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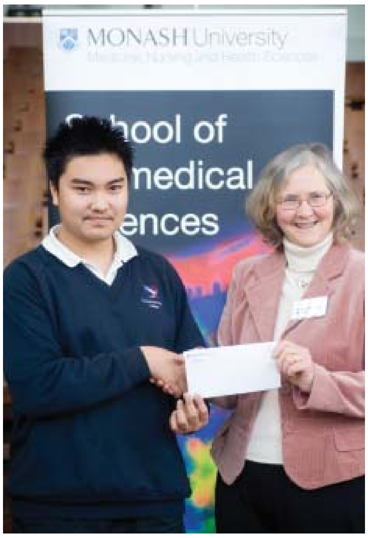
Biomed Benchmark

News from Biomedical Science at Monash – November 2007, Issue 4

Biochemistry pioneer inspires next generation of scientists

Internationally renowned biochemist Professor Elizabeth Blackburn spent three weeks visiting the School of Biomedical Sciences as the Louis Matheson Distinguished Visiting Professor.

During her intensive tour, the Australian-born scientist and Professor at the University of California San Francisco appeared as the key note speaker at the Careers in Science Symposium. Organised by the School of Biomedical Sciences in conjunction with VESKI (Victorian Endowment for Science, Knowledge and Innovation) and Invest Victoria, the symposium drew over 135 science-mad secondary school students to the BMW Edge theatre at Federation Square.



Tom Nguyen from Eumemmerring Secondary College and Professor Elizabeth Blackburn.

Professor Blackburn gave students a rare opportunity to hear about her research, career path and even some of her struggles as a student! It's a history that led to *Time Magazine* recognising her this year as one of the 100 most influential people in the world.

Professor James Whisstock, Dr Alyssa Barry and Dr Leslie Yeo also shared their experiences of choosing the path that led them to careers in science. The talks aimed to encourage students who already have a passion in science to continue in their interest and pursue a career. Students were then split into small break-out groups, which gave them the opportunity to ask more detailed questions of the speakers. Tom Nguyen from Eumemmerring Secondary College was selected by Professor Blackburn to spend a day in a laboratory in the School of Biomedical Sciences.

During two subsequent Monash University research seminars Professor Blackburn detailed her latest research into the structure of telomeres, the caps on chromosomes that prevent them from fraying. She discovered telomerase, an enzyme in chromosomes that adds a specific sequence of DNA to the telomeres after they divide. Telomerase diminishes as people age.

Professor Blackburn won the Albert Lasker Award for Basic Medical Research last year, which is seen by many as a precursor to being awarded a Nobel Prize. 70 winners of the Lasker Award have gone on to win a Nobel Prize.

Professor Elizabeth Blackburn

Over 135 secondary school students filled the BMW Edge Theatre at Federation Square to hear Professor Blackburn.

Researchers' grant success

Professor James Whisstock and his program team will receive more than $11 million from the NHMRC for research to develop new treatments for a range of diseases.

Professor James Whisstock

The program's chief investigators, James Whisstock, Ian Smith, Philip Bird, Stephen Bottomley, Rob Pike and Ashley Buckle will research the control of proteases and their inhibitors in infectious, degenerative and cardiovascular diseases.

The program grant will focus on the role of proteases in a wide range of diseases such as cancer, heart disease and dementia. It will aim to develop compounds for therapeutic use in hypertension, heart disease and stroke.

The team also aims to understand how the human immune system fights bacterial and viral infection. Recently, the NHMRC program team published a paper in the international journal *Science* that describes how the immunity protein perforin functions to protect humans against infection and cancer. Professor Whisstock said the NHMRC grant renewal was great news for his team.

"This funding will allow us to address the role of proteases in a range of important human diseases" Professor Whisstock said.

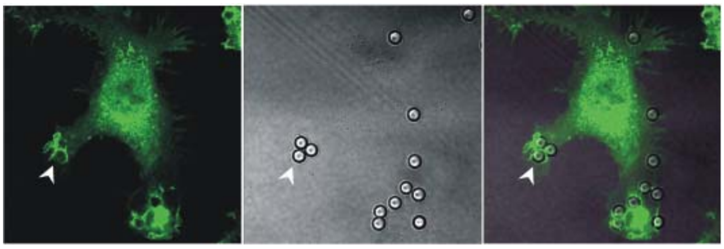
Also successful in program funding, Dr Ed Stanley from the Monash Immunology and Stem Cell Laboratories received one of only five Special Program Grants. He has been allocated $2.9 million to explore the derivation of pancreatic B-cells from embryonic stem cells. The project is part of a nationwide search for treatments for Type 1 diabetes, in conjunction with the Juvenile Diabetes Research Foundation International. In 2008, the School of Biomedical Sciences will receive a total of $28 million from project and program grants from the NHMRC. The school received 50% of Monash University's overall NHMRC funding.

Novel protein to help battle infection

In research that could have implications for fighting infections, scientists have discovered a protein that regulates the ability of white cells to engulf foreign particles including bacteria.

White blood cells, which include structures called macrophages, kill foreign particles that could potentially harm the body. For the body to successfully kill these cells, they must first be engulfed by the macrophages.

Professor Christina Mitchell and Dr Kristy Horan from the School of Biomedical Sciences have identified a novel protein, known as 72 kDa inositol polyphosphate 5-phosphatase (72-5ptase), that actually reduces the ability of macrophages to engulf particles.



Cell 5: Internalization of antibody-coated latex beads by macrophage cells is regulated by the 72kDa inositol polyphosphate 5-phosphatase. The white arrowhead (left panel) indicates that this 5-phosphatase enzyme is recruited to sites of phagocytosis upon addition of latex beads (middle panel). Right panel shows an overlay of the fluorescence and brightfield images.

Their findings revealed that by decreasing the cellular levels of 72-5ptase, the engulfing of particles by macrophages could actually be increased. Macrophages play a critical part in the immune system by resolving infections and may play a role in clearing damaged or dead cells. They not only directly fight disease by swallowing up infectious organisms but also promote the growth of new healthy cells to aid in healing."We hope by slowing down 72-5ptase activity, we may effectively allow macrophages to more efficiently engulf and kill bacteria" Professor Mitchell said. The 72-5ptase regulates the process by removing molecules that promote macrophages to kill and digest unwanted material.

"By altering the effectiveness of 72-5ptase, there is the potential for it to be used to enhance the fight against bacterially-infected cells. It could allow macrophages to more efficiently recognise tumour cells and therefore be more efficient about killing them off," Professor Mitchell said.

While previous research has looked at the activity of 72–5ptase, this is the first study that has investigated the function of the protein. The results have been published in the latest issue of *Blood*, the world's leading haematology journal. The study was funded by the NHMRC and the ARC Centre of Excellence in Functional and Structural Microbial Genomics.

Gut infection regulator identified

Scientists have found a gene that controls toxin production in an endemic human gut disease.

Dr Glen Carter and Dr Dena Lyras, working in Professor Julian Rood's laboratory in the Department of Microbiology, have found a new gene that regulates toxin production in the bacterium Clostridium difficile, which can cause gastrointestinal intestinal disease syndromes known as C. difficile– associated disease (CDAD).

CDAD is the most commonly diagnosed bacterial cause of infectious hospital–acquired diarrhoea in developed countries. In severe cases, it can result in death.

Dr Glen Carter and Dr Dena Lyras

The incidence of CDAD has been steadily increasing especially among the elderly and children.

Dr Carter said scientists in the UK, US and Canada, had seen the emergence of a new hypervirulent strain of C. difficile that results in a higher than average mortality rate, and the closure of entire hospital wards. C. difficile produces three known toxins, but until this research was carried out, little was known about how the expression of one of these toxins was regulated. "Identifying the regulatory gene is the first step towards understanding it. It gives us an extra target to work with to try and shut off the toxins that cause infection" said Dr Carter.

The onset of the infection is associated with the use of antibiotics that disrupt the usual intestine environment, enabling C. difficile spores from the environment to colonise the gut and cause diarrhoea.

"We know that the toxin regulated by this regulatory protein is not essential for the development of the disease because not all C. difficile strains produce the toxin" Dr Lyras said.

"Our next step is to work out exactly what it does. If we can understand how C. difficile produces the toxin, we can work towards trying to prevent its expression."

Spiny mouse aiding stem cell research

The spiny mouse is helping scientists to understand stem cell function for the development of regenerative therapies.

Professor Graham Jenkin and Dr Hayley Dickinson from the Monash Immunology and Stem Cell Laboratories (MISCL) are using the spiny mouse to investigate different sources of stem cells and how they behave in the body.The results of the study will help with the selection of the most appropriate type of stem cells for future clinical therapies.

Professor Jenkin and Dr Dickinson's research is unique as it is the only stem cell research being carried out on the spiny mouse in the world. The research investigates three sources of stem cells found in the umbilical cord, the human embryo and the placental tissues and what happens to these cells when they are administered to the spiny mice.

The stem cells are administered to the fetus of the spiny mice to ensure that the cells are not rejected. Researchers then readminister the cells to the spiny mice during their adult lives. They use a tracking system to monitor the fate of the cells.

"The tracking system helps us to determine which of these cells have the potential to attach or implant themselves into major organs and tissues and become blood, heart, liver, brains or muscle cells. It also tells us whether or not they can adjust to their new environment and survive or if they remain as neutral 'stem cells'" Professor Jenkin said.

To determine how successful the administered stem cells are, researchers also monitor the immune system of the mice. The immune response allows the researchers to determine whether the adult recipients have tolerated or rejected the cells. They hope that the stem cells will be tolerated by the adult animal, following exposure of the animal to the stem cells during its own fetal development.

The spiny mouse is a nocturnal species that is native to regions of Egypt and Israel. They are an ideal candidate for this type of research because, like humans, they have a long gestation period and are therefore very highly developed at birth. The development of the kidney, liver, lungs and brain of the spiny mouse are essentially completed at the time of birth.

"We hope that because of the similarities between the early development of the spiny mouse and humans that the information we learn about the spiny mouse will tell us more about stem cell behaviour in humans" Professor Jenkin said.

The spiny mice were imported five years ago from The University of Amsterdam by Associate Professor David Walker (Department of Physiology, Monash University) and are the only colony in the southern hemisphere. The research is being undertaken in collaboration with colleagues at the Monash Immunology and Stem Cell Laboratories and the Department of Obstetrics and Gynaecology.

Spiny mouse

Moo-ving forward in the search for new vaccines for malaria

Monash University scientists have found a striking resemblance between human malaria and an infection in cows called babesiosis (or tick fever), which may shed new light on the prevention and treatment of malaria in humans.

Associate Professor Brian Cooke and his team have extended their malaria research efforts to learn more about babesiosis, an endemic disease of cattle in Australia and many other countries.

The parasite babesia infects and grows inside red blood cells. The disease costs the beef and dairy industries millions of dollars each year in avoidable economic losses. Using synthetic blood vessels to investigate how babesia-infected red blood cells behave, Dr Cooke's team has shown that babesia parasites cause cow red blood cells to stick to the inner wall of blood vessels in a similar way to malaria. Malaria is frequently fatal because infected red blood cells adhere to the inside of blood vessels and block blood flow to vital organs such as the brain.

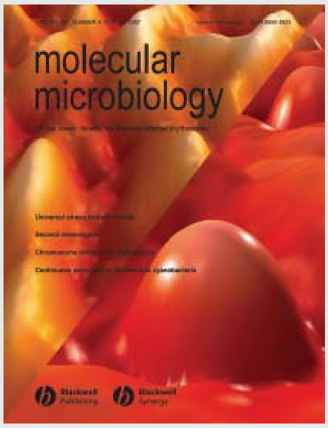
In collaboration with colleagues at The Department of Primary Industries in Queensland and the National University of Singapore, Dr Cooke's team has used cutting-edge imaging technologies to visualise structures on the surface of infected cow red blood cells that make them abnormally sticky. Interestingly, these nanomolecular structures are similar to those that appear on the surface of human red blood cells infected with malaria parasites.

"Studying babesia infections in cattle offers us a huge potential to learn more about precisely how malaria parasites cause disease – and in a much more amenable experimental system than humans" Dr Cooke said.

Dr Cooke's team will now look even more closely at the surface of these infected blood cells, to investigate precisely how Babesia parasites cause disease. They are working to identify the specific genes and proteins involved in this process, since they could represent possible targets for new and urgently required drugs and vaccines.

"With such a similarity between the two diseases, we hope that these findings and our continued work on Babesia will help us to understand and uncover more about how to find an effective vaccine for Babesiosis, and also to identify new drugs and vaccines for malaria," Dr Cooke said.

Their recent findings have been published in the international journal Molecular Microbiology and can be downloaded at *www.blackwell-synergy.com/doi/abs/10.1111/j.1365 2958.2007.05850.x.*



Associate Professor Brian Cooke's images are featured on the front cover of Molecular Microbiology www.mol-micro.com

Breakthrough gives scientists a promising gut feeling

Advances in intestinal cell growth will lead to a better understanding of the link between the initial stages of colon and bowel cancers, and gut development.

The lead researcher, Dr Helen Abud was the first scientist to genetically modify pieces of the intestine out of the body in cell culture. Having easier access to the cells now allows her to study the genes that control gut development and bowel cancers in ways that were not previously possible. Dr Abud is specifically interested in the relationship between gut cells in the embryo and comparing them to early-stage intestinal tumours. Several researchers believe that the genes that are normally switched on during early embryonic development may be the very same cells that reappear and cause cancer.

"By understanding embryonic development, we hope to understand more about cancer. In many cancers, there is increasing evidence that genes that have very normal roles in early development are inappropriately activated during cancer" said Dr Abud. Colorectal cancer, commonly known as colon or bowel cancer is cancer that develops in the colon or the rectum. It is the

Dr Helen Abud

second most common cause of cancer-related death after lung cancer. One in 20 Australians, mostly over the age of 50, develops the disease in their life time.

Dr Abud is studying mouse intestinal stem cells to explore the genesis of cancer development. She is examining the genes that control the initial differentiation of the inner layer of cells that line the intestinal tube in early development, which is also where the cancerous tumours form.

"We are looking at how potential cancer-causing genes disrupt the development of the intestinal epithelial cells in our novel culture system. By looking for changes in cell growth, shape and movement we are hoping to identify certain behaviours and links which should give us a better understanding of tumour formation" said Dr Abud.

Contact us

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