recognised for their excellence in science by receiving a Victor Chang School Science Award. This is the eighth year we have given these awards with more and more schools being added each year.

Institute Deputy Director, Professor Jamie Vandenberg, says the awards are about inspiring dedicated science students to continue with their passion.

"Each and every one of these students has shown a dedication to science and a passion for discovery, and they all have the potential to go on to become Australia's next science hero, like Victor Chang, Howard Florey, Elizabeth Blackburn or Brian Schmidt".

"We have one of the most robust and innovative group of scientists here in Australia Many of our future thoughtleaders are here today, and we want to inspire them to continue their passion and turn that into a rewarding career," added Professor Vandenberg.

Former Award recipient, Garry Niedermayer was the Guest Speaker at the 2011 Campbelltown-Bankstown Awards ceremony. He said the award gave him his passion for scientific research, which carried into his PhD research on Alzheimer's disease and other forms of dementia.

At the ceremony he told the 2011 recipients to enjoy the experience and to take advantage of the opportunity to visit the Institute as part of the Award.

"The award itself was inspirational but going to the Institute, meeting the researchers, seeing the massive machines - that was really inspirational, my driving force."

# **Nurturing our** bright young stars of science



Garry Neidermayer, Victor Chang Science Award recipient in 2005 with the 2011 winner from his old high school, Sarah Redfern High School, Jessie Wheildon.

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#### **Bequests**

If you are thinking of leaving a bequest to the Institute, we would like to acknowledge your generosity by making you a member of the newly formed Victor Chang Bequest Club – 'YOUNG@HEART'. Membership will entitle you to attend a biannual 'YOUNG@HEART' Institute tour and luncheon.

The following wording, depending on the type of bequest, should be used when leaving a legacy to the Victor Chang Cardiac Research Institute:

"I give to the Victor Chang Cardiac Research Institute, (ABN 61068363235) Liverpool Street, Darlinghurst NSW

- a) The sum of \$\_\_\_ or
- b) \_\_\_\_% of my estate or
- c) Residue of my estate

(insert a, b or c) to be used for the purposes of research and I direct that the receipt of the Executive Director of the Victor Chang Cardiac Research Institute shall be sufficient discharge to my Executor(s).

# Leaving a legacy, shaping the future

#### Herbie's Story

Herbert Sydney Smith – 13 April 1919 to 8 December 2003

Herbie was a Paddington boy. A returned soldier and a wharfie for 30 years. In 1974, his life changed when he won \$60,000 in the lottery.

For 50 years, Herbie enjoyed life around the corner from where the Institute sits today, as a 'Paddo' boy, with his wife Iris, affectionately known as "The Boss". When Iris passed away in 2002 and Herbie in 2003, they willed the proceeds of the sale of their home, which they had purchased in 1952 for \$850, to the Victor Chang Cardiac Research Institute, to purchase equipment...

"To continue the work of the Great Doctor."

The house sold for \$710,000.

As the Institute was in the process of building its new state-of-the-art facility, Herbie's legacy was invested until it was time to purchase the equipment. By that time, the legacy had grown to \$950,000 and the Institute was able to put the money towards purchasing a state-of-the-art, live scanning confocal microscope, worth over \$1,000,000. At the time of purchase there was only one other similar microscope in Australia.

Sally Dunwoodie's laboratory uses the microscope on a daily basis; she says the vital work that has been carried out in her laboratory in recent years would not have been possible without the generosity of Herbie.

"This is one of the most advanced confocoal microscopes available, and allows us to see inside cells and watch as its protein components drive the cell to function. This microscope has enabled us to do experiments this year that we could have only dreamt of in the past.

"It's hard to sum up our thanks to Herbie and his family. But it's safe to say, his legacy is shaping our future."



Left: Professor Sally Dunwoodie with Herbie's tribute plaque, in the Confocal Microscope facility.

Victor Chang Cardiac Research Institute Annual Report 2011

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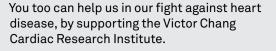


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Please call the Fund Development Office on 1300 VICTOR, or visit www.victorchang.edu.au

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