Established by the Health Research Council Act (1990), the Health Research Council of New Zealand (HRC) is the Government’s principal funding and investment agency for health research. As a Crown agency, the HRC is responsible to both the Minister of Health, and the Minister of Science and Innovation. HRC funding comes primarily from Vote Science and Innovation.
FOREWORD

By the Minister of Health, Hon Tony Ryall, and the Minister of Science and Innovation, Hon Dr Wayne Mapp

Health research is central to New Zealand’s ability to continually develop an efficient world-class health system, and deliver leading edge services. Clearly New Zealand nurtures many individuals who are insightful and creative and can advance novel solutions to the problems facing human health and health system delivery. The investment the Government makes in research is capable of excellent value; the evidence for this is illustrated in the pages of this publication.

We are particularly impressed by the outcomes of HRC-supported research that contribute significantly to enabling New Zealanders to lead more fulfilling and productive lives. An example is the innovative work of researchers to prevent cerebral palsy in some new born babies that have suffered brain injury. Furthermore, the potential for New Zealand to benefit economically from realising a commercial opportunity for products of research will help the nation prosper. The real challenge for investors in research is to select winners; those that are able to follow their fundamental research ideas through to application in the form of a service or product. As you read through the many cases that follow, it is clear that the HRC has done a very good job of doing just that – picking winners.

We wish the HRC every success in continuing to support our researchers and the best research ideas so we may all benefit from their commitment, inspiration and achievements.

Hon Tony Ryall
Minister of Health

Hon Dr Wayne Mapp
Minister of Science and Innovation
# CELEBRATING 20 YEARS OF HEALTH RESEARCH IN NEW ZEALAND

## CONTENTS

<table>
<thead>
<tr>
<th>Page</th>
<th>Section</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>Introduction - By Dr Robin Olds, HRC Chief Executive</td>
</tr>
<tr>
<td>5</td>
<td>A Snapshot of the HRC</td>
</tr>
<tr>
<td>6</td>
<td>A Brief History of the HRC</td>
</tr>
</tbody>
</table>

## RESEARCH HIGHLIGHTS

### Infant Health
- Keeping a cool head improves outcomes for newborns

### Child Health
- A sore throat can break your heart
  - *Case Study* – School-based primary prevention of rheumatic fever

### Understanding the Origins of Adult Disease
- Liggins Institute
  - *Case Study* – Long-term safety of treatment for fetal anaemia

### Preventing and Controlling Diabetes
- Is lifestyle the drug of choice?
  - *Case Study* – Managing diabetic kidney disease

### Māori Health Research
- Culture at the core of health and wellbeing
  - Whakauae Research for Māori Health and Development
  - International Indigenous Health Research Collaboration

### Pacific Health Research
- Navigating the way to Pacific health solutions
  - Stories lay path to healthier communities: Minimising harm from alcohol use
  - Growing future Pacific health research stars
    - Applying indigenous knowledge to manage mental health
    - Family focus on Pacific health

### Injury Prevention
- Providing new insights into the causes and consequences of injury in New Zealand
  - *Case Study* – The New Zealand Drivers Study

### Longitudinal Studies
- Nature versus nurture
  - The Dunedin Multidisciplinary Health and Development Study
    - *Case Study* – Long-term consequences of low levels of self-control during childhood
  - The Christchurch Health and Development Study
<table>
<thead>
<tr>
<th>Page</th>
<th>Section</th>
<th>Subsection</th>
</tr>
</thead>
<tbody>
<tr>
<td>37</td>
<td>Mental Health and Addiction</td>
<td>Finding effective treatments for depression and eating disorders</td>
</tr>
<tr>
<td>40</td>
<td>Housing and Health</td>
<td>Demonstrating the impact of poorly insulated houses</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Case Study – The interplay between housing and infectious diseases</td>
</tr>
<tr>
<td>44</td>
<td>Understanding Occupational Risks to Health and Wellbeing</td>
<td>How our work affects our health</td>
</tr>
<tr>
<td>47</td>
<td>Harnessing the Power of the Immune System</td>
<td>Malaghan Institute of Medical Research</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Immune Cell Biology research programme</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Top honour for young scientist</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Case Study – New technology for better cancer vaccines</td>
</tr>
<tr>
<td>53</td>
<td>Developing New Ways to Fight Infections</td>
<td>Super drugs for super bugs</td>
</tr>
<tr>
<td>56</td>
<td>Bioengineering Will Change the Face of Modern Medicine</td>
<td>Scientists unite to build a virtual human</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Case Study – Virtual heart and real hearts combine</td>
</tr>
<tr>
<td>59</td>
<td>The Role of Genes in Cancer</td>
<td>Many things affect the behaviour of genes and our susceptibility to cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Case Study – Targeted cancer chemotherapy using prodrugs</td>
</tr>
<tr>
<td>63</td>
<td>Exploring the Brain</td>
<td>Understanding how the brain can regenerate itself and unravelling the mystery of memory</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Case Study – Brain mechanisms through which our memories are made</td>
</tr>
<tr>
<td>66</td>
<td>Stroke and Traumatic Brain Injury</td>
<td>New Zealand researchers are finding new ways to reduce disability and casting the spotlight on the stroke epidemic in developing countries</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Case Study – Rehabilitation after a stroke</td>
</tr>
<tr>
<td>69</td>
<td>Bone Health</td>
<td>Advances in bone biology have revolutionised the treatment of Paget’s disease and osteoporosis</td>
</tr>
<tr>
<td>72</td>
<td>Cardiovascular Disease</td>
<td>PREDICT – Embedding research into practice</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Case Study – Research can take you down paths you never imagined</td>
</tr>
</tbody>
</table>
The Health Research Council of New Zealand (HRC) is a publicly funded Crown agent, with the mission of benefiting New Zealand through health research. This year we celebrate twenty years of doing exactly that, by publishing highlights of just some of the groundbreaking research we have supported during that period. There are many highlights to choose from. The HRC has supported a wide range of top-class health researchers performing research of international standing. In making our selection of what to include, we wanted to illustrate both the quality of health research and also the breadth of subject material.

The HRC officially came into being on 1 October 1990. To mark our 20 year anniversary, the HRC has published Celebrating 20 Years of Health Research in New Zealand, which profiles 20 years of HRC-funded research achievements.

Over the years, the HRC has placed a major focus on developing a robust investment process, geared towards identifying and supporting our nation’s best and brightest researchers. In short, we seek to support the people and the research that is most likely to make a difference. Our research stories show the importance of maintaining this world-class system and the value of the contribution hundreds of top scientists make to our policy and assessment committees every year.

In the last year alone, around 900 health research experts from New Zealand and across the world freely gave their time and their expertise to help the HRC decide how best to invest the public’s health research money. We can only reward them with the knowledge that their time has been well spent, and the quality of New Zealand health research is evidenced in this account of the extraordinary advances that HRC-funded researchers have made.

From its inception, a major role of the HRC has been to build capacity and capability in priority areas to ensure that New Zealand can address the health needs of its unique and diverse populations. We have worked hard to do this, developing models
A Snapshot of the HRC

• Key roles for the HRC, as defined in the Health Research Council Act (1990), include determining priorities for health research investment, initiating and supporting health research, supporting the development and retention of the health research workforce, and supporting knowledge transfer from health research.

• In 2010/11, the HRC received $83.5M of public money to invest in health research for the benefit of New Zealand.

• The HRC has determined four broad priority areas for health research investment:
  - New Zealand Health Delivery: Providing improvements and innovations for healthcare services and planning;
  - Health and Wellbeing in New Zealand: Keeping people healthy and independent throughout life;
  - Improving Outcomes for Acute and Chronic Conditions in New Zealand: Improving the understanding and management of disease and disability, and
  - Rangahau Hauora Māori: Utilising Māori knowledge and capability to address Māori health issues.

• Within the broad policy framework set by the HRC, about 60 per cent of the health research investment supports the best ideas, about 33 per cent supports more needs-driven research, and seven per cent directly targets health research career development.

• At any one time the HRC is managing around 330 separate research contracts, including about 90 career support awards.

• As of 1 April 2011, the total value of active research contracts was $268M, awarded to more than 30 research organisations, including universities, District Health Boards and independent and community-based institutions and organisations.

• HRC funding supports a health research workforce of more than 570 full time equivalents, spread over about 2,300 positions.
A BRIEF HISTORY
OF THE HRC

Although we are currently celebrating two decades of achievements for the Health Research Council of New Zealand (HRC), the HRC and its previous incarnations actually date back 74 years. In effect, the HRC is the oldest specialist research-purchasing agency in the country.

The HRC has its origins in the Medical Research Council (MRC), a departmental committee of the then Department of Health, created in 1937 under the Health Act (1920). In 1951, the Medical Research Council Act established the MRC as an autonomous entity, owned by the Ministry of Health. At this stage in the life-cycle, the MRC focused almost entirely on biomedical research.

Through the Health Research Council Act (1990), the MRC was dissolved and the HRC in its current form was created. The Act included sweeping changes to the scope of activities for the agency, including the creation of the Biomedical Research Committee, the Public Health Research Committee, the Māori Health Committee and the Ethics Committee. The HRC was henceforth charged with promoting all research relevant to health.

In 1997, the Minister of Health transferred the funding for the HRC from Vote Health to Vote Research Science and Technology (RS&T). Ownership of the agency still rested with the Minister of Health, but the funding was allocated by the Minister of Vote RS&T. From that point onwards, the HRC has had accountability to two Government ministers.

The 2004 Crown Entities Act designated the HRC as a Crown agent, rather than a Crown entity, requiring the HRC to ‘give effect to’ ministerial advice rather than ‘give regard to’ it. The HRC must work closely with both ministries to ensure that policies and directions are well aligned and that health research is actively contributing to the Government's goals.

Acknowledgements

The HRC would like to thank everyone who has been involved in the production of this publication, which celebrates the 20th anniversary of the HRC. In particular, we would like to acknowledge the following people:

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The HRC would also like to thank everyone who has assisted with sourcing images and photographs for Celebrating 20 Years of Health Research in New Zealand.
INFANT HEALTH

Keeping a cool head improves outcomes for newborns

Even with the advances in obstetric care over recent decades, up to three babies in every thousand births will have abnormal brain function due to restricted oxygen from a twisted cord, inadequate placenta or contractions that are too strong. Cerebral palsy is one of the most devastating consequences of exposure to low oxygen levels or infection before, or at birth. The costs to society are huge.

In 2002, a US study estimated the cost as US $8.2 billion, with 800,000 persons affected in the USA alone. The costs include loss of potentially productive members of society and the direct burden of life-long care on the individual, family, and social institutions. Brain cooling is the first ever practical treatment for brain injury in babies.

This is the extraordinary story of how the first cooling cap for babies was developed by an HRC-funded team at The University of Auckland.

Alistair Gunn is a Professor of Physiology at The University of Auckland’s School of Medical Sciences. He first became interested in this field of research when working as a paediatrician, twenty years ago. When he was called upon to resuscitate babies that had been deprived of oxygen at birth, he noticed that they often improved initially and then declined – sometimes with severe seizures. At that stage, there was nothing in the literature to suggest why that might be but specialists wondered if this occurred because the damage to the brain was still progressing. Professor Gunn decided to undertake his own research, and did a PhD with Professor Sir Peter Gluckman at the Liggins Institute to try and understand what was happening to these babies and how they could be helped.

Professor Gunn conducted his initial studies in rats. He gave them drugs intended to protect the brain from injury and noticed that these drugs also made them cold.
When he tried to keep the animals warm, the protective effects of the drugs were lost. Professor Gunn and his colleagues then went on to show that cooling was a side-effect of such drugs and had a protective effect in itself. They also discovered that brain damage developed progressively over time, following the initial injury. It seemed that clinical perceptions were right: the team found that when the brain was deprived of oxygen at birth, a complex biochemical cascade was launched that resulted in the delayed death of neurons. Cooling the brain interrupted this cascade and could reduce disability in the long term. However, cooling was only effective at preventing damage if it was started relatively early in the process. They developed a system for measuring brain activity to identify accurately the precise point at which cooling should be applied. They also found that the babies’ brains had to be cooled continuously for several days whilst secondary injury and inflammation settled down.

Professor Gunn was helped in his endeavours by his mother, the late Professor Tania Gunn, an eminent paediatrician specialising in the care of newborn babies at the National Women’s Hospital. She joined the team in using the knowledge gained from animal studies to develop a prototype cooling cap and cautiously testing cooling in newborn babies with signs of brain injury. These studies also yielded practical innovations that have been widely taken up overseas, such as a simple neurological examination and brain monitoring after birth to identify babies that would benefit from this treatment.

The first international clinical trial was published in the *Lancet* in 2005 – the CoolCap Trial. This study showed that the cap was effective in preventing brain damage in babies with all but the most severe brain injury, in which seizures had often already developed before cooling commenced. There have now been a number of large clinical trials and more are ongoing. The results indicate that brain cooling prevents later disability in about one in six babies, providing the first practical and effective treatment for this devastating condition. These trials have also led to licensing of the CoolCap by the FDA in the USA, through the company that has bought the rights to develop it – Olympic Medical, USA.

Through their work, Professor Gunn and his colleagues have changed the standard of care for infants deprived of oxygen at birth and brought new hope to parents facing the tragic consequences of neonatal brain injury. However, they are not content to stop there and are working to increase the efficacy of the treatment through combining cooling with other interventions, and are testing whether it is also effective in other situations, such as after premature birth. Professor Gunn hopes that one day it will be possible to prevent or treat all cerebral palsy in newborn babies.

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**2010 Sir Charles Hercus Medal**

The Royal Society of New Zealand’s 2010 Sir Charles Hercus Medal for scientific or technological work of great merit in clinical sciences and technologies and public health was awarded to Professor Alistair Gunn, FRSNZ. The award citation noted that Professor Gunn is one of the world’s leading clinician-scientists in perinatal physiology and neuroscience. His studies in animal models revealed that hypothermia could be used therapeutically to improve outcomes for newborn babies experiencing asphyxia at birth.
Natural born enemies – Getting good bacteria to fight the bad

New Zealand has one of the highest rates of rheumatic fever and rheumatic heart disease in the world. It is a disease that mainly afflicts the young, and is strongly linked to poverty.

A recent New Zealand study found particularly alarming rates of rheumatic fever in 5-14 year old Māori and Pacific Island children, who had rates of 34 and 67 cases per 100,000 respectively. That equates to ten and 20 times the rates seen in New Zealand Europeans.

In every case, it starts with a sore throat - caused by the streptococcal family of bacteria. For many it leads to irreversible damage to their heart valves and, consequently, every year tens of thousands die from rheumatic heart disease worldwide.

Professor John Tagg has devoted a lifetime of research to finding ways to protect children from these infections.

Professor John Tagg's quest to find a way to counter childhood streptococcal infections began in a very personal way when, as a 12-year-old, he experienced his own fight with rheumatic fever - one of the more dangerous complications of the all too common strep throat.

At its worst, rheumatic fever can result in fatal, or at least debilitating, heart damage and for a young John Tagg that meant spending the next decade or so on penicillin to avoid any further Streptococcus pyogenes infections.

“I didn’t really care for that because all through my teenage years I was popping penicillin pills and therefore smelling like a fungus - and for me that was strong motivation to find another way,” he says.

Just what that other way could be did not become apparent until he was at Melbourne University and heard a lecture from Dr Rose Mushin, who had just been on study leave in the United States and was talking to the class about her new research interest in microbial interference. She wanted to explore the possibility of putting friendly bacteria in the gut to protect against intestinal infections.

Although only a student at the time, it was a seminal moment for Tagg who immediately thought about the possibility of doing the same in the throat. He freely admits that this notion has dominated his thoughts ever since.

By 1989 he had identified 10 children - out of an initial sampling of 100 - who were harbouring one particular type of bacteriocin-producing Streptococcus salivarius, and who appeared to be relatively free from pyogenes infections.

It was that specialised S. salivarius that would go on to be used as the basis for K12 Throat Guard, which is produced by the listed company BLIS Technologies formed with the
The K12 strain is widely accepted in New Zealand and is now on sale in the massive North American market, where it is sold as the world's first probiotic gum. It is marketed mainly for its effectiveness in fighting bad breath, but at the same time it confers greater natural protection against strep throat. Further products are on the way, with Professor Tagg describing K12 as ‘the bug for all ages’.

Currently Professor Tagg and his team are colonising mothers with K12 in the third trimester of their pregnancy, in the hope that they will in turn colonise their baby as they cuddle it and look after it. It is relatively easy to colonise a baby with K12 because there are no competitor bacteria, so the baby will hopefully acquire the organism and potentially benefit from its protection right from birth.

K12 can also have a part to play right through the remainder of life. Aside from protection against strep throat infections, it can also help teenagers and young adults concerned about bad breath. For older people a major concern is oral thrush, so if they can increase the levels of *salivarius* on the tongue this could and should reduce the problem.

Professor Tagg firmly believes that every course of antibiotics should be followed up by a course of K12. The levels of naturally-occurring *salivarius* will have dropped off, opening a window of opportunity to colonise with K12.

BLIS Technologies is also working on M18, a *salivarius* strain that is effective against some of the bacteria that cause tooth decay. They are also investigating a micrococcus that lives harmlessly on the skin and may be able to prevent skin infections and reduce body odour by acting on some of the bacteria that break down lipids in sweat.

They are also looking to see if they can use this micrococcus to deal to *Staphylococcus aureus* in the nasal cavity, because hospital nurses can’t work in intensive care if they are carrying it.

For Professor Tagg the focus is now on working with the company to find new probiotic prospects by doing what he feels he does best, going back to the culture collection to select potential candidates for commercial application.

Time in the laboratory is, of course, where it all started for him and he is grateful to the HRC for the consistent funding support that allowed him to pursue fundamental research that, decades later, has led to the development of products with commercial application.

“I felt the freedom to pursue my research interests and I was never discouraged from just following my intuition along the way,” he says.

Looking ahead there are still projects he would like to pursue, key amongst them being prospective trials involving the colonisation of children with BLIS-producing *S. salivarius* to further assess the impact of this on the occurrence of ear infections, particularly otitis media. He would also like to do more work on the application of BLIS-producing *S. salivarius* to the reduction of bad breath and candida infections in adults.

“That’s still the residue of the dream – to go full circle and to do the final, critical, clinical proof for some of these potential applications is what needs to be done. There are snippets of the jigsaw puzzle already in place, but you really like to go in with a big, independent multi-centre study and look at the degree of efficacy you can actually achieve,” says Professor Tagg.
BLIS Technologies has been very much a local success story but Professor Tagg is quick to acknowledge the international connections he has enjoyed and developed along the way. He is part of an international streptococcal club called the Lancefield Society, which meets every three years and he has served on its international organising committee. His main collaborators in the field are in Australia, England and the United States.

Professor Diana Lennon is a paediatrician who has spent many years trying to reduce the impact of infectious diseases on children. Her research at The University of Auckland has had a particular focus on rheumatic fever, because of the high-incidence in New Zealand children and the strong association with poverty and disadvantaged populations. Rheumatic heart disease resulting from acute rheumatic fever is the commonest cause of childhood heart disease globally, and 150 people in New Zealand die from heart damage caused by the condition every year. The cause of rheumatic fever is well-established, a sore throat resulting from infection with the group A streptococcus family of bacteria – a ‘strep throat’.

It is known that the disease can be prevented. With paediatrician Professor David Teele, Professor Lennon conducted a randomised trial of a school-based intervention programme in an area where infection rates were high. The intervention was supplied by the school nurse, who prescribed penicillin if a strep throat was suspected. Over four years, 53 schools and 22,000 students were involved. Despite the large size of the study, it was still necessary to combine the results with those of other studies to see the full-effects of the intervention – that rheumatic fever is reduced by 60 per cent when actual or suspected strep throats are treated with penicillin in high-risk groups.

Their findings led to new national guidelines for rheumatic fever prevention in New Zealand. These include assessing a patient’s risk of contracting rheumatic fever using criteria that the research team developed based on known risk factors, and taking throat swabs from those that are thought to be at high-risk. This means that unnecessary antibiotic use can be avoided in low-risk patients. As a result of the study, school-based sore throat clinics have been established in Northland, the Bay of Plenty and Hawke’s Bay. More clinics are planned for other areas, including Auckland. A sore throat clinic in the Northland town of Kaeo has been so successful in eliminating rheumatic fever over a nine-year period that an international workshop held in Auckland in 2009 set the goal of reducing the rheumatic fever rates of Māori and Pacific peoples to Pakeha levels by 2020.
UNDERSTANDING THE ORIGINS OF ADULT DISEASE
Liggins Institute

Named after Sir Graham (‘Mont’) Liggins, the Liggins Institute at The University of Auckland is testament to the value and power of multidisciplinary research.

Established in 2001, the Liggins Institute initially brought three research teams together under the one roof, to focus on four key areas: pregnancy and birth; fetus and newborn; growth, development and ageing; and brain and behaviour.

The Liggins Institute soon attracted two HRC Programme grants as well as grants from the Marsden Fund and other sources.

In 2003, the National Research Centre for Growth and Development – a New Zealand Centre of Research Excellence – was established and headquartered within the Liggins Institute umbrella. Others units followed, such as the Maurice and Agnes Paykel Clinical Research Unit and LENS, the Liggins Educational Network for Science.

Over the past decade the Liggins Institute has made a string of important discoveries over a range of areas, such as the effects of poor maternal nutrition and pre-term birth, the links between pre-term birth and diabetes, and the relationships between early life environment and later risk of disease.

Researchers from the Liggins Institute were also involved in the development of a cooling cap to protect the brains of newborns that have suffered asphyxia during birth.

Professor Sir Peter Gluckman, New Zealand’s first Chief Science Advisor to the Prime Minister, and the founding director of the Liggins Institute, had always intended to be a researcher.

His 35-year research career pretty much began from the time he graduated from Otago medical school. In his house surgeon year, he headed to the Himalayas where he worked with Sir Edmund Hillary, examining iodine deficiency and its effect on development.

“This experience set the course for Sir Peter’s life-long research focus on developmental endocrinology.”

A research fellowship followed, trying to understand the role of IGF1 in fetal growth and he then went to the United States in 1976, where he became heavily involved in developing a model for studying developmental endocrinology. When Sir Peter returned to New Zealand in 1980, to take up a position at The University of Auckland, Sir Graham Liggins generously shared his facilities - even though they were working in different areas of development.

He also came back with the view that, to understand fetal development, a multidisciplinary approach was needed and he set out to build a relatively broad group of people that understood the fetus from different points-of-view; endocrinology, growth, metabolism, neuroendocrinology, neuroscience, respiratory control and temperature regulation.
Over the next two decades Sir Peter developed a large group of 60 to 70 research staff working in a multidisciplinary way, under firstly an MRC and later an HRC Programme grant.

At one stage, Sir Peter had the rather unusual experience of being both Dean of a medical school and running a large research group. When he stepped down as Dean, he had an ambition that New Zealand had to have research institutes, similar to those in Australia, which were focused on research and graduate studies.

He persuaded The University of Auckland that they should do that, opening the way for the Liggins Institute with its focus on growth, developmental endocrinology and the developmental origins of health and disease - his own particular areas of interest.

Working with colleagues, such as the late Professor Tania Gunn, Professor Alistair Gunn, Professor Jane Harding, Dr Mark Vickers, and Dr Barbara Johnston, they made major strides in a number of areas - ranging from the neuroprotective effects of cooling for babies that suffered birth asphyxia, to research into the effects of maternal nutrition on the health of offspring.

On the commercial front, the Liggins Institute spun out a couple of companies, including Neuren Pharmaceuticals, which has products under clinical trial. They include therapeutics that are designed to target brain repair and rescue after brain injury, and another range of compounds targeting growth hormones in both cancer and metabolic disorders.

Sir Peter himself has become more and more focused on developmental epigenetics and the developmental origins of health and disease, in a quest to understand more about the relationship between evolutionary biology, developmental biology and human medicine.

It is that intellectual challenge of science that he says interests him the most now and he thinks that understanding more about the relevance of developmental plasticity and human health will turn out to be very important and change the whole approach to non-communicable disease.

Sir Peter maintains a small research group working in evolutionary medicine here and also manages the Epigen academic consortium, which has a group of about 100 people in Singapore - with additional partners in AgResearch and the UK - working in epigenetics, fetal growth and the life-long effects of a poor start to life.

"Most of my work is managing large groups, like the group in Singapore. I think my skill has always been to integrate across disciplines and understand. That’s how I got caught up in evolutionary biology and evolutionary medicine because, at the end of the day, it is the only integrating principle that integrates all aspects of biology together. There is no other principle that does."

Professor Sir Peter Gluckman

Sir Peter has long-standing collaborations with AgResearch, understandable given much of his work has had implications for agriculture as well.

He also works closely with Professor Mark Hanson, the Director of the Developmental Origins of Health and Disease Division and the Institute of Developmental Sciences at the University of Southampton School of Medicine in the UK.

The Epigen Consortium is a valuable avenue for collaboration, involving researchers from New Zealand, Singapore and the UK working in the area of developmental epigenetics and its relevance to nutrition.

He heads the International Healthy Start to Life project which looks at aspects of perinatal health from an economic perspective and spans eight countries, both developed and developing.
Events before birth can change the risk of developing several diseases in adulthood. Animals made anaemic and treated with blood transfusions before birth have altered structure and function of their hearts as adults. It is not known if this occurs in people.

In humans, rhesus disease is a common cause of fetal anaemia, and treatment of this problem with blood transfusions before birth was first developed in Auckland by the late Sir William Liley in 1963. Professor Jane Harding and her team are studying the babies, now adults, who received this revolutionary treatment. As this technique was pioneered in New Zealand, the cohort being studied by Professor Harding and her team includes the oldest surviving in-utero transfusion recipients in the world. Assessments include the structure and function of their hearts using MRI, and measurement of other risk factors for adult disease.

Findings from this study will provide the first evidence in man of long-term structural changes in the heart following in-utero events. This study will assess the long-term safety of treatment for fetal anaemia. Importantly, it will also provide key information of relevance to the future treatment of babies who become anaemic after birth, such as those born preterm or after some kinds of twin pregnancy.

“The study is now about at the half-way mark, and we have been delighted at how willing these very special people are to contribute to the study. Early results are suggesting that heart function may indeed be altered after fetal anaemia, although it is too soon to be sure of this, or what this might mean for long-term health.”

Professor Jane Harding
PREVENTING AND CONTROLLING DIABETES

Is lifestyle the drug of choice?

Statistics suggest that the number of people diagnosed with diabetes in New Zealand has now exceeded 200,000 and there could be half as many people again who have yet to be diagnosed. The disease also affects a disproportionately high number of Māori and Pacific peoples.

Type 2 diabetes is the predominant form. It usually occurs in adults, although it is increasingly seen in children, and is linked to obesity and other conditions as wide-ranging as heart disease and cancer.

That means researchers like Professor Jim Mann and colleagues from the University of Otago in Dunedin’s Edgar National Centre for Diabetes and Obesity Research, along with colleagues from the University’s Departments of Human Nutrition, Medicine and Preventive and Social Medicine, find themselves covering many of the important causes of serious ill-health and mortality seen internationally.

Professor Jim Mann has always liked being able to look at the big picture. Although he was drawn to clinical medicine, he was also vitally interested in biochemistry (in which he completed his PhD thesis) and epidemiology (the discipline of his Doctor of Medicine thesis), so getting involved in diabetes research seemed logical.

While working under Sir Richard Doll, then Regius Professor of Medicine in Oxford and best known for his work in cancer epidemiology, Professor Mann was also influenced by Professor Philip James, a physician and researcher at Cambridge who was doing obesity-related research in Britain in the 1960s and ’70s. He involved a young Jim Mann in the first Royal College of Physicians report on obesity.

What was ignored in that report, and for many years after, was the prediction that obesity was going to become the epidemic of developing and developed countries if people didn’t do something about it.

That prediction stayed with Professor Mann and he decided that, when the opportunity arose to pursue research of his choosing, that would be his focus.

His connection to Otago came at Oxford when he found himself working with a New Zealand epidemiologist by the name of David Skegg.

Professor Mann’s mentors wanted him to become a molecular epidemiologist, an area he was not that interested in, so when he was given the opportunity to do everything he wanted to do at Otago, he grabbed it.

At Otago there was acceptance of his research in all kinds of areas, from epidemiology and public health – the big picture work – to basic research in his well-equipped laboratory.
One of his first research grants – from the MRC in pre-HRC days – enabled a pilot study that suggested it was possible to reduce the chances of people with impaired glucose tolerance (prediabetes) going on to develop the disease, if they made major lifestyle changes. Confirmatory evidence came some years later, from large randomised, controlled trials in Finland and then the USA. The potential for appropriate diet and exercise to help stem the tide of the diabetes epidemic is arguably one of the most important developments in diabetes research in the past half century.

That sort of internationally recognised research has continued with projects such as the HRC-funded LOADD (Lifestyle Over and Above Drugs in Diabetes) study, led by Dr Kirsten Coppell, published in the British Medical Journal in 2010. This was a follow up to earlier work published in The Lancet and BMJ showing the potential benefits of dietary fibre and the importance of fat modification in the treatment of diabetes.

The LOADD study showed that, even when people were on a maximised drug regime, these dietary principles could produce an improvement that was as great as any of the new drugs. It received considerable publicity worldwide.

Other dietary research has involved comparisons of high-carbohydrate, high-protein and high-fat diets in the management of overweight people at risk of diabetes. They found comparable weight loss could be achieved regardless of diet composition, though more recent studies suggest that diets relatively high in protein may confer some benefits.

Weight regain following weight loss is a major issue for many but the group has shown that a simple nurse-led programme involving occasional weigh-ins and supportive phone calls is as effective as a more intensive and costly programme. Diet composition had little effect on the likelihood of weight regain.

They have also investigated how best to identify people at risk of developing diabetes before they have developed any abnormalities of blood glucose. Research by Dr Kirsten McAuley, Associate Professor Sheila Williams and Professor Jim Mann into the early diagnosis of insulin resistance eventually led to the development of the McAuley Index which has now become an internationally accepted measure.

More recently they have also worked with Professor Geoff Chase and colleagues at the University of Canterbury to develop a more sophisticated early stage test to be used for screening and for understanding the effects of interventions on insulin action.

The over representation of Māori in diabetes statistics has led to research describing appropriate use of BMI cut-offs and studies to establish the most appropriate diet composition for Māori.

HRC funding has also allowed a number of younger researchers working with Professor Jim Mann to undertake research leading to PhD degrees and researchers in the early stages of their careers to develop to the point where they now have major HRC-funded research programmes of their own.

For example, Associate Professor Rachael Taylor led the APPLE Study, one of the first community studies in the world to show that it is possible to halt excess weight gain in children through physical activity and dietary intervention. She and colleagues now have substantial HRC grants to examine ways of preventing obesity at the earliest possible stages of life.
In addition to her work on the LOADD study, Dr Kirsten Coppell - a public health physician who has also trained in general practice - has undertaken a number of epidemiological studies in diabetes including a collaborative project involving the University of Otago and Ngati Porou Hauora on the prevention of diabetes. In 2007, that was expanded to include the prevention of chronic disease and a whole-health approach, which is now being used on the East Coast of the North Island. The initial collaborative project, the Ngati and Healthy - Prevent Diabetes Project, received the gold award in the Whanau Ora Awards for Māori health initiatives.

In addition to the work on early prevention of obesity, future research will include the metabolic syndrome, in particular its relationship to gout and non-alcoholic, fatty-liver disease, and ways of reducing the risk of developing these conditions.

Professor Mann and colleagues have also set up the Centre for Translational Research, as an offshoot of the Edgar National Centre for Diabetes and Obesity Research, as an avenue to put their research into practice. One of their greatest contributions has been in the area of guidelines, with Professor Mann chairing the European Diabetes and Nutrition Guidelines group, and the Expert Advisory Group on Diabetes and Cardiovascular Disease in New Zealand. He has also chaired or served on several other relevant national and international groups, including the nutrition advisory group to the World Health Organisation – evidence of the quality of the research work of his group.

Professor Mann's hope is that governments in New Zealand and worldwide will see the relevance of their findings and encourage implementation of the interventions they have developed.
The HRC’s Clinical Research Training Fellowship was established in 2006 to support clinicians to undertake research training and obtain postgraduate qualifications. The scheme contributes to clinical research capacity, bridges the gap between scientists and clinicians, and enables translation of research findings. Clinicians are well placed to identify research questions, as they apply evidence-based clinical practice.

An evaluation of the Fellowship in 2010 found that it has successfully increased clinical research capacity and contributed to the translation of research into clinical practice. Recipients of the Fellowship have undertaken innovative research with implications for the clinical setting, and have maintained a combination of clinical work and research after their Fellowship has concluded.

The impact of the Fellowship on the career and clinical practice of the Fellows has been significant. Without financial support from the HRC, many of the Fellows would not have been able to undertake research training.

Some of the research results have had important implications for policy and clinical practice. Dr Cheri Hotu, a renal fellow at Auckland Hospital, conducted a randomised, controlled pilot study to determine whether community-based monitoring could improve blood pressure control in Māori and Pacific patients with early diabetic nephropathy. The DEFEND (Delay Future End Stage Nephropathy due to Diabetes) study investigated whether monthly community visits by nurse-led Māori or Pacific healthcare assistants could break down barriers and achieve better results than usual clinic practice. The community model provided more frequent monitoring, more adjustments to medication regimens, the removal of language and transport barriers, and encouragement of medication adherence, which led to a higher utilisation of antihypertensive medications. A significant decrease in systolic blood pressure and a significant reduction in urinary protein levels provided evidence of an overall improvement in diabetic nephropathy for patients who received community care.

The study results led to the Department of Renal Medicine at Auckland Hospital adopting the DEFEND model of care for outpatients with chronic kidney disease. Healthcare assistants undertake frequent home-based visits to patients with chronic renal impairment, monitoring their blood pressure and assisting with transportation to clinic appointments.

The Clinical Research Training Fellowship led to Dr Hotu’s appointment as an honorary clinical lecturer with The University of Auckland, and contributed to the training and professional development of the Māori and Pacific healthcare assistants, leading to employment for one assistant in a similar healthcare role.
MĀORI HEALTH RESEARCH
Culture at the core of health and wellbeing

By Professor Sir Mason Durie, CNZM
(Ngāti Kauwhata, Ngāti Raukawa, Rangitane),
Assistant Vice-Chancellor (Māori and Pasifika), Massey University, Palmerston North

As a South Pacific nation, Aotearoa New Zealand has a distinctive identity and a distinctive heritage. Moreover, it has a tradition that reflects Polynesian voyages as well as voyages from the Northern Hemisphere. In order to address that reality and to be useful to the peoples who make up New Zealand in modern times, we need knowledge and information that is relevant, grounded, and applicable to modern times. While old knowledge is integral to the modern agenda, new knowledge is also needed to better understand contemporary challenges. In that respect, over the past twenty years, health research has played a significant role in shaping New Zealand so that all people have a better chance to participate fully in society.

Māori health research has largely been about the interpretation of indigenous knowledge and Māori custom so that Māori patients can have genuine access to health care that draws on two sets of values, two traditions, and two systems of knowledge. Interface research occurs at the boundary between health sciences and mātauranga Māori (Māori knowledge) and reflects insights from both. To a large extent, over the past 20 years, Māori health research has operated around the interface. It has led to fresh approaches to understanding health and sickness, health services that recognise the significance of culture to wellbeing, a Māori paradigm for health literacy, evidence-based health policies for Māori, research methodologies that incorporate Māori world views, and greatly increased Māori capability in research and in the health sector.

The HRC’s proactive approach to Māori health research has been a critical factor for those developments and establishing two Māori health research centres in 1993 was...
an important catalyst. Both centres were initially known as Te Pūmanawa Hauora and were led by Professor Eru Pōmare from the Wellington Clinical School at the University of Otago and Professor Sir Mason Durie from the Department of Māori Studies at Massey University in Palmerston North. They had worked together as friends and colleagues in earlier years, and in the early 1900s their grandfathers had worked together in Wellington. After Professor Pōmare’s sudden death in 1995, the Wellington Centre was renamed in his honour. In the intervening years, four other Māori health research centres have been established.

“A new cadre of 30 or more Māori health researchers with doctoral degrees has emerged, due in no small part to the provision of doctoral scholarships by the HRC.”

The gains made in Māori health research have not only been reflected in the generation of new knowledge that has had direct application to health services and better understandings of the determinants of health, but has also been a core part of a renewed health movement among Māori. A translational approach to research has seen active engagement with iwi, Māori communities, health agencies and government agencies so that a wide platform for Māori health advancement has become evident. The movement has also reached out beyond New Zealand to touch other indigenous peoples, especially in Australia, Canada, Hawaii and the Pacific. Within indigenous communities Māori health researchers are recognised as leaders for better indigenous health.

The past 20 years has demonstrated that with the right levers, transformation is possible. The impacts of decisions taken in 1990 have led to gains that would not have been thought possible in earlier decades. There is now a critical mass of competent Māori researchers, a greater appreciation of research ethics by all researchers, methodologies that make sense to Māori, and clear evidence that health research can be translated into Māori health gains.

“There is a keenness within the Māori sector for ongoing research to evaluate progress and to tackle new frontiers.”

The challenge for the next 20 years will be to build on the gains made in the past two decades so that the insights learned can be applied more evenly and with greater reach. But new research will also be necessary to meet a changing New Zealand and a changing globe. Epidemiological transitions, demographic shifts, natural disasters, environmental stresses, climate change, global overpopulation, widespread malnutrition, and continuing indigenous exclusion will require fresh approaches. Māori health researchers will have key roles to play in the years ahead and will be challenged to develop new methodologies that focus on greater inter-disciplinary alliances, increased uptake of research findings, and participation in arenas that have yet to be defined. Co-construction, collaboration and improved instruments of research translation will be necessary.
Whakauae Research for Māori Health and Development

By Dr Heather Gifford (Ngati Hauiti)
Director, Whakauae Research for Māori Health and Development

Whakauae Research for Māori Health and Development (WRMHD) is a distinctive model of Māori community-based research that has been strongly supported by the HRC since its inception. WRMHD was established by Te Rūnanga o Ngāti Hauiti in 2005, its aim being to not only develop the research capacity of Ngāti Hauiti, but also to offer a broad range of Māori-centred research services both nationally and internationally. Whakauae has focused primarily on Māori public health research, health promotion evaluation and primary-care research. With the addition of new staff in 2008, we have broadened this focus to include health services and health policy research. The team has grown from two staff initially to six staff members currently. Whakauae utilises largely kaupapa Māori qualitative research methodologies. However, through research partnerships, we are able to offer a mixed-method approach if required for the research.

Our research is important for three reasons: we contribute to Māori health research capacity building; we model effective community-based research practice; and we are passionate about research making a difference “on the ground” - therefore bridging a critical gap between research and practice. While much of this bridging occurs at a health services level - we are also very interested in generating an interest in research at a whānau and hapū level. I think we have managed to achieve this in a small way through activities like our Families Commission Parent Panels, where we ask Hauiti whānau what they think about a range of social policy issues; our work with Hauiti whānau as research participants in a range of projects; and marae-based hui with our Rūnanga whānau and wider Hauiti whānau, at which we discuss various research results and research practice. If we can make research exciting and interesting to our community, there is a much stronger likelihood that our whānau members will go on to further study that involves research and will think about using research to inform decision-making within whānau.

Whakauae’s current research projects include investigator initiated research on topics as diverse as tobacco control, and the impact of government policy on health inequalities and whanau ora, through to various evaluations of both general population and Māori-focused public health interventions. The mix of research we undertake can in the longer term, through increasing the evidence base and informing and strengthening practice, make a difference to Māori health outcomes. However, to achieve this, it is critical that research results are widely disseminated and that there is a political will from a range of partners to receive and act on advice.

I asked my team how they all came to be at Whakauae and why they had left various secure positions in academic and health provider institutions to come to work at Whakauae. The answers were very similar - I think as researchers we all want to make a difference on the ground - this is expressed in different ways such as “I can contribute to being a conduit between the evidence and practice and encouraging people to use the evidence to inform their practice”, and “to help bridge the disconnection between what the actors are doing on the ground and what the research and evidence is telling them”. The team also talked about the disconnect going both ways, “because what was happening at the policy level wasn’t translating to what was needed on the ground I guess”. Other reasons for team members making a deliberate choice to work in an iwi-based research centre was that the organisation had a reputation for high standards of work and ethical practice; it was a place where people were supported but also challenged to extend themselves; and as a community-controlled organisation, the principles reflected by the owners (iwi), were reflected in practice within the organisation itself.

The HRC has been critical to Whakauae’s development. They have supported Whakauae in a number of ways: from funding our first establishment grant that was targeted directly at growing community research, through to grants received in both...
the mainstream and Māori HRC grant rounds. Three of our research team have received career development awards that have supported advancement through an academic career pathway. In addition to financial support, we have received other types of support, such as a visit by the HRC’s Chief Executive, Dr Robin Olds, to our marae to discuss the role of Māori community-based research and support and advice from the wider Māori health directorate. In turn, two of our team have been able to contribute to the HRC through participation as reviewers, as assessors and as committee members.

We are very hopeful that some of our direct research results can inform practice and service delivery outcomes. For instance we have just completed, in partnership with ALAC and our local PHO, an evaluation of a brief alcohol intervention in primary health care that demonstrated some very positive outcomes. The research results can be used to influence decision-making at all layers of the health system, with policy makers by suggesting how to intervene in a significant public health issue, with funders by suggesting how the model could be implemented nationally, and with health providers by offering detailed advice regarding systems and processes for implementation.

As a team we value and contribute to building strong networks internationally. Dr Heather Gifford is a partner on the International Union of Health Promotion, South West Pacific Working Group, and Dr Amohia Boulton is on the Executive of the Health Research Services Association of Australia and New Zealand. Both Dr Boulton and Dr Gifford have had extended periods of study and work in Canada. Dr Boulton is currently working with health services researchers in Canada and Australia to investigate research opportunities across three countries regarding contracting for health outcomes with vulnerable populations. In addition, Whakauae has hosted a Trans-Tasman hui on indigenous partnerships within tobacco control to strengthen a joint approach to tobacco control research with indigenous populations.

Our next steps in our research plan are to further consolidate the work we are currently doing and continue to build our profile both nationally and internationally. Building Whakauae's profile is about extending the opportunities to influence health services delivery and practice through high quality research, with a focus on improving Māori health outcomes. We need to keep a watchful eye on what is happening politically that may influence our sustainability, for example, changes in funding priorities, and attempt, where possible, to influence decisions and adapt our approach if necessary.

As a team, we have a number of hopes and dreams for our research, including contributing or finding ways to make the big evidence base over here more accessible for ordinary people and ordinary practitioners on the street.

My dream, as the team leader, would be that we have a reputation as an excellent example of community-based research; we make a difference (even in small ways) to health service delivery and practice; we continue to enjoy working in a small community-controlled research organisation; and that, through our work, research is seen as interesting and accessible by whānau.
International Indigenous Health Research Collaboration

Dr Pamela Bennett (Te Arawa: Ngati Whakaue, Ngati Pikiao), from The University of Auckland, led a team of New Zealand researchers and health professionals who, in collaboration with indigenous researchers from McGill University and the University of British Columbia in Canada, examined factors and processes that promoted resilience in mental health among indigenous people. This project, entitled Roots of Resilience: Transformation of Identity and Community, is one of a number of academic projects both groups have collaborated on in the past decade.

Dr Bennett, together with Dr Jane McKendrick, examined the ways in which Māori coped with adversity and psychological distress to identify the concepts that underpinned resilience. They looked at examples in history by examining traditional songs and stories, and academic publications that portrayed traumatic events and instances of resilience. This initial phase of the study was further informed by interviews with kaumatua and kuia, and group discussions with Māori from several areas in New Zealand, that identified the distinctive features and concepts of resilience in Māori communities. A recurring theme was that resilience is inextricably linked to long held Māori beliefs about themselves, their relationships with each other, and the natural environment around them.

The concepts identified were used to inform solutions to different scenarios constructed by the research team, in consultation with Māori mental health practitioners and past consumers to ensure authenticity. The scenarios and solutions helped provide informed and practical models to support the application of the concepts to a clinical setting for the assessment and management of psychological distress in Māori.

The Canadian team, led by Dr Rod McCormick from the University of British Columbia, and the international lead investigator Professor Laurence Kirmayer from McGill University, also undertook similar research for First Nation and Métis people. Both New Zealand and Canadian teams found similar concepts that promoted resilience, and took great care in recording any differences between their respective communities. Both teams have documented a range of indigenous ways of addressing issues, either solely or alongside Western approaches, pertaining to indigenous mental health. The models and information that led to their construction have been disseminated widely through various international networks to allow for modification by other groups, local and international, to meet their own needs. The research findings will inform the ways in which health professionals diagnose and treat indigenous people with mental health problems.
The term ‘Pacific peoples’ encompasses a range of cultures, languages and world views that are as diverse as they are valuable. Pacific New Zealanders make a major contribution to the nation, from the economy to the arts and form an increasingly large part of our demographic.

For a number of reasons, Pacific peoples in New Zealand consistently experience poorer health outcomes than other citizens. They are six times more likely to be diagnosed with cardiomyopathy (a disease of the heart muscle) and gout, and four to five times more likely to suffer from rheumatic fever, gastric ulcers and diabetes compared with other New Zealanders. Many other conditions are also more common in Pacific New Zealanders, and the outcomes less favourable.

Reversing this trend means engaging people in a way that is meaningful and respectful to them, and this means greater participation of Pacific peoples in all areas of health research.

The HRC has worked hard to make this goal a reality. We are fortunate to have trained and retained talented individuals who are focusing their considerable skills on defining and addressing key Pacific health issues. Their role in building a body of Pacific health knowledge is invaluable, as is their influence in training and inspiring the next generation of Pacific researchers.

“Pacific communities in New Zealand are many and varied and there is no coherent ‘Pacific’ body of knowledge.”

Dr Margaret Southwick
Stories lay path to healthier communities: Minimising harm from alcohol use

Through the HRC’s Partnership Programme; the HRC, the Alcohol Advisory Council of New Zealand and the Accident Compensation Corporation formed a partnership to fund research to reduce the harm caused by alcohol in New Zealand. In 2005, a Le Ala project was funded as a result of this Partnership – Searching for Pacific Solutions: A Community-based Intervention Project. Together with Dr Helen Warren, Dr Ieti Lima and Moana Solomona, Dr Margaret Southwick formed Le Ala. The project aimed to increase understanding in Pacific communities about alcohol and drug-related harm and to encourage activities that reduce the likelihood of such harm.

Good Pacific health research involves understanding the cardinal Pacific value of reciprocity and returning to communities what is learned in an appropriate way. No-one understands how to work with Pacific communities better than Dr Southwick, Dean of Faculty, Health Education and Social Science, at Whitireia Community Polytechnic. Of Tuvalu and Pakeha decent, she has been making a major contribution to Pacific health research for many years. Dr Southwick initially trained as a nurse but went on to gain a BA in Anthropology and Sociology, a postgraduate diploma in business studies and PhD in Nursing. This diverse range of skills has been invaluabale as a senior academic, Pacific researcher, lecturer and mentor, and she has made a major contribution as an advisor on health and research policy.

The Le Ala intervention embodies Pacific philosophies, values and approaches that are common to all Pacific communities. A total of seven community groups participated in the study, involving up to 100 individuals at a given time, and living in a range of locations across New Zealand - from Auckland to Christchurch.

The model behind Le Ala places the power to effect change with the communities involved, and not with the research team. The academics involved facilitate and guide the process but the knowledge generated and the outcomes gained are owned by the communities themselves. Interviewers were all highly knowledgeable about Pacific protocols and values, and spoke at least one Pacific language fluently. The participants decided how the meeting should be conducted, in terms of the languages used and the customs observed. Some communities also chose to broaden the remit to include other issues of concern, such as youth suicide, at-risk behaviours and intergenerational conflict. Rather than developing a response focused solely on alcohol use, they were able to address the broader social, behavioural, psychological and cultural determinants that influence alcohol use and look at improving the health of the whole community.

The key to the intervention is the use of ‘narrative therapy’, basically story-telling, which builds on the strong oral tradition in ‘cultural communities’. Participants were encouraged to tell their stories, in a safe environment, deconstruct them to find the issues, and then rebuild new stories that would relegate painful memories to the past and guide the way forward to a future where these issues were addressed. The rationale behind this method is simple, yet powerful - the way in which we make sense of a problem invariably gives rise to the intervention.

The researchers developed three archetypal narratives from the ‘wounding stories’ that participants told. The ‘Smart Cookies’ (mainly women in their thirties with degrees and good jobs) have integrated well into Palagi society and appear as outward successes in both Pacific and Palagi systems. They are pressured by expectations from their Pacific families, and perhaps also non-Pacific partners - who may not understand Pacific culture and their role and responsibilities as
a husband within it. Sometimes ‘Smart Cookies’ are unmarried and face criticism for failing to produce grandchildren. Alcohol is used to help them manage competing demands and tensions in their lives.

The ‘Young Dudes’ feel estranged and disconnected both from New Zealand society and from the Pacific society with which their parents and grandparents identify. Alcohol provides a means of filling the void and connecting with like-minded others. It becomes the norm. The ‘Old Hacks’ have ‘come to a world where they have no place’. They have lost their traditional roles as head of the family, leaders and mentors and also drink to fill the void.

During the course of the story-telling, the groups moved beyond these wounding stories into what they saw as the intervention. They transformed the negative archetypes to positive ones, ‘Smart Cookies’ became ‘High Flyers’, reconnecting with their ‘culture’ and traditions; ‘Old Hacks’ were transformed to ‘Wise Old Owls’, reprising their roles and responsibilities as fathers and husbands; and ‘Young Dudes’ became ‘Vikings of the Sunrise’, acquiring a secure identity as the future navigators of Pacific people in New Zealand.

Le Ala achieved a lot in the few months that it was running. It was proven to be a valuable model for engagement with Pacific communities; raising awareness of alcohol issues and providing opportunities for them to take ownership of these issues. It functioned as a primary prevention intervention and revealed a serious gap in the public health promotion of safe drinking levels in Pacific communities. More than this, the Le Ala intervention provided a way of generating new understandings between generations and this is key to maintaining strong Pacific communities.

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Growing future Pacific health research stars

Applying indigenous knowledge to manage mental health

Through the Pacific Career Development Award Programme, the HRC hopes to engage Pacific peoples with research and then provide funding vehicles for them to travel along the career pathway to become credentialed researchers addressing Pacific health issues. Dr Karlo Mila-Schaaf is an ideal example of what the HRC hopes to achieve.

Of Tongan and Pakeha decent, Dr Mila-Schaaf started her contribution to Pacific health research as the HRC’s Manager, Pacific Health Research from 2000 until 2004. In this role, she built on the wisdom and expertise of the HRC’s Pacific Health Research Committee to craft some valuable and inspirational policies - including the ‘Flax Roots Model’ for supporting and mentoring students, the Pacific Health Research Strategic Plan and the Guidelines on Pacific Health Research.

Her ability to cement in words the values, paradigms, beliefs and hopes for Pacific health research was founded on years of writing her own poetry. She has already published two volumes of her work, Dream Fish Floating (2005) and A Well Written Body (2008). In 2006, Dream Fish Floating won the NZSA Jessie McKay ‘best first book of poetry’ category at the Montana Book Awards.

On joining the HRC, Dr Mila-Schaaf already had a Masters degree in Social Work and after leaving to start her family, she decided to apply for an HRC scholarship to do her PhD at Massey University. Her recently completed PhD focused on identifying the relationship between culture, identity and health, and wellbeing for the New Zealand-born Pasifika generation. She began with an analysis of the health and culture information provided by more than 1,000 Pacific High School students, who participated in the HRC-funded Youth2000 Adolescent Health Survey.
She discovered that feeling accepted by others, feeling proud of your ethnic identity, continuing to place importance on Pacific values and speaking Pasifika languages, were all statistically associated with a range of advantageous health and educational outcomes. Feeling accepted was associated with being more likely to try hard at school, more than twice as likely to report doing well at school, being half as likely to report suicidal thoughts and being 70 per cent less likely to report a suicide attempt in the previous twelve months, compared with those who did not feel accepted.

Dr Mila-Schaaf went on to interview a small sample of successful, high-achieving, second-generation Pacific peoples to further understand the relationship between identity, culture, resilience and optimal health and wellbeing among this population. She was also able to interweave her own experiences as a Pacific New Zealander to create a narrative that gives real insight into this unique group.

Dr Mila-Schaaf is currently a Postdoctoral Fellow at the Department of Public Health, University of Otago, Wellington. She was recently awarded a HRC Pacific Health Postdoctoral Scholarship to develop an intervention for mild to moderate mental health problems that builds on Tongan and Samoan indigenous knowledge traditions, and the experiences of Pacific consumers, their families and mental health practitioners to identify what is therapeutic.

**Family focus on Pacific health**

His mother’s experience of living with severe heart disease inspired Dr Gerhard Sundborn to embark on a career in health research. Surgery gave his mother a new lease of life and made him question why Pacific peoples are less likely to access surgery, when they actually have a higher incidence of heart disease than other New Zealanders. This was the topic of his Masters thesis and he discovered that issues arose in the primary-care setting and the referral process for Pacific peoples. Most did not receive surgical treatment until their condition became a medical emergency and so their outcomes following surgery were generally poorer.

In 2004, Dr Sundborn went on to study cardiovascular disease risk factors in Auckland’s Pacific peoples, supported by an HRC Postgraduate Scholarship. As part of a research team at the School of Population Health, The University of Auckland, he collected data on risk factors for heart disease and diabetes through the Diabetes Heart and Health Survey. The team found that the risk of heart disease was significantly higher among Pacific groups studied (Samoan, Tongan, Niuean and Cook Islanders) when compared with the European group. However, the risk varied between ethnic groups, with Niueans having the lowest estimated risk and Samoans the highest.

Tongan women had a diabetes prevalence that was over double that of their men, but this gender difference was not seen in other Pacific groups. They also found a particularly high prevalence of undiagnosed diabetes in Cook Islanders, compared to the other groups. The study highlighted the importance of not treating Pacific peoples as a single ethnic group for the purposes of research.

Dr Sundborn went on to become Co-Director of the Pacific Islands Families (PIF) Study and a Senior Research Fellow at AUT University. The PIF study is a longitudinal study following 1,398 Pacific children born in 2000 for the first eleven years of their lives, funded in part by the HRC. It is providing a wealth of information about health and development in Pacific communities. The research team have published detailed findings on a range of areas, including oral health, glue ear and child development by ethnicity, paving the way for public health interventions that are culturally relevant and appropriately targeted. The study has found that being strongly aligned with Pacific culture leads to better health outcomes for both mothers and children. The importance of the PIF study extends beyond the knowledge that it is generating, to the opportunities that it is providing to engage and train the next generation of Pacific researchers, and Dr Sundborn has a key role in this. The HRC is currently funding a further two Pacific students to contribute to the research programme.
INJURY PREVENTION

Providing new insights into the causes and consequences of injury in New Zealand

A paper by the former Injury Prevention Research Unit Director at the University of Otago, Dunedin, Emeritus Professor John Langley, published in the New Zealand Medical Journal in December 2010, put the total social and economic cost to the country at more than $9.6 billion in 2008.

The Accident Compensation Corporation’s (ACC) treatment and rehabilitation costs were almost $1.4 billion alone. Other costs include weekly compensation ($1.16 billion), lost income due to premature mortality ($908 million) and human costs ($6.21 billion), based on disability-adjusted life years.

The New Zealand Injury Prevention Strategy has identified six priority areas: assault, falls, drowning, motor vehicle accidents, suicide/self harm and the workplace. These areas account for 84 per cent of the total social and economic costs of all injuries.

By far the biggest injury group is young people - from adolescence through to 35 or 40 - who make up a disproportionately high proportion of the motor vehicle crashes and sporting injuries. While heart disease and cancer may affect more people, they tend to do so in their later years, rather than in their prime productive years.

Injury is an important facet of health because it causes so much premature loss of life and premature disability in New Zealand.

The origins of the University of Otago’s Injury Prevention Research Unit (IPRU) go back to the days of the HRC’s predecessor, the Medical Research Council. It recognised injury as an important area of research and called for tenders to establish an injury research unit, and the Dunedin group won the funding. The HRC has remained a key funder ever since, through both Programme and Project funding.

One of the key figures in the IPRU has been Emeritus Professor John Langley, who retired as Director in 2009, when Professor Hank Weiss took over the role.

A psychology graduate of the University of Otago, Professor Langley specialised in industrial psychology, taking a role with BRANZ – the Building Research Association of New Zealand – working on safety projects.
He was working in Wellington when he successfully applied for a position analysing injury data generated from the HRC-funded Dunedin Multidisciplinary Health and Development Study, one of the HRC’s longest supported research programmes.

When the tender was released to set up the IPRU, Professor Langley and long-time colleague Associate Professor David Chalmers put in a successful bid and launched the unit under the Department of Preventive and Social Medicine umbrella.

A lot of their early research was stimulated by the Dunedin Multidisciplinary Health and Development Study. For example, they noticed that many kids were getting injured on playground equipment and their analysis showed that it was due to a combination of height and surfacing.

They then did a case-control study to see how a change in height and surfacing would change the risk. They found the critical factor was the type of surface because while soft, some surfaces also allowed rebound and that was often what caused the injury. The research resulted in new standards for playgrounds.

Over the years the IPRU has been involved in a range of prominent research projects, such as the Rugby Injury and Performance Project, which followed a large cohort of rugby players and produced a series of valuable studies on injury incidence and the effectiveness of protective measures, such as mouth guards.

Sport and recreational injury prevention has continued to be an important area of research, along with child safety, road safety, occupational injury, intentional injury, injury surveillance, alcohol-related harm, disability and rehabilitation, and biomechanics of injury. By the end of 2010 the IPRU had published 85 reports across all those areas.

There is ongoing research in each area. Examples include Child Home Safety, looking at factors affecting parental perception and response to risk; and in the disability and rehabilitation field, the HRC-funded Prospective Outcomes of Injury Study (POIS), headed by Dr Sarah Derrett.

POIS follows a group of people who have made a claim on ACC, to see why some make good recoveries and others don’t, by examining a range of things from access to services to their personal perception of whether or not it is a serious injury.

Professor Langley says there are areas which continue to cause concern, such as serious assault, which doubled in the five years up until 2008. It is of particular concern when statistics show victims have a five per cent chance of dying.

Serious self-harm also continues to worsen, increasing by 45 per cent between 2003 and 2008. In both cases, the two main groups are the 15–24 and the 24–45 year-old age brackets. Dr Shaymala Nada-Raja’s Recovery via Internet from Depression project is looking to tackle self-harm by evaluating a web-based self-help programme using cognitive therapy.

Alcohol has also been a key area of focus, with studies examining gender drinking patterns and alcohol-related harm by area, and the e-SBI National Trial to evaluate the effectiveness of an electronic screening and brief intervention developed for use with university students.

On the basis of these findings, Professor Langley says they actually lobbied to get the alcohol purchase age raised again, but failed.

Professor Langley acknowledges the critical role HRC support has played, funding the core of the unit and many projects.
Dr Begg is another IPRU staff member who began work on the Dunedin Multidisciplinary Health and Development Study. The study cohort just happened to be the right age to be among the first learner drivers in the world to go through a comprehensive Graduated Drivers Licensing System. Much of this research led to the development of the NZDS.

The overall aim of the NZDS is to identify the main driving and driving-related crash risk factors for newly licensed drivers. They are asking questions such as how much supervised driving do they get as learner drivers? Who is teaching them to drive? Do they use professional instructors? Do they drive unsupervised, or at night or with passengers when they are not supposed to?

They are also looking at other factors such as drug and alcohol use, impulsivity, sensation seeking and aggression. They examined the pre-licence driving behaviour of the cohort and found that around 50 per cent had driven on road before they got a licence.

One of the other key things Dr Begg and her colleagues have noticed is that many young drivers are progressing only slowly through the Graduated Drivers Licensing System and they are investigating the reasons for this.

The NZDS cohort
- 3,992 newly licensed drivers, recruited face-to-face, from various locations throughout New Zealand;
- Gender: 51% female; 49% male;
- 21% identified as Māori; (n=825);
- Age at learner licence: 49% were aged 15 years, 18% were 16 years, 11% were 17 years, 22% were 18+ years.

Follow-up at restricted and full licence stage (as of 30 April 2011)
- 2952 (74%) of cohort have passed their restricted licence test;
- 87% of whom completed the first follow-up interview;
- 1576 (39%) of cohort have passed the full licence test;
- 93% of whom completed the second follow-up interview.

“Non-progressors” (i.e. those who had not progressed to a restricted licence)
- 548 (46%) completed a brief telephone interview to ascertain reasons for not progressing;
- 540 (47%) were unable to be contacted;
- 101 (9%) refused the interview.

Parent study
Of the 1,405 parents eligible for this study:
- 1200 (85%) participated and completed a telephone interview;
- 205 (15%) refused or were unable to be contacted.

Traffic crash and infringement records
- Of the 3,992 in the cohort, 98% gave signed consent for access to all traffic crash and injury records listed on the consent form (traffic crash reports, traffic infringement, offences, and convictions, hospital traffic records, ACC records for traffic injury) for 10 years after they gained a full licence;
- Less than 1% refused access to all records;
- 1% denied access to police records.
Over the past 39 years, 1,037 Dunedin-born individuals have been closely monitored as part of the widely acclaimed Dunedin Multidisciplinary Health and Development Study.

The HRC-funded study, which was established by Phil Silva in the early 1970s, has followed the cohort from birth, collecting data every two years, from the age of three until 15, and then again at the ages of 18, 21, 26, 32, and most recently, 38 years of age. It boasts a 96 per cent participant retention rate. At each step along the way researchers have assessed a comprehensive range of biological, psychological, social and economic factors to see how they come together to shape good and poor psychosocial, mental, cardiovascular, respiratory, oral, sexual and reproductive health outcomes.

To date, the Dunedin Multidisciplinary Health and Development Study has generated more than 1,100 scientific publications and reports.

When, as a fourth year clinical psychology student in 1985, Professor Richie Poulton took a walk through the student union at the University of Otago, he couldn’t have imagined he would eventually be heading the Dunedin Multidisciplinary Health and Development Research Unit.

His attention was drawn to an advertisement for a part-time interviewer for the age-13 assessment. He applied and was employed by a post-doctoral researcher from America, Terrie Moffitt, who is now the associate director of the study and Professor at the Institute of Psychiatry in London, and the Departments of Psychology and Neuroscience, Psychiatry and Behavioral Sciences at Duke University, USA.

Professor Poulton used data he collected in his Masters Thesis and went on to do a PhD in anxiety disorders at the University of New South Wales in Sydney. He eventually returned to Dunedin to become Deputy Director under Phil Silva, before taking the reigns himself in 2000.

It has given him the opportunity to broaden his horizons and move beyond his interest in the behavioural area, getting more involved in understanding psychosocial determinants of physical health, and focusing on risk for cardiovascular disease, as well as oral health.
With a publication list of more than 1,100 papers from around 400 different authors, there have been many highlights for the Dunedin Multidisciplinary Health and Development Study. The quality of the data gathering, the size of the cohort and the excellent retention rate has given it international credibility, but over the last decade, it has been the groundbreaking gene-environment work which has grabbed worldwide attention, by turning the long-standing nature versus nurture debate on its head.

Papers generated from the study have highlighted the interplay between genes and environment, for example, showing that people with a shorter form of the gene 5-HTT (which helps in the production of the neurotransmitter serotonin) are twice as likely to suffer from depression if they faced some major trauma or stress in their life. In other words, a genetic predisposition can interact with an environmental stress to trigger a significant illness.

They have also been able to bring together the behavioural data they have collected with the medical and dental information they have built up. For example, a study involving Murray Thomson, the Professor of Dental Epidemiology and Public Health at the University of Otago’s Faculty of Dentistry, identified cannabis smoking as a major predictor of gum disease, an area previously unexplored. The study was one of the few dental and oral health papers to appear during the last 20 years in the Journal of the American Medical Association, and included commentaries and even an educational piece for medical practitioners.

The quality of the data has also allowed the research team to look into areas such as the age-old psychosomatic concept that suggests social or psychological issues can get under the skin to cause physical damage. They showed that childhood maltreatment will predict levels of systemic inflammation in adulthood, even after taking account of all other known risk factors, increasing the risk of health problems, such as cardiovascular disease and poor lung function.

Such is the Dunedin Multidisciplinary Health and Development Study’s international standing that over the years it has attracted millions of dollars in funding from four branches of the National Institutes of Health in the United States, as well as extensive funding from Britain.

While the study doesn’t generate commercial outcomes as such, it does generate data that can feed into decisions about how best to allocate vast amounts of money for social good – be it health, education, social development or justice.

Professor Poulton says HRC funding has been critical in both getting the study started and then keeping the core of the organisation operating.

Looking ahead, the age 38 assessments have been taking place during 2010 and 2011, and Professor Poulton says one of their plans is to come up with a measure of premature ageing. They want to identify predictors in earlier life that are modifiable, in the hope they can slow or even stop a person heading down the premature ageing track and improve their quality of life in later years.

His hope is that the multidisciplinary database will continue to be used to make valuable and relevant contributions to both science and policy.
Spin-off studies
Several spin-off studies have been developed, including the parenting study which has generated home visits with over 500 children now. The next generation study involves 15-year-old offspring of the study members, and so far over 100 people have been involved. By adding those to the interviews they conducted with the grandparents of study members, they now have information on three generations.

CASE STUDY
Long-term consequences of low levels of self-control during childhood

“We are all born with certain innate capacities but there are skills that you can acquire. The good news is that parents can teach their children these skills using sensible parenting strategies, at whatever age.”
Professor Richie Poulton

“We have shown that it does matter, and it matters a lot, above and beyond the usual suspects: things like low socio-economic status during childhood and childhood IQ, which are good predictors of life outcomes. After we hold those things constant, self-control adds significantly to prediction.”

This will feed directly into current debates among policy makers and governments about what they should invest in, in the early years, because it seems that targeted programmes early in life can influence later life outcomes.

This HRC-funded study, led by Professor Richie Poulton from the University of Otago, Dunedin, and Professors Terrie Moffitt and Avshalom Caspi, both of Duke University and King’s College London, provides the first hard evidence that childhood self-control does influence adult outcomes in the general population (Photograph: Otago Daily Times)
The Christchurch Health and Development Study

Why use longitudinal studies?

“A longitudinal study provides a powerful means of addressing the question of how early disadvantage influences later development. Such questions are hard to answer using retrospective studies, asking people at the age of 30, what happened in their childhood. People seldom remember these things particularly accurately.

Longitudinal studies provide quite powerful methods of addressing causal questions. For example, examining the question of to what extent cannabis use is associated with mental health problems. If you find a correlation between cannabis use and mental health problems, you could dismiss it by saying that people with mental health problems are more prone to using cannabis. But having data about how they were before they started to use cannabis helps you address those problems.”

The Christchurch Health and Development Study has been following the health and development of a cohort of 1,265 Christchurch children from birth up to the age of 30. This group represented 98 per cent of all the children born in the Christchurch urban area from April to August 1977. The cohort was studied 22 times by the time they were 30. The study is ongoing.

Principal Investigator of the Christchurch Health and Development Study, Professor David Fergusson, didn’t set out to become a researcher. In fact, the first two years of his working life were spent in the British Merchant Navy.

His first brush with academia actually came when he was a cleaner at Victoria University’s Department of Geography. The debates he entered into with staff and students helped him realise he too could obtain a university degree. After earning a degree in psychology at Victoria University of Wellington in the late 1960s, he went to work for the child welfare division of the Department of Education, which had gathered all sorts of interesting data but had no-one to analyse it.

With the aid of a card-sorter and an electronic calculator, he analysed a survey of child abuse and published his first book on the topic. He then worked on a long-term study of the delinquency behaviour of 25,000 children and on a survey of the aged.

The work gave him a broad background in survey research methodology and data analysis and when the University of Otago’s Christchurch School of Medicine advertised for someone to run a longitudinal study, Professor Fergusson applied and was successful.

Over the 35 years since work first began on setting up the Christchurch Health and Development Study, the findings have been many and diverse, but Fergusson points to several of particular interest.

The earliest was their research linking passive smoking and lower respiratory illness in infancy. They were amongst the first to demonstrate that children whose parents smoked, and particularly mothers, had higher rates of lower respiratory illness. That research has led to a whole series of public health measures - the most recent of these being the publicity about the adverse effects of smoking in cars.

They have also produced a series of studies showing that the provision of preventive health care and preschool education in New Zealand is unevenly distributed, so that children from affluent, privileged backgrounds having greater utilisation of these services, such as immunisation.

Their next major research with policy implications was research into lead exposure and childhood education and behaviour. In the 1980s, they estimated the lead levels of kids in

“The aims of the research have not just been to publish interesting scientific papers for people to cite and refer to – there was a genuine desire to have some practical outcomes. A whole series of practical outcomes have happened since the inception of the study in 1977 to the present.”

Professor David Fergusson
the Christchurch study by collecting baby teeth and were able to show that even sub-clinical levels of lead had harmful effects. This fed into major policy debates regarding the regulation of lead in petrol, as well as environmental lead.

One of the backbones of the Christchurch Health and Development Study has been research into early conduct problems, which has shown they are a precursor of a wide range of later difficulties including crime, mental health problems, substance abuse and suicidality. They have been working with Government agencies to develop policies addressing these needs.

**Translating research into policy and service development**

The Christchurch Health and Development Study has an impressive track record of translating research into policy and service development.

For example, their research showed that children who came from homes marked by multiple social, educational and other disadvantages were also prone to multiple life-course problems. This raised the issue of what can be done for children in multiple problem families and the Early Start programme was set up as a home visiting service attempting to provide support, mentorship and assistance to at-risk families.

A randomised control trial was used to test the programme’s effectiveness. It passed with flying colours and was then used to form the foundation of the Government’s major Family Start initiative. Aside from the value of Family Start, the approach represents an important shift towards the use of evidence-based programmes and the development of methodologies for evaluating their effectiveness.

The Christchurch Health and Development Study has not shied away from controversial subjects, including a series of studies which showed that children exposed to childhood sexual abuse were at increased risk of mental health problems. They also found that these problems applied to both males and females.

They have also published a series of papers showing that cannabis users appear to be at increased risk of psychotic symptoms, mental health problems, educational failure, motor vehicle accidents, other illicit drug use and further negative outcomes.

The most volatile area has been their research into abortion and mental health, where a series of studies found that abortion appears to slightly increase the risk of mental health problems, rather than decreasing them.

Another significant contribution of the Christchurch Health and Development Study has been in developing research methodologies, such as models for estimating errors of measurement in the reporting of behaviour and the development of statistical models for testing causality. The next step in the research will be the age-35 follow up, to see how things turn out when the cohort reaches mature adulthood.

Professor Fergusson is looking forward to seeing if the difficulties of adolescence - such as cannabis use, smoking and substance use - really matter when they reach adulthood, and how much damage early disadvantage and difficulty impose on your later life outcomes.

Another area where they are developing greater interest is in the role of genetic factors in human development and they are working more closely with the University of Otago’s Dunedin Multidisciplinary Health and Development Study. Between them they have a remarkable amount of powerful information on phenotypical variations for both physical and mental health, and this provides abundant opportunities to study the ways in which genes interact with environment.

Professor Fergusson says the success of the project has been a team effort involving many people, especially his long-time colleague, Associate Professor John Horwood, who has worked with the study since its inception, and the 1,265 families who have given freely of their time.
Illnesses such as depression, bipolar disorder and eating disorders contribute substantially to the health burden of every country, including New Zealand.

Depression is predicted to become number two on the list of disorders having the largest worldwide burden by the 2020s.

Professor Peter Joyce is the Director of the Mental Health Clinical Research Unit and Dean of the University of Otago, Christchurch. He never set out to be a psychiatrist. His first choice was to be a professional cricketer, but his parents thought he needed to have a proper job.

He headed to the University of Canterbury to study chemistry, but became attracted to medicine as the most interesting place to do research, probably as a chemical pathologist.

But in another of life's twists Professor Joyce discovered he enjoyed talking with patients and, out of the blue, decided that psychiatry would be the most interesting specialty - partly because there were many unknowns and much more to discover.

Key amongst those questions has been why do some people do very well with certain treatments but others do very badly, and why do some experience drug side-effects while others don't?

“At the moment, so many treatments for disorders like depression work for 50 per cent of the people but they don’t work for the other 50 per cent.”

Rather than simply setting out to see what works, many of the Mental Health Clinical Research Unit's depression studies have focused on understanding what is behind this variability and how clinicians can best match a treatment to an individual.

Right from their earliest HRC-funded trials, they have made a significant contribution internationally as to which types of antidepressant worked better for certain groups of patients.

For example, the unit found that people under 25, especially women, do better on the more modern Selective Serotonin Reuptake Inhibitors (SSRI) compared to the older tricyclic drugs, while for men over about age 45, the drugs like the tricyclic Nortriptyline was much better than the SSRI Fluoxetine.

Professor Joyce has found that when he presents that data to clinicians, they often say that has been their experience as well.

“But that still hasn’t permeated all clinicians’ awareness and many older men are getting the wrong antidepressant.”
They have also helped dispel the idea that people with impulsive personality traits shouldn't be given antidepressants, by adding to a growing body of evidence that shows they actually do very well when treated with an SSRI rather than a tricyclic.

Another interesting finding revolves around a subgroup of people with depression who find their mood gets worse during the day, rather than better, which is the usual pattern. The Mental Health Clinical Research Unit found that those who experienced a dropping mood did much better with Nortriptyline.

They also identified a marker for inflammation in about 10 per cent of their depressed patients. That group responded much better to antidepressants than psychotherapies.

Professor Joyce's unit has also compared cognitive behaviour therapy and interpersonal psychotherapy, finding there wasn't a big difference between the two treatments. As is the case with drug treatments - some do well while others don't.

He says they worked with a number of people that mental health services had partly given up on because they were said to have a difficult bipolar disorder, yet they have done remarkably in the structure of a clinical trial. This has reinforced his belief that the best way to get good treatment is to participate in a good treatment trial.

At the time of publication the Mental Health Clinical Research Unit was about to start analysing the data from a major bipolar trial.

Eating disorders have also been an important area of research. The group's earliest HRC-funded trial involved a bulimia nervosa trial using cognitive therapy. As with their depression studies they found that, contrary to clinical beliefs, the presence of a complicating personality trait or personality disorder was not associated with a worse outcome.

Another interesting finding was that although many came to them and said they thought they were depressed because of their bingeing and purging, over time they came to realise that their mood was independent of their eating.

The only real predictor they found of long-term outcome of bulimia was a personality trait called self-directedness – part of the model of personality developed by Robert Cloninger, a colleague in the United States. It predicted both short-term and long-term outcome but not the severity of the bulimia.

A study into anorexia treatment also produced a surprise finding. It was a three-way trial comparing interpersonal psychotherapy, cognitive therapy and what they called specialist supported clinical management as a control therapy.
One of the group’s long-standing collaborations has been with Robert Cloninger, a psychiatrist in the United States who has been developing what Professor Joyce describes as the most original approach to thinking in psychiatry during his lifetime.

The other long-standing collaboration he has had has been with Philip Mitchell at the University of New South Wales. They have parallel interests and jointly wrote a book five years ago on mood disorders, using largely New Zealand and Australian authors.

Contrary to all expectations, what Professor Joyce describes as “sensible clinical management” produced better results than both specific psychotherapies. He says the study has been replicated several times overseas, causing a quantum shift in international thinking about treatment approaches for anorexia nervosa.

While doing these studies, Mental Health Clinical Research Unit researchers have collected DNA. Working with Professor Martin Kennedy and his Gene Structure and Function Laboratory at the University of Otago, Christchurch, they have followed up several interesting leads that include how variations in the dopamine transporter gene relate to borderline personality disorder and impulsive behaviour. Dopamine is a neurotransmitter that is associated with movement and learning, but also with the brain’s pleasure and reward system. The dopamine transporter is a protein that literally removes dopamine from the nerve synapse and terminates its action.

Professor Joyce explains that people in their clinical cohorts with particular forms of this gene are much more likely to have borderline personality disorder. But interestingly, even those in a non-clinical population with the same forms of the gene rate themselves as more impulsive.

“It shows how a common genetic polymorphism that deactivates dopamine may be relevant to impulsivity in the general population and to personality disorder in a mental health population.”

Looking ahead, Professor Joyce is involved in initiating a new project called Canterbury Health Aging Life Course Study (CHALICE). They are recruiting a random cohort of 50-year-olds with a view to following them for the rest of their life, effectively tracking the second 50-years of life rather than the first years of life.

It is especially relevant for the Canterbury District Health Board because it has by far the biggest proportion of 75-plus year-olds in the country.

“Something the South Island can do well is longitudinal studies – either with patient cohorts or with population samples. We can out-compete the rest of the world in ways we can’t with the latest technology.”

When asked what his “greatest hope” for his research was, Professor Joyce said:

“It would be wonderful if, at some stage in the future, when a clinician sees someone with depression or someone with bipolar disorder we could better predict which are going to be the treatments that are going to work for them – rather than so many months or years of life wasted through trial and error with different treatments.”
Professor Philippa Howden-Chapman is Director of He Kainga Oranga/the Housing and Health Research Programme at University of Otago, Wellington, a multidisciplinary team that primarily examines how housing can be improved to benefit health. It includes Professor Julian Crane, who heads the Wellington Asthma Research Group, and Associate Professor Michael Baker, a public health physician and infectious diseases researcher. Other co-directors are Professor Chris Cunningham, the Director of the Research Centre for Māori Health and Development at Massey University, Wellington, Dr Malcolm Cunningham at BRANZ – the Building Research Association of New Zealand – and Associate Professor Robyn Phipps, the Director of Built Environment cluster in the School of Engineering and Advanced Technology at Massey University, Palmerston North.

Originally a clinical psychologist, Professor Howden-Chapman was always interested in the drivers of behavioural and social systems. When working as a family therapist in an alcohol and drug unit she became especially interested in the types of housing people went to when they left the psychiatric hospital. She realised that having continuity in the community was crucially important, because people who were hospitalised faced big reintegration problems when finding a job and somewhere to live again.

We spend more than 75 per cent of our time inside our homes and if we are old or young the figure is more like 90 per cent. It is little wonder that improving the living environment is a practical way of improving health.
Once Professor Howden-Chapman went into the area of public health and reducing inequalities, she decided that improving housing was a very practical way of improving people’s health.

Professor Howden-Chapman has identified three key strengths of He Kainga Oranga/the Housing and Health Research programme and describes them as follows:

1) We are multidisciplinary and link researchers from public health, medicine, building science, architecture and Māori health and development to work on the broader social determinants of health.

2) We try to do the most robust studies we can: community trials, where we work closely with local communities, community organisations, and policy-makers. We also carry out cohort, case-control and qualitative studies so as to better understand the effects of housing on health.

3) We also recognise that you can’t just look at health in isolation – it is part of current concerns such as energy security and climate change.

One of their earliest HRC-funded studies, the Housing, Insulation and Health Study showed that retrofitting insulation not only improved health and wellbeing, but also produced energy savings and reduced carbon emissions, providing a 2:1 benefit to cost ratio.

Their second community trial, the Housing, Heating and Health Study also showed that a well-insulated house with effective heaters, which replaced unflued gas or portable electric heaters, made a big difference to asthma. Changing that environmental factor had as much impact as a new generation pharmaceutical drug, in terms of reducing wheezing, coughing and lost days off school.

The fact that these community trials are carried out as partnerships is reflected in the 85 per cent retention rate of study participants. The Insulation Study involved 4,407 people, while the Housing, Heating and Health Study included 409 children with asthma, as well as their parents and siblings. Professor Howden-Chapman puts that down to people wanting to understand more about how they live and how they can make a difference for family, friends and other communities.

HRC funding has been absolutely critical and their Programme grants have allowed them to build up a team of internationally respected researchers across a number of disciplines.

Making the connection between energy efficiency in residential houses and the potential impact on carbon emissions has influenced Government policy and led to a big investment in insulation and more efficient and sustainable heaters. They regularly work with a whole range of agencies, including the Energy Efficiency and Conservation Authority, the Building Research Association of New Zealand, the Department of Building and Housing, the Ministry of Economic Development, Housing New Zealand, the Ministry of Social Development, the Ministry of Health, District Health Boards and the Treasury.

Professor Howden-Chapman is particularly proud of the prototype extended-family housing for a family of 11 people they developed and built in consultation with the Tokelau community and Housing New Zealand.
They have analysed the health and socio-economic consequences of leaky buildings and had input into the new Building Code. They are keen to continue to make recommendations for new and existing houses based on the medical and building science they have developed. They may be a little bit more expensive to build, but they provide health benefits and lower operating costs.

They are working with councils around the country on the roll-out of the Healthy Housing Index, which links health science with building science, and provides a way of ranking houses for health, safety and sustainability. Before the Christchurch Earthquake they had assessed all the Council houses in Christchurch and in the future plan to re-appraise the houses again in order to see the validity of the earthquake part of the Index.

Currently, Dr Michael Keall is currently carrying out an HRC-funded large trial on reducing injuries in the home in Taranaki. The Housing Injury Prevention Intervention study involves 800 homes and about 2,007 people have agreed to take part. No-one has dropped out.

After the houses are insulated, the houses in the intervention receive between $500 and $1,000 dollars worth of home repairs by a local builder working for the research team. The study will be able to show whether this lowers the rate of slips and falls by tracking Accident Compensation Corporation claims.

Older people are often cold in their homes in winter and for people with Chronic Obstructive Pulmonary Disease (COPD), this can increase the risk of them being hospitalised. Helen Viggers is leading the HRC-funded Warm Homes for Elderly New Zealanders study, a community trial of 550 older people with COPD, where those in the intervention group receive $500 in their electricity accounts over winter.

Following his long-term interest in the effect of housing on asthma, Professor Julian Crane is examining whether mouldy homes cause children to have asthma – not simply exacerbate asthma symptoms.

Overall, He Kainga Oranga community trials have involved over 10,000 people in almost 4,000 households and are helping to show that improving the indoor living environment produces tangible health results.

In future, they want to continue their work with the rental housing sector, which now makes up 32 per cent of all New Zealand households. It represents some of New Zealand’s poorest housing, because there is so little regulation, so they are looking at ways to improve conditions for people who rent and cannot afford home ownership.

Professor Howden-Chapman says their interest extends to neighbourhoods and understanding the link between where people live and how they get to work. Her hope for the future is that they will be able to look at these really important issues between not just housing, but also land use, transport, air quality and climate change.

**COLLABORATIONS**

Professor Philippa Howden-Chapman also directs the New Zealand Sustainable Cities Centre, which links most universities in New Zealand with the National Institute of Water and Atmospheric Research and Landcare Research.

She is a member of the International Council of Science for Asia and Pacific which is looking at urban settings and how housing and other infrastructure can be improved, and a group commissioned to report on urban systems and the built environment for *The Lancet*. She has been asked to lead a World Health Organization group that is developing international guidelines for housing and health.

“Creating sustainable housing and cities is an intergenerational issue and we’ve got to put resource into it over the longer term. The economic value of maintaining and improving health needs to be recognised as being as important as returns from generating patents.”

*Professor Philippa Howden-Chapman*
Associate Professor Michael Baker’s key focus has been on the interplay between housing and infectious diseases.

Infectious diseases are a major reason people are hospitalised. Twenty years ago they accounted for about 18 per cent of acute hospitalisations in New Zealand – but that figure has now risen to 26 per cent which represents more than 20,000 extra hospitalisations a year.

A trained physician, he started working at ESR at the time New Zealand’s meningococcal disease emerged in the early 1990s and was the main epidemiologist describing the inexorable rise in disease incidence.

In just five years, New Zealand went from 50 or 60 cases a year to 10 times that number - a dramatic epidemic for a developed country.

Associate Professor Baker secured HRC funding to investigate risk factors for this disease in children and identified that household crowding markedly increased the risk of infection.

These findings were cited as a key reason for Housing New Zealand to start the Healthy Housing Programme for its houses and their occupants. Subsequent research shows the programme has created measurable health improvements for tenants.

Associate Professor Baker has also played a prominent role in influenza research, including tracking influenza transmission in a cohort study of 65,000 Housing New Zealand households - established using HRC funding as part of the Housing and Health Research Programme.

The cohort includes over 240,000 people and over the past eight years has accumulated well over 1.5 million person years of data, creating a resource that now attracts overseas funding.

“We now have enough statistical power to examine multiple hypotheses about disease burden and how it relates to housing conditions. It’s a very valuable resource.”

Associate Professor Michael Baker
To the average person, the term occupational health calls to mind the deaths and injuries that occur every year in high-risk industries, such as construction, agriculture, forestry, transport and mining. More difficult to quantify are the deaths that occur as a result of long-term exposure to something harmful in the work environment.

In New Zealand, the average death toll in the high-risk industries over the past decade has been about 100 people each year. Occurring mostly in summer, these preventable deaths gain headlines as families struggle to come to terms with their loss. Researchers at the Centre for Public Health Research at Massey University, estimate that around 1,000 lives a year are lost to work-related illness, and 200-400 of these deaths are thought to result from occupational cancers. This is two to three times our annual road toll. These deaths, they argue, go unrecorded, or may never be linked to the original cause. More recent studies in the UK put occupational cancers at nearly five per cent of all cancers, rising to eight per cent in men (half of which are asbestos related), and Australian research suggests it may be even higher. Fewer than 40 of the cancer deaths are notified to the Department of Labour, and most of these involve asbestos-related cancers; there are very few reports for other occupational cancers.

The argument for more research in this area is compelling, because these deaths are preventable, and because more suspected hazards are being identified every year. We describe the work of Professor Neil Pearce, and Professor Jeroen Douwes, and the outstanding contribution their work has made to our understanding of occupational health.
A period as a bus driver in the 1980s initiated Professor Neil Pearce’s interest in occupational health. He still remembers what it felt like to breathe in diesel fumes, whilst driving daily for periods that most people would only contemplate on family holidays.

Fortunately, he decided to put his degree in statistics to full use as a public health researcher, and is now an expert on occupational respiratory diseases and cancer in New Zealand. Formerly the Chair of the National Occupational Safety and Health Advisory Committee, he has built a strong team at the Centre for Public Health Research, Massey University.

In September 2010, the tenth anniversary of the founding of the Centre for Public Health Research, Professor Jeroen Douwes took over as Director. Also in 2010, Professor Pearce received a life-time achievement award for services to occupational health, for his research into workplace disease risks, from Safeguard magazine. The HRC has been funding Professor Pearce, Professor Douwes, and their team since 1990, including Dr Andrea t’Mannetje, Dr David McLean, and Dr Lis Ellison-Loschmann, and they have attracted HRC support ever since.

Since he first developed an interest in this area, Professor Pearce has covered an extraordinary array of topics to gather evidence about occupational health risks in New Zealand. He was part of the team that first described the increased risk of leukaemia associated with exposure to electromagnetic fields in electrical workers, and particularly those exposed to the highest doses – welders/flame cutters and electrical line workers.

Over the years, the Centre for Public Health Research has amassed large amounts of data on cancer risk related to different jobs and has collaborated with The International Agency for Research on Cancer, which regularly reviews the research evidence and has compiled a list of about 40 occupational carcinogens. Professor Pearce points out that that this information is supposed to be available to everyone, but most of it never finds its way to the workplace.

Studies at the Centre for Public Health Research have identified a broad, and at times surprising, list of occupations in which there is increased risk of certain cancers.

The team were the first to demonstrate significant excess risk for cancers of the lung and blood among meat workers, perhaps related to breathing in micro-organisms when slaughtering animals and processing meat. They are now investigating further, with HRC funding to look at the bioaerosols (air-borne viruses, bacteria, proteins or other fine particles from the animals slaughtered) that meat workers are exposed to, and test whether they have the potential to cause cancer. The findings will allow the team to understand why meatworkers are at risk and develop effective interventions to protect them from occupational exposures.

Research at the Centre for Public Health Research has also highlighted the risks of occupational cancers in agricultural workers, cleaners, painters, truck drivers, sales assistants, hairdressers and machinists. In one study of occupational bladder cancers, the team found that truck drivers had an excess risk. No-one knows exactly why this may be, but an inability to take frequent drinks and toilet breaks has been suggested as a possible factor, as a small increased risk has also been observed in sales assistants. Carcinogens from fumes, smoking and other toxic exposures are excreted in the urine.

The team at the Centre for Public Health Research have also studied health risks in timber workers exposed to pentachlorophenol (PCP). They found that high exposure was linked to nerve damage, mood disorders, lung infections, heart palpitations and loss of libido. More recently, the team have analysed dioxin levels in New Zealand sawmill workers exposed to PCP, and showed that they remain elevated twenty years after

“Current exposures take priority over historic exposures because we can stop them now. However, if you have asbestos in your lungs or dioxin in your body fat, you’re still being exposed.”

Professor Neil Pearce
exposure to PCP ceased. Dioxin is known to increase the risk of developing cancer, and there was an increased risk of cancer in the PCP-exposed workers in the study.

Another risk for timber workers is of respiratory diseases from breathing in wood dust. Work by the group has shown that exposure to both green and dry sawdust is related to lower lung function, and exposure to green pine sawdust increases the risk of asthma. The HRC is currently funding the Centre for Public Health Research to establish whether these exposures actually cause lung disease or just make existing disease worse. In another study, they have shown that sawmill labourers are three times more likely to currently have asthma. Other occupations with high asthma risks included metal processing plant workers and bakers. Earlier work showed that food processors other than bakers are at elevated risk of chronic bronchitis and that the risk for chemical processors is 18 times that of other workers.

**Working across Government**

Collaboration and co-operation between Government agencies is essential for real progress to be made in occupational health. This is a strong focus for the HRC’s Partnership Programme. Through the Occupational Safety and Health (OSH) Joint Research Portfolio, the HRC has partnered with the Accident Compensation Corporation and the Department of Labour, OSH, to support research on risks encountered in a wide variety of work situations. Currently, the initiative is supporting research on: interventions to reduce wood dust exposures; workplace exposure to carcinogens; indicators to improve surveillance for occupational disease, and prevention of noise-induced hearing loss.

**Building research in occupational health**

In 2008, the HRC partnered with the Department of Labour to provide $3.5 million for a three-year programme of studies on occupational health and cancer risk. The Building Research in Occupational Health in New Zealand programme brings together investigators with a broad range of skills to address gaps in what we currently know and, crucially, will provide training for the next generation of researchers. The programme is based in, and coordinated by, the Centre for Public Health Research.

The primary risk for metal processing plant workers appears to be in welding. The team has shown that lung function is reduced in welders working without local exhaust ventilation, illustrating the preventable nature of most workplace illnesses.

Most adults spend a third of their waking life at work, Professor Pearce points out. During this time they could be exposed to any number of toxins, including dust, oils, solvents, pesticides, chemicals, fumes, smoke or magnetic fields. In addition there are the hazards associated with lifting, loud noises and accidents. Future challenges will not be restricted to addressing the large gaps in our understanding of current hazards, as there is no shortage of new and emerging risks to consider.

“We must also seek to understand the challenges that our changing world will have on occupational health. Such issues include an ageing workforce, global pandemics, nanotechnology and the 24/7 operating environment that takes a toll on social functioning, sleep and mental health.”

Professor Neil Pearce
In New Zealand one in five people are affected by asthma and allergy. They are significant diseases, because they affect the growth and development of young New Zealanders. Furthermore, asthma is one of the most poorly diagnosed conditions in the elderly. The economic burden runs into the hundreds of millions of dollars each year, primarily for symptomatic relief. Globally, billions of dollars are spent annually on controlling asthma and allergy.

Although asthma has been described for 100 years, and we have gained significant insight into what drives disease symptoms, we still do not understand the underlying pathological processes that initiate asthma and allergy. This issue has been the research focus of Professor Graham Le Gros, the Director of the Malaghan Institute and Group Leader of the Institute’s Asthma and Allergic Diseases research programme.

“By creating understanding of how the allergic disease process starts, I hope to shift the current mindset away from simply treating the symptoms of asthma and allergy, and actually effect change in the onset and prevalence of this disease.”

His research is helping scientists, clinicians and public health officials to be very aware of the influence that the environment has on the development of allergic diseases. In particular, his research was the first to provide a biological basis for the so called hygiene hypothesis.
- which states that a lack of early childhood exposure to infectious agents increases susceptibility to allergic disease.

The flip-side to allergic responses is that they are the ones that protect against parasitic diseases. To maximise return, Professor Le Gros has, in parallel, a parasitology research programme dedicated to the development of a vaccine against human hookworm, one of the great neglected tropical diseases that keeps over a billion people in a state of poor health. His research team has developed world-leading skills and knowledge required to make a real difference in these areas. This work represents an important contribution to the global vaccine initiative against human hookworm that New Zealanders can be proud of.

Professor Le Gros entered the field of asthma and allergy because he had always been interested in how the body can protect itself against disease.

“In my early years, I witnessed first hand how great breakthroughs in immunology had just led to the eradication of smallpox, and prevented polio. Also, the study of immunology was providing an amazing new wave of fundamental knowledge to other medical disciplines of how the genes, cells and hormones work in the body.”

Professor Le Gros says he was drawn into the excitement of learning about the unknown and he wanted to be doing the most important scientific research, and research into the immune system attracted him.

Through the support and reputation of Professor Jim Watson he was able to gain entry to one of the leading immunology groups at the National Institutes of Health in the USA, to further his knowledge in immunology. There he was involved in one of the great advances in understanding how allergic immune responses develop. He says he was then faced with the question of what to do with all this exciting new knowledge - academia or applied research - and chose the latter. He joined the leading preclinical asthma team at Ciba-Geigy in Basel, Switzerland - an experience which he says taught him both the power and limitations of pharmaceutical research. After five years at Ciba-Geigy he was offered the opportunity to come back to New Zealand and direct and grow an independent medical research institute.

“This was an incredibly exciting time and I knew that if I could attract the right backing and support, the opportunities existed to make a significant contribution to the fields of asthma and allergy here in New Zealand.”

His scientific interests have also been coloured by his experience of having lived in the tropics as a child, where he experienced firsthand the debilitating effects of worm infection and subsequent treatment. Parasitology has a natural link with asthma and allergy because they all use the same Th2 immune response pathways, so there is a natural synergy that can potentially be exploited for the benefit of both areas.

Professor Le Gros says that the HRC funding and application process challenged the investigator to focus on making a big discovery, leading to the aims of his research programmes going well beyond the minor incremental research outputs. In the early days, sufficient funding was provided within the one grant to enable breakthrough research to be undertaken.
The scientific papers resulting from his HRC-funded research have been highly cited by leading authorities in the asthma and allergy fields. His research has led to the establishment of a spin-off company, and intellectual property rights being passed on to preclinical development groups. Professor Le Gros has a close working relationship with scientists from leading organisations from around the world, such as the National Institutes of Allergy and Infectious Diseases, Bethesda, Maryland, USA and pharmaceutical companies.

Professor Le Gros says his greatest hope for research in this field is that we can apply our knowledge about allergic immune responses to the development of effective therapies for asthma and allergy sufferers. He also hopes that the significance of this field of basic biomedical research, and its potential contribution to other research disciplines, is recognised and better supported.

Immune Cell Biology research programme

Professor Franca Ronchese is the Group Leader of the Malaghan Institute’s Immune Cell Biology research programme. Her research on basic immunology has led to exploration of better treatment options for cancer, and more recently, allergic disease.

“I really believe that immunology has an important contribution to make to the field of cancer therapy and that it is worthwhile coming to terms with the complexities of the immune system, as they can be used for a good purpose."

Cancer affects a large proportion of the population and is one of the major causes of death in this country. Although there are several treatment options for individuals affected by cancer, the instances of complete cure are still relatively rare. Furthermore, the economic burden of cancer in New Zealand is enormous because it affects so many people and requires the use of expensive drugs and treatments.

Cancer immunotherapy is based on exploiting the properties of the immune system to attack tumour cells. There are a number of advantages to this approach. The immune system is highly specific in targeting cancer cells, resulting in fewer side-effects, and can attack and eradicate small tumours that are spread around the body. These small scattered tumours are difficult to target with other therapies.

However, at this point in time, immunotherapy is relatively expensive to administer because each cancer vaccine is tailor-made for each individual cancer patient. Professor Ronchese’s
team are working on the proof of concept that appropriate activates of a patient's immune system can eradicate their tumours. With continued basic research, she believes that the treatments will become simpler and cheaper to apply.

Professor Ronchese's research centres on dendritic cells and, in particular, the involvement of these cells in the early phases of an immune response, and how they can be used in immunotherapies. Her research has led to the clinical development of a dendritic-cell-based therapeutic cancer vaccine that has been tested in three clinical trials, including the current phase I glioblastoma multiforme trial being overseen by Dr Ian Hermans from the Malaghan Institute.

This work is supported by a close working relationship with clinicians from the Wellington Blood and Cancer Centre and Wellington Hospital, and access to the Institute’s state-of-the-art GMP (Good Manufacturing Practice) accredited vaccine production facility. One of Professor Ronchese’s main goals is to make cancer vaccines easier to use.

Professor Ronchese trained as an immunologist and has worked in the field of immunology for 30 years. Before arriving at the Malaghan Institute, her main interest was in basic immunology and she wasn’t trying to apply this knowledge to any specific disease.

However, at the time that she started at the Malaghan Institute, a critical breakthrough was made overseas that showed that the immune system could detect differences between normal and cancer cells, and that these differences could be defined at the molecular level. This fundamental discovery encouraged her to explore how the immune system could be manipulated to activate a targeted and specific immune response against the different components (antigens) on a tumour cell.

“"It was very easy for me to enter this line of research because of the interest and enthusiasm of those around me. On my arrival in New Zealand, I met a number of people that were very enthusiastic about becoming involved in this emerging area of tumour immunology. This is one of the nice things about basic research - you can apply your knowledge or findings in many different directions."" 

Professor Ronchese’s early research was initially funded by the Cancer Society of New Zealand, which allowed her to show that the approach she was proposing was going to work. After this, the number of projects and people involved in the research grew considerably and the HRC funding she received was critical in enabling her to expand her work from one experimental project in mice, to a small-scale clinical trial, through to the more extensive basic research and translational programme it is today, involving numerous scientists, patients and clinicians.

As a result of HRC funding, Professor Ronchese has been able to establish a research group at the Malaghan Institute that has specialist expertise and laboratory tools for working in tumour immunology. A number of up-and-coming young New Zealand researchers have received their training in her laboratory group and have since gone on to secure very successful positions around the world, where they can further their training and hopefully gain new knowledge that they can bring back. The research group plays a significant role in informing the general public and clinicians about immunotherapy and the opportunities it presents for curing disease.
Professor Ronchese's work with the cancer vaccine has been part of an international effort in trying to demonstrate that dendritic cells can be applied to the treatment of cancer.

She says they have been in the unique position where they have been able to combine this vaccine with other treatments that also enhance the ability of the immune system to attack tumours. Some of this work has been undertaken in collaboration with international colleagues, and published in widely read international scientific journals.

Professor Ronchese's group are now applying their knowledge of dendritic cells to other diseases where overactive immune responses are a problem, such as in allergy. She would like to test the proof of concept that the impact or symptoms of inflammatory allergic diseases can be reduced by targeting immune cells.

Professor Ronchese says she looks forward to cancer vaccines becoming accepted as a mainstream therapy for cancer that supports other treatments, such as radiotherapy and chemotherapy. She thinks that immunologists are fairly confident that as we further our understanding of the immune system, we will be better poised to treat cancer patients with immunotherapy.

“I hope that soon there will be improved immune-based treatments for cancer but we are still currently in the discovery phase. Through good-quality basic research, we hope to evolve the individualised cancer vaccine to a simpler immunotherapy that can be used to treat any cancer patient.”

Professor Franca Ronchese

Top honour for young scientist

For her groundbreaking research into the development of designer vaccines for the treatment of cancer, Malaghan Institute PhD student Dianne Sika-Paotonu was named winner of the HRC Advancing Human Health and Wellbeing category of the 2008 MacDiarmid Young Scientist of the Year Awards.

These awards were presented by the former Foundation for Research, Science and Technology in recognition of the New Zealand-born Nobel Laureate, Professor Alan MacDiarmid, to celebrate the achievements of New Zealand’s future leaders in science.

The focus of Dianne’s PhD research was to improve the activity of a rare group of immune cells called dendritic cells. These cells are able to stimulate the immune system to attack cancerous tissue and are a critical component of the cancer vaccines created at the Malaghan Institute. By developing ways to make the cancer vaccines work even better, Dianne's cutting-edge research meant it was one step closer towards a highly effective more natural cancer therapy that doesn’t have the side-effects of conventional cancer treatments.

“Cancer is a terrible disease and we need to support bright young New Zealanders such as Dianne to ensure our future,” says Professor Graham Le Gros, Director of the Malaghan Institute.
Dr Ian Hermans is investigating the development of new vaccines for human diseases. He is looking at a series of compounds that can activate a certain set of immune cells. This may form the basis of distinctive new vaccines against the bacterial and viral diseases for which no effective vaccine currently exists. The research also has direct implications for the development of vaccination strategies against cancer.

The HRC has been supporting Dr Hermans to undertake this work since he was awarded the Sir Charles Hercus Postdoctoral Fellowship in 2004, which supplied a secure salary for four years for him to take up the position of Team Leader at the Malaghan Institute of Medical Research. The HRC funding provided an incentive for Dr Hermans to return to New Zealand from the UK, where he had been working as a staff scientist at Oxford University.

Dr Hermans believes that while there is a pressing need to make successful vaccines for global threats like HIV, malaria and tuberculosis, appropriately designed vaccines may also be used in the future as effective therapies for a number of common, non-infectious conditions.

“There is accumulating evidence that vaccines can be used to treat conditions like cancer, allergy and autoimmune disease. For all of these applications, it is critical that vaccines are designed to stimulate immune responses of the correct ‘character’,” Dr Hermans says.

Research to date has shown that some patients respond very well to cancer vaccine therapy, but the overall response rate is relatively low. There is little or no associated toxicity to the treatment and so the incentive to realise the full potential of such vaccines is high. To do this, the vaccine technology needs to be improved.

One of the issues that need to be addressed is that, because of genetic differences between individuals, tumour fragments that stimulate a strong response in one individual may not do so in another. The team are tackling this by synthesising longer tumour fragments with new technology. The longer fragments can incorporate several different antigens derived from tumours and this should increase the number of people that will mount a good response to the vaccine.

The team has also found that immune cells called natural killer T-cells (NKT) provide support to the dendritic cells and the response may be improved if they can be stimulated by adding a synthetic substance to the vaccine.

The improved vaccine technology will be tested in patients with advanced melanoma by the end of the study period and a synthesis pipeline to produce vaccines for other cancers will also be established. This direct relationship between chemists, immunologists and oncologists is invaluable, providing the means to propel discoveries in the lab into the clinical arena where they can benefit patients at the earliest opportunity.
Infectious diseases have always been a close companion of humankind. Microscopic bacteria and viruses are behind many of the diseases that have had a massive human price, such as tuberculosis (TB), HIV/AIDS, meningococcal disease and pneumonia. While the rates of tuberculosis have been falling around the world in recent decades, we now face the challenge of newer forms that are highly resistant to antibiotics.

In New Zealand, our rate of seven to ten cases per 100,000 people is low compared to the UK, but nearly double that of the United States and Canada and higher than the six per 100,000 in Australia. Poverty, overcrowding and migration from countries with high rates of infection have all contributed to the resurgence of tuberculosis in New Zealand.

The vaccination campaign that started in 2004 has been instrumental in controlling our epidemic of Group B meningococcal disease, however, people continue to die from it. Of those that do die, 70 per cent will do so within 24 hours of their first symptom - with the median time being just 12 hours.

Some of the other challenges New Zealand faces from infectious diseases include avian flu, the resurgence of diseases thought to be controlled - such as polio - and the ever present risk of a flu epidemic caused by a strain for which people have no immunity.

At The University of Auckland, structural biologist Professor Ted Baker, immunologist Professor John Fraser and microbiologist Associate Professor Thomas Proft are working towards the development of entirely new ways of fighting infections. Over the last 20 years they have demonstrated the effectiveness of strong scientific collaboration in the push to understand more about the mechanisms these organisms use to infect their host and the way they develop immunity.
Professor Ted Baker's molecular-level research is based on the premise that biological mechanisms – whether involved with disease or normal body processes – depend mostly on proteins. There are thousands of different proteins in a cell, each one with its own particular job to do, which it does very efficiently over and over.

Understanding how they do this depends to a large extent on seeing their three-dimensional, atomic-level structures. Professor Baker describes it as being like a lock and key system – each protein is designed to do exactly its own task and nothing else. Provided this proceeds as it should, then everything is fine.

Professor Baker uses x-ray crystallography to actually ‘see’ molecules in atomic detail. This leads to important applications. For example, if you want to make a drug to specifically target a virus, then the most powerful way of doing this is to identify a protein that the virus depends upon, examine its exact structure and then design a small molecule that is going to block the active part of that protein. This is the way in which current HIV drugs were developed.

Professor Baker's original degree was in chemistry but after completing his PhD at The University of Auckland he headed to Oxford to do postdoctoral research with Nobel Prize Winner Professor Dorothy Hodgkin, as part of the team that solved the structure of insulin. She encouraged him to develop a similar research programme in New Zealand on his return.

An example of research in which Professor Baker is using his structural biology expertise today involves *Streptococcus pyogenes*, the bacterium that is behind conditions such as rheumatic fever, septicemia, toxic shock, and a range of other illnesses. Just five years ago, it was discovered that these bacteria use long hair-like assemblies called pili to attach to host cells when infecting them. Professor Baker has been working with Associate Professor Thomas Proft investigating how these pili are assembled and how they stick onto host cells.

They have discovered that they are long, thin collections of protein molecules arranged like a single strand of beads on a string. Each protein is joined to the next by a covalent bond. Professor Baker and a PhD student, HaeJoo Kang, also discovered that each molecule has a novel type of cross-link, that has never been seen before. This means that while the pili are very thin they are also very strong.

Professor Baker says that this work suggests several new ideas for combating these bacteria. They could stop bacteria from attaching to cells by disrupting the pili so they do not assemble, they could try to block the parts of the pili which join onto the host cells, or they could block the enzyme which makes them.

The next stage would be to collaborate with chemists who can design molecules to target the structures they have discovered.

Professor Baker and his colleagues are already doing this in their TB programme, where they have identified a number of promising drug targets and are working with medicinal chemists who design inhibitors that will block the activity of these proteins.

This work began when the genome of the bacteria that causes TB, *Mycobacterium tuberculosis*, was sequenced in the late 1990s. About 4,000 different genes were identified but it was realised that practically nothing was known about any of the proteins produced by the organism.
They launched a large programme to work on the structures of important TB proteins, joining forces with researchers in the United States, India and other countries to form a large consortium to help define new drug targets.

Professor John Fraser has had research funding from the HRC since the 1980s, focusing on *Staphylococcus aureus* and *Streptococcus pyogenes*, two of the most common but also virulent human pathogens.

He and Associate Professor Thomas Proft attracted widespread international attention for their research into understanding the function and mechanisms of the potent superantigens produced by these bacteria.

While Associate Professor Proft has gone on to focus on understanding *S. pyogenes* pili and the role of streptococcal DNases in immune evasion, Professor Fraser has now moved his attention to a set of microbial virulence factors called SSLs (staphylococcal superantigen-like proteins) which are produced by *S. aureus*. These target the innate immune response and have potential as targets for vaccine therapy.

*S. aureus* is probably the most common form of microbial infection around the world and is the most common cause of nosocomial infections in hospitals. There are also serious outbreaks of what is called community-acquired *S. aureus* which causes severe acute illness throughout the world.

Professor Fraser explains that there are now strains that have developed in the USA and Europe which are causing severe pathology. Infections from these new strains are very difficult to treat with standard antibiotics, so there is clearly a need for developing other methods for treatment of these severe acute infections. This is where their focus is now directed.

SSLs provide a potential new direction for attacking *S. aureus*. What makes them particularly interesting is that they are conserved across all strains of *S. aureus*, which suggests they are extremely important in terms of the organism's survival and therefore have considerable potential as a vaccine target. It means it could be possible to develop a vaccine that is going to work against all strains.

One of the curious features about SSLs is that they are human-specific. Professor Fraser says they don't work on other animals and it is extremely intriguing as to why this particular organism has developed these very human-specific molecules. It also makes them difficult to work on because they can't use animal models of infection to study what role they play in staphylococcal defence.
BIOENGINEERING WILL CHANGE THE FACE OF MODERN MEDICINE

Scientists unite to build a virtual human

Bioengineering is the use of engineering principles to understand the function of the body, and provide innovative solutions to healthcare issues. Bioengineering is now providing us with a whole new area of medical science, virtual models of human organs and systems.

The Physiome Project (‘Physio’, meaning life; and ‘ome’, as a whole) takes what is known about our genome and the chemistry, physics and anatomy of the human body to create computerised models of how we function at the level of cells, tissues and organs.

Initiated by the International Union of Physiological Sciences, the project involves co-ordinating efforts from scientists across the globe working towards creating, in essence, a digital human. Standardising programming language so that data and models can be easily shared, their contributions could change the way that modern medicine is practiced - even though the task is so vast it will never be complete.

Integral to this endeavour is the work of Professor Peter Hunter, Professor Bruce Smaill and their team at The University of Auckland’s Bioengineering Institute, whose work in this area precedes the project by decades. We catalogue some of their remarkable achievements, including producing the first computerised model of the human heart.

Professor Hunter started his academic career as an engineer, with a degree in Theoretical and Applied Mechanics. He appreciated at an early stage the importance of engineering...
principles in medicine, and his PhD from the University of Oxford focused on modelling the mechanics of the ventricles of the heart. His work on producing a virtual heart began over 20 years ago, when he returned to The University of Auckland and formed a collaboration with Professor Bruce Smaill. Peter Hunter’s skills lay in the mathematical modelling of the behaviour of the heart, whilst Bruce Smaill’s expertise in experimental physiology enabled the detailed measurement of the heart structure. The melding of these skills proved highly productive. As a result, the Bioengineering Institute at The University of Auckland was established in 2001 and now boasts over 100 researchers from many disciplines and around 70 postgraduate students. Professor Hunter continually stresses the contribution that each member of this large team makes to the extraordinary successes of the Institute. The HRC has been supporting aspects of the research since 1996, and Professor Hunter is currently an HRC Programme Director. 

The team at the Bioengineering Institute has now developed a model of the heart that links the organ and tissue structure to how the heart functions at a cellular level, allowing them to predict how the heart will react to a given event, such as the administration of a drug. The implications are phenomenal. The virtual heart can be programmed to do everything that a real heart will do naturally, in health, disease, or in response to stressors such as a toxin or surgery. This has great benefits not just for predicting how a patient will respond to a certain treatment, but also for surgical planning and diagnostic tests. In the future, it will be possible to predict the effects of stress on a patient’s heart without the risks attendant to stress tests.

Developing a new drug costs approximately $8 billion US dollars; partly because of the ‘scattergun’ approach of developing multiple candidate molecules in the hope of finding one that will be safe and effective. Many experimental drugs are abandoned because of toxic effects on the heart. Some of these toxic effects are not discovered until after the drug has been marketed, exposing patients to increased risk and drug companies to the exponential costs of class-action suits. All of these costs are ultimately translated to consumers. If drugs can first be tested in computer models, the risk to patients and the cost of development can be greatly reduced.

Perhaps the most exciting aspect of this work is that the heart model is the first and most complete virtual-organ model in the Physiome Project. Through the Human Genome Project, the entire human genome was mapped for the first time in a collaborative effort that spanned the globe. It was a phenomenal achievement and captured the imagination of an entire generation. However, this was just the first step in what will be a far greater feat - linking the knowledge of an individual’s genome with what is actually occurring, or likely to occur, in their body.

By the time the Human Genome Project was complete in 2003, the Physiome Project was already underway. Professor Denis Noble of the University of Oxford's Physiology Department, a key figure in The Physiome Project and a collaborator with Professor Hunter’s team, has said that relying on the genome alone to understand the human body “is like looking at a telephone directory and thinking you have the secrets of the city”. Professor Hunter agrees that, while the data on the genome is very important, it must be integrated with the vast amount of the knowledge that we have about the human body before we can appreciate the full picture. The key to doing this lies in creating mathematical models of how these data are related. These models must be consistent with the laws of nature, and take into account how each of the systems of the body interact with, and impact on, each other.

Professor Hunter says that the ultimate aim is to develop a virtual human body that would enable us to look at a change in a single gene and follow the effect of that change through from cell, to tissue, to whole organ. The dream is to link what we now know of the human genome to the whole organism, in a way that accounts for environmental influences on the body as well.

“\textbf{You can look at an aeroplane and see its shape and describe its electrical and mechanical systems, but to understand its function – that it will fly – you need to use the laws of physics and the mathematics that describes them.} \vspace{-0.5cm}

\begin{flushright} \textit{Professor Peter Hunter} \end{flushright}
Alistair Young and Brett Cowan are Associate Professors at The University of Auckland’s Bioengineering Institute and Department of Anatomy with Radiology. Together they direct the Auckland MRI Research Group, and have won international recognition for their work in developing analysis software known as the Cardiac Image Modeler (CIM). The software combines the mathematical heart model developed at the Bioengineering Institute with information obtained from a patient’s tagged MRI scan.

In tagged MRI scans, a temporary pattern of lines is created across the heart muscle, by modifying the magnetisation at specific points. This creates a pattern of lines that will bend and distort as the heart contracts, giving information about movement within the muscle. With CIM, clinicians and researchers can accurately measure tissue structure and deformation – showing shape, motion and strain.

CIM has proved invaluable in trials of new drugs, monitoring patients with heart conditions and in heart transplants. It has already been used in clinical trials, where the accuracy of measurements reduced the number of people needed to effectively test the drug. The team won funding from the National Institutes of Health, USA, to create a worldwide database of cardiac MRI studies, which will allow clinicians to compare their patient’s results with those from specific study populations. Working with scientists at UCLA, the team have created a database of scans from patients with and without symptoms, and are developing downloadable tools for classifying studies, standardising protocols, and classifying population subgroups. In effect, they will create an invaluable resource for clinicians and researchers alike.
THE ROLE OF GENES IN CANCER

Many things affect the behaviour of genes and our susceptibility to cancer

Professor Anthony Reeve feels fortunate to have got in on the ground floor of DNA research, while undertaking postdoctoral research at John Hopkins University in the United States.

For more than a decade, the Cancer Genetics Laboratory has benefited from extensive HRC support and now comes under the Genetics and Epigenetics of Cancer Programme grant held by Professor Reeve, Associate Professor Parry Guilford and the Head of the Department of Pathology, Professor Ian Morison.

One of their major discoveries, which put them on the front page of *Nature*, was the identification of a new epigenetic mechanism of cancer initiation involved in Wilms Tumour, which affects the kidneys of young children.

They realised that the imprinting – or switching on and off – of the gene insulin-like growth factor 2 (IGF2) was being disrupted.

In addition, they found that this epigenetic change could occur before birth, perhaps due to an environmental exposure *in-utero*, which also means the cancer actually started before birth.

Epigenetics recognises that while genes are passed on from one generation to another, the way they are expressed – or switched on or off – can be affected by factors other than the underlying DNA sequence. It examines changes to the structure of the chromosomes, not the genetic code itself.

In the case of the work of Professor Anthony Reeve, Director of the Cancer Genetics Laboratory at the University of Otago’s Department of Biochemistry, the focus has been on the way DNA gets ‘decorated’ with methyl groups or molecules which bind to it. This can affect the way the information held in the DNA is read or transcribed, and can silence a gene which should be active at a particular time during development.

“*When I was doing my post-doc I was really lucky to be doing it at a time when the whole recombinant DNA and DNA sequencing area got going for the first time. I was very, very lucky to be there in that window of time because it allowed me to bring a number of those skills back to New Zealand.*”

Professor Anthony Reeve
They also found that the Asian population lacks the particular epigenetic mechanism seen in certain types of Wilms Tumours and Professor Reeve says the next step will be to try to identify the environmental trigger they seem to lack.

“Now that Japan, for example, is Westernised and a lot of the Western cancers are now occurring at a far higher rate, it will be interesting to see if this trend continues with this particular tumour. It may well be something to do with the diet affecting the developing fetus that triggers this epigenetic change.”

The Cancer Genetics Laboratory has also turned its attentions to the epigenetics of colorectal cancer. Women of European descent in New Zealand have one of the highest rates in the world and about a third of colorectal cancers are thought to have an epigenetic mechanism which might be triggered by some aspect of the western diet.

Looking to the future, Professor Reeve believes earlier detection is the best the way to deal with cancer because it is more curable than at the advanced stage.

**Pacific Edge Biotechnology**

Pacific Edge Biotechnology was formed in 2001 to develop tests for cancer detection and management.

The company is currently commercialising Cxbladder, a bladder cancer test which they hope will be used as a screening tool in New Zealand and be taken into the North American and European markets as well.

Bladder cancer ranks around number eight in terms of prevalence worldwide but it is the most expensive to treat because it has a very high risk of recurrence. Cxbladder allows patients to be closely monitored with a simple urine test, rather than a highly invasive cystoscopy. It is also able to pick up more than 95 per cent of the high-grade tumours at stage one.

Pacific Edge is also developing a colorectal cancer prognostic assay developed through HRC-funded research by Professor Reeve. The aim is to better predict what course of treatment would be best for that particular patient.

Associate Professor Parry Guilford has held the position of Chief Scientific Officer at Pacific Edge since it was launched but has now reduced his time in that role to focus more on the discovery aspect of the process in the Cancer Genetics Laboratory.

“The links are still very strong. We still see Pacific Edge as the commercialisation arm of this lab and we'll do the basic work here to get the proof of principle up and running, and then move it on to Pacific Edge.”

**Gastric cancer breakthrough**

An Otago graduate in molecular biology, Associate Professor Guilford started out his research career gaining his PhD in plant viruses at Cambridge University in the UK.

A desire to get involved in human research saw him spend three years in Paris mapping genes involved in human deafness.

Soon after he returned to Dunedin looking for a research role, Professor Reeve told him about an extended Māori family that appeared to have a gene for stomach cancer. They needed someone to identify the gene involved, just the sort of work he had been doing in Paris.

They developed a special relationship with the family and the Kimihauora Health and Research Clinic in Mt Maunganui. This helped Guilford’s research team identify E-cadherin as the gene implicated in this form of stomach cancer.

“We now, hypothetically, impinges on a lot of adult cancers where people think that maybe these epigenetic changes occur much, much earlier – even in-utero, such that they can predispose people to diseases later in life.”

Professor Anthony Reeve
About 50 people from that family who had a 70 – 80 per cent chance of dying from gastric cancer had cancer detected early through being screened for mutations using genetic tests.

Equally importantly, there are 100 people who now know they do not have the gene and no longer live with that threat hanging over them.

The research team have now identified 13 New Zealand families with mutations in the E-cadherin gene and worldwide, reports on about 150 families have been published so far.

Associate Professor Guilford says they now want to try and find a way to diminish the risk of these mutation carriers, without surgical intervention, by focusing on changes in the epigenome.

He believes they will be able to find drugs or chemopreventative agents that will inhibit these epigenetic changes and stop the cancer.

Their research with E-cadherin has given them a very good model to work with because they have people who are under close surveillance and that allows them to examine a cancer at a very early stage.

“To me one of the great joys and the great powers of the research we’ve done is that close interaction with families. It is powerful because you get a lot more done when the families are behind you and things work much better. Your motivation stays a lot higher because you know why you are doing the work.”

Associate Professor Parry Guilford

An immunofluorescence image of the gastric mucosa
(Image: University of Otago, Dunedin)

COLLABORATIONS

Associate Professor Guilford is part of a strong international consortium for inherited gastric cancer, which met last year to develop new guidelines on how to manage the disease.

New Zealand Genomics Limited

Professor Anthony Reeve has been a key figure in the establishment of New Zealand Genomics Limited - a genomics research infrastructure that brings together expertise from The University of Otago, Massey University, The University of Auckland and AgResearch.
The problem with drug therapy for cancer is that drugs that damage cancer cells are also toxic to healthy tissues. Prodrugs were developed to get around this issue, because they offer a way of attacking tumours selectively, without harming other cells. Inactive when first given, they are converted to the active drug within the body, once they have reached the target region - preferably within tumours.

Preclinical research in this area has been supported by the HRC since Professor Bill Denny and Professor Bill Wilson began their search for effective prodrugs, around 20 years ago. Based at the Auckland Cancer Society Research Centre at The University of Auckland, their groundbreaking work has led to major advances, and some disappointments, as they tackle the myriad of complex issues that tumour biology raises.

One of these issues is hypoxia, essentially, oxygen depletion within tumours. Hypoxic regions occur in tumours that grow so fast that they outstrip the development of their blood vessel network. The vessels are generally malformed and contain inclusions and blind ends that mean that parts of the tumour will receive a poor blood supply. These kind of tumours also tend to be more aggressive and spread quickly. More than 65 per cent of the 10 million people who are diagnosed with cancer each year have significant hypoxia in their tumours. Hypoxia is known to increase a tumour’s malignancy and resistance to current cancer treatments, particularly radiation therapy, but to date there are no effective treatments that can reach and destroy hypoxic tumour cells.

The ability to kill these hypoxic cells may dramatically improve the outcomes of patients with cancer. Professors Denny and Wilson, in collaboration with colleagues at Stanford University in the United States, have become world-leading authorities in the field of hypoxia.

Proacta Inc is the company that has been formed to commercialise the findings at both Auckland and Stanford University, California. In 2004, it acquired Proacta Therapeutics Ltd – the company founded by Professors Wilson and Denny in 2001 to develop the drug targets discovered through their research at The University of Auckland. Proacta Inc has a number of prodrugs in development and has raised $43 million in investment capital to date. Phase 1 clinical trials for Proacta’s first product began in January 2006.

Proacta’s lead research programme is the development of a unique anti-cancer drug, PR 104, which has very small molecules and can easilycross cell layers and penetrate hypoxic areas. Once absorbed into the oxygen-deficient areas of tumours, it is converted into a toxic agent that damages the DNA and destroys the cells. The product is now in clinical trials in the USA. Clinical trials of their second compound, PR509, should start in 2011.

Professors Wilson and Denny’s research into anti-cancer drugs also includes gene-dependent enzyme-prodrug therapy (GDEPT). GDEPT therapy involves genetically modifying tumour cells to produce an enzyme that is not present, or only present in low levels, in normal tissues. Once this has been done, a prodrug is given to the patient that will only become toxic when it is activated by the enzyme in the tumour cells. Researchers believe combining this treatment with hypoxia-targeted therapy will be a major advantage because hypoxic cells are resistant to the actions of GDEPT. If the same active drug can be simultaneously administered to non-hypoxic tumour cells by GDEPT therapy and hypoxic cells through small-molecule prodrug technology, then all areas of the tumour can be attacked simultaneously.

Pre-clinical research was funded by the HRC, the former Foundation for Research Science and Technology, and the Auckland Cancer Society. Further funding was provided by the National Cancer Institute (USA).
EXPLORING THE BRAIN
Understanding how the brain can regenerate itself and unravelling the mystery of memory

The HRC’s investment in neuroscience research supports discoveries on movement disorders, such as Parkinson’s disease, Huntington’s disease and motor neurone disease, as well as epilepsy, Alzheimer’s disease and other dementias, brain injury, stroke and mental illness.

Our ageing population means that the number of people with dementia is projected to quadruple over the next forty years. Alzheimer’s disease currently affects more than 40,000 New Zealanders, and a quarter of those aged 80 and over. Without new treatments, the burden on the health system and families will reach unprecedented levels. Scientists studying these diseases are making frequent advances, but with this progress comes greater understanding of how complex these conditions really are, and how little we can achieve with our current treatments. Consequently, the HRC has a strong focus on neuroscience research.

HRC-funded neuroscientists are world leaders in their field, and their publications make a major contribution to the international literature that informs the fight against these devastating disorders. Here, we profile just a few of their remarkable discoveries.
The high international impact of New Zealand neuroscience research is in part due to the work of Professor Richard Faull and Professor Mike Dragunow, and their teams. Professor Faull is the Director of the Centre for Brain Research at The University of Auckland, and the HRC has been supporting the research of his group for 20 years. The group is multidisciplinary and involves pharmacologists, geneticists, psychologists and clinicians, including Associate Professor Bronwen Connor, Professor Russell Snell, Dr Lynette Tippett, Dr Henry Waldvogel, Dr Maurice Curtis, and Associate Professor Michelle Glass. Together they have made discoveries that radically changed our understanding of the human brain.

It was only comparatively recently that scientists reported the presence of stem cells in the human brain. Up to this point it was widely accepted that the adult human brain could not generate new brain cells, and that cells lost to injury or disease could not be replaced. In 2003, Professor Faull and his team reported their discovery of stem cells in the basal ganglia, the part of the brain that is involved with the control of mood and movement. The basal ganglia is profoundly affected in movement disorders like Parkinson's and Huntington's disease. They showed, not only that this part of the brain could create new nerve cells, but the pathway through which these cells travelled through the brain. These discoveries raised the possibility that this process could be exploited to stimulate the creation of new cells in sufficient numbers to combat injury and disease, and direct the new cells created to the parts of the brain that are damaged. Suddenly, the search for an effective treatment for some of the worst diseases of the brain was heading in a whole new direction.

The advances that have been made would not be possible if it were not for the existence of the Human Brain Bank (HBB), which Professor Faull established in 1993. This is one of the best collections of human brain tissue in the Southern Hemisphere, including brains affected by the major neurodegenerative illnesses. The HBB is invaluable for the group's research on Huntington's disease, an inherited disorder that leads to uncontrolled movements and mood disturbances. There is currently no cure. Professor Faull and his team have spent years working closely with affected families and earning their trust. This is reflected in the number of people that have bequeathed their brains to further the research.

Using healthy and diseased tissue from the HBB, the team have been able to study which nerve cells die, how they die, and also understand how the pattern of cell death relates to symptoms. Most recently they have developed techniques for growing human brain cells for functional studies. They apply the knowledge gained across a wide range of neurodegenerative disorders. Most recently, Professor Faull, Professor Linda Tuhiwai Smith, Pro Vice Chancellor Māori at the University of Waikato, and Dr Melanie Cheung, also from the University of Waikato, have received HRC support to work with Māori families living with Huntington's disease, developing a model of partnership between indigenous communities and biomedical researchers.

In order to make significant breakthroughs in treatment of disease, it is necessary to induce the same condition in animals so that we can learn more about the disease process, and effective treatments can be developed and tested before human trials begin. Professor Faull and Professor Snell’s team has been working with researchers at the South Australian Research Development Institute and Harvard University on a sheep model of Huntington’s disease. This will be the first time a model of human brain disease will have been created in a large animal with a brain very similar to humans. This is a crucial and exciting advance towards effective treatments for the disorder.

“Knowing that stem cells were present in the brain - that the brain had the potential to renew itself - took the search for treatments for neurological disorders down new paths that did not involve the use of embryos.”

Professor Richard Faull
At the University of Otago’s Department of Psychology, Professor Wickliffe Abraham has spent many years studying the brain mechanisms through which our memories are made.

This work focuses on plasticity at the synaptic connections where nerve cells communicate with each other. As the word ‘plasticity’ suggests, the synapse is capable of changing its shape and function for minutes, hours or years. It is through synaptic plasticity that memories are formed. In 2002, Professor Abraham’s group was the first to report that these changes could be enduring ones, meaning that the process of learning literally remodels the brain. Professor Abraham’s group has identified specific genes and proteins which are active during the learning process and contribute to laying down long-term memories. Understanding how memories are formed in the healthy brain is key to understanding how they are affected in disease, and how they can be protected by treatments.

Professor Abraham is the Director of the University of Otago’s multidisciplinary Brain Health Research Centre. The Centre brings together 35 research teams from a broad array of science disciplines to understand the healthy brain, and how it can be protected from and repaired in disease and injury.

Through the Centre, Professor Abraham, Professor Warren Tate and Dr Joanna Williams have collaborated for over 20 years to study the complex neural changes that occur during memory formation, and in Alzheimer’s disease. In 2010, the HRC awarded $5 million to this research team to undertake groundbreaking clinical research that will build on these advances in knowledge to test potential treatment molecules in rodent models of Alzheimer’s disease.

The team will also search for markers of cognitive decline and Alzheimer’s disease in the blood of elderly people. Identifying such markers could revolutionise the treatment of Alzheimer’s disease by allowing better planning of therapies and long-term care. The team also includes Dr Ping Liu, Dr Stephanie Hughes, Professor Robert Knight, Professor Murray Skeaff, Dr Nick Cutfield and Dr Hu Zhang.

In 2010, Professor Tate was awarded the Rutherford Medal by the Royal Society of New Zealand for his outstanding contribution to science - including his pioneering work on understanding how proteins are synthesised in living cells. This knowledge has profound implications for determining how proteins influence memory formation and Alzheimer’s disease.
STROKE AND TRAUMATIC BRAIN INJURY

New Zealand researchers are finding new ways to reduce disability and casting the spotlight on the stroke epidemic in developing countries.

“Stroke is one of the most fearful disorders and imposes a huge physical, emotional and financial burden on stroke patients, their families and society.”

Professor Valery Feigin

Stroke

There are about 7,000 new strokes in New Zealand annually and some 45,000 New Zealanders live with the aftermath of stroke. One in four are younger than 65 years of age.

Stroke costs $450 million yearly in direct costs but other costs include lost productivity, payment for medications and private rehabilitation. Three-quarters of stroke survivors are moderately to severely disabled and almost half require help in their everyday activities.

In New Zealand, it ranks second only to ischaemic heart disease in terms of total disability-adjusted life years lost and premature mortality.

Traumatic Brain Injury

Traumatic Brain Injury (TBI) is also a significant health problem in New Zealand, costing the country $100 million a year in direct costs. About three-quarters of traumatic brain injuries are due to car accidents, while the remainder are due to falls, violence, sport and other causes.

Preliminary findings of a recent study have shown that New Zealand is likely to have 50–60,000 traumatic brain injury patients every year, outnumbering stroke survivors.

Moderate to severe TBI patients have physical problems as well as an emotional and psychological burden. While the majority of them are considered mild, TBIs can lead to quite significant disability.
Professor Valery Feigin’s interest in stroke began after his father died from one 30 years ago. At that time, the World Health Organization was performing the first stroke epidemiological study. As a neurologist, he started developing his own research in the early 1980s.

Over the last 10 years he has been involved in twelve HRC-funded Projects in stroke, TBI and cardiovascular disease and now heads the National Institute for Stroke and Applied Neuroscience at AUT University.

His New Zealand stroke research began with the Auckland Regional Community Stroke Study (ARCOS) Group’s series of studies and the HRC-funded Project, Auckland Regional Stroke Outcomes (ASTRO). ASTRO was designed to follow-up all stroke survivors over five years, with the emphasis on neuropsychological outcomes – the largest population-based, follow up study of that kind ever done.

The latest HRC-funded ARCOS IV Programme, Measuring and Reducing Stroke Burden in New Zealand, began in 2010.

The ARCOS studies have shown that, while stroke incidence in New Zealand has declined over the last 20 years, the rate of decline (11 per cent) is over four times slower than in other developed countries. At the same time, stroke incidence for Māori and Pacific peoples increased.

The recently completed ASTRO also produced groundbreaking findings that captured international attention. It was the first five-year population-based follow-up of 418 stroke survivors and spanned virtually all areas of functional outcomes – from neurological impairment to cognitive impairment and disability – and found that over 60 per cent of stroke survivors have a complete recovery by five years.

They also found that Māori and Pacific peoples have significantly worse outcomes in terms of cognitive impairment, including dementia and reduced economic self-sufficiency, when compared to European New Zealanders. At the same time, they identified that men do better than women in terms of outcomes post-stroke.

Importantly, they also found that cognitive rehabilitation may help influence all other functional outcomes, such as disability, handicap and quality of life. This finding could mean a significant change in the current practice of stroke management, by getting neuropsychologists involved earlier.

A rehabilitation technique called attention process training was also successful in stroke survivors who have attention deficit - the most prevalent cognitive deficit, accounting for about 50 to 90 per cent of all cognitive deficits from stroke. It has already been included in the current New Zealand guidelines as an evidence-based rehabilitation recommendation.

Internationally, they have also had an impact. In 2009 they published a systematic review of stroke epidemiology world-wide in The Lancet Neurology, using data from 56 different population-based studies. It showed that stroke incidence in developed countries has decreased by 42 per cent, but in developing countries it has actually increased by over 100 per cent.

Nobody expected such results and Professor Feigin predicts it will lead to a change in perspective on the importance of stroke in developing countries, leading them to put stroke on the government agenda and do something to stop the epidemic.

The stroke research has also led to some commercial developments, such as the world’s first stroke rehabilitation DVDs for people discharged from hospital, to improve their chances of recovery. They have been endorsed by the World Federation for NeuroRehabilitation and reviewed positively by leading medical journals.

Work in traumatic brain injury has also made significant progress through research, such as the Brain Injury Outcomes New Zealand in the Community study, designed to gauge the impact of head injury in New Zealand, which is the first population-based study of that kind here and the largest in the world.

They have already made two remarkable and unexpected findings. First, preliminary results suggest that TBI incidence here is far greater than anticipated and, significantly, a greater proportion of children are affected by TBI (30-35 per cent rather than the expected 25 per cent).
Professor Feigin says New Zealand has a good reputation internationally for carrying out top-quality, population-based epidemiological studies and many of these were pioneered 30 years ago by Professor Ruth Bonita, who is currently still involved in the ARCOS IV Programme as a named investigator. That international reputation is also underscored by his own role as editor in chief of *Neuroepidemiology*, a well-regarded international journal.

Looking ahead, Professor Feigin thinks it is time to do more research into understanding why there are differences in stroke burden – for example, between Māori, Pacific and European New Zealanders – and getting to grips with why Māori and Pacific are at greater risk.

What he hopes for is to use all this research to improve the outcomes and reduce the burden of stroke and TBI here, save lives, reduce the burden on families and contribute to international knowledge as well. To achieve this goal, his institute has established good collaborative links with key stakeholders, including the Ministry of Health, the Stroke Foundation and the Brain Injury Association of New Zealand.

“Improving the outcomes and reducing the burden of stroke and TBI is achievable in New Zealand. We are a small country and if we have something that is effective we can implement it relatively easily compared to other countries.”

Professor Valery Feigin

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**CASE STUDY**

Rehabilitation after a stroke

Professor Winston Byblow at The University of Auckland’s Centre for Brain Research has shown that combining magnetic brain stimulation with simple rehabilitation exercises can help people recover arm and hand function, even more than six months after a stroke.

Working with PhD student and physiotherapist Suzanne Ackerley he found that the stimulation appears to prime the brain to be more receptive to the rehabilitation exercises, helping it relearn how to control fine movement.

This research is part of an ongoing programme, led by Professor Byblow along with Professor Alan Barber and Dr Cathy Stinear in the Department of Medicine, that has led to the development of an inexpensive arm and hand rehabilitation device, that can be used by patients at home. They can make hundreds of arm movements in a few minutes with minimal effort and this repetitive movement boosts plasticity in motor areas of the brain.

Plasticity is the process through which the brain reorganises itself following damage, injury or exposure to new situations - including nerve cells sprouting new connections. For nerve cells to make beneficial connections, they need to be correctly stimulated.

In a recent HRC-funded clinical trial, patients who experienced stroke at least six months prior used the device immediately before self-directed therapy, three-times per day, for one month. They improved upper-limb function to a greater extent than patients who did therapy alone.

In a new trial, the team is working with Auckland District Health Board nurses and therapists to determine if their interventions enhance brain plasticity and improve outcomes for patients undergoing physical therapy in the weeks immediately following stroke.
Advances in bone biology have revolutionised the treatment of Paget’s disease and osteoporosis

Maintaining independence and mobility in later life depends to some extent on the state of our skeleton.

Osteoporosis, a gradual loss of bone mass with increasing age, is a major issue for older New Zealanders. Thanks to research, we now better understand how this condition can be best prevented and treated, but it will continue to have a major impact on the health and well-being of our ageing population. After the age of 60, over 50 per cent of women and nearly 30 per cent of men can expect to suffer a fracture as a result of this bone loss. The most important fracture is of the hip, an event from which many elderly people never fully recover. The estimated cost to New Zealand is $1.1 billion per year.

There are many different diseases of the bone, related to the rate of bone loss or bone re-growth, or production of new bone. The HRC has been supporting The Bone Research Group at The University of Auckland for two decades. Internationally renowned for their contribution in the area, Professor Ian Reid and his team have made some major breakthroughs in our understanding of the human skeleton and the treatment of bone diseases. Here we profile some of their key discoveries.

Professor Ian Reid is a clinician and a Professor of Medicine and Endocrinology at The University of Auckland Medical School. As the Director of the Bone Research Group, he has built a world-class research team whose findings have had a major impact on the way that certain bone diseases are prevented and treated, and on our understanding of the biology of the human skeleton. The multi-disciplinary group includes Professor Jill Cornish, Professor Tim Cundy, Associate Professor Andrew Grey and Dr Anne Horne, and undertakes a broad range of research activities from molecular studies of bone growth and animal models of disease to drug development and clinical trials of treatments.

Professor Reid became interested in bones whilst working with his mentor Kaye Ibbertson, a former Professor of Endocrinology in Auckland. Historically, the medical profession thought of bone as a chunk of calcium but advances in technology and biology have revealed that bone is a responsive, dynamic tissue. Ibbertson saw the potential in a field that excited few others at the time. Professor Reid remembers conferences that attracted just a couple of hundred participants, and now attract over 6,000.

We now understand that bones are living tissues, in a continuous cycle of degeneration and renewal. Professor Reid has spent much of his career understanding this cycle and looking for ways to prevent the breakdown of bone and strengthen the skeleton. Greater knowledge on the biology of bone cells has led to strategies to manipulate their behaviour and protect the skeleton. This research becomes particularly important as our demographics change and our population starts to age and conditions, such as osteoporosis, reach epidemic proportions.
Osteoporosis is a condition in which the honeycomb-like inner matrix of bones thins and becomes weak, increasing the chance that they will break. As we age, the process of renewal is slowed and we lose bone mass, greatly increasing the risk of developing this condition. Until comparatively recently, osteoporosis was an inevitable consequence of ageing for many people. A dire one for some, leading as it might to collapse of the vertebrae in the spine, hip fractures and permanent disability.

In the 1960s, a group of drugs were developed that slowed the bone breakdown in the body - the bisphosphonates. These drugs were used to treat Paget's disease and by the 1980s, there were isolated reports that they could slow bone loss in osteoporosis, but there was no hard evidence. Professor Reid and his team provided that evidence through a clinical trial that revolutionised the treatment of this condition. They showed that use of these early drugs led to a dramatic increase in bone density in people with osteoporosis. Publication of their findings in *The Lancet* attracted the interest of pharmaceutical companies, Merck and Novartis, who worked with Professor Reid and the Bone Research Group in creating much stronger forms of the drugs.

The Bone Research Group contributed over 20 years of research to developing stronger bisphosphonates and took the lead in the development of zoledronate, working with Novartis. Zoledronate is 10,000 times more potent than the agents first available in the 1960s, and Andrew Grey and Mark Bolland in the Bone Research Group have shown that it is only necessary to give this drug once every few years to maintain its effects.

Having shown dramatic improvements in the treatment of osteoporosis, the team has moved its focus to osteopenia, a condition in which the bone mineral density is lower than normal and a precursor to osteoporosis. Concentrating prevention measures solely on those with existing osteoporosis ignores the fact that only 20 per cent of fractures occur in this group. In 2009, the Bone Research Group started a six-year study to test the effectiveness of bisphosphonates in preventing fractures in osteopenia. The findings of this trial will have major implications for treatment.

One of the issues clinicians who undertake research face is in seeking to improve treatments for patients suffering from relatively rare diseases. The fewer the number of patients suffering from a condition, the more difficult it is to interest pharmaceutical companies in investing in the development of new drugs. Such was the case with Paget's disease, a chronic condition of the bones that affects around one per cent of older adults worldwide, and 5-10 percent in New Zealand. The normal process of bone breakdown and renewal is disturbed and the new bone that is formed is misshapen, brittle and weak. Although only a few bones are involved in each person affected, the condition is painful and can lead to fractures, arthritis in affected joints and pinching of the nerves. If the bones of the skull are affected, headaches and vision and hearing loss are possible. A very rare form of the disease can also occur in children, and Professor Tim Cundy of the Bone Research Group has identified the gene that causes that form.

Understandably, drug companies were not initially interested when Professor Reid approached them with the suggestion that they support the extensive clinical trials necessary to get the new, more potent, bisphosphonates approved for treatment of Paget's disease. However, this is precisely what Professor Reid managed to achieve and the results were

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“Zoledronate is so effective that elderly people don’t even have to remember to take it - a doctor can administer an injection once every one to three years and they will still get the bone-strengthening effects.”

Professor Ian Reid
astounding. After a single dose of zoledronate, 98 per cent are still free of disease over six years later.

In addition to strengthening the bones through slowing the rate that they are broken down, the treatment of osteoporosis and Paget’s disease also involves giving calcium supplements to strengthen the bones from within. The Bone Research Group were the first to prove that calcium supplements were effective in increasing spine and hip bone density in normal post-menopausal women, and in older women and men.

However, they have also made another very important discovery. This, apparently harmless, supplement increases the risk of heart attack in men and women by 27 per cent.

Professor Reid and Dr Mark Bolland first noticed this increased risk in a clinical trial of calcium supplementation that they were undertaking, and subsequently confirmed it by analysing the results of 15 similar trials that had been conducted around the globe, involving a total of 12,000 people. So far, the risk has only been observed when calcium levels are increased through supplements and there is no data available to show any increased risk in those with a high calcium intake through diet alone.

One possible reason is that supplements raise calcium levels in the blood much more than ingested dairy products do, leading to higher blood levels, and that these high levels may affect the blood vessels. Professor Reid points out that calcium is a metal and high blood concentrations may result in calcium being laid down in the artery walls, causing stiffening. As calcium supplements are far less effective at preventing fractures than bisphosphonates, Professor Reid and his team have called for a review of calcium supplements in the treatment of bone diseases. This is another instance of the work of the Bone Research Group having an impact on clinical treatment.

The Bone Research Group is also researching a number of other avenues for new treatments, and Professor Jill Cornish has identified hormones found in fat for which levels are lower in thin people, which may explain why fatter people have stronger bones. These hormones now become potential treatments for osteoporosis and have been licensed to drug companies. Their research on bone biology has yielded two key regulators of bone cell growth that could potentially be manipulated as treatments for conditions in which there is bone overgrowth or bone loss. Research has previously focused on restraining the activity of the cells that break bone down (osteoclasts) and not increasing the activity of the cells that build bone (osteoblasts). Professor Reid points out that we need therapeutic agents that will do both and research efforts will be increasingly focused in this direction.

The work of the Bone Research Group has had a major impact on clinical practice and is an excellent example of the translation of fundamental biomedical research to the clinic - where the outcomes actively improve peoples’ lives. Their success is in no small part due to the team’s ability to work with large pharmaceutical companies in a relationship that is mutually beneficial and does not compromise the integrity of the researchers. The changes that have occurred were led by clinicians and basic scientists, and supported by pharmaceutical companies who realised the potential of the work and maintained an ongoing dialogue with the team to build on therapeutic opportunities.

The funding provided by ‘big pharma’ allows the research team to act on their ideas, follow-through on developments and explore clinical questions as they arise. Professor Reid emphasises the importance of having multiple funding sources in ensuring success, and acknowledges the support of the Auckland Medical Research Foundation, Lotteries Health, the former Foundation for Research, Science and Technology and Fonterra, as well as the continuous support from the HRC.

Professor Reid was recently the recipient of the Frederick Bartter Award from the American Society of Bone and Mineral Research, an accolade that has not been granted to a physician in the Southern Hemisphere for many years. He stresses that this is an award for the whole group and their successes are due to the collective contributions of every member of the team.
Cardiovascular disease (CVD) is still the leading cause of death in New Zealand, accounting for 35 per cent of deaths annually. One in twenty adults have been diagnosed with CVD – that’s about 280,000 people.

The basis for over 80 per cent of CVD events can be explained, and so many of these deaths are not only premature, but preventable.

Drug-based management of CVD risk has previously been initiated when blood pressure or cholesterol exceeded specific levels. Clinical guidelines now focus on the absolute CVD risk, which is determined by the cumulative effect of multiple risk factors, such as age, gender, smoking, blood pressure, cholesterol, diabetes and previous CVD history, rather than high levels of one or two risk factors.

Professor Rod Jackson and his colleagues at The University of Auckland developed colour coded paper-based risk charts for clinicians to estimate their patients’ absolute CVD risk based on combined risk factors. Later, as clinics became more computerised, they developed a computer version, resulting in the PREDICT software – which combines a clinical decision support system and a research tool.

PREDICT is a web-based decision support system, used mainly to assist primary care practitioners to assess and manage cardiovascular disease risk. It has been developed by a research team at The University of Auckland, led by Professor Rod Jackson from the School of Population Health, and software company Enigma Publishing Limited.

The software is based on the colour risk charts developed by Professor Jackson’s team in the early 1990s. The charts were well received and used not only locally but internationally. However, their subsequent research revealed that clinicians were not using the risk charts frequently enough. Jackson’s team concluded that a computerised system would be more effective as the use of a computer during consultations was becoming more commonplace for GPs.
The computerisation of CVD risk prediction started simply as a PDF version of the colour chart but rapidly developed into a sophisticated, evidence-based, clinical decision support programme.

Partnering with a software developer, Professor Jackson's team provided the academic and evidence rigour, and Enigma, the commercial skills and services. They designed and built PREDICT's first product in 2002, a CVD risk assessment and management module. The programme is currently used by about 80 per cent of Auckland and Northland PHOs, and has generated a cohort of around 150,000 patients so far, becoming one of the world's largest CVD cohort studies. The research component of PREDICT has been supported mainly by two consecutive HRC project grants and multiple National Heart Foundation research fellowships.

PREDICT automatically extracts CVD risk factors in a patient's medical record, loads them into the prediction template and within seconds estimates the level of CVD risk. It then applies this risk profile to current CVD risk management guidelines and provides personalised management recommendations. PREDICT simultaneously captures the risk factors in an external database as an anonymised record of the data generated. This data can then be anonymously linked to hospitalisations, deaths, laboratory results and drug dispensing, and is used to develop new risk prediction tools for multiple New Zealand population groups.

The rapid growth of the PREDICT dataset is now enabling the research to move from a primary focus on risk prediction to a broader focus on addressing disparities in CVD burden and quality improvement. In the next few years, PREDICT will be able to develop a comprehensive CVD risk profile on over one-third of adult New Zealanders as well as up-to-date information on their management.

The next step for Professor Jackson and his team is to see PREDICT used more frequently in hospitals nationwide, primarily for people with acute CVD. Later this year they will produce new CVD and diabetes risk prediction tools specifically designed for Māori and Pacific, and other high risk groups, resulting in more tailored information which will help provide better targeting of interventions.

The PREDICT model could also be applied to other common conditions such as mental health and respiratory disease, but as Professor Jackson explains, it is not for the faint-hearted. He would like to see groups with expertise in several other common conditions develop PREDICT equivalents. However only very common conditions where there is good evidence for effective interventions can justify the huge amount of on-going effort required to develop and maintain electronic decision support systems like PREDICT.

Professor Jackson has a long term commitment to epidemiology and population health research but he continues to be driven by a focus on embedding research into practice.

"The easiest way to make research relevant to practice is to generate research from within everyday practice. That's what I have been doing for the last 10 years and is what makes PREDICT unique – it all happens from practice."

How a ‘population bomb’ forged a career path

Reading the book *The Population Bomb* at the age of 15, had a significant impact on Professor Jackson. The work by Paul Ehrlich warned of mass starvation of humans in the 1970s and 1980s due to overpopulation and suggested we would never improve our health unless we slowed the world's population growth. The concept of a population bomb and the impact this would have on health influenced and guided Professor Jackson's career step into medicine – without realising it, he has always linked health and populations.

As a young clinician/house surgeon he became interested in smoking as a major population health problem, and the main adverse smoking outcome, CVD, became his focus. Supported by the opportunity to work with Professor Robert Beaglehole, then a CVD epidemiologist in the Department of Community Health, at The University of Auckland, Professor Jackson spent ten years working in public health epidemiology which focused on CVD in whole populations.
Following the completion of a postdoctoral fellowship in the United States in 1989-90, Professor Jackson returned to The University of Auckland as Senior Lecturer in Epidemiology. He was required to teach medical students and soon realised that to keep them awake he had to make his teaching more clinically relevant. This led him to explore the clinical epidemiology of CVD and he developed an increasing interest in the clinical management of CVD risk.

At about the same time he was invited by the Ministry of Health to lead the development of clinical guidelines for managing high blood pressure and he has subsequently been involved with every CVD risk management guideline developed in New Zealand. Together with his clinical epidemiology teaching, his involvement in clinical guideline development has had a major influence on Professor Jackson’s subsequent career. However, he still maintains a strong interest in public health epidemiology and believes that his role is to apply epidemiology across the clinical – public health spectrum.

A passionate and popular lecturer, Professor Jackson and his research focus has been immortalised by his students with a special YouTube tribute, *I’m Sorry Rod Jackson*. And, as a renowned cardiovascular health expert, Professor Jackson appeared on *Test the Nation – Just how healthy is New Zealand?* in 2006, and was responsible for developing with the production team, the Southern Cross Health online test, which provided the format for the show.

### Assessing cardiovascular risk and treatment benefit

#### Risk level women

<table>
<thead>
<tr>
<th>Total Cholesterol/HDL ratio</th>
<th>Non-smoker</th>
<th>Smoker</th>
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</thead>
<tbody>
<tr>
<td>55/6</td>
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<tr>
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<td>70/5</td>
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</table>

<table>
<thead>
<tr>
<th>Blood Pressure mm Hg</th>
<th>AGE 70</th>
<th>AGE 60</th>
<th>AGE 50</th>
<th>AGE 40</th>
</tr>
</thead>
<tbody>
<tr>
<td>180/105</td>
<td>160/95</td>
<td>140/85</td>
<td>120/75</td>
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</tbody>
</table>

#### How to use the Tables

- Identify the table relating to the person’s sex, diabetic status, smoking history and age.
- Within the table choose the cell nearest to the person’s age, blood pressure and TCHDL ratio. When the systolic and diastolic values fall in different risk levels, the higher category applies.
- For example, the lower left cell contains all non-smokers without diabetes who are less than 45 years and have a TCHDL ratio less than 4.5 and a blood pressure less than 130/80 mm Hg. People who fall exactly on a threshold between cells are placed in the cell indicating higher risk.

*(Tables: The University of Auckland)*
Globally 50,000 people will die from heart failure in the next 12 months and 3,000 will be saved by a heart transplant. However, donor numbers will continue to fall short of demand.

The artificial heart pump was designed to keep patients with congestive heart failure alive while they wait for a donor heart transplant, or to give the patient a chance to recover by allowing their heart to rest and heal. Current heart pump technology requires a bulky wire cable to pass through a patient’s skin to power the heart pump. These wires cause serious infections, sometimes leading to death, in about 40 per cent of patients. The wires are also prone to breaking and restrict a patient’s activity, and if a pump stops, the patient has only about a minute to live.

Recent research however, initiated by an HRC-funded Project, has been instrumental in addressing these challenges in the form of a wireless heart pump and the commercialisation of the technology.

Associate Professor Simon Malpas of the Department of Physiology, School of Medical Sciences, and the Auckland Bioengineering Institute at The University of Auckland, did not envisage his research career would emerge into the commercial realms of a start-up R&D company, with himself at the helm driving the research team and pursuing business relationships.

It was a Wellcome Trust Major Equipment grant and then an HRC grant in 1998 that were the impetus for the technology that ultimately grew to the formation of Telemetry Research Limited.

The pioneering research project that initiated this path required recording a variety of physiological signals in laboratory animals and studying interventions and disease states in a more natural environment, in contrast to collecting data from an anaesthetised animal. This was the genesis of the technology - Associate Professor Malpas found he was unable to buy the instrumentation to create the implantable monitoring devices needed for this research.

Recognising the opportunity to enter the market, he teamed up with Dr David Budgett of the Bioengineering Institute, and in 2005 they founded Telemetry Research to commercialise their technology.

Telemetry’s ‘break through’ product was the ability to transfer power to implantable pumps, in particular a heart pump. Currently infection caused by a cable entering the skin is the largest problem for the industry.

“The development of the instrumentation grew out of a basic research need, we couldn’t buy it so we had to build it ourselves, and then we became aware of the tremendous market need for this technology.”

Associate Professor Simon Malpas

The transcutaneous energy transfer technology (TET) developed by Dr Budgett and Associate Professor Malpas sends power through the skin with no wires required. This gives patients back their mobility. The unique feature of the technology is that there are no heat generation issues as experienced with earlier models. The focus now for Associate Professor Malpas, Dr Budgett and the team is on the basic core technology.

At the same time, Associate Professor Malpas is looking at potential relationships with medical device companies to take the technology to market.

“...it wasn’t the intention but it was a consequence of the research, and also the realisation that there was an opportunity in taking biomedical device instrumentation to the market.”

Associate Professor Simon Malpas

Research can take you down paths you never imagined

CASE STUDY

Associate Professor Simon Malpas

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Associate Professor Simon Malpas

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Associate Professor Simon Malpas
“Broadly speaking we are looking at how wireless power can be adapted for a range of medical devices that need lots of power. It’s the ‘chicken and egg’ concept. Because implantable device companies haven’t had wireless power, they haven’t developed these technologies, but now we can offer the power.”

“We don’t want to provide the whole device but to partner with another company to get their device with our power to clinical trial and on the market. I think this is a good model for a New Zealand company, as implantable clinical devices have probably the highest level of difficulty with residual requirements such as safety.”

Telemetry’s aim is to be the preferred supplier of wireless power and they are currently developing a broad platform of technology that can be tailored to meet the specific needs of devices being powered. They are also working on another concept that uses conductive wireless power to monitor pressure, which could be used to measure arterial or intracranial pressure.

Associate Professor Malpas appears to be thriving in his dual researcher/Chief Executive role, and enjoying the demands of academic research, coupled with the formation and development of a R&D biotech company.

He says: “It is very much about the team that is the key part of the success of research groups. Much credit for the R&D team goes to fellow founder Dr David Budgett whose instrumentation experience has created a unique platform for new devices to be developed.”

He is conscious though of the challenges for emerging researchers to grow and fund their careers, and find a research team, and says that while you may be in a position to do a PhD, you have to be particularly proactive to find a Postdoctoral Fellowship, a laboratory to work in and also the funding. “This is not dissimilar to where he is today, still seeking funding: “That’s always a challenge,” he says.
About the HRC

The HRC is the principal Crown agency responsible for the management of the Government’s investment in public good health research in New Zealand. Our mission is ‘benefiting New Zealand through health research’, with a vision of improved health and quality of life for all.

To find out more about the HRC, go to: http://www.hrc.govt.nz/about-us.