HOW WHITE BLOOD CELLS BEAT BACTERIAL INFECTION

PhD candidate, Melanie Coker and Professor Tony Kettle analyse results using a mass spectrometer.

Poisonous gas was used as a weapon in World War 1, but when it comes to fighting invading bacteria, it appears that gas might also be a key factor in how we control infection in the human body.

Scientists from the the Free Radical Research Group, Professor Tony Kettle and PhD candidate Melanie Coker, have recently added another crucial piece to the jigsaw puzzle of how our body defends us against bacterial infection, but which paradoxically can cause other inflammatory problems.

For the first time ever Kettle and Coker have discovered that a part of this bacteria killing process may involve gassing the invading bacteria within the white blood cell itself, after bacteria have been enveloped and 'eaten'.

It's a unique discovery which has just featured in two overseas publications *Chemical and Engineering News* and is a cover story in the American journal, *Chemical Research in Toxicology.*

The scientists have shown that the interaction between proteins and hypochlorous acid (household bleach) in white blood cells, results in the production of toxic chloramine gas, which has a lethal effect on any bacteria. Although this finding has not been proven within living cells it has been demonstrated in the laboratory.

Over recent years Christchurch medical researchers have been steadily enhancing our understanding of how we fight infections. What exactly are the precise mechanisms and chemical reactions in that basic unit of the body, the human cell?

This latest research from the Free Radical Research Group significantly advances previous findings which demonstrated that bacteria-fighting foot soldiers, or white blood cells, actually use the equivalent of chlorine bleach to kill invading bacteria.

Now the researchers have discovered that the body's arsenal is even more effective, and has another powerful weapon in its fight against bacterial infections, chloramine gas.

Why is this important? One of the key reasons is that for some time it's been known that the action of white blood cells, when they attack bacteria, can cause inflammation that destroys healthy body tissue in chronic diseases like rheumatoid arthritis or cystic fibrosis; and even promote certain cancers.

Now that chloramine gas has been identified as a likely player in this process, new approaches can be developed to control inflammatory response in numerous diseases.

This research was funded by the Health Research Council of New Zealand and supported by the National Research Centre for Growth and Development.

University of Otago
NEW ZEALAND

University of Otago, Christchurch, February 2009

Connecting with the Community

It is a great pleasure for me to introduce the February 2009 newsletter, which connects the University of Otago, Christchurch with our community. Our vision is to be: "A research-led campus with an international reputation for excellence." We are proud to be the top rated of the four Schools of Medicine in the country, and part of New Zealand's top rated University for research.

I would like to welcome David Meates, the new Chief Executive Officer of the Canterbury District Health Board (CDHB) back to Christchurch. The University of Otago, Christchurch and the CDHB work closely together to improve the health of our community. While the CDHB is responsible for the provision of health care, the University contributes to tomorrow's health by research and education, and by being an 'attractor' organization for health professionals who choose Christchurch as the place to live and to work.

The current economic climate will mean challenging times for health, tertiary education and health research in New Zealand. However, shortages of health professionals mean we will continue and even expand the teaching of medical students and other health professionals. The University of Otago, is already planning for a larger intake of nearer 270 medical students, which in a few years will mean medical student classes for Christchurch of about 90, rather than 80.

Last year, our staff competed well for research money, with notable successes for Health Research Council funding, Marsden Grant funding and Lottery Health funding. Our staff continue to make substantive contributions to national and international research across a range of health areas.

This year we will begin planning for our 40th anniversary, with celebrations being planned for February 2012. We welcome any ideas for these celebrations.

Professor Peter Joyce
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DEFECTIVE GENE PUTS MIDDLE-AGED MALES AT RISK

Heart disease and heart attacks are the big 'killers' in New Zealand, with some 30,000 people being admitted to hospitals every year with heart problems. Researchers from the Christchurch Cardioendocrine Research Group have recently identified a gene variant which may help doctors tailor better treatment to individual heart attack patients.

"It's been known for some time that a defective ACE2 gene is associated with high blood pressure, but our research has now clearly linked one variant of this gene to a greater likelihood of mortality after heart attack. This is particularly so with middle-aged males who have acute coronary syndromes, or reduced flow of blood to the heart," says lead researcher Dr Barry Palmer.

However Dr Palmer also points out that the ACE2 gene variant is only one of a range of risk factors, both physiological and environmental, which can affect survivability after angina or heart attack.

"This is the first time ever that this variant of the ACE2 gene has been identified in terms of survivability," says Dr Palmer." It will be useful in terms of other research we're doing on tailoring heart disease treatment more accurately to the patient."

"If we can identify those people at greater risk we may be able to do more earlier in their treatment, and it's easy enough to identify if someone has this variant of the gene."

Males are more prone than females to the effects of the ACE2 gene variant because of their chromosomal make-up. That's because males have only one copy in each cell of the ACE2 gene on the X chromosome, and none on the Y chromosome, whereas females have two X chromosomes.

This means that if a male has a defective ACE2 gene variant there is no complementary chromosome which can compensate for that ineffective gene. Females have an alternative copy of the gene on their second X chromosome which can compensate and provide normal blood pressure to the heart.

In its normal form on the X chromosome the ACE2 gene produces an enzyme which controls blood pressure by influencing hormone levels. It is only when that gene is defective that blood pressure may increase.

Dr Palmer says techniques for analysing links between gene variants and heart disease are advancing rapidly, enhancing understanding and improving treatment for one of our most serious health problems.

This research has been published in the October 2008 issue of the *American Heart Journal* and was funded by the University of Otago, Health Research Council, National Heart Foundation and Maurice and Phyllis Paykel Trust.

Recent grants from the Canterbury Medical Research Foundation and Lottery Health are allowing further research on genes from the X chromosome and heart disease to continue.

Dr Barry Palmer.

VOLUNTEERS KEEN TO LEARN ABOUT RESEARCH STUDIES

Dr Lisa Stamp, speaking to research participants.

Around two hundred research volunteers packed halls on two separate occasions in Christchurch in December to learn about studies in which they participated. The level of interest surprised and gratified the research teams.

Dr Lisa Stamp from the Rheumatology and Immunology Research Group presented results of a study into the administration of the 'frontline' drug for rheumatoid arthritis, Methotrexate. Dr Tony Merriman from Dunedin also outlined research into the genetic background to the disease.

Dr Stamp's study looked at dosing regimens with Methotrexate when people are first diagnosed with rheumatoid arthritis. There is some doubt as to the best dose levels of this key drug in terms of getting a rapid response and limiting the spread of the disease.

"The problem is that at present the accepted clinical approach is that Methotrexate dosing levels should be slowly increased over a number of months because of concern about side effects," says Dr Stamp.

"However our research results suggest that higher dose levels earlier after onset and diagnosis may have better results in controlling joint damage in the early stages of what can be a crippling disease."

This study has been published in *Arthritis and Rheumatism* and was funded by the Health Research Council and Arthritis New Zealand.

At the second meeting researchers from the Van der Veer Institute also presented short talks on Parkinson's and brain research. Chief scientist Dr Michael MacAskill discussed his work investigating eye movements and Parkinson's, while PhD students Tracy Meltzer and Phoebe Macrae described how MRI brain scans are used in research and the nature of swallowing disorders.

Research participant Allan Wright reflected the general feeling of participants saying it was great to meet other volunteers, and learn more about Parkinson's disease and the excellent health research in Christchurch.

DISTINGUISHED RESEARCH MEDAL AWARDED TO CHRISTCHURCH CARDIOLOGIST

World leading cardiac researcher Professor Mark Richards, has recently been awarded the University of Otago's highest research honour, the Distinguished Research Medal.

Professor Richards received the medal for leading-edge research over two decades as director of the 40 member Christchurch Cardioendocrine Research Group (CCERG) and the discovery of the crucial role played by heart hormones in heart failure and heart disease.

"I was delighted to receive the medal, in fact flabbergasted," he says. "I don't think it relates to any one particular piece of work we've done, but simply the accumulated impact of the group over a long period of time, and the fact that we've made a clinical difference in the caridiovascular area internationally."

The ground breaking research by the CCERG discovered that the level of hormones secreted by the heart, such as ANP and NTpro-BNP, can be used as more accurate markers for cardiac stress, and therefore better diagnosis and more accurate treatment of heart failure and heart disease.

These innovative findings have been internationally recognised by leading research journals and clinicians and incorporated into clinical guidelines and tests in Europe and North America. They have had a huge impact on the lives of thousands of heart disease and heart failure patients world-wide.

Further research by the CCERG is developing these innovative hormone studies by investigating patients' genetic links to heart disease. Professor Richards, who is also a cardiologist at Christchurch Hospital, has published more than 300 papers and been cited more than 9400 times by the international research community.