Magazine of the Harry Perkins Institute of Medical Research

Breakthrough technology to reduce breast cancer surgeries

Antibiotic resistance: a modern medical emergency

# Stopping the spread of melanoma

Issue 2 2016

What you need to know about prostate cancer

# Perkins recognises philanthropic partners



At a special function at Government House Ballroom on 1 June, the Patron of the Perkins, Her Excellency the Honourable Kerry Sanderson AC, presented citations to MACA and the Prendiville Family.



Ashok and

Renu Kumar

and family

MACA was awarded the Perkins Corporate Partner Award for 2016. MACA is not only the title sponsor of the MACA Ride to Conquer Cancer but has a team of up to 300 riders in this event which raises critical funding for cancer research at the Perkins. The award was accepted by MACA's Director of Operations, Geoff Baker.

The Prendiville Family received the Community Partner Award for their outstanding contributions to the Kirkbride Melanoma Centre, established at the Perkins in memory of young professional golfer, Scott Kirkbride who lost his battle with melanoma at just 27 years of age. The award was accepted by Garry Prendiville on behalf of Dr Jamie Prendiville and the family.



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# From the Director - my Father's Day message

### Have you had a conversation recently about prostate cancer?

Prostate cancer is the most commonly diagnosed cancer in Australia. Nine men die from the disease every day but many men are reluctant to talk about it, even with their doctors.

As a doctor and a scientist, I've witnessed how prostate cancer behaves, both in my patients and in the laboratory. As a specialist in endocrinology I treat men with prostate cancer and as a scientist I conduct research into how hormones act in this cancer.



I have also experienced the devastating effects of prostate cancer on a personal level as it claimed the life of my father.

Here at the Perkins, the team in the Cancer Medicine Laboratory has made key discoveries involving a tiny microRNA molecule that could ward off prostate cancer.

We found that prostate cancer cells contain less of microRNA molecules, spurring their rapid growth. MicroRNAs are small and, unlike double-stranded DNA, consist of a single strand of nucleotides, encoded in plant and animal genome.

Our research suggests that this microRNA normally works as a brake on prostate cell growth, so perhaps if we can put it back into prostate cancer cells then we can restore that brake.

While we continue to drive research into prostate cancer it is also important to remind everyone that early diagnosis is a critical factor.

**Professor Peter Leedman** Director, Harry Perkins Institute of Medical Research

# About prostate cancer

### What is the prostate?

The prostate is a small gland that sits below the bladder. It surrounds the urethra, the passage through which urine passes. The prostate needs the hormone testosterone to grow and develop. Often the prostate is the size of a walnut, but it is normal for it to grow as men age. Prostate cancer occurs when abnormal cells develop in the prostate.

### Symptoms

It's not uncommon for there to be no noticeable symptoms when prostate cancer is in the early stages. In the later stages, some symptoms of prostate cancer might include: finding blood in the urine, the frequent or sudden need to urinate, difficulty or discomfort when urinating or experiencing pain in the lower back, upper thighs or hips.

### **Risk factors**

The risk of prostate cancer increases with age, men over 50 years are particularly at risk. Family history has also been strongly linked to developing the disease. Fatty diets and those high in processed meat, as well as lifestyle factors like lack of exercise could increase the risks.



About 1 in 7 men will be diagnosed with prostate cancer during his lifetime.



The average age at the time of diagnosis is 66 years



In Australia, prostate cancer is the most commonly diagnosed cancer in men, with more than 3,000 men dying of prostate cancer every year. The team is currently testing a targeting molecule that functions like a GPS navigator and sends the nanoparticles straight to the tumour site.

Dr Anabel Sorolla

### New method to fight hard to treat breast cancers

Researchers at the Harry Perkins Institute of Medical Research have developed a new, more effective method to tackle aggressive breast cancers.

The research, led by Dr Anabel Sorolla, involves the use of nanoparticles to deliver anti-cancer agents directly to a tumour.

The research focused on triple negative breast cancer, an aggressive cancer with few treatment options that becomes highly resistant to chemotherapy and results in patients relapsing after remission.

The investigation found that chemotherapy resistance in this type of breast cancer is linked to a DNA-altering protein.

The protein is found in two places in the body, in the brain and in the breast. In the brain the protein works to protect

neurons from damage, warding off brain cell death that could lead to Parkinson's Disease.

In breast tissue, the protein triggers cancer cell growth, spread and chemotherapy resistance.

The new nanoparticles work by blocking the DNA-altering protein and delivering chemotherapy drugs directly to the tumour, while also making the cancer cells more susceptible to chemotherapy.

Dr Sorolla said her team's nanoparticles have been shown to be more effective than those currently used to treat patients. "We have found that our nanoparticles only trigger cell death in this highly aggressive form of breast cancer, not in healthy cells," Dr Sorolla said.

"Our method works better than nanoparticles currently used in the clinic, partly because existing nanoparticles don't have targeting molecules," Dr Sorolla said.

"On the whole, when we combine existing anti-cancer drugs with our nanoparticles we can greatly reduce the dose of chemotherapy needed, with better results and less side effects."

The study was published in the high impact, international journal *Nanoscale*.

### About Triple Negative Breast Cancer

Cancers that test negative for progesterone receptors, estrogen receptors and a protein called HER2 are known as triple negative.

Triple negative breast cancer does not respond to the most widely used breast cancer treatments. Triple negative breast cancers have a higher rate of recurrence than other types of breast cancer.

Five-year survival rates are lower for women with triple negative breast cancer.

More than one in every ten breast cancers are found to be triple negative.



### Breakthrough technology to reduce breast cancer surgeries

Thousands of breast cancer patients might be spared a second surgery thanks to groundbreaking new technology.

Up to one in four women undergoing surgery to remove breast cancers will have to return to the operating theatre within weeks to remove further tissue, as small traces of tumour can be left behind.

Currently, surgeons use their finger to distinguish the edge of the tumour because cancerous tissue is much harder and stiffer than normal tissue, but this method doesn't detect tiny cancerous cells which could allow the tumour to rearow.

#### World first

To solve this problem Perkins biomedical engineer, Dr Brendan Kennedy and his team of researchers from the Perkins and The University of Western Australia, have developed the world's first 3D printed fingermounted optical imaging probe - a 'smart surgical glove'.

Dr Kennedy said the probe measures tissue stiffness at a microscopic level using high resolution imaging, allowing surgeons to detect cancer cells that are too small to see or feel but can continue to grow if left in the breast.

"The finger can only identify large tumours so the ability to detect cancer at a cellular level is key to ensuring effective removal of the tumour," Dr Kennedy said.

"The surgeon will be able to run their gloved finger around the edge of the tumour and the super sensitive probe will project an image of what they're touching on to a high resolution screen for far better visibility."



surgical glove prototype

#### Surgeons to test late this year

Dr Kennedy is working with surgeons and pathologists in Perth to test the first generation prototype on tissue taken from mastectomies and he believes the glove will be ready to test in surgeries by the end of 2016.

He said the ability to translate research outcomes into patient benefits was fundamental, and he hoped consultations between surgeons and scientists would allow patient outcomes to continuously improve at a faster rate.

Dr Kennedy is developing the glove in association with leading breast surgeon Professor Christobel Saunders and UWA's Professor David Sampson.

The project is funded in part by the National Breast Cancer Foundation.

# Cause of mitochondrial dysfunction discovered by Perkins researchers

Researchers have found a connection between a mutation in the power source of our cells and a devastating disease that causes vision loss, heart disease and muscle defects in patients.

The disease, known as Leigh Syndrome, has previously been linked to a genetic mutation, but Perkins researchers were able to determine how the mutation led to mitochondrial dysfunction.

Mitochondria are responsible for converting energy from food into a power source for our body and are essential for the normal function and survival of our cells.

The researchers discovered that this mutation stopped production of a particular protein, which helps our cells generate energy.

Lead researcher on the project, Dr Tara Richman, said without this protein the energy production system falls apart, which leads to symptoms similar to those seen in patients with Leigh Syndrome.

"When we investigated further, we discovered that this protein works like a chaperone, guiding vital components of our energy production system to the right area," Dr Richman said.

In patients with Leigh Syndrome, the symptoms often show up later in life as the function of mitochondria diminishes over time.



"Your body can compensate for quite a lot of horrible things, even without the right components, but eventually things start to go very wrong," Dr Richman said.

"There's still so much that is not understood about mitochondria and how they power every single part of our body".

"If we don't understand this, we've got no hope of understanding any disease at all."

### Eureka finalist announced

A project, FANTOM5, led by Professor Alistair Forrest of the Harry Perkins Institute of Medical Research, has been named as a finalist for the Scopus Eureka Prize for Excellence in International Scientific Collaboration.

With 260 specialists from 20 countries, including 22 Australian researchers, the FANTOM5 project is mapping the sets of genes expressed in each of our cell types. The map is being used to interpret genetic diseases and engineer new cells for therapeutic use.

The prestigious Australian Museum Eureka Prizes were established in 1990 to reward outstanding achievements in Australian science and science communication.

FANTOM5 Australian collaborators are from the Harry Perkins Institute of Medical Research, the University of Melbourne, the University of Queensland, the Translational Research Institute and Telethon Kids Institute, and the project is based at RIKEN Japan.

### Top British award for Perkins researcher

One of the Perkins brightest medical scientists has been recognised with a prestigious award by the British Pharmacological Society.

Associate Professor Kevin Pfleger, Head of Molecular Endocrinology and Pharmacology, has won the Novartis Prize in recognition of his work, which focuses on receptors throughout the body that are the target of many commonly used medicines.

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

The winners will be announced on 31 August.

# Stopping the spread of melanoma

Researchers from the Harry Perkins Institute of Medical Research may be a step closer to reducing the growth and spread of melanoma.

A team from the Perkins Laboratory for Cancer Medicine found that a tiny molecule in our cells works as a powerful tumour suppressor, stopping the growth and spread of cancer.

Perkins Director and Head of the Cancer Medicine Laboratory, Professor Peter Leedman, said microRNA-7 functions as a molecular gate around the cancer, keeping the tumour locked in one spot in the body. As the cancer grows, it can unlatch the molecular gate and spread to other parts of the body.

"Our research found that microRNA-7 was reduced when the cancer progressed from one spot on the skin and spread to other organs," Professor Leedman said.

"We put the microRNA-7 back in the melanoma cells and were able to slow down the cancers growth and ability to spread through the body."



### Melanoma is the most aggressive type of skin cancer and Australia has the highest incidence in the world.

When melanoma is confined to the skin and removed the prognosis is very good, but if the melanoma spreads the survival rate is drastically reduced.

After decades of little progress in the fight against melanoma, we now have targeted drugs providing hope for patients, but melanoma often recurs so new treatments are still urgently needed.

### Another step towards better treatment

Leading investigator on the study, Rikki Brown, said that patients with low levels of microRNA-7 in their cells have reduced long-term survival rates.

"We found a particular protein that runs rampant when there are low levels of microRNA-7. This protein instructs cancer cells to divide, migrate and resist killing by anti-cancer drugs," Rikki said.

"When levels of microRNA-7 are increased in melanoma cells, it turns down this protein and reduces those harmful effects," Rikki said.

"We hope this discovery is another step towards developing treatments that may delay or prevent melanoma spreading and new research will look at combining microRNA-7 with other approved anti-cancer drugs to see if they are more effective together."

The study was funded in part by the Kirkbride Melanoma Centre at the Perkins.

To find out more about the Kirkbride Melanoma Centre at the Perkins and how you can support research into melanoma visit: www.kirkbride.org.au



# Antibiotic resistance: a modern medical emergency

PhD student Kieran Mulroney is undertaking cutting edge research in antibiotic resistance under the supervision of Dr Aron Chakera From treating common infections to allowing organ transplants, antibiotics have extended average lifespans by decades. But bacteria can develop resistance and their misuse and overuse is making them less effective. As a result, doctors are now seeing once curable infections they can no longer treat.

### How does antibiotic resistance affect me?

Using antibiotics when you don't need them or not finishing your prescribed dose of antibiotics may mean that they won't work for you when you need them in future. The more antibiotics you use, the more chances bacteria have to become resistant. Once a strain of bacteria becomes resistant to antibiotics they are known as 'superbugs'.

Antibiotic resistance is fast becoming one of the most serious threats to human health.

### How the Perkins is helping

Dr Aron Chakera, who heads the Perkins Translational Renal Research Laboratory, and his team are currently investigating ways to minimise antibiotic resistance and help improve the effectiveness of the antibiotics we have.

### Finding the right drug quickly

The team is working on the fastest and most reliable method to diagnose bacteria. By identifying the bacteria quickly, doctors can prescribe the 'right' antibiotic to treat the specific infection. This means that patients will get better faster, with less exposure to unnecessary antibiotics.

They are looking at using other drugs that destroy the bacterial barrier, so we can use less antibiotics but in a more targeted way.

### Rapid detection of antibiotic resistance

Perkins researchers are also helping develop a screening test that will rapidly detect whether bacteria present in an infection will be susceptible to common front-line antibiotics. Their method is much faster than the current tests and could help doctors select the best medicine very soon after the patient presents.

## Using non-antibiotic bacteria killers to treat infected wounds

Treating infections on the skin before they escalate to system-wide infections is an important strategy in managing antibiotic resistance. Perkins researchers are exploring the use of non-antibiotic alternatives, such as vinegar, as bacteria killing agents for infections on our skin. You can see the history making petri dish and Fleming's hand written inscription at the Perkins Open Day on Saturday 27 August 2016 from 10am to 3.30pm.

# A piece of history that saved millions of lives

### Many of us know the story!

In 1928, Alexander Fleming was growing bacteria in petri dishes in his cluttered office. Fleming went on holiday without sterilising his plates or closing the windows to his laboratory. When he returned he found his culture dishes covered in a common mould, the kind that grows on a slice of bread.

## It was a stroke of luck that has since saved millions of lives.

Fleming noticed there was a clear ring around the mould that had killed the bacteria in his petri dishes. He labelled and saved the dishes. With the help of Australian Howard Florey and Ernst Chain, this discovery became the first ever antibiotic and went on to cure millions of people of bacterial illnesses that had previously been largely untreatable and often deadly.

Today, the Harry Perkins Institute of Medical Research has a priceless piece of this history in its Nedlands facility. In 2013, the Hon. Liz Behjat MLC and her family donated a sample of the antibiotic mould, signed and dated by Alexander Fleming.



Liz's father, the late John Williams (who was also a Member of Parliament in the Legislative Council from 1971 to 1989) worked with a former laboratory assistant of Alexander Fleming's in the 1960's. The laboratory assistant had been gifted two samples of the historic mould. The co-workers became friends and the lab assistant gave Williams one of the mould samples.

Liz says she did not realise the significance of Fleming's petri dish growing up.

"We had it for all these years but it was something we'd take to school for show and tell."

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> "I brought it to the Perkins where they were extremely excited to see this piece of history. I went home and told my mum that this little petri dish had an impact far beyond what we thought."

The Williams/Behjat family donated the antibiotic mould sample to the Perkins in 2013. It is displayed in a special case at the Perkins headquarters in Nedlands By recognising what is unique amongst children with an autism spectrum disorder, will enable us to diagnose autism earlier and intervene earlier.

# A new genetic player in autism

A study aimed at detecting the genetic triggers of autism spectrum disorder has uncovered a new gene mutation which could lead to better diagnosis and treatment outcomes.

The investigation was led by Associate Professor Julian Heng from the Harry Perkins Institute of Medical Research, who heads the Brain Growth and Disease Laboratory.

The research revealed a connection between autism spectrum disorder and mutations to a gene known as DENR.

Julian said the research looked at two children with autism spectrum disorder; each had a unique genetic mutation to DENR that changed the way this gene functioned.

The study found that foetal brain development seems to be disrupted by the DENR gene malfunction, which appears to affect the assembly of neural circuits in the brain. By uncovering the ways through which genes such as DENR shape brain development, it is hoped that scientists might be able to recognise how the autistic brain is unique.

"Finding the genetic triggers of brain developmental disorders such as autism helps us identify the most important elements required for a great start to life and good mental health," Heng said.

He said this sort of research can improve the diagnostic precision for autism and can also lead to personalised treatments in coming years. "We believe that by studying genes such as DENR in the context of brain development, we might be able to tinker with this element to our mental health for therapeutic gain," Professor Heng said.

"We know that early intervention is critically important to the management of mental health conditions such as autism."

This study involved research teams in Germany, Austria and the United Kingdom.

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

# Philanthropy funds genetic disease prevention program

A \$60,000 grant from the Perpetual Foundation, through the Helen Leech Endowment, will fund the development of a screening test to help reduce fatal recessive diseases.

The grant was awarded to the Perkins Neurogenetic Diseases Laboratory, led by Professor Nigel Laing AO, for a project entitled 'Prevention of genetic diseases through pre-conception carrier screening'. It will involve analysing DNA samples to find genetic mutations that could cause devastating and often fatal diseases.

### **Genetic roulette**

"Most of us do not know which recessive lethal disorders we carry. Therefore, when any couple decides to have children, we play what I have called 'genetic roulette'," Professor Laing said.



"If both partners carry the same lethal recessive disorder then the couple has a one-in-four chance of a child with that lethal recessive disorder."

Implementing a screening test will give parents an opportunity to uncover what disease genes they and their partner carry, and the likelihood of passing those genes on to future offspring.

# Sean's battle with cancer

Cancer survivor, Sean Tucker, is one of the many amazing riders who will be cycling over 200km in this year's MACA Ride to Conquer Cancer.

Now 20, Sean was diagnosed with Stage 3 Non-Hodgkin Lymphoma when he was just 13 years of age.

After being told that he had cancer, Sean had one big question: "Am I going to die?"

"I asked my dad this question, and he looked me in my eyes and held my shoulders, and he said to me that I was in for a big fight, like a boxing match.

"12 rounds Sean, except you aren't going the full 12, you are going to knock this cancer out in round 1, because you are the strongest person I have ever met, and because we need you, we aren't ready to say goodbye yet."

Sean says his experience in hospital taught him a valuable life lesson: "You never truly know what it is to be alive until something out of your power threatens to take it from you."

"For a few years things began to get back on track, until May last year when I was rushed to hospital with severe abdominal pains. I had the first of three operations on my bowel they say because of the toll that chemo had on my body.



My last operation was only on the 24th March this year. I am getting worried again. This ride will help me find my strengths again," said Sean.

Sean says no one should have to go through the experience he did, which is why he's participating in the Ride.

All funds raised through MACA Ride to Conquer Cancer come directly to the Perkins for our cancer research.

It's not too late to register for the Ride on 15-16 October 2016 at: pr16.conquercancer.org.au

# **Perkins Open Day**

Saturday 27 August, 10am to 3.30pm

**QEII Medical Centre, Nedlands** 



### Experience the wonders of medical science when the Harry Perkins Institute of Medical Research opens its doors to the community.

Join us for talks on the very latest in research and treatments, hands-on activities, guided tours of the building by medical researchers and a rare walk through our state-of-the-art laboratories where our researchers tackle the most challenging human diseases.

10.50am	Breast cancer - the good, the bad & the ugly Dr Andrew Redfern
11.30am	We are how we think - investigating the genetic basis for early onset brain disorders Associate Professor Julian Heng
12.10pm	Hunting genes in Western Australia Professor Nigel Laing AO
12.50pm	Why understanding fundamental biology is fundamental to your health Associate Professor Kevin Pfleger
1.30pm	Biomedical engineering for heart disease Dr Barry Doyle
2.10pm	Fighting cancer: a glimpse into the future Woodside Professor Ruth Ganss
2.50pm	Heart research is vital Professor Peter Thompson AM



### Visitors' paid parking: Carpark 3A, 7, 7B (off Monash Avenue)

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