Biomed Benchmark
News from the School of Biomedical Sciences
March 2011, Issue 13

Punching holes with killer proteins

An international team of researchers has solved the 3D structure of a key immune protein and shown how it kills cancerous and virally infected cells. For their painstaking efforts, the scientists from the School of Biomedical Sciences, Peter MacCallum Cancer Centre and Birkbeck College in London have been rewarded with a paper in the prestigious medical journal *Nature.*

For the challenging project lead author Dr Ruby Law, from the Department of Biochemistry and Molecular Biology, purified a protein called perforin, produced crystals and then exposed these crystals to X-ray beams at the Australian Synchrotron, in Clayton. Back in the lab, the scientist spent several months solving perforin's structure.

What did she see?

"In its soluble form, perforin looks like a house key. It is flat, with a big head, skinny tail, plus a key hole in the middle," Dr Law says.

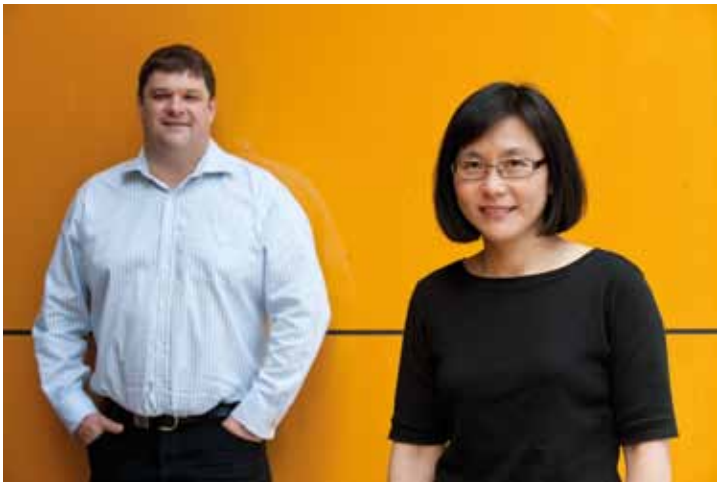
Her colleagues at Birkbeck College, who performed electron microscopy studies, also collected images of this protein. They showed that the 'head' of the key can exist in two forms, diamond or square. This feature might help explain how perforin can move and change from a soluble to insoluble cell-surface-bound form, with lethal consequences.

Dr Law explains: "Perforin is a beautiful protein where everything works perfectly. The perforin 'tail' seeks and latches onto an infected cell, before molecules interact together to form a doughnut-shaped complex. Then, in a master stroke, the 'head' region punches a hole into the cell through which killer enzymes (granzymes) can be injected to eliminate the foe."

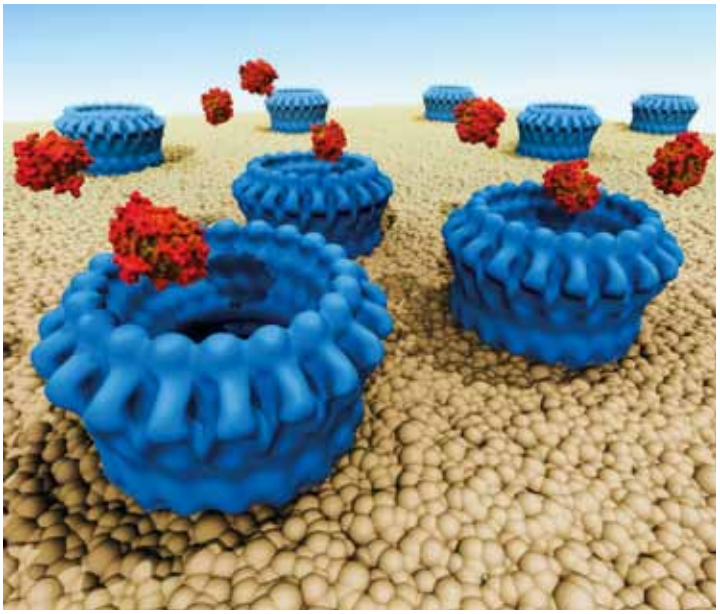
With the protein structure now known, the next step for the research team is to learn how to inhibit its function. That's because over-functioning perforins attack pancreatic beta cells and cause diabetes, and are responsible for transplant rejection.

While there is much work to do on the perforin front, Dr Law acknowledges the importance of teamwork. "By jointly pooling our data together, we could look at perforin from different angles and gain a better understanding of how it works and causes disease."

Dr Law, who was funded by the NHMRC and ARC Centre of Excellence in Structural and Functional Microbial Genomics, collaborated with research project leaders: Professor James Whisstock, Department of Biochemistry and Molecular Biology; Professor Joseph Trapani, Peter MacCallum Cancer Centre; Professor Helen Saibil, Birbeck College; and colleagues from the Australian Synchrotron and Victorian Partnership of Advanced Computing.



Dr Ruby Law (right) with Professor James Whisstock.



Perforin pores (blue) on a membrane landscape (beige). Granzyme toxins (red) are shown moving through the perforin pores. Image: Mike Kuiper, VPAC.

MONASH University
Medicine, Nursing and Health Sciences

Grants success

School of Biomedical Sciences researchers are successful recipients of $24.7 million of funding from NHMRC commencing in 2011. This includes support for 36 project grants and 13 fellowships.

In addition, our researchers secured $7.6 million of funding from ARC. This includes support for 15 project grants and three Future Fellowships.

Several scientists achieved outstanding results. Head of School, Professor Christina Mitchell scored a career-topping four grants worth $2.2 million from ARC and NHMRC. Recent recruit Dr Di Yu also received four grants while colleagues Professors Gail Risbridger and Jamie Rossjohn were awarded three grants each. A summary of the top 10 grant recipients is listed.

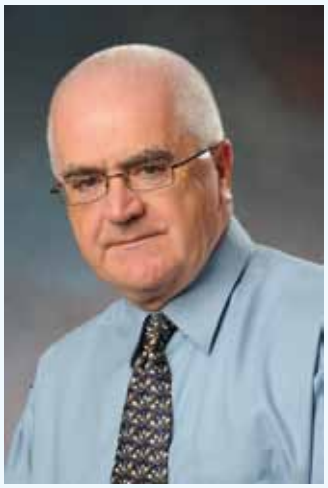
Funding was also secured from other Australian grant funding agencies to the value of $1.2 million.

Top 10 Grant Recipients*

	Name	Grants received	Amount ($ million)
1	Professor Christina Mitchell	4	2.2
2	Professor Gail Risbridger	3	1.7
3	Professor Jamie Rossjohn	3	1.7
4	Professor Tony Tiganis	2	1.4
5	Associate Professor Jane Black	2	1.2
6	Professor David Jans	2	1.2
7	Professor Andrew Elefanty	2	1.2
8	Dr Di Yu	4	1.1
9	Dr Zane Andrews	2	1.1
10	Dr Helen Abud	2	1.0

**Funding sources: NHMRC, ARC and/or other Australian grant funding agencies.*

An eye for anatomy



Professor Paul McMenamin

Paul McMenamin is a rare breed of anatomy professor, who combines his passion for medical research with academic teaching.

Born and educated in Scotland, the University of Western Australia staffer for 23 years has moved eastwards where he now heads the Centre for Human Anatomy, at the Monash Clayton campus.

Professor McMenamin has ambitious goals. "I want to break away from anatomy being seen as a dead science," he says. "It's a living thing and I want to encapsulate that in the teaching for students studying biomedical sciences, medicine, radiography, psychology and psychiatry."

Professor McMenamin uses both novel and conventional approaches to teach anatomy. Students dissect and reconstruct a 'virtual' human body using interactive software, body paint organs onto each other, as well as study cadaver specimens and attend tutorials. He also plans to collaborate with clinical skills teachers so that theoretical and practical aspects of anatomy can be taught at the same time to enhance learning.

Also on his 'to do' list, Professor McMenamin hopes to raise funds from philanthropic donations to renovate teaching spaces, build a cool room and expand the anatomy facilities. He believes an infrastructure upgrade is needed for the centre to become the best anatomy teaching centre in the country.

In addition to his role as an educator, Professor McMenamin heads a team of scientists who study the eye, a life-long interest. His group at the Department of Anatomy and Developmental Biology study corneal inflammation, which affects people who wear contact lens or have eye injuries; the role of the immune system in diabetic retinopathy and age-related macular degeneration; and eye evolution in marsupials.

"You can work on so many problems: allergic diseases at the surface of the eye; neurological, connective tissue and parasitic diseases; and disorders such as cataracts," Professor McMenamin says. "The eye encapsulates almost everything that is amazing about the body."

"I want to break away from anatomy being seen as a dead science. It's a living thing."

School of Biomedical Sciences staff are successful recipients of NHMRC and ARC grants. Here are a selection of research projects that received funding for 2011.

First time success

Dr Natalie Borg was awarded an ARC discovery project grant to further her research into tripartite motif-containing proteins which are involved in immunity and cell growth. She plans to study how some of these molecules add 'tags' to other proteins and how this function relates to their 3-dimensional structure. Dysfunctional tripartite motif-containing proteins play a role in cancer, and neurodegenerative and immunological disorders.

Dr Catherine Itman, who received an NHMRC project grant, studies how the growth factor activin and hormones such as testosterone influence critical events during testis development. She is interested in how these molecules 'talk' to one another, how abnormal hormone actions in boys affect their fertility as adults, and how endocrine disrupting chemicals in the environment impact on hormone signals, impairing both testis development and sperm production.

Dr Belinda Henry was awarded an NHMRC project grant to further her obesity research. She studies the role that skeletal muscle plays in body weight regulation, and how it expends energy. In muscle, energy can be expended via thermogenesis, a process of specialised heat production. Belinda analyses animal models that have differing predispositions to obesity. She hopes to explain how muscle thermogenesis determines our susceptibility to obesity and how disease risk can be predicted.

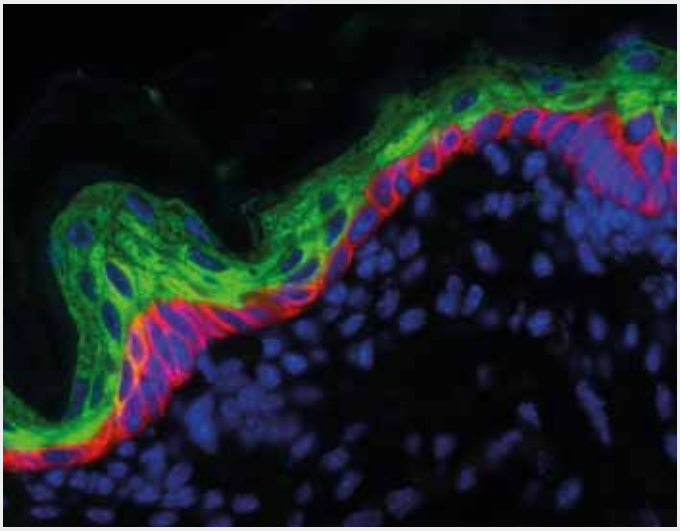
Dr Kylie Wagstaff was awarded both an ARC discovery project grant and ARC Australian postgraduate fellowship to continue her research into DNA delivery for gene therapy. She plans to develop a safe, non-invasive and cost-effective means to deliver DNA into living cells, which could potentially treat incurable genetic disorders. Kylie will also use this approach to coax normal adult cells to become precursor stem cells, which could be used as an alternative to harvesting stem cells from embryos.

New ARC future fellows

Dr Sheena McGowan conducts research into the design of novel drugs which can better treat malaria, the world's most deadly parasitic disease. She studies enzymes that break down human blood products, which the parasites use as a 'food' source. By designing compounds that inhibit these enzymes, it may be possible to 'starve' these organisms and therefore treat malaria.

Dr Ian Smyth studies our largest organ, the skin. He will use mouse models to understand skin disease and fundamental processes in cell biology. Despite the advances that have been made identifying genes which make up our genomes, we still remain ignorant of many of their functions. In collaboration with the Wellcome Trust, Ian is using genetic approaches to find new genes involved in embryonic development and skin disease.

Dr Zane Andrews studies how POMC neurons in the hypothalamus, at the base of the brain, suppress appetite, regulate body weight and maintain blood glucose concentrations at a constant level. He will generate transgenic mouse lines with selectively deleted mitochondrial genes only in POMC neurons. By examining these genetic defects, Zane hopes to understand how mitochondrial metabolism in these brain cells affects appetite, and predisposes individuals to diseases such as obesity and diabetes.



Expression of keratin in the developing skin. Image: Dr Ian Smyth.

Spotlight on obesity

Medical researcher Professor Michael Cowley is using his expertise and passion for obesity to establish the Monash Obesity and Diabetes Institute (modi).

Here, he discusses the big issue.

What is obesity?

Obesity is having too much fat; we believe it is a disease of the brain. The brain tells you when to eat, how much energy to burn and how fat it wants you to be.

High levels of abdominal fat cause inflammation that is associated with insulin resistance and diabetes; and sticky blood vessels in the heart, plaque adhesion and cardiovascular disease.

How do men differ from women?

Men put fat down around their abdomens, where it causes inflammation, and women around their hips and bottoms, where it doesn't occur. However, after menopause women have similar cardiovascular risk profiles for obesity that men do.

Is Body Mass Index the right measure for obesity?

BMI is a great measure to apply to populations. It's easy – you divide weight by your height, squared. However, it's not accurate on an individual basis such as footballers, where their BMI would be considered high because their body composition is much more muscular than it is fat.

Depending on your nationality, a normal BMI ranges from 18.5–25; less than that you're unhealthily lean; more than that you start having increased rates of disease associated with obesity.

Another useful measure is waist circumference. Women with a waist circumference greater than 80 cm have an increased risk of obesity-related health conditions; the corresponding number for men is 94 cm.

Is there a transgenerational component to obesity?

The mother's health during pregnancy strongly influences the baby's health after birth. We know this for smoking and drinking; the same appears to be true for both maternal obesity and maternal diet.

There's also emerging data showing that the health of the father has a direct impact on the health of his offspring.

How do we ensure that pregnant women receive good advice about metabolic health?

GPs know it's important that mums are healthy, but I don't think they realise the dramatic impact that maternal metabolic health can have on a fetus' metabolic health and later in adult life. When GPs, nurses and public health professionals know this, they can start educating mums.

How do we address childhood obesity?

We have a much greater responsibility to kids because while they make some choices, we control access to food and physical activity. Also, how we set that child up as a young person will determine what their adult life is going to be like.

We can encourage children to exercise and eat a treat food occasionally, but ultimately we can't prevent them from making bad decisions.

How do we treat obese children?

There's no approved surgical or drug therapy for children, only medical messages about exercise and healthy diet which are not working.

Professor Michael Cowley

Lapband surgery has a net positive benefit for obese adolescents, although there is debate [1] if this approach is appropriate for teenagers. Drugs don't do very much, so lapband surgery is all we have at the moment.

Another paper stated that nine per cent of type 2 diabetic teenagers will die by age 35 [2].

Obese teenagers need to eat less and exercise. If that doesn't work, we have to do something. It's contentious as the options that we have are not good, but the option of doing nothing is worse.

What advice would you give to an obese adult?

Start exercising, build up muscle strength and endurance. At the same time, eat less and clean up your diet.

Physical activity is the most important component of good metabolic health as it reduces insulin resistance and inflammation.

1. *JAMA*, 2010. Feb 10; 303(6): 519-526.
2. *Diabetes*, 2002. June; 51 (Supplement 2): A24 - A25.

What is modi?

The Monash Obesity and Diabetes Institute is being established at the Monash Clayton campus.

Our team of scientists are working on new treatments for obesity, and breaking the link between obesity and disease. We want to develop better drug and surgical therapies, identify natural extracts of foods, which may improve insulin sensitivity, and work on better exercise regimes.

> "Start exercising, build up muscle strength and endurance. At the same time, eat less and clean up your diet."

For more information:
www.modi.monash.edu.au
www.diabetesaustralia.com.au
www.heartfoundation.org.au

Asthma and the diet-gut connection

Professor Charles Mackay isn't afraid to put forward radical new ideas on how we should deal with the 'asthma epidemic'.

The immunologist from the Department of Immunology believes that bad diets cause asthma, not super-clean homes, since asthma is linked to obesity. He believes that the types of bacteria in our gut determine disease susceptibility, which opens up new avenues for diagnosis, treatment and prevention.

"Microbes in our gut break down dietary products and dietary fibre, and make molecules called short chain fatty acids," Professor Mackay says.

"We identified the receptor for short chain fatty acids, GPR43, and showed that it regulated inflammatory responses, which fitted in beautifully with our ideas around diet affecting asthma and auto-immune diseases in western countries."

If diet matters, how can we reduce our chances of getting asthma? "Eat beans, fruit, nuts, bran and cereal," says Professor Mackay, "since high-fibre foods activate the GPR43 receptor, which we believe is playing a preventative role."

Other researchers have identified a second receptor called GPR120 that is triggered by omega-3 fatty acids, which might explain why fish-eating Eskimos don't get asthma.

Professor Mackay believes that if we can understand the role of gut flora, we could potentially replace the bad 'bugs' there with good 'bugs', and tackle asthma and other inflammatory diseases at the same time. In the future, at-risk people could take probiotics or receive a faecal transplant of bacteria from healthy donors - delivered by colonoscopy.

"For us to be part of this radical new direction in immunology and inflammation is exciting," says Professor Mackay.

"One of the fascinating things about this story is that the fields of microbiology, nutrition, immunology and metabolism are converging, and ultimately this will help us understand asthma, diabetes, obesity and metabolic syndrome."

While these novel ideas are yet to be tested in the lab, the NHMRC Australia Fellow and Fellow of the Australian Academy of Sciences is also discussing junk food policy with interested politicians.

"There are parallels about where we are with obesity and diet, and where we were with smoking 40 years ago when people felt it was their right to do what they wanted. But when the disastrous effects of smoking became known, legislation was put in place to help people do the right thing," Professor Mackay says.

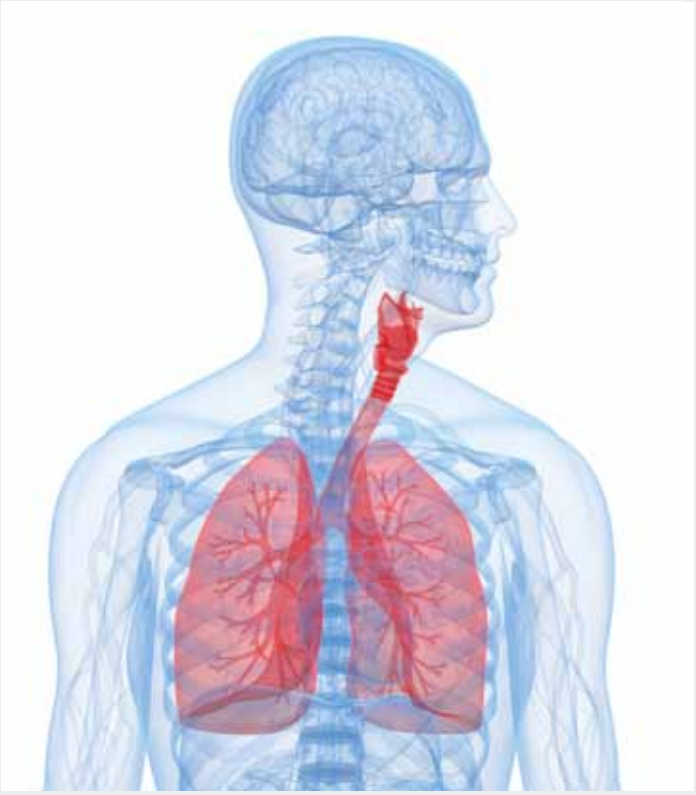
"We need to do the same thing with diet as obese people will have a reduced life expectancy through cardiovascular and inflammatory diseases. They will also develop type 2 diabetes and their children are more likely to get these illnesses, as well as asthma."

Professor Mackay believes we can intervene. Options include: regulating what is sold in school canteens, taxing junk food, banning TV advertisements, limiting the number of fast food outlets in the suburbs and ensuring these outlets have a larger proportion of healthy food.

In the meantime, the maverick scientist and his team are continuing to explore the asthma and diet-gut connection.

"We're on the ground floor of this new research direction and hopefully there will be productive outcomes for world health."

Professor Charles Mackay



News in brief

Professor Julian Rood (right) receives his award from the Dean Professor Steve Wesselingh.

Professor Julian Rood was presented with a 25 Year Service Award on 3 November by faculty Dean Professor Steve Wesselingh. He received a silver medal.

Since coming to Monash in 1985, Professor Rood has combined teaching with research into bacteria that cause human and animal diseases. He was Associate Dean (Research Degrees) in the Faculty of Medicine (1997–2000) and Head, Department of Microbiology (2001–2003).

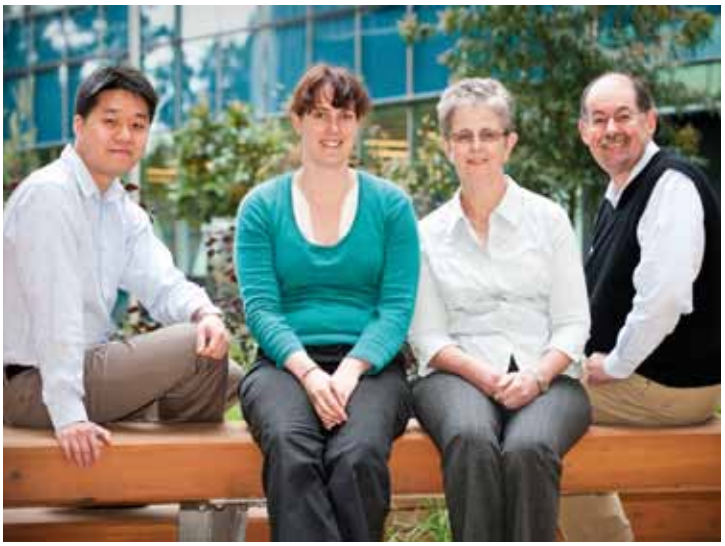
Currently, Professor Rood holds a Personal Chair in the Department of Microbiology and is a Chief Investigator in the ARC Centre of Excellence in Structural and Functional Microbial Genomics, also at Monash University.

Associate Professor Brian Cooke, also from the Department of Microbiology, has been appointed as Deputy Editor of the *International Journal for Parasitology.* The journal publishes original research articles, reviews and commentary about parasites which are biologically, socially and economically important in human and veterinary medicine, and agriculture.

Associate Professor Brian Cooke

A delegation from the Philippine Embassy in Canberra visited the faculty to explore collaborative opportunities in research and research training in health, biomedicine and malaria with government agencies and universities in the Philippines. The group also met with Associate Professor Cooke, who discussed how the two countries could join forces in infectious disease research.

From left to right: Associate Professor Brian Cooke, Mrs Melinda Macalintal-Rada (Labour Attache), Mr Alexander Ngie Go (Third Secretary) and Ms Mary Anne Alfonso Padua (Charge d'Affaires, Ambassador to the Philippines in Australia).



From left to right: Wilson Wong, Dr Corrine Porter, Dr Ruth Kennan and Professor Julian Rood.

Destructive protein causes debilitating sheep disease

A team of Melbourne and Sydney researchers have shown how a protein called AprV2 damages the hooves of sheep after they become infected with footrot. Their discovery of the structure of this molecule, published in the open-access medical journal *PLoS Pathogens,* helps explain how this micro-organism can cause lameness in affected livestock.

Footrot is a contagious bacterial disease commonly affecting sheep in Australia, the UK and Europe. In its severe form, infected sheep become lame and are unable to eat properly, reducing the quality of their wool, which negatively impacts on financial returns to the grazier.

"We knew that strains of *D. nodosus,* the bacteria that causes footrot in sheep, secreted three proteases, and the theory was that they damaged the hoof. But it had never been proven," says Dr Ruth Kennan, a microbiologist at the ARC Centre of Excellence in Structural and Functional Microbial Genomics.

"So we mutated each of these genes, stopped them from being expressed and showed that the mutant strains behaved differently in the lab. We also had to confirm their role in this disease."

Dr Kennan's research collaborators from the University of Sydney, Camden, and NSW Department of Primary Industries, led by Professor Richard Whittington, then tested these genetically-modified bugs in controlled trials with healthy sheep.

"When you knock out AprV2, there is no disease and the sheep are happy," says Dr Corrine Porter, a structural biologist at the School of Biomedical Sciences.

"Therefore, AprV2 is essential for footrot to develop in these animals."

But what makes AprV2 unique?

Dr Porter says this virulent protein differs from a closely related counterpart by one single amino acid, an important finding.

"The three-dimensional structure of AprV2 showed us that this single amino acid is found on a loop, away from the active site of the enzyme. We think this loop acts as a hook to capture its bait, proteins which it then degrades."

The Monash team, led by Professors Julian Rood and James Whisstock, hope to identify what this disease-causing molecule binds to, and then use that information to develop inhibitors to proteases in the future.

Zeroing in on aggressive breast cancers

Dr Clare Fedele, from the Department of Biochemistry and Molecular Biology, studies how one protein plays a key role in both aggressive breast cancers and healthy breast cells. In Australia, about 1 in 9 women and 1 in 767 men are diagnosed with breast cancer, amounting to over 12,700 new cases each year. In 2006, 2625 women and 25 men died from this disease.

The molecule, inositol polyphosphate 4-phosphatase II (also called INNP4B) is found in only a small number of breast cells. However, when INNP4B levels are manipulated in the lab, it's possible to see how cultured breast cancer cells respond to these changes. Low concentrations of this protein trigger cell division and tumour growth in breast cancer cell lines, so they become more cancerous, while high INPP4B levels inhibit these harmful effects from occurring.

Some breast tumours express this protein while others are deficient in INPP4B–usually basal-like breast cancers, which do not express estrogen receptors. Therefore, these cancers cannot be treated with conventional drugs such as tamoxifen, which targets this hormone.

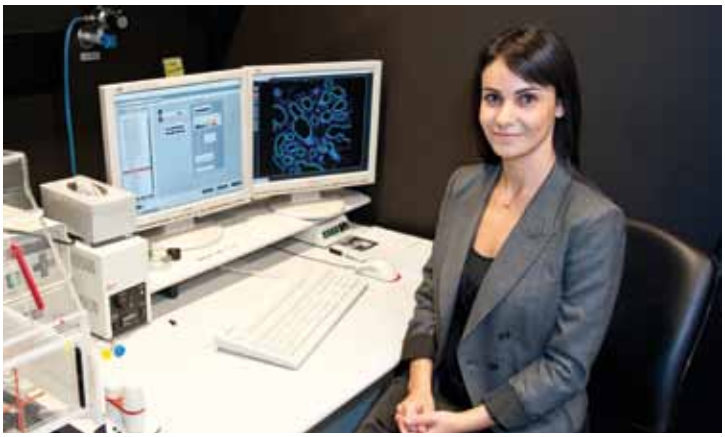
"These results, which were published in the journal *Proceedings of the National Academy of Sciences,* indicate that INPP4B is a new tumour suppressor protein that acts to inhibit cell division in the mammary gland," Dr Fedele says.

"Also, the loss of this protein may contribute to the development of these aggressive breast cancers which are currently very difficult to treat."

As INNP4B is absent in the majority of basal-like breast cancers, it is possible that drugs, which inhibit molecules in INNP4B's signalling pathway, may better treat this disease in the future.

While Dr Fedele has discovered important details about this tumour suppressor molecule, her team has also developed highly-specific antibodies which detect INNP4B in cancer cells. "Our screening technique could be easily integrated into pre-existing pathology labs, where these antibodies could be used as both diagnostic and prognostic tools for specific breast cancers," she says.

Dr Fedele, who was funded by the NHMRC and during her PhD by a Cancer Council Victoria scholarship, collaborated with Professor Christina Mitchell, Head of the School of Biomedical Sciences; Professor Catriona McClean, Head of Anatomical Pathology at the Alfred Hospital; and colleagues from Cancer Council Victoria, Garvan Institute of Medical Research and Centenary Institute.



Dr Clare Fedele

Brian Lee

Harnessing bubbles for cancer detection

Brian Lee embraces new challenges. After 15 years maintaining and improving artificial ventilation and pain relief devices at Royal Melbourne Hospital's intensive care unit, he changed tack, combining his passion for clinical technology with direct patient contact.

That meant coming to Monash, where Brian enrolled in the postgraduate diploma of medical ultrasound course before combining sonography work at Northern Hospital with part-time PhD research at the Department of Medical Imaging and Radiation Sciences, where Dr Michal Schneider-Kolsky is his supervisor. The 47-year-old student hopes to develop an ultrasound contrast agent that will detect small breast cancer tumours which would otherwise be missed, potentially reducing the need for invasive biopsies.

Ultrasound doesn't instantly come to mind as a cancer screening tool. But this technique, which can be used to detect liver tumours, has its advantages. "Ultrasound doesn't require ionising radiation, it's relatively safe and cheap, and is important for patients with poor kidney function who can't have contrast CT scans," Brian says.

He believes that the key to this emerging field are tiny microbubbles that can be made up of fats, proteins or polymers. These microbubbles are injected into the bloodstream and can improve ultrasound detection of soft tissues or masses. Brian has created protein coated microbubbles with a dense gas core, which, when injected into mice, can be 'seen' using ultrasound. His co-supervisor at CSIRO Parkville, Dr Judith Scoble has attached a tumour-specific antibody onto the microbubbles and shown that the bubbles bind to the receptor *in vitro.*

"Our next step is to attach a suitable antibody to our microbubbles, inject these into mice with known breast tumours and look for attachment under ultrasound," Brian says.

He hopes to continue his research subject to future funding. Despite the challenges ahead, Brian is focussing on writing a paper about the development of his protein coated microbubbles and planning future experiments.

"It's our goal to get rapid, early detection of breast cancer at the bedside," he says.

"Hopefully one day we can inject these microbubbles into patients suspected of having cancer and be able to visualise tiny cancer cell clusters using ultrasound."

Of scales and scans

Lizards fascinate Gina Westhorpe.

So the keen Bachelor of Radiography and Medical Imaging student undertook a research project at Melbourne Zoo, where she determined the gender of lizards.

For some lizard species, sex differences are not obvious until adulthood. Also, the standard screening methods used are invasive and can give incorrect results. Therefore, Gina reasoned that ultrasound might represent a new approach to solve this gender problem.

For her project, Gina studied sail-tailed water dragons, green iguanas, frilled lizards and Fijian crested iguanas. Using ultrasound, she looked for structures called hemipenes – a pair of sex organs located in pockets flanking the tail of male lizards.

When an ultrasound transducer is placed onto the base of a reptile's tail, hemipenes can be seen sliding within the hemipenal pocket of male lizards only. This technique is reproducible and a reliable indicator of sex. Melbourne Zoo is now using ultrasound for other lizard species.

For her innovative research work, Gina received two prizes: Best Presentation (Radiography) at the Australian Institute of Radiography annual meeting (Victorian branch), and more recently, the AIR Harold Anderson Memorial Diagnostic Student Prize at the 16th ISRRT annual scientific meeting, at the Gold Coast last September.

"I am honoured to receive this award," says Gina, who received a plaque, $250 and a one-year membership to the AIR.

"It's a wonderful reward for all the hard work that my supervisors Dr Michal Schneider-Kolsky and Paul Lombardo (Monash University), and Dr Helen McCracken (Melbourne Zoo) and I put into this project."

Gina has since graduated and is combining a Masters of Medical Ultrasound at Monash University with clinical training at St Vincent's Hospital.

Gina Westhorpe (right) with Gillian Tickall, Chairperson of the Victorian branch of the Australian Institute of Radiography and Chief Radiographer, Alfred Hospital.

Dr Ruud Segers (left) from Intervet-Schering Plough Animal Health with Centre Advisory Board member Professor Joachim Frey (right) during a lunch session at the conference.

Veterinary pathogens the highlight at Monash Prato

Veterinary diseases were the talk of the town in Tuscany last October when 130 delegates from over 30 countries gathered at the Monash Prato Centre for the first Prato conference on the Pathogenesis of Bacterial Diseases of Animals.

The event, which was hosted by the ARC Centre of Excellence in Structural and Functional Microbial Genomics and an organising committee chaired by Professor Julian Rood from the Monash Department of Microbiology and ARC Centre Chief Investigator, brought together leading researchers, veterinarians, students and pharmaceutical representatives who have an interest in bacterial diseases affecting livestock. Themes discussed at the four-day conference included: epidemiology, genomics, mechanisms of pathogenesis, extracellular pathogens and toxins, host-pathogen interactions, host responses and immunity, and vaccines.

Sponsors for the event included: Intervet-Schering Plough Animal Health, CSIRO Livestock Industries, Faculty of Medicine, Nursing and Health Sciences, Pfizer Animal Health, BioX Diagnostics and Don Whitley Scientific. Travelling scholarships were also awarded to four participants from developing countries.

The feedback from attendees was positive, so a second conference will be held in 2012.

For more information:
www.vetpath2010.org
www.microbialgenomics.net

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