Perkins

HARRY PERKINS INSTITUTE
OF MEDICAL RESEARCH

Annual Report

Highlights 2015

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Chairman's report

2015 – The year in brief

Following 2014, a year which was marked by the appointment of a new Director to the Perkins and the opening of two new facilities, this year has seen a renewed focus on ensuring our research translates into a lasting impact on the health of our community.

Good governance is essential and I am grateful for the support of my fellow Directors for their commitment to the mission of the Perkins.

My particular thanks go to three board members who resigned this year, Mr Peter Leonhardt, Dr Gary Geelhoed and Ms Erica Smyth.

Peter Leonhardt joined the Board in 1998, commencing with the interim Board of the Western Australian Institute for Medical Research (WAIMR), as the Institute was then known. Peter was responsible for the Finance Committee and involved in the Fundraising Committee from the beginning of the Institute, crucial roles in its early development. He brought with him vital skills as an experienced Chartered Accountant, being then a Senior Partner with PricewaterhouseCoopers and previously the Managing Partner of the predecessor firm of Coopers & Lybrand in Western Australia. Peter also brought his personable and consensual style to the Board, and his experience was invaluable in dealing with all aspects of the Institute's business, from visionary expansion projects to crisis management. At a special General Meeting Peter Leonhardt was recognised for his long and distinguished service to the Institute by the passing of a Special Resolution conferring on him Honorary Life Membership of the Institute.

Dr Gary Geelhoed, the Chief Medical Officer of WA, joined the Board in June 2013. Ms Erica Smyth also joined the Board in 2013. They have both made very valuable contributions as Directors of the Institute. This year saw the Board welcome two new members, Mrs Jan Stewart PSM and Mr Roger Port.

Having served as Chief Executive Officer of Lotterywest from 1992 to 2014, Mrs Stewart brings invaluable skills to the Board which she joined in February 2015. A social worker by profession, her career prior to Lotterywest included eight years as Chief Social Worker at Perth's major paediatric teaching hospital.

Mrs Stewart has held many voluntary board positions both locally and internationally including that of Senior Vice President on the Executive Committee of the World Lottery Association, as well as the inaugural position of President of the Asia Pacific Lottery Association. She is also a graduate of the Australian Institute of Company Directors.

Mr Port, who joined the Board in April 2015, is a chartered accountant and a partner in PricewaterhouseCoopers. He brings 30 years of experience in financial analysis, company and business valuations, transaction due diligence and mergers and acquisitions to the Board. Roger has previous board, audit and finance committee experience over a period of more than 15 years at Amana Living, the Financial Services Institute of Australasia and Perth Diocesan Trustees. Mr Port became Treasurer of the Institute following Peter Leonhardt's retirement.

I thank Professor Leedman for his leadership and commitment over 2015. His dedication and hard work continues to serve the Institute's scientific aims very well, and he has made good use of quite limited resources. I also commend the researchers and research support staff of the Perkins for their passion and dedication. We are blessed with very talented and able researchers, and a highly professional research support team.

In the following pages you will be able read about the Institute's achievements and the generosity of its many donors. The ongoing support of the community, through our major events and other fundraising and community activities is highly valued by the Board and the researchers. I thank each and every donor who demonstrates their commitment to making a difference to the health of the community through their generous gifts. Ongoing funding provided by the WA and Federal governments is vital to sustain the quality of our work and we are very grateful for their support.

It has been an honour and pleasure to work with everyone at the Institute and with our supporters.

Laurence Iffla
Chairman

Our researchers and doctors are working to save more lives and to bring tomorrow's health closer to today for people in Western Australia

Director's report

Making progress towards preventing disease

Collaboration within and across the Perkins flourished in 2015 as a result of the restructure of the Perkins last year into three research divisions, Cancer and Cell Biology, Clinical Science and Molecular Medicine.

Within each Division we are working in multidisciplinary teams where our top scientists are working side by side with medically trained doctors, pathologists, biostatisticians and bioinformatics experts who can translate huge amounts of data and make it clinically relevant.

Significant discoveries were made during the year. They included a new way to treat preeclampsia (high blood pressure in pregnancy), a new way to make liver cells from stem cells and a new cause of prostate cancer due to an abnormality in the energy powerhouse of the cell, the mitochondrion, amongst numerous other breakthrough discoveries.

New genes were also found including a gene signature that can identify people who are at higher risk of heart attack and stroke, several genes that cause muscle and nerve disease and a new gene associated with autism. Further information about these discoveries is detailed in this report.

Scientific review

A highlight of the year was the Perkins Scientific Review and Strategy Meeting held in September. Our new structure and all Laboratory Heads were reviewed by a prestigious panel which included Professor Doug Hilton, Director of the Walter and Eliza Hall Institute, Melbourne, Professor Kathryn North AM, Director of the Murdoch Children's Research Institute, Melbourne, Professor Joseph Trapani, Director of the Peter MacCallum Cancer Centre, Melbourne, Professor Peter Little AO, University of Queensland, Professor Ian Constable, former Director of the Lions Eye Institute, Professor Lawrie Beilin AO (Chair) and Professor John Challis (Perkins board). The review resulted in very positive affirmation of the new divisional structure, the capacity of the Perkins to translate its discoveries, clinical linkages and the quality of new recruits.

We are actively recruiting new world-class scientists and clinicians to the Perkins who are being attracted to the environment which is one of cutting edge innovation mixed with passion, collaboration and a focus on the translation of our discoveries into improving clinical outcomes.

New Professors recruited

Two Professors with international reputations and their laboratories moved to the Perkins in 2015.

In February 2015, Professor Alistair Forrest established the Systems Biology and Genomics Laboratory which applies new genomic and bioinformatic approaches to studying basic biology and cancer. A Western Australian by birth, Professor Forrest had been at RIKEN in Japan since 2007 where he was scientific coordinator of the FANTOM5 (Functional Annotation of the Mammalian Genome) Project. He continues to be very involved in this project which includes a consortium of over 250 scientists in 20 countries.

Professor Ryan Lister joined the Perkins in mid-2015, establishing the Epigenetics and Genomics Laboratory. An award winning researcher with a national and international reputation, Professor Lister gained his PhD at UWA and then worked overseas including time at the Salk Institute in California. In 2009, he successfully constructed the first complete maps of the human epigenome. These pioneering maps identified unexpected complexity in the epigenome of embryonic stem cells, and are already serving as an important reference for medical researchers.

Clinical trials critical

Critical for the community is the ability of the Perkins to translate its discoveries into new treatments. Throughout 2015 the Perkins undertook a range of clinical trials aimed at fast tracking our research outcomes for the community. The trials included testing colchicine, a drug used for gout, to prevent heart attacks, a new treatment that may reduce development of diabetes in kidney transplant recipients, determining the optimal treatment approach to patients with acute shock,

and developing ways to improve the health outcomes of elderly patients.

In addition, multiple early phase cancer clinical trials were conducted in Linear Clinical Research Ltd and by Perkins researchers based at Fiona Stanley Hospital.

Our researchers and doctors are working to save more lives and to bring tomorrow's health closer to today for people in Western Australia and throughout the world. Every day, they are making progress towards preventing disease, diagnosing disease earlier, and developing new treatments.

I thank the staff, the Board of Directors and the community for their support as together we strive to defeat disease.

Professor Peter Leedman
Director

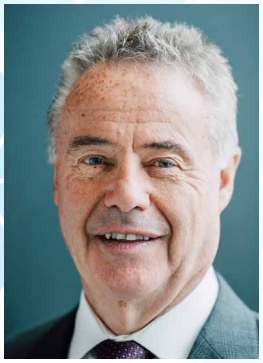
Board of directors

2015

Mr Laurence Iffla
Chairman

Mr Iffla has been Non-Executive Director since March 2005 and Chairman of the Board from May 2009.

He is a partner in the legal firm, Iffla Wade and practices primarily in the area of commercial property law, State taxes and trusts and joint ventures.



Professor John Challis

Professor Challis joined the Board in June 2014 as proxy for the Vice Chancellor of The University of Western Australia.

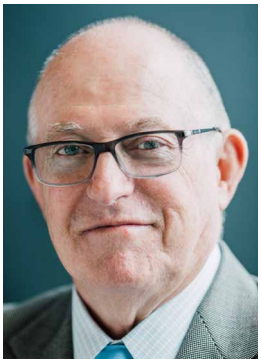
He commenced his position as Pro Vice-Chancellor for Health and Medical Research in February 2014.

Professor Challis is an internationally recognised expert in reproductive biology.

Dr Stephen Davis

Dr Davis joined the Board in 2012. He is a Radiologist and Partner of Perth Radiological Clinic.

He is a medical graduate of UWA, a Member of the Royal College of Physicians UK and Fellow of the Australian and New Zealand College of Radiologists.



Dr Bob Every AO

Dr Every joined the Board in April 2013. He is a Metallurgist by profession having completed his Bachelor's Degree in 1968 and a Doctorate in 1971. In 2000, he was awarded a Centenary Medal and in 2012 was recognised as an Officer of the Order of Australia.

He is Chairman of Wesfarmers Limited and Chairman of Boral Limited.

Professor Garry Geelhoed
(resigned December 2015)

Professor Geelhoed, the Chief Medical Officer of WA, joined the Board in June 2013.

He is a Paediatric Emergency Physician and is a past President of the Australian Medical Association WA.

Mr Keith Kessell

Mr Kessell joined the Board in August 2010.

He was Executive General Manager, Corporate Affairs at Wesfarmers Limited for 12 years, retiring in 2008.

Mr Roger Port

Mr Port joined the Board in April 2015. He is a chartered accountant and is a partner in Pricewaterhouse-Coopers.

He has 30 years' experience in financial analysis, company and business valuations, transaction due diligence and mergers and acquisitions and has led the PwC Perth Deals team since 2009.

Dr Erica Smyth

(resigned December 2015)

Dr Smyth joined the Board in 2013. She has over 30 years' experience in the mineral and petroleum industries.

A geologist, she was the Chair of Toro Energy Limited for nine years before stepping down in 2015.

Mrs Jan Stewart PSM

Mrs Stewart joined the Board in February 2015. She held the position of CEO of Lotterywest from 1992 until December 2014.

Mrs Stewart is a social worker by profession, having graduated from UWA with a Bachelor of Arts and Master's Degree in Social Work.

She is a graduate of the Australian Institute of Company Directors.

Perkins divisions, laboratories and centres

The Cancer and Cell Biology Division

The Cancer and Cell Biology Division is co-led by Professor Ruth Ganss and Associate Professor Andrew Redfern.

Cancer Epigenetics Laboratory

Associate Professor Pilar Blancafort and her team joined the Harry Perkins Institute of Medical Research in 2014. Associate Professor Blancafort is a specialist in genome engineering and gene targeting and her laboratory has pioneered the development of engineered DNA binding proteins to modulate the epigenetic state of cancer cells and delivery strategies for tumour targeting in pre-clinical studies. The team has begun the generation of targeted nanoparticles to encapsulate the aforementioned agents in both human cells and tumour tissues in mice models. The overall goal of the laboratory is to bring these new agents in pre-clinical and Phase I trials for metastatic basal-like breast cancer.

Laboratory for Cancer Gene Regulation

Led by Dr Archa Fox, the Laboratory for Cancer Gene Regulation investigates how genes are turned on and off in cancer and a variety of other diseases. Specifically, the group studies unusual sub-nuclear bodies termed 'paraspeckles', and investigates their role in diseases, as well as how these can be used as a model system for understanding oncogenic complexes.

Laboratory for Cancer Medicine

Professor Peter Leedman leads the Laboratory for Cancer Medicine. The research focuses on the mechanisms that regulate hormone action in various cancers (e.g. breast and prostate cancer) as well as identifying and utilising microRNAs as therapeutics in cancer. In the hormone action group, the focus has been on nuclear receptors and their coregulators, whilst in the microRNA group the focus has been on microRNA-7 (miR-7) and miR-331. The two arms of the laboratory are linked by their common interest in RNA biology and applying these findings in a translational sense in preclinical animal models with a longer-term view towards therapeutic application.

Cell Signalling Group

Cancer cells have over active enzymes of the type called protein tyrosine kinases (PTK) that function as on/off switches to control cancer cell growth and malignancy. Associate Professor Evan Ingley and his team investigate the functions of a subtype of PTK, known as Src Family kinases (SFK). They have discovered new interactions and pathways that SFK enzymes regulate in leukaemia and bone cancer (sarcoma) cells that influence their ability to survive and become invasive.

Iron Metabolism Laboratory

The Iron Metabolism Laboratory, headed by Associate Professor Debbie Trinder, investigates the molecular mechanisms in normal iron metabolism and in the development of iron overload disorder hereditary haemochromatosis. The team has expertise in the area of molecular and cellular biology of iron including cell isolation and culture, iron transport, gene and protein expression, gene knockdown and immunohistochemistry.

Leukaemia Research Laboratory

The Laboratory, led by Dr Louise Winteringham, is studying new ways that leukaemia genes are regulated. In particular it focuses on the role of gene enhancers and microRNAs (miRNA). MiRNAs are small pieces of RNA that can regulate gene expression by degrading the gene message before it can be translated into a protein. We have identified a number of key miRNAs that regulate blood cell development, and these appear to be deregulated in leukaemia. Importantly, miRNAs are now being trialled as a new form of treatment for some cancers.

Liver Disease and Carcinogenesis Laboratory

The objective of the Laboratory, headed by Professor George Yeoh, is to realise the use of a liver progenitor cell (LPC) for cell therapy to treat liver disease. Currently organ transplant is the only successful solution to cure end-stage liver disease. Large numbers of mouse LPCs can be generated and they readily differentiate into functional hepatocytes in culture. They can be used to treat mouse models of liver disease. We have also produced LPCs from mouse embryonic stem cells.

Systems Biology and Genomics Laboratory

Headed by Professor Alistair Forrest, the Systems Biology and Genomics Laboratory was established in 2015. The Laboratory's research focuses on using cutting-edge genomic techniques, in particular next generation DNA sequencing and computational approaches (bioinformatics) to understand how cells work at a system level. Professor Forrest has extensive experience in next generation sequencing (NGS) and has published using a variety of platforms (Roche, SOLiD, Illumina and Helicos) and protocols (RNA-seq, CAGE, small RNA, ChIP-seq).

The move to Perkins in 2015 is allowing him to translate his basic research on mammalian systems onto clinically relevant questions such as identification of novel cancer biomarkers and drug targets.

Targeted Drug Delivery, Imaging and Therapy Laboratory

The Laboratory, led by Assistant Professor Juliana Hamzah, focuses on developing strategies to specifically target diseases such as cancer and atherosclerosis for diagnostic imaging and local therapeutic interventions. A major challenge to detect and treat chronic inflammatory diseases such as cancer and atherosclerosis is to effectively deliver contrast agents and therapeutics into the pathological tissues whilst avoiding off-target binding and consequent cytotoxic effects. The team focuses on developing tools and strategies to target the microenvironment of cancers and atherosclerotic plaques for imaging and therapy.

Vascular Biology and Stromal Targeting Laboratory

Woodside Professor Ruth Ganss heads the Vascular Biology and Stromal Targeting Laboratory which focuses on blood vessels as a crucial component of normal tissue function and in disease.

The Laboratory studies the role of blood vessels in cancer, and importantly, designs new treatments to manipulate blood vessels within the cancerous tissue for improved anti-cancer drug delivery. This treatment also enables better access of immune cells into malignant tissue which is particularly interesting with the arrival of immunotherapy in the clinic.

Kirkbride Melanoma Centre

The Kirkbride Melanoma Centre, led by Scientific Director, Professor Peter Leedman, is dedicated to finding improved treatments for melanoma skin cancer. Current research projects undertaken within the Harry Perkins Institute of Medical Research include the use of proteins to slow down and destroy tumours, the examination of genes that can prevent UV-induced melanoma and screening drug combinations (compound) to find a new compound with the ability to destroy melanoma cells.

Clinical Science Division

The Clinical Science Division is co-led by Professor Grant Morahan and Professor Peter Thompson.

Western Australian Centre for Health and Ageing

Ageing research is conducted through the Perkins affiliate centre the Western Australian Centre for Health and Ageing (WACHA) which is led by Professor Leon Flicker. WACHA's research aims to extend healthy lives, prevent the onset of disabling illnesses, find better ways to treat diseases common amongst older people, and to improve the way health services are delivered. Researchers, clinicians, and students collaborate to identify and overcome the most critical obstacles to healthy ageing, including dementia, depression and frailty.

Centre for Clinical Research in Emergency Medicine

The Centre for Clinical Research in Emergency Medicine (CCREM), led by Professor Daniel Fatovich, is a unique unit established at Royal Perth Hospital that brings together clinical staff working in the Emergency Department (ED) and laboratory scientists using immunological and molecular biological techniques. CCREM investigates a number of conditions within the spectrum of disease treated by EDs including, sepsis, trauma, anaphylaxis, chest pain and drug dose.

Centre for Diabetes Research

At the Centre for Diabetes Research, led by Professor Grant Morahan, the research is aimed at understanding and preventing diabetes and its complications. Diabetes is recognised as a major public health problem and is Australia's fifth "national health priority area". Diabetes is characterised by increased blood sugar levels, and has two major forms: Type 1 diabetes, which results from the person's own immune system destroying the insulin-producing cells; and Type 2 diabetes, which results from the person's growing inability to respond normally to insulin. Both forms of diabetes are caused by complex interactions between many genes and environmental factors. Our particular focus is on the genetics of Type 1 diabetes.

Translational Renal Research Laboratory

The Translational Renal Research group, led by Dr Aron Chakera, aims to improve outcomes for patients with renal diseases, by translating advances in basic science from the bench to the bedside. Research is focused on the immune system and how it is affected by immunosuppression, particularly in the setting of transplantation. Infectious diseases are a common problem in immunosuppressed patients. By studying host responses to pathogens, levels of immune function can be defined that may predict the likelihood of disease and help better understand the factors that influence disease development.

Molecular Medicine Division

The Molecular Medicine Division is co-led by Professor Nigel Laing AO and Professor Phillipa Lamont.

Brain Growth and Disease Laboratory

Established in late 2014, the Brain Growth and Disease Laboratory is led by Associate Professor Julian Heng. The goal of the research is to understand the genetic causes of childhood brain disorders such as intellectual disability, epilepsy and autism spectrum disorder. This work will enable health practitioners and clinicians to improve the diagnosis and treatment of children with these conditions.

Epigenetics and Genomics Laboratory

Established in early 2015, the Epigenetics and Genomics Laboratory is led by Professor Ryan Lister. Almost every cell in the body contains essentially the same genome sequence, however differential usage of the genetic information enables cells with vastly different features and functions to be formed. The epigenome is a molecular code superimposed upon the genome that can control how genes are turned on and off, without altering the underlying DNA sequence.

The Laboratory's research uses advanced genomic, molecular, genetic and computational techniques to study the epigenome, including using next-generation sequencing technologies to generate whole-genome high-resolution maps of the epigenome and associated molecular processes. The research aims to elucidate the mechanistic underpinnings of how the epigenome is established and dynamically modified, how it affects the cellular readout of the underlying genetic information, and to develop molecular tools for editing the epigenome.

Mitochondrial Medicine and Biology Laboratory

The Mitochondrial Medicine and Biology Laboratory is headed by Professor Aleksandra Filipovska. Mitochondria are microscopic, energy producing machines that are found in all human cells. Mitochondria contain a small set of genes that must work properly to make the energy our bodies require for health.

Defects in the expression of mitochondrial genes cause debilitating diseases for which there are currently no cures. We have identified several different disease causing mutations in human cells, developed a complete new set of analyses to understand how these mutations cause disease and provide insights into possible treatments. We have developed several different models of mitochondrial disease in mice.

Molecular Endocrinology and Pharmacology Laboratory

The Molecular Endocrinology and Pharmacology Laboratory, led by Associate Professor Kevin Pfleger, investigates how different molecules, particularly hormones, bind to our cells and transmit distinct signals into them. This communication is absolutely essential for coordination of our cells, tissues and organs. This laboratory is developing and successfully applying our world-leading patented technologies, including the Receptor-Heteromer Investigation Technology (Receptor-HIT).

This research is being translated through the Perkins spinout company Dimerix Bioscience Ltd, of which Associate Professor Kevin Pfleger is Chief Scientific Advisor.

Molecular Endocrinology – Cellular Regulation Laboratory

Led by Professor Tom Ratajczak, the Laboratory investigates hormone action with a translational bias in several different paradigms including prostate cancer and speech defects, as well as disorders of calcium homeostasis and bone disease. The work presents a great example of clinically relevant "translational bench-to-bedside research" in action. The Ratajczak lab is credited with the discovery of cyclophilin 40 (CyP40), an estrogen receptor-associated protein involved in modulating steroid receptor function.

Neurogenetic Diseases Laboratory

Professor Nigel Laing AO, heads the Neurogenetic Diseases Laboratory which is one of the world's foremost research groups in the investigation of the genetic causes of muscle diseases. It has five themes to its research: 1) Disease gene discovery (finding genes which, when they are mutated, cause genetic diseases. 2) Functional genomics (proving that a novel variant in a gene is in fact disease causing 3) Development of therapies for selected neurogenetic diseases. 4) Development of better molecular diagnostic tools to provide more patients with a diagnosis 5) Research into the prevention of genetic diseases through newborn and preconception carrier screening.

Synthetic Biology and Drug Discovery Laboratory

The Synthetic Biology and Drug Discovery Laboratory, led by Associate Professor Oliver Rackham, focuses on re-engineering bacteria and yeast for use as microscopic drug factories, and in the manipulation of mammalian gene expression. Large, high quality libraries of new drugs are absolutely essential resources to find new medicines. However, their use is restricted to a few pharmaceutical giants. We are engineering cells to make a wide variety of drug-like molecules, providing a unique drug discovery resource accessible to almost any scientific laboratory. As each cell can make a different molecule of interest, billions of different potential drugs could be produced in a single tube. This technology provides an opportunity to put the future of drug discovery in the hands of the wider scientific community and provides new tools for Australian industries.

Facilities

Monoclonal Antibody Facility

The Monoclonal Antibody Facility, led by Kathy Davern, provides a service for researchers, clinicians, and commercial groups across the nation and overseas. The Facility generates top-class serum-based products, including novel antivenom agents and multiple monoclonal antibodies for use in a variety of clinical and preclinical arenas. The facility continues to generate multiple antibodies to a range of target antigens including human Hepatitis C virus, mesothelioma, human carcinomas, and molecules involved in muscular dystrophies, cancers, diabetes and lung disease.

Australian Cancer Research Foundation Cancer Imaging Facility

Officially opened in 2015, the Perkins established a high end preclinical imaging facility (the ACRF Cancer Imaging Facility) at its main headquarters. This preclinical equipment is essential in the fight against human cancer, by helping experts in the field move towards earlier disease detection, prevention strategies and assessment of the efficacy of new cancer treatments. The preclinical MRI, PET/CT and SPECT/CT scanners in the CIF are non-invasive, high resolution monitoring tools that are smaller versions of human imaging equipment, allowing researchers to examine tumour development in preclinical models of cancer and determine effective forms of treatment. The ACRF Cancer Imaging Facility offers unparalleled access to an imaging platform unsurpassed in Australia.

Linear Clinical Research Ltd

Founded by the Perkins, Linear is a purpose built facility that supports first in human through to phase II clinical trials and is co-located within a major research precinct and tertiary teaching hospital, Sir Charles Gairdner Hospital. It is headed by Dr Janakan Krishnarajah. Linear has the Australian advantage of fast regulatory approval time to achieve first-in-human clinical data and extensive experience in adaptive healthy volunteer/ patient protocol designs. Linear is Western Australia's only dedicated early phase clinical trials facility and the most advanced of its kind in Australia.

In 2015 Linear won the Business Services Export Award and was a finalist in the Health and Biotechnology Award categories of the Western Australian Industry and Export Awards.

Research highlights

Neurogenetic disease findings

Dr Gina Ravenscroft, from the Perkins Neurogenetic Diseases Laboratory, was the lead author of a review published by the prestigious journal Brain in February.

Traditionally clinicians and researchers have approached muscle diseases, which mainly affect newborn children, by grouping patients according to the gene or genes which cause the disease.

However, now that more and more genes are being identified as a result of new gene sequencing technology, Dr Ravenscroft found that patients may have a mutation in a large number of different genes, which might not have been considered in that disease.

Mutations in many different genes can cause the same type of disease. On the other hand, mutations in the same gene can affect patients differently.

It is hoped that the findings will allow researchers to develop new treatments, by using therapies which are applicable to more than one genetic disorder.

Mitochondria link to Fatty Liver Disease

Perkins researcher, Dr Tara Richman from the Mitochondrial Medicine and Biology Laboratory, was lead author on the paper *Mutation in MRPS34 Compromises Protein Synthesis and Causes Mitochondrial Dysfunction*, published by, PLOS Genetics.

The paper explored the strong influence that mitochondria have on fatty liver disease.

Mitochondria are the tiny, energy producing machines which are found in all cells and their dysfunction causes a number of diseases and disorders. The parts of the body which are affected the most severely by mitochondrial dysfunction are the ones which use the most energy.

Dr Richman found that even though there may be a mutation in the mitochondria in other cells of the body, the liver is most severely affected which was a major step forward in knowledge that will provide an effective model for future testing of treatments for fatty liver disease.

Fatty liver is a condition in which fat builds up within liver cells and is a common health problem in countries where there is a high rate of obesity among adults.

Muscular Dystrophy breakthrough

Findings by a Perkins PhD student, published in Brain, have changed the way neurologists across the world will look at the disease Muscular Dystrophy.

Dr Macarena Cabrera-Serrano, from the Laboratory for Neurogenetic Diseases, was lead author on the paper, *Expanding the phenotype of GMPPB mutations* which was published in May.

Although Congenital Muscular Dystrophy has several forms and can stem from mutations in many different genes, it generally causes debilitating muscle weakness and can also involve the brain. Congenital muscular dystrophies most often present at birth, or become obvious during the first six months of a child's life. Some other kinds of muscular dystrophies can present later in life.

The muscular dystrophy caused by mutations in the GMPPB gene was known as a severe disease presenting by the age of four years and frequently associated with epilepsy, intellectual and developmental disabilities and other defects of the brain. This latest study looked at patients in Perth and Sydney with a mutation in the GMPPB gene and showed that this Muscular Dystrophy can appear as a late onset condition, affecting adults with no abnormalities of the brain.

Genetic breakthrough helps couples hoping for healthy child

In June, the American Journal of Human Genetics published significant findings from the Perkins Laboratory for Neurogenetic Diseases relating to a lethal muscle disease.

The genetic research found that babies with the rare condition, Arthrogryposis Multiplex Congenita, are paralysed and don't survive because nerves aren't signalling to the patients' muscles.

The group analysed data from the exome sequencing of all the genes in a newborn baby who had passed away within an hour of birth due to severe muscle weakness.

The researchers were able to pinpoint the gene which had mutated to cause the disease; a task which was simplified because the parents, from Sydney, were both carrying the same defective copy of the gene, GPR126. The Perkins team then worked with colleagues in France and Brazil and at Stanford University in California to fit pieces of the puzzle together.

DNA diagnostic panel tests can now be extended to include the new gene, so that families can find out early during pregnancy whether their child has inherited the disease.

Research could help pregnant women and babies

Exciting research led by Woodside Professor Ruth Ganss found new answers for pregnant women with high blood pressure, which is also a characteristic of the serious condition, preeclampsia.

Preeclampsia is a problem in 5% to 10% of all pregnancies in Australia and can threaten the lives of the mother and unborn child. There is currently no cure except delivering the baby, which can cause health problems for the child if the birth is pre-term. Most traditional medications for high blood pressure, or hypertension, are harmful for the foetus.

Pregnant women produce more blood and fluid, and therefore their blood vessels need to relax and expand to meet the baby's demands. When the vessels stay constricted and the mother experiences hypertension, the mother and the placenta can't provide enough nutrients for the foetus.

Professor Ganss' research on a regulator called RGS5 has led to a new understanding about the somewhat mysterious process which makes blood vessels constrict or relax during pregnancy. It also shows that a woman, with no previous experience of high blood pressure, can become hypertensive during pregnancy which then can cause preeclampsia.

The research has opened the door for a potential treatment, using an existing drug which is currently being utilised to help female infertility.

The paper, *Regulator of G protein signalling 5 is a determinant of gestational hypertension and preeclampsia*, was published in June in the high impact factor journal "Science Translational Medicine". It was a national interdisciplinary collaboration with groups from Perth, Canberra, Melbourne and Sydney.

Twitter for Cells

A research team from Western Australia, Japan and Germany, led by Perkins Professor Alistair Forrest, collaborated to create the first map of cell-to-cell communication between the hundreds of cell types which make up our bodies.

The work, published in Nature Communications in June, revealed for the first time that there are literally hundreds of messages passed between any two cell types. Imagine twitter for cells; hundreds of cell types telling each other what is happening via hundreds of different messages (status updates).

While traditional biology is focused on one or two genes at a time, the ethos behind systems biology is to study all elements (typically genes or proteins) simultaneously to see how they work together in a system (or network). Humans have evolved into complex multicellular organisms made of hundreds of different specialised cell types.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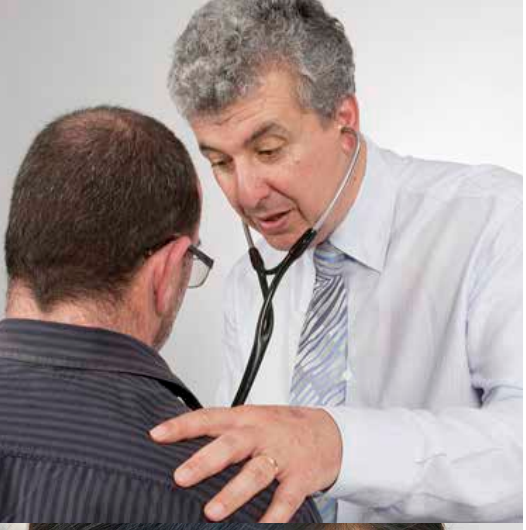
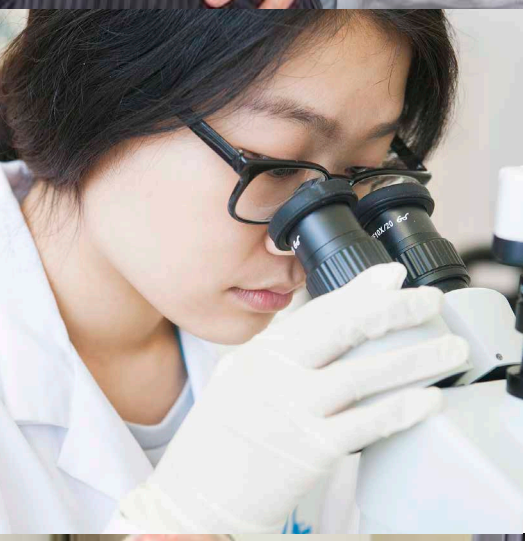
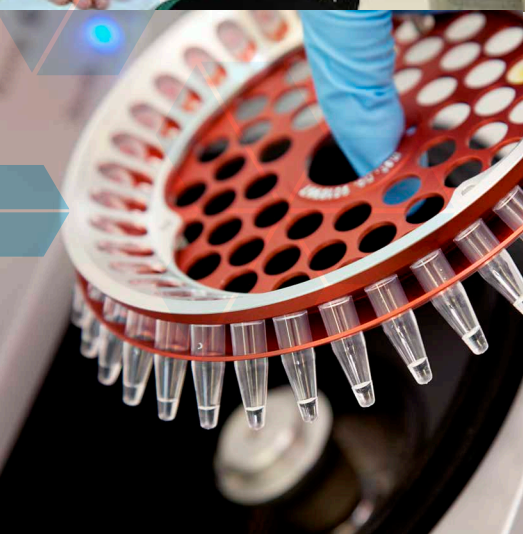






Division of labour between these specialised cell types allows us to have more complex functions than simple single cell organisms like yeast and bacteria. Cell specialisation allows us to see, hear, pump blood, walk etc.

To make all of this work the human body has evolved protein messages that are used to communicate between these different cell types to coordinate their activity. This study has revealed that they have many ways of talking to each other.

Professor Forrest said the work has important implications for medicine.

The proteins involved are actually well known to the general public. Insulin, human growth factor and leptin and their receptors are important in diabetes, height and obesity. This type of signalling is also very important in our immune response to infectious diseases. It is also important in cancer, particularly neuroblastoma and lung cancer.

Research providing clues about Motor Neurone Disease

Dr Archa Fox found that the molecules studied in her work on cancer are also involved in Motor Neurone Disease, or ALS.

The findings were published in a paper, *'Prion-like domains in RNA binding proteins are essential for building subnuclear paraspeckles'*, in the Journal of Cell Biology.

Dr Archa Fox is known for her discovery of a tiny cellular structure within the nucleus of cells, called the paraspeckle.

MND mainly affects adults and only a small number of cases have a family history of the disease. There is currently no understanding of the cause of the disease.

Researchers don't know what's going wrong in the motor neurones that are dying, but now think there could be a common pathway involving paraspeckles that is faulty in MND patients.

The research showed that while different molecules are involved in MND, many of them come together within paraspeckles.

Paraspeckles are formed by accumulations of proteins and are important in human cells because they help the cells to cope with stress. However, when the same proteins accumulate in the wrong places this causes diseases including MND and other lethal conditions.

While the research is at a very early stage and being tested in human cells within a laboratory setting, it provides hope for people with neurodegenerative diseases and their families.

Search for a diet to protect against Diabetes

A new WA research project was commenced with the aim of uncovering what type of diet works best to protect people against Type 2 diabetes based on a person's specific genes.

Professor Grant Morahan, who heads the Centre for Diabetes Research at the Perkins, said that the study aimed to help people choose the ideal diet to help reduce their chances of developing Type 2 diabetes depending on their individual genetic makeup.

Professor Morahan said the study would be done using The Gene Mine resource, which was created by the Centre and harnesses the power of the entire mouse genome for accelerating medical research discoveries. A human study into this would take millions of dollars and thousands of participants and would need to be followed up over 20 to 30 years. Using the incredible power of The Gene Mine, the study aims to complete the task in five years.

New step towards early cancer detection

A study, by Professor Alistair Forrest from the Harry Perkins Institute of Medical Research and Dr Bogumil Kaczkowski from RIKEN Japan, has uncovered a pattern in genes that could lead to improved diagnosis for a range of cancers.

The study, which was published in October in Cancer Research, discovered a trend of genetic patterns, known as markers, which are switched on or off across the majority of cancer types. Cancer markers are substances that are produced by tumours and are used to help detect, diagnose and manage some types of cancer.

Many cancer types have no known useful markers, so this important research is the first step to diagnosing these cancers and could help identify new drug targets, potentially helping millions of people.

Professor Forrest said he was delighted that the team had been able to detect so many significant cancer markers and was optimistic about the research leading to improvements in early diagnosis methods.

How a deep sea shrimp could change medical research

An enzyme squirted out of deep sea shrimp causing a bright blue burst to scare away predators is the key to innovative scientific work to develop new therapies for serious human diseases.

Associate Professor Kevin Pfleger and colleagues from the Harry Perkins Institute of Medical Research, The University of Nottingham and Promega Corporation tested a derivative of the bioluminescent protein and found it was a "game-changer" for monitoring the way hormones and pharmaceuticals bind to receptors on the surface of living cells.

Associate Professor Pfleger says that understanding how medicines bind to receptors on the cell is incredibly important for discovering and developing new therapies to help patients.

"The key to future breakthroughs is through understanding the nuances of how medicines need to work. If cell function is like playing the piano, most medicines slam the keys or close the lid. The idea is to get back to the tune the body is trying to play," he says.

This work was funded by an Australian Research Council Linkage Grant and the results have been published in the July edition of the very high impact scientific journal Nature Methods.

Awards and honours

Fellowships honour Perkins Professors

In March, Professor Peter Leedman and Professor Nigel Laing were elected Fellows of the Australian Academy of Health and Medical Sciences.

The Academy aims to mentor the next generation of health and medical science researchers and provide a forum for discussion on progress on medical research with an emphasis on translation of research into practice.

Leading health and medical science minds from across the country came together to establish the Australian Academy of Health and Medical Sciences, which will provide independent advice to government, industry and the community on issues relating to evidence-based medical practice and medical research in Australia.

Queens Birthday Honour for Perkins Professor

The Governor General has appointed Professor Nigel Laing an Officer in the General Division of the Order of Australia. Neurogenetic Diseases Laboratory and has made significant contributions to the field over the course of his career.
He was honoured for his "distinguished service to medicine in the field of neuromuscular disorders, as an academic and researcher, to medical education and through contributions to professional associations."

Gene investigation reached finals in Eureka Prizes

A major international project, led by Professor Alistair Forrest from the Perkins, was a finalist in the 2015 Australian Museum Eureka Prizes for the Scopus Eureka Prize for Excellence in International Scientific Collaboration.

The FANTOM5 project was started in RIKEN Japan and involves researchers systematically examining the sets of genes used in most cell types of the human body. The project has generated many notable discoveries resulting from the investigation over the past 15 years.

Award for medical researcher's global impact

An outstanding Perkins researcher, who has been praised for making his mark on Australian and global science, has been honoured with the Vice Chancellor of UWA's Mid-Career Research Award.

Associate Professor Kevin Pfleger is Head of Molecular Endocrinology and Pharmacology at the Harry Perkins Institute of Medical Research and his team study how hormones and medicines act in the body.

Associate Professor Pfleger holds patents for both technological innovations and a novel therapy for chronic kidney disease. These are being commercialised by spin-out company Dimerix Bioscience Limited which has recently been acquired by ASX-listed Sun Biomedical Limited.

Professor Leedman said the Vice Chancellor's award was also a recognition of Associate Professor Pfleger's contributions to the broader scientific community, including his extensive advocacy, mentoring and transdisciplinary activities.

Perkins researchers win NHMRC awards

Perkins researchers behind new work to improve treatments for heart and kidney disease were recognised in Canberra in September with National Health and Medical Research Council (NHMRC) Research Excellence Awards.

The Deputy Director of the Perkins, Professor Peter Thompson, won the Marshall and Warren award for his innovative grant application which will be used for a study on patients with stable coronary heart disease.

Professor Thompson and his team will follow up on the promising results of a clinical trial to confirm whether a new use for an old drug can reduce heart attacks in patients. The drug is colchicine, widely used for gout and is known to be low cost and relatively free of side effects. This follow-up study will involve around 5,000 participants.

Associate Professor Kevin Pfleger received an award for having the top-ranked fellowship application in his category. His research focuses on receptors throughout the body that are the target of many currently used medicines.

Many treatments result in unexplained effects due to a lack of understanding of their mechanism of action at the molecular level. Associate Professor Pfleger will generate new knowledge about these mechanisms with a view to improving the effectiveness of current and future medicines, and reducing their side effects.

2015 WA Health Excellence Award for Deputy Director

Professor Peter Thompson received the Minister of Health's award.

Presented by Health Minister, the Hon. Dr Kim Hames MLA, at the WA Health Excellence awards, the accolade recognises individuals who have made an outstanding commitment to longer, healthier lives for Western Australians.

Dr Hames said that Professor Thompson, a cardiologist, was recognised as one of the State's leading medical practitioners, researchers and health advocates focused on better health outcomes for all.

Throughout his career he has contributed to professional and community organisations, been an active researcher and publisher and supervised one of the largest cardiovascular clinical trial units in Australia.

Merit Grants awarded to Perkins researchers

Four researchers from the Harry Perkins Institute of Medical Research won competitive Project Grant Merit Awards in August from the WA Department of Health.

Associate Professor Julian Heng who heads the Brain Growth and Disease laboratory, Dr Gina Ravenscroft from the Neurogenetic Diseases laboratory, Dr Glenn Arendts from the Perkins Centre for Clinical Research in Emergency Medicine and Dr Andrew Ford from the Perkins WA Centre for Health and Ageing each received a $75,000 award to sustain their valuable research projects.

The award is in recognition of their highly ranked NHMRC Project Grant applications in 2014, which narrowly missed out on federal funding.

National funding to fight dementia

Researchers at the Harry Perkins Institute of Medical Research have received Federal Government funding to tackle the impacts of dementia – the second-leading cause of death in Australia behind heart disease.

The funding was from the National Health and Medical Research Council (NHMRC) and the Australian Research Council. At the Perkins a fellowship was awarded to Dr Sarah Rea, from the Neurogenetic Diseases Laboratory. Her work will focus on how gene mutations in self-degrading cell receptors cause dementia.

Two other recipients were Dr Kate Smith and Dr Andrew Ford, from the WA Centre for Health and Ageing (WACHA). With dementia five times more prevalent in Aboriginal Australians than non-Aboriginals, Dr Kate Smith's project aims to help develop a better quality of life for patients as well as identifying factors associated with a better quality of life. Dr Andrew Ford will investigate factors contributing to the development of depression in adults with Alzheimer's disease and the effect of a simple, safe and cost-effective treatment.

New research on childhood brain disorders

A team of researchers headed by Associate Professor Julian Heng has been awarded a grant to investigate the role of genetic mutations in childhood brain disorders.

The research project will address mutations which disrupt normal foetal brain development and lead to intellectual disability. The long-term goal of the investigation is to generate new ways to predict and manage intellectual disability. It is hoped the research can also be applied to other brain disorders.

Community Engagement

MACA Ride to Conquer Cancer

More than a thousand riders participated in the fourth annual MACA Ride to Conquer Cancer in October and raised a total of $4.5 million.

MACA, the title sponsor of the Ride, had a team of 300 riders who raised more than $1.2 million of the total.

Geoff Baker, the driving force behind the MACA team, said that the Ride is about the company's journey to support the community in conquering cancer as we have all been affected by cancer in one way or another. He said that as able bodied persons, we owe it to our community to make a difference. Ride-generated dollars support Perkins researchers and clinicians and provides state-of the-art equipment required for vital cancer research programs improving the health of Western Australians.

In four years, the MACA Ride to Conquer Cancer® has raised over $19.5 million for the Perkins. The annual two-day, 200km Ride draws thousands of participants and brings together communities of survivors, cyclists and supporters who train and fundraise for months in order to participate.

Top Fundraisers 2015

1.	Grant Menhennett	$43,357.00
2.	Martin Howley	$39,052.20
3.	David Edwards	$32,540.00
4.	Peter Leedman	$23,550.00
5.	Ross Williams	$20,025.00
6.	Dave Harwood	$15,378.00
7.	Derek English	$15,071.50
8.	Derek Milford	$13,128.00
9.	Andrew Holben	$13,013.15
10.	Suzanne Philpot	$12,700.00

Top Teams 2015

1.	Team MACA	$1,263,782.44
2.	Team Woodside	$223,949.17
3.	TCD Group Of Companies	$110,973.21
4.	Team Iluka	$110,212.15
5.	Rullo Group	$95,450.32
6.	Team Perkins	$91,737.45
7.	MAMILS	$64,960.15
8.	F@T Dads	$54,439.09
9.	Sock It To Sarcoma	$53,142.45
10.	Crack Cycling	$51,146.24

Striding towards a better future

Hundreds of dedicated walkers who took part in the 2015 Weekend to End Women's Cancers, presented by Hawaiian, raised $1.8 million to support breast and ovarian cancer research at the Perkins.

The 60 kilometre walk over two days was the culmination and celebration of a year of fundraising.

Top fundraiser and cancer survivor, Liza Carpene, who single handedly raised more than $40,000 for women's cancer research, shaved her head for the event and received enthusiastic applause from the large crowd gathered at the finish line.

Lotterywest BioDiscovery Centre

The Lotterywest BioDiscovery Centre was established by the Perkins to increase community awareness about the importance of medical research.

The Centre provides hands-on interactive scientific experiences. The activities explore the intricacies of our most challenging human diseases such as cancer, diabetes, cardiovascular and neuromuscular diseases. The Centre employs a team of talented medical researchers, including Honours and PhD students from within the Perkins to help visitors with activities that are run in both a "wet lab" laboratory environment and a "dry lab" Community Resources Room.

Visitors to the laboratory are immersed in a fully interactive experience, which reveals how our scientists work with molecules that aren't visible to the naked eye. This includes being taught how to extract DNA, look at cells under a microscope and use the technical tools of a medical research scientist.

Customised programs have been developed for the school students and community and corporate groups.

Inaugural Perkins Open Day

In August the Perkins opened its doors during national science week and welcomed 720 visitors to its headquarters in Nedlands to explore, experiment and learn more about research into cancer, cardiovascular disease, diabetes and other diseases.

One of the activities at the Open Day was to 'Kill a Cancer Cell," a hands-on activity in the Lotterywest BioDiscovery Centre which involved using pipettes, staining cells and looking at their magnified images.

Talks by top Perkins researchers included information on stem cells, breast cancer and melanoma, the exciting new technologies which will benefit patients and also shone a spotlight on heart attacks and stroke.

Public forum focus on stroke

More than 300 people attended the Perkins flagship annual community forum, the Wesfarmers' Harry Perkins Oration in November.

Professor Graeme Hankey, a world-renowned neurologist, addressed the audience on the impact of stroke on the community and explored prevention measures. He said that the incidence of stroke was rising, with 5,000 Western Australians having a stroke each year, or 13 a day.

He said that more people were also surviving stroke which meant the health burden was also increasing, with 30 to 50% of survivors living with a disability.

Professor Hankey also emphasised that stroke was preventable.

"90 percent of all strokes are attributable to high blood pressure, lack of exercise, high fats and a poor diet, diabetes, alcohol, smoking and heart problems," he said.

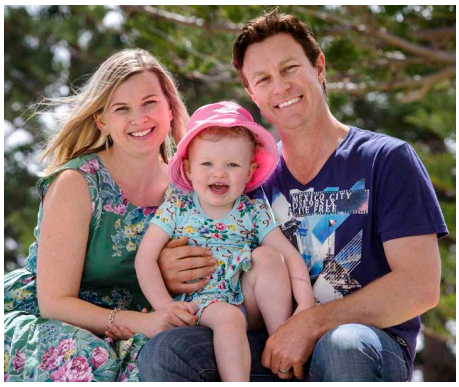
Melanoma forum

National and local experts gathered in Perth in December for the Kirkbride Melanoma Centre's Research Symposium and Community Forum.

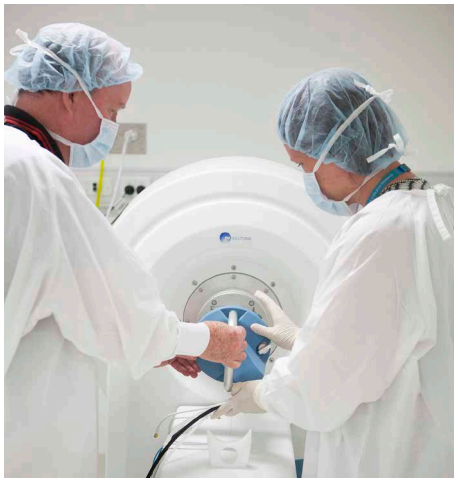
The symposium held by the Harry Perkins Institute of Medical Research, involved presentations from 15 melanoma experts and gave scientists and clinicians an opportunity to discuss the latest in research and treatments for the disease.

The Forum offered an overview of the progress in the field, with talks on how to reduce mortality from melanoma and the need for clinical trials in Western Australia.

Professor Grant McArthur from the Peter MacCallum Cancer Centre in Melbourne said during his keynote presentation, that there was a critical need for research into personalised medicine. He said that we have breakthroughs but not for all patients and that's why we need to stop rolling the dice and hoping that people will respond to the drugs.



Power of partnerships



Cancer patients to benefit from unique collaboration

Research in Western Australia is set to benefit from an exciting new collaboration between the Harry Perkins Institute of Medical Research and Perth Radiological Clinic's charity the PerthRadClinic Foundation.

Together they have established the Perth Radiological Clinic Associate in Translational Imaging - a three year clinical research position at the Perkins headquarters in Nedlands.

The Associate in Translational Imaging will be involved in the investigation of tumours in preclinical models of disease; a critical bridge between discoveries in the laboratory and their translation into new treatments for cancer patients.

The new appointment will be part of a team involved in fast-tracking a number of current projects and the translation of successful outcomes into new human clinical trials.

The Perth Radiological Clinic Chairman Dr Martin Blake said one of the key drivers when they established the PerthRadClinic Foundation was to support innovation in medicine and being involved with the Perkins in this way was a perfect fit.

Woodside Cancer Research Fellow announced

Internationally renowned cancer researcher, Professor Ruth Ganss, was awarded the prestigious Woodside Cancer Research Fellowship in April.

The Fellowship was established in 2015 with a donation to the Perkins of $1M by Woodside.

Professor Ganss, who is scientific head of the Cancer and Cell Biology Division at the Perkins, also leads her own Laboratory which is focused on finding a way to effectively treat pancreatic and liver cancer tumours.

Perkins and Hawaiian form partnership to end women's cancers

Hawaiian, a Western Australian property company, partnered with the Perkins by sponsoring the major fundraising event, The Weekend to End Women's Cancer. The walk supports cutting-edge cancer research at the Perkins.

Director of the Perkins, Professor Peter Leedman, said that there is a great synergy between the values of the Perkins and Hawaiian as both organisations are committed to helping people and to giving back to the community. Hawaiian Director, Kate O'Hara, said Hawaiian's initial interest in supporting the Perkins was inspired by staff who had experienced the impact and trauma of women's cancer.

She said it was exciting to be partners with an organisation that was not only a leader in its field but also shared Hawaiian's passion about making a difference in the community.

$2.4 million ACRF Cancer Imaging Facility opens

A ground-breaking State Cancer Imaging Facility was officially opened at the Perkins in July.

The $2.4 million facility, which uses specialised imaging equipment, was funded by the Australian Cancer Research Foundation, thanks to a bequest from a strong advocate of cancer research.

The Acting Chairman of the ACRF, Stephen Rix, said that the donation in the will of Mr Kevin McCusker had provided the ability to significantly expand the cancer imaging capability in WA.

The MRI, PET/CT and SPECT/CT scanners in the Cancer Imaging Facility are all non-invasive, high resolution monitoring tools that are smaller versions of human imaging equipment, allowing researchers to examine tumour development in pre-clinical models of cancer and determine effective forms of treatment.

Director of the Perkins, Professor Peter Leedman said the preclinical equipment in the facility would assist researchers move towards earlier disease detection, prevention strategies and assessment of the efficacy of new cancer treatments.

Financial report

Statement of comprehensive income for the year ended 31 December 2015

REVENUE	2015	2014
Funding and grants – operating	3,796,181	3,847,835
Grants – capital works	385,303	5,763,978
Rendering of services – clinical billings	7,663,592	5,869,408
Donations	1,913,094	604,872
Event income	6,476,241	7,953,667
Facility income	8,061,010	2,662,026
Other income	992,061	526,860
Interest income	542,246	581,022
	29,829,728	27,809,668

EXPENSES	2015	2014
Employee costs	(6,371,300)	(5,393,813)
Laboratory and clinical expenditure	(4,952,084)	(4,714,946)
Cost of sales – clinical billings	(3,196,299)	(2,902,640)
Depreciation and impairment	(7,527,234)	(7,110,965)
Administrative, office, event and utilities expenditure	(10,216,892)	(8,191,490)
Net deficit from continuing operations	(2,434,081)	(504,186)
Other comprehensive income / (loss)	13,613	(3,007)
TOTAL COMPREHENSIVE LOSS	(2,420,468)	(507,193)

Financial report

Statement of the financial position for the year ended 31 December 2015

ASSETS	2015	2014
CURRENT ASSETS		
Cash and cash equivalents	30,967,441	27,710,754
Cash held in trust	417,303	6,949,185
Trade and other receivables	10,424,247	5,613,677
Inventory	10,725	17,024
Prepayments	181,606	215,352
TOTAL CURRENT ASSETS	**42,001,322**	**40,505,992**
NON-CURRENT ASSETS		
Cash held in trust	–	38,905,471
Available-for-sale financial assets	264,893	261,600
Property, plant and equipment	139,541,402	141,779,403
Investment in subsidiary	–	–
TOTAL NON-CURRENT ASSETS	**139,806,295**	**180,946,474**
TOTAL ASSETS	**181,807,617**	**221,452,466**

LIABILITIES	2015	2014
CURRENT LIABILITIES		
Trade and other payables	11,860,141	5,608,753
Grants held in trust	12,295,058	12,889,697
Lease liabilities	1,991,783	5,754,683
Non interest-bearing liabilities	2,000,000	2,000,000
Employee entitlements	627,360	470,303
TOTAL CURRENT LIABILITIES	**28,774,342**	**26,723,436**
NON-CURRENT LIABILITIES		
Grants held in trust	–	39,251,449
Loan from related entity	–	–
Employee entitlements	111,953	135,791
TOTAL NON-CURRENT LIABILITIES	**111,953**	**39,387,240**
TOTAL LIABILITIES	**28,886,295**	**66,110,676**
NET ASSETS	**152,921,322**	**155,341,790**
Accumulated surplus	152,815,866	155,249,947
Available for sale revaluation reserve	105,456	91,843
TOTAL SURPLUS	**152,921,322**	**155,341,790**

The Statement of Financial Position provided above, together with the attached Statement of Comprehensive Income, have been extracted from the audited special purpose financial statements of the Harry Perkins Institute of Medical Research and its controlled entity. The summary financial information does not include all the information and notes normally included in an audited financial report. The audited special purpose financial report can be obtained upon request to the Chief Financial Officer.

The audited financial report (from which the summary financial information has been extracted) has been prepared in accordance with the requirements of the Associations Incorporation Act (WA) 1987, Australian Charities and Not-for-profits Commission Act 2012 and Regulations 2013, Australian Accounting Standards and other authoritative pronouncements of the Australian Accounting Standards Board.

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