Perkins

Issue 1 2016

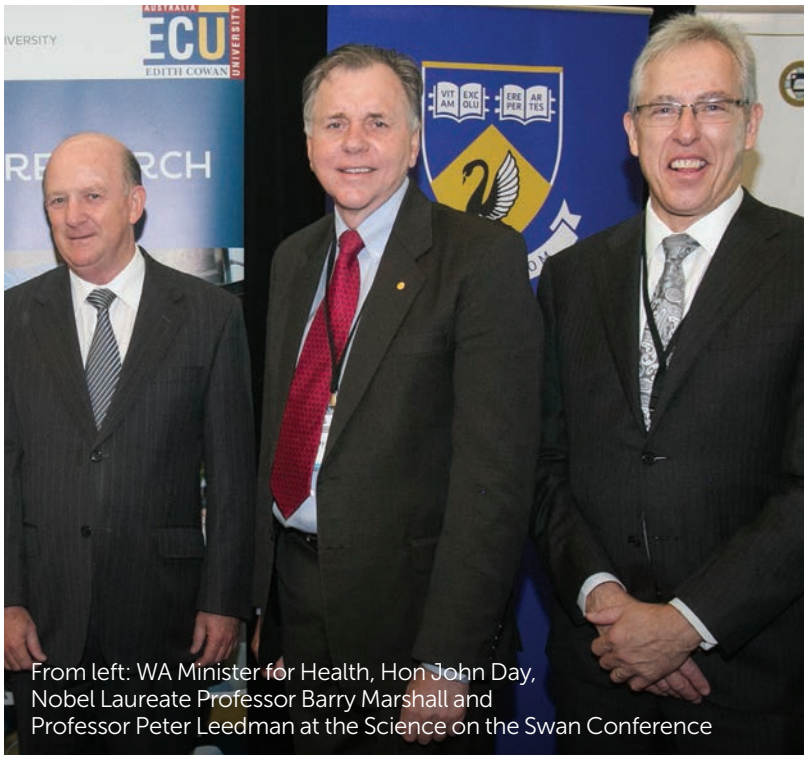
Magazine of the Harry Perkins Institute of Medical Research

Frogs and humans not so very different

Drug to break down tumour defences

New biomedical engineering program

From the Director



From left: WA Minister for Health, Hon John Day, Nobel Laureate Professor Barry Marshall and Professor Peter Leedman at the Science on the Swan Conference

This month I had the privilege of chairing WA's premier annual health and medical research conference, *Science on the Swan*.

With the theme of "cutting edge", the conference showed that medicine and medical research are in the middle of an unsurpassed decade of technology driven discovery.

Speakers highlighted big data and its application to precision medicine, advances in DNA sequencing and how MRI and PET scans are being used to beat cancer.

It is exciting to imagine where this technology might take us in the next few years as scientists from around the world tackle formidable challenges such as 3-D printing a whole organ like the liver or a kidney.

The Perkins is focused on recruiting the brightest minds, securing cutting-edge technology and producing innovative research for improved patient outcomes. We are already delivering on that vision, with the opening of a new floor in our state of the art facility at Nedlands. The new floor will house scientists working in areas including cell reprogramming, tissue bioengineering and revolutionary cancer imaging.

Enjoy this magazine, which features some of our recent research breakthroughs.

Professor Peter Leedman
Director, Harry Perkins Institute of Medical Research

PS – Date for your diary
Perkins Open Day on Saturday 27 August 2016

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New biomedical engineering program to change the face of medicine

> “Such grand plans are transformative, like putting a man on the moon”
> Dr Barry Doyle.

Dr Barry Doyle with Dr Brendan Kennedy and their teams.

A ground breaking vision to integrate bioengineering, medicine and science has led to the creation of a biomedical engineering program aimed at delivering revolutionary medical breakthroughs, such as transplantable 3D printed organs.

The Biomedical Engineering@Perkins program will fast track fundamental discoveries and develop cutting-edge clinical services to improve community health outcomes.

It has brought together biomedical engineers, clinicians and scientists in the Perkins state-of-the-art facility in Nedlands.

The program consists of two laboratories, a Vascular Engineering Laboratory headed by Dr Barry Doyle and a Cancer Imaging Laboratory headed by Dr Brendan Kennedy.

Dr Doyle said the program would be strengthened by the integration of a dedicated tissue-engineering lab within five years.

“Our grand vision is to 3D bioprint the world’s first implantable heart,” Dr Doyle said.

“This will require an immense effort from researchers from every facet of science, and beyond.”

Perkins Director Professor Peter Leedman said the program was the first of its kind in the State and would ultimately deliver improved health to the broader national and international communities.

“The first two laboratories will form the nucleus of a much larger critical mass over coming years”, said Dr Kennedy.

“This in turn will attract new researchers from throughout local universities and the broader biomedical engineering world”.

The program is a joint venture between the Harry Perkins Institute of Medical Research and the UWA Faculty of Engineering, Computing and Mathematics.

Linc Codd and Dr Liesl Celliers

New imaging expert welcomed

Radiologist and nuclear medicine specialist, Dr Liesl Celliers, has joined the Perkins in a new position which aims to fast-track cancer research.

Dr Celliers has been appointed as the inaugural *Perth Radiological Clinic Associate in Translational Imaging*, a position established by the PerthRadClinic Foundation to help scientists optimise research conducted in the high-end cancer imaging facility located at the Perkins.

After receiving her Bachelor of Medicine and Surgery from the University of Melbourne, Dr Celliers trained as a radiologist and a nuclear medicine specialist.

Perkins Director, Professor Peter Leedman, said he was pleased to welcome Dr Celliers to the Institute.

"This is the first time we've had a radiologist specialising in nuclear medicine at the Institute," Professor Leedman said.

"We are extremely grateful to the PerthRadClinic Foundation, chaired by Dr Martin Blake and his colleagues who have made this possible with a generous gift over a number of years."

Dr Celliers said her role involved evaluating cancer research projects and offering strategic advice, using her background in molecular imaging and oncology.

Dr Celliers said she hoped her work would lead to earlier disease detection, discovery of better prevention strategies and new cancer treatment tests.

Dr Michael Winlo

Linear Clinical Research welcomes new CEO

Linear, the clinical trials arm of the Harry Perkins Institute of Medical Research, has welcomed Dr Michael Winlo as its new CEO.

Dr Winlo is originally from Perth and earned his Bachelor of Medicine and Surgery with Honours from The University of Western Australia in 2005.

Dr Winlo spent the last six years between Silicon Valley and New York growing the health practice of the highly regarded data analysis firm Palantir Technologies.

Throughout his career Dr Winlo has gained strong skills in global business development, medical technology investment, health data analysis and project management.

"Linear is a world-class organisation with a compelling mission to improve patient access to new treatments and accelerate clinical research. I'm thrilled to return home and apply the unique experiences I gained overseas to serve as CEO," Dr Winlo said.

The Gene Detective

Professor Nigel Laing AO has dedicated his life to chasing covert disease genes in the genetic code of families desperate for answers.

This April, Professor Laing – one of the longest serving and most respected researchers at the Harry Perkins Institute of Medical Research – celebrated his 200th primary journal article, surrounded by scientists young and old, a large number of whom had either been mentored by or collaborated with Professor Laing.

Through the 200 journal articles, and the 34 years it's taken to reach that milestone, Professor Laing has made a truly astounding impact on the health of patients around the world.

Of his 200 articles, 25 describe new human disease genes, each of which signifies critical answers for thousands of families.

"I had an email today from a clinical colleague in the US saying they had solved a 50-year-old puzzle by showing the mystery condition a family suffered from was Laing distal myopathy," Professor Laing said.

Laing distal myopathy is a genetic condition that exhibits progressive muscle weakness in the feet and hands, often presenting in children under five years of age. The disease was named after Professor Laing.

"Most times with a genetic disease, you can't cure the patient because there is no treatment currently available but we can provide closure because the patient knows what their disease is and what they can expect in terms of disease progression."

Laing's illustrious career in science began in Edinburgh, when he chose to take a hiatus from his medical degree to accept a paid research role and a PhD in neurobiology.

Upon hearing that young Laing was pursuing a career in research, the Dean of the Faculty of Medicine pleaded with him to return to medical school.

"He grabbed me by my jacket lapels and hoisted me into the air, physically shook me and said 'you must promise me you'll come back and finish your medical degree' and I said 'don't worry, I'm coming back.'" Professor Laing said it was a deal he was happy to defy after discovering his true passion.

"One of the key things I love about research is that we're able to witness our work translated into health outcomes for thousands of patients and families," Professor Laing said.

Professor Laing's 200th paper describes a recessive disease gene that induces paralysis in babies before birth. Professor Laing says this research will lead to prenatal diagnosis for future families.

Perkins expands into new laboratories

Professor Ryan Lister with his team in the new laboratory at the Perkins

> "It feels like a defining moment, to be moving into a space that will enable the discoveries of tomorrow...."

More than 50 researchers from five laboratories have moved into new facilities at the Perkins this month.

When Perkins moved into its headquarters in Nedlands two years ago it allowed room for growth. Now, just over two years since the opening of the state of the art facility, a new floor has been opened which will house up to 100 Perkins researchers.

Three of the laboratories are new to the Perkins: the Epigenetics and Genomics Laboratory, headed by Professor Ryan Lister; the Cancer Imaging Laboratory, headed by Dr Brendan Kennedy; and, the Vascular Engineering Laboratory headed by Dr Barry Doyle.

Perkins Chief Operating Officer, John Fitzgerald, said that this is such an exciting time for the Institute.

"The opening of level 6 will not only allow us to bring both the new epigenetics and biomedical engineering teams into the Perkins, it will also allow us to relocate the WA Centre for Health and Ageing from Royal Perth Hospital, enabling us to increase the critical mass of medical research within our fantastic facility".

Perkins

HARRY PERKINS INSTITUTE
OF MEDICAL RESEARCH

Tour the new laboratories at the Perkins Open Day

Date for your diary

Saturday 27 August
10am to 3pm
Updates perkins.org.au

Professor Ryan Lister

Frogs and humans not so very different

An international team of researchers, led by Perkins researchers Dr Ozren Bogdanovic and Professor Ryan Lister, has found the genetic "switch" that causes one species of animal to look similar to another.

Fish, frogs, mice and even humans look remarkably similar at early embryonic stages and appear to share the same molecular instructions that generate the formation of body structures, such as a heart, limbs and the nervous system.

The researchers used powerful genome analysis technologies to map the biochemical signals, known as epigenetic changes, which effectively switch off certain genes during embryo development.

Their findings have improved the scientific understanding of the epigenetic process of development, which could be used in the future to show how these processes may go awry and cause disease or disability.

Dr Bogdanovic, the first author of the study, said the researchers were comparing the way that these epigenetic switches changed throughout embryo development in different species in order to form a blueprint for normal development.

"By looking at early stage embryos of different species, we were able to find the existence of multiple epigenetic switches that appear to be critical for limb formation or brain development" Dr Bogdanovic said.

"The switches change similarly in all these different organisms, even though they're separated by hundreds of millions of years of evolution."

Professor Lister said that this is fundamental research into how normal vertebrate development takes place.

"Through this we open a window into the processes that likely also occur during human development," said Professor Lister.

The research has been published in the prestigious journal *Nature Genetics.*

New drug to break down tumour defences

A drug developed by Woodside Professor Ruth Ganss and her team from the Harry Perkins Institute of Medical Research could be used to repair blood vessel defects and allow for more targeted and effective drug delivery.

Current anti-cancer treatments like chemotherapy and immunotherapy, which harness a person's own killer immune cells, can struggle to enter a tumour because the blood vessels that fuel it become malformed.

While investigating this problem Professor Ganss and her team in the Perkins Vascular Biology and Stromal Targeting Laboratory found that smooth muscle cells that line blood vessels to give them shape and help them pump blood, often break down in tumours. Once the smooth muscle cells break down, the blood vessel becomes leaky, reducing blood flow and preventing chemotherapy and immune cells travelling into the tumour.

Professor Ganss said the new drug developed in her laboratory worked by repairing the smooth muscle cells and returning normal blood flow to the vessels, allowing other anti-cancer drugs to reach the tumours core.

"To achieve greater absorption of anti-cancer drugs, the blood vessels are really key," Professor Ganss said.

Professor Ganss said the defect in smooth muscle cells lining blood vessels in cancer could be a catalyst for other problems.

"It could be that once the smooth muscle cells break down and the blood vessels become leaky, cancer cells are able to slip out of the tumours and migrate through the blood stream to spread to different parts of the body."

"We are currently investigating whether our drug could help stem the spread of cancer in a patient by repairing the leaky blood vessels."

The research has been published in the prestigious journal *Cell Reports*.

Dr Anna Johansson-Percival, Dr Zhi-Jie Li and Woodside Professor Ruth Ganss.

Professor Alistair Forrest

Perkins researcher wins Millennium Science Award

Perkins Laboratory Head, Professor Alistair Forrest, has won the Millennium Science Award and become the first West Australian based researcher to win the award since its inception.

The Award, which is granted to a young researcher who has made outstanding contributions to Australian scientific research, was presented at this year's 37th Annual Lorne Genome Conference in Victoria.

Professor Forrest heads the Systems Biology and Genomics Laboratory at the Perkins and investigates how cells work at a system level.

"Eleven years ago I was at Lorne presenting as a nervous PhD student, it's great to come back as an 'academic adult' and win this award," Professor Forrest said.

Professor Forrest joined the Perkins in 2015. He was recruited to the Institute using funds raised from the MACA Ride to Conquer Cancer and a fellowship grant from the Cancer Research Trust.

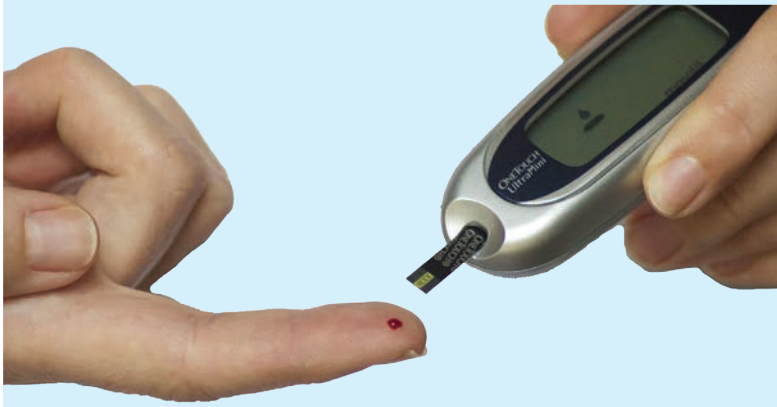
Study improves understanding of Type 1 Diabetes risk

A study led by Perkins researchers has uncovered a complex web of factors that impact a person's risk of developing Type 1 Diabetes.

Previous investigations had identified 60 disease genes that affect a person's risk of developing Type 1 Diabetes.

Professor Grant Morahan, Director of the Centre for Diabetes Research, said the purpose of this investigation was to uncover how these disease genes caused diabetes.

"Some genetic diseases, for example cystic fibrosis, are simple genetic diseases. They are caused by a mutation in one gene and this mutation makes a faulty protein," Professor Morahan said.



"People thought complex diseases, such as diabetes, would also be due to variants that changed proteins but our study found that's not the case."

The researchers used powerful analysis technologies to reveal how the disease genes functioned.

"We tested 30,000 different genes in four cell types provided by people from some 4000 families. We discovered that most of the diabetes genes controls the amount of activity of nearby genes," Professor Morahan said.

"Previously people thought that if you wanted to prevent someone getting Type 1 Diabetes, scientists would need to develop a drug that would counter faulty proteins but this study suggests we need a different approach."

"We need to come up with a treatment that will control the way the disease genes affect the immune system."

The published results were highlighted for its importance in the April edition of the leading *Journal of Immunology*.

Breakthrough in childhood disability

A dynamic research team, including Perkins scientists, has uncovered the cause of microcephaly and intellectual disability in a young West Australian.

Microcephaly is abnormal smallness of the head, a congenital condition associated with incomplete brain development. Microcephaly has recently been linked with the Zika virus outbreak sweeping South America.

First author on the paper, Perkins researcher Isabel Hemming, said the team had uncovered a strong link between a specific chromosome mutation and intellectual disability, which helped them establish the cause of the child's condition.

"Our study was significant in that we were able to conclude that the genetic mutation is almost certainly responsible for the child's symptoms," Ms Hemming said.

Head of the Perkins Brain Growth and Disease Laboratory, Associate Professor Julian Heng, said the study opened the door to important new research into chromosomal triggers of brain growth defects, and possible methods of treatment.

Associate Professor Julian Heng

Perkins researchers decipher world-first muscle disorder cases

Perkins scientists have discovered crucial information that could lead to improved treatments for young patients with a devastating muscular disorder.

The Neurogenetic Diseases researchers were asked to help solve the case of two unrelated patients a one-year-old and four-year-old experiencing severe muscle stiffness and limited movement.

The multi-national team focussed their study on a muscle protein, known as tropomyosin-3 (TPM3).

The protein is vital for skeletal muscle development and plays a crucial role in healthy movement and when defective, this protein was known to cause a range of muscle disorders.

Dr Kristen Nowak from the Perkins Neurogenetic Diseases Laboratory said this is a world-first case where a TPM3 defect has produced these symptoms.

"All diseases caused by defective TPM3 up to now have had muscle weakness as a common feature. The children in this case had very severe muscle stiffness from birth, the absolutely opposite effect," Dr Nowak said.

Clinicians treating patients with similar symptoms will be able to provide targeted gene screening as a result of this study.

The first muscle disease associated with TPM3 was discovered by Neurogenetic Diseases Laboratory Head Professor Nigel Laing 20 years ago.

Leading cardiologist calls for urgent heart research

Professor Peter Thompson, cardiologist and Deputy Director of the Harry Perkins Institute of Medical Research, has called for a renewed focus on fundamental heart research.

Professor Thompson said that while WA has excellent clinical research into the treatment of heart disease, basic research into really understanding the causes of heart disease is very limited.

"We urgently need to understand heart disease better and tackle the basic causes with an intensive effort to reduce the toll from heart disease in our community," Professor Thompson said.

"A focus on finding treatments for heart disease has produced dramatic results, for example if you had a heart attack 30 years ago your risk of dying in the first week was 13% and now the risk of dying from a heart attack in the first month is down to 4%."

"But while treatments have improved, we still don't have answers to some fundamental questions about heart disease and hence why it remains the biggest killer of both men and women."

Professor Peter Thompson

He said that high blood pressure is an area where a breakthrough is urgently needed.

Professor Thompson said that the Perkins is focused on building a critical mass of expertise in heart disease here in WA to answer these questions.

"The Perkins needs the continued support of the community to keep our best heart scientists and doctors here in WA if we want to ensure that we find the answers and at the same time have access to the latest clinical trials."

AXIS scholarship supports promising cancer researcher

An early career scholarship donated by AXIS Financial Group has enabled Perkins researcher, Joanne Van Vuuren, to focus on investigating a gene that could reduce cancer cell growth.

"The partnership with AXIS CEO John Exton and his team has given me the opportunity to share the important work we do with people from the community", Joanne said.

"My project focuses on investigating the role of a gene, known as HLS5, in liver cancer."

"Our aim is to directly investigate whether loss of HLS5 increases the risk of liver cancer and if so, can we then use HLS5 as a drug target," Joanne said.

Joanne said cancer research was often reliant on philanthropic funding from organisations like AXIS and she commended the foresight of AXIS in supporting research that would pay dividends in community health.

AXIS scholarship recipient, Joanne Van Vuuren with AXIS CEO, John Exton

Walkers support life saving cancer discoveries

The third Weekend to End Women's Cancers presented by Hawaiian saw 752 walkers raise $2.3 million.

Twelve months of high teas, sausage sizzles, quiz nights and fundraising dinners culminated on the weekend of 2 and 3 April when the city became a sea of pink as hundreds of walkers wound their way through the streets and Hawaiian shopping centres including the Carillon in the city, Melville Plaza and The Mezz at Mount Hawthorn.

With funding raised through the Weekend, the world-leading researchers, doctors, scientists and clinicians at the Perkins can continue to advance cancer research programs, aimed at translating our discoveries into improved patient care.

Thank you to walkers, sponsors, volunteers, crew members and donors who made the Weekend a great success.

In May 2017, the Perkins is holding a 30km walk with a $1,000 fundraising minimum.

Register your interest to walk with us and help in our quest to defeat women's cancers.
Visit thankyou.everydayhero.do/perkins

Macquarie Group riders support Perkins cancer research

Staff at the Macquarie Group are contributing to cancer research at the Perkins by raising vital funds through the MACA Ride to Conquer Cancer.

David Walker, an Associate Director of Macquarie Group Limited, said he signed up for his first Ride in 2014 and found that his Macquarie colleagues were keen to get involved by signing up for the Ride or supporting the teams fundraising efforts.

David Walker and his son at the Ride

Riders from the Macquarie Group participate as members of Team MACA.

"In the first year, it was just a bit of fun and a good reason to get fit but after the emotional opening ceremony and then visiting the Perkins laboratories, it started to sink in that it was more than just fun – it was really important," David said.

"After signing up for the second Ride my grandfather died of cancer and it made it all the more real for me."

The Macquarie Group Foundation rewarded the determination of their staff members by matching their fundraising efforts with a donation of $61,000.

The Macquarie Group Foundation is the philanthropic arm of Macquarie Group, facilitating pro bono programs and funding a range of community projects including cutting-edge research.

The 2016 MACA Ride to Conquer Cancer will take place on 15 – 16 October. To find out more about how you can register for the Ride visit www.perkins.org.au

MACQUARIE

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