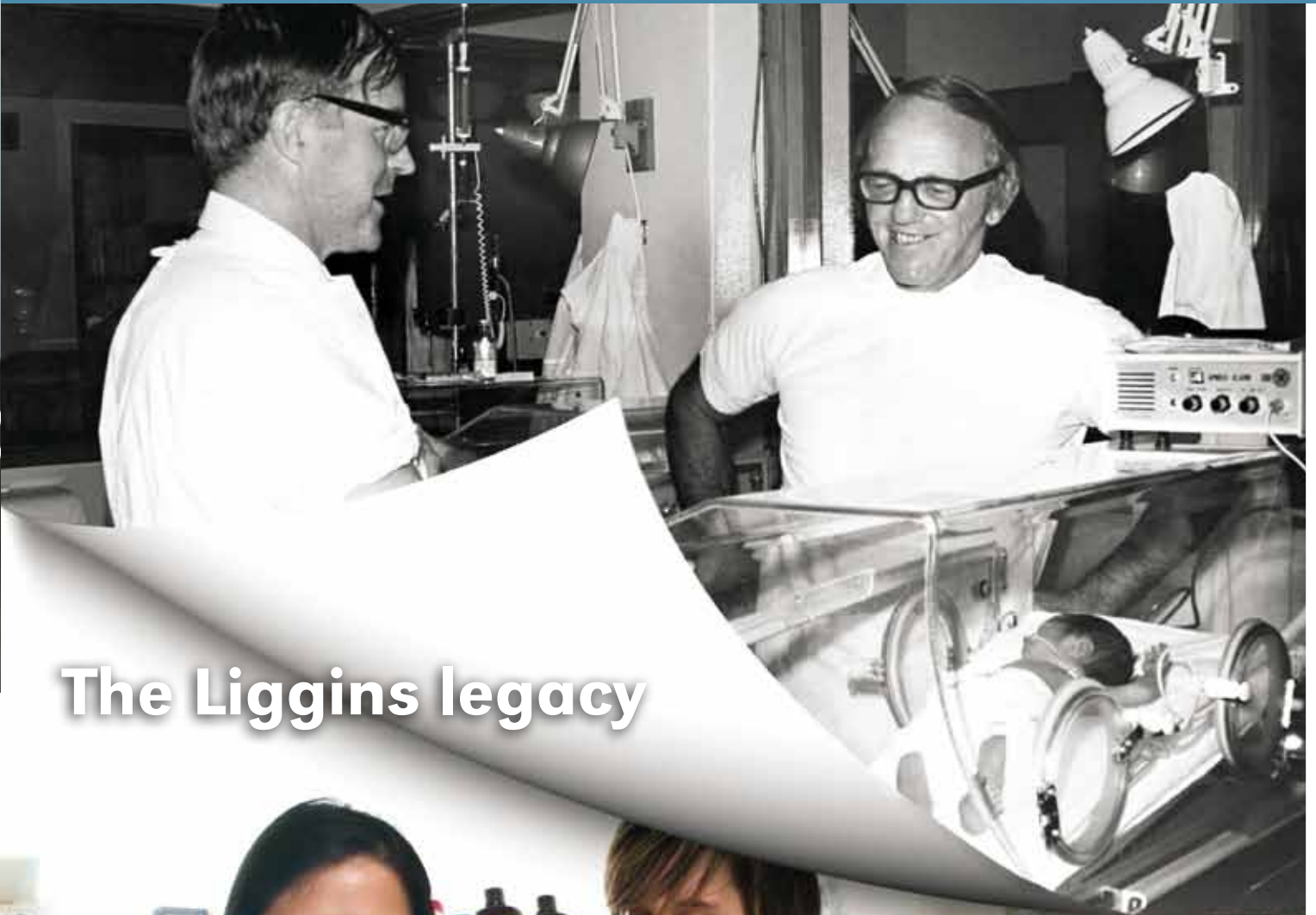


Dialogue

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The Liggins legacy



LIGGINS INSTITUTE
THE UNIVERSITY OF AUCKLAND
NEW ZEALAND

Te Whare Wānanga o Tāmaki Makaurau

On our cover: The Liggins legacy

In this issue we celebrate the legacy of scientific enquiry and integrity which successive generations of researchers at the Liggins Institute have inherited from the renowned medical scientist for whom the Institute is named.

The top picture shows paediatrician Dr Ross Howie (left) and Sir Graham (Mont) Liggins in the early 1970s. Together they proved the efficacy of a new treatment based on Mont's scientific research. The landmark clinical trial they conducted changed obstetric practice and halved the death rate for premature babies at that time. Read more on page 3.

Directly and indirectly the Liggins-Howie trial has been a starting point for new generations of researchers at the Liggins Institute investigating how events at the beginning of life affect development and health throughout life. Some are even following the health of the children (and their children) born during the trial.

Mont Liggins was keen to encourage and support young researchers and his legacy is an inspiring example to the Institute's many postgraduate students such as Cassandra Yap (left) and Zöe Clayton in the bottom picture. Read about their research on page 7.



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The Liggins legacy

Mont Liggins' achievements and approach to life continue to inspire.

Sir Graham 'Mont' Liggins died on 24th August, aged 84. His research achievements were such that many believe he should have won the Nobel Prize. He was New Zealand's most distinguished medical scientist, known for his intellectual rigour, elegant experimental design, shrewd questioning, academic generosity and dry wit.

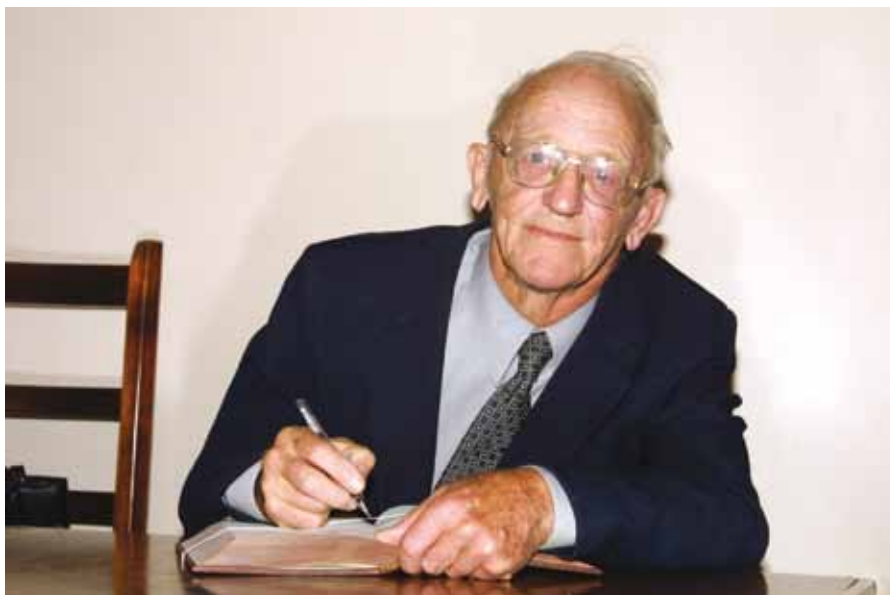
When Mont embarked on a career at National Women's Hospital in 1959 – then a hub of medical discovery – his ambition was to discover what triggers premature birth, which was then often a death sentence. During his day job as an obstetrician he saw its tragic outcomes.

In 1963, America's best doctors could not save a son of President John F Kennedy and his wife Jackie, who was born five weeks early. Like most preterm babies, his lungs were immature and unable to inflate sufficiently.

Squeezing his research into one day a week and after hours, Mont experimented with sheep. He firstly turned upside down the theory held since Aristotle that the mother's body instigated labour. He discovered that the fetus triggers birth by releasing a steroid hormone called cortisol. Suddenly everyone wanted to know him.

But his most fantastic breakthrough was made accidentally. During the course of his experiments he noticed that even very premature lambs born to ewes that had been given cortisol could breathe. With typical generosity he immediately shared the results with a colleague, who established how cortisol matures lungs early.

Realising the possibility this presented for babies, Mont swiftly teamed up with paediatrician Ross Howie, and they designed and conducted a trial giving a synthetic cortisol (betamethasone) to women in premature labour. It was an enormous success, halving the babies' death rate. The simple, inexpensive treatment remains the gold



Emeritus Professor Sir Graham Liggins mentored and inspired a new generation of biomedical researchers.

standard around the world and has saved hundreds of thousands of lives.

Mont, nicknamed after childhood favourite Monty the Mouse, followed in his GP surgeon father's footsteps to train in medicine, his first preference having been for engineering.

His academic ability was balanced by an adventurous streak. He grew up in Thames, which he described as an adventure playground. His outdoor upbringing prepared him well for the several summers he spent in Antarctica starting in 1977, studying seals and how they manage to hold their breath underwater for so long. He won a Polar Medal for this research. It was one of many accolades, including a Knighthood in 1991.

Mont Liggins has been a source of inspiration to scientists at the Institute that is proud to bear his name.

Associate Professor Frank Bloomfield, also a clinician-scientist, admired Mont's personal integrity. "He was a wonderful example of how you can achieve great research without being overtly ambitious or trampling on people to get there," he says.

"Mont was always willing to spend time properly talking to people, no matter who they were."

Dr Mark Vickers, who works on nutrition before and after birth, is inspired by the way Mont thought laterally and explored new research threads.

"Like Mont Liggins, we use a lateral approach to problem solving and it has resulted in some of our most important observations. We too have relatively limited research funding and to maximise its use we have to think outside the box and innovate," says Dr Vickers.

"He's a wonderful role model."

Ten years of innovative biomedical and clinical research

In 2011 the Liggins Institute will celebrate its 10th anniversary and we would like to contact and include as many former staff and students as possible. The Alumni and Friends section of our website has further information and a form to update your details. Please relay this request to other former staff and students of your acquaintance.

Liggins' research alive and well

New questions are still being asked of Mont Liggins' findings.

The landmark 1972 clinical trial by Liggins and Howie has a legacy entering its fourth decade. With the help of the original trial data, passed on by the authors to a new generation of researchers, new discoveries are still being made.

The first was in the 1990s, when clinicians were unsure whether steroid treatment also helped the babies of women whose waters had broken prematurely.

A team led by Professor Jane Harding, who was to join the Liggins Institute and is now Deputy Vice Chancellor (Research) at The University of Auckland, analysed Ross Howie's meticulously handwritten records.

Without having to recruit any further patients, they confirmed that treating such women does boost their babies' chance of survival.

Other studies have checked for long term health problems caused by exposing unborn babies to steroids. Although life-saving at birth, steroids are powerful hormones that could potentially have long term effects on growth, heart and lung function, diabetes risk, bone density and more.

Ross Howie had checked the first 318 surviving babies in his study at ages four and six years and found no ill effects. But Dr Stuart Dalziel, Professor Harding and researchers from the University's Faculty of Medical and Health Sciences carried it further. In 2002 and 2003 they performed the almighty feat of tracking

down and testing more than half (534) of the 'babies' in the original trial, who were by then aged around 30 years.

Reassuringly, the results, published in the prestigious journal *The Lancet*, showed no clinically important effects – enough to be certain that the benefits of the treatment in reducing death in infancy and severe disability in childhood vastly outweigh any potential risk in later life.

Now, the researchers are looking at the next generation: the children born to the now grown 'babies' born in the original trial.

Lead author Dr Dalziel, an honorary member of the Liggins Institute and a paediatrician at Starship Children's Hospital, points out that it is one of the longest follow-up periods ever undertaken following a trial conducted in pregnancy.

"The original trial conducted by Mont Liggins and Ross Howie remains a superb example of how to take experimental findings in animals through to clinical practice. The exceptional quality of their trial design and their meticulous record keeping have allowed us to answer questions that were not anticipated 40 years ago," he says.

In the 30 years after their original trial, it became commonplace for women who were at risk of preterm delivery but had not delivered their babies within a week of the first steroid course to be given further doses.

Amidst concern at a lack of evidence that this practice was effective and safe, a major multi-centre study was launched to clarify its benefits and risks. The study recruited 982 women at hospitals throughout Australia and New Zealand. Professor Harding co-ordinated the New Zealand component of the study.

The results support the use of repeat doses of steroids. Babies whose mothers received repeat doses had fewer breathing and other health problems than those whose mothers received only a single course, and there was no difference in the health of the two groups of children at age two.

These children are now being followed up at six to eight years of age. The 300 New Zealand children in the study were assessed by paediatrician and neonatal paediatrics trainee Dr Chris McKinlay. The Australian children are also being re-assessed, but Dr McKinlay's study, which he is carrying out for his PhD at the Liggins Institute, is more comprehensive, including extra measurements of hormone concentrations, blood pressure and body fat. The results are expected later this year.

The above studies were funded by the Health Research Council, the Auckland Medical Research Fund, Lottery Health and the National Health and Medical Research Council of Australia.



Generations of researchers, from left: Dr Stuart Dalziel, Dr Ross Howie, Professor Jane Harding and Sir Graham Liggins in 2002.

Cosmopolitan science

Accents and languages from around the world are resonating through the offices and laboratories of the Liggins Institute as budding scientists from all corners of the globe recognise it as a desirable place to be.

The Institute's international reputation continues to grow, and has currently attracted more than 30 PhD students and scientists in the early part of their career. They come from Canada, the United States of America, the United Kingdom, Ireland, Croatia and other parts of Europe, Israel, Singapore, Sweden, China, Korea, India, Oman, Mexico and Brazil.

Some are clinicians branching out into research, while others are biomedical researchers with science backgrounds. A common thread is their desire to learn from the Liggins Institute's expertise in the way early life events can contribute to health and disease in adulthood.

The young researchers are often a conduit for collaborations between the Institute and other Universities and research institutions.

One such collaboration has drawn together scientists from New Zealand, France, Sweden and India who are examining how babies born after prolonged pregnancies fare in later life.

Babies born after more than 42 weeks of gestation have generally been subjected to poor nutrition towards the end of their gestation, because the placenta gradually loses its ability to deliver adequate amounts of nutrients.

To see how these babies are affected, French paediatrician Dr Jacques Beltrand analysed data from 525 Swedish children born after 42 weeks.

During a postdoctoral fellowship at the Liggins Institute, which he completed last year, he used mathematical modelling, in collaboration with AgResearch scientists, to discover a clear increase in body weight in teenage boys born post-term.

"Astoundingly, we found that boys – not girls – who were born post-term are almost three times as likely to be overweight at age 16 compared to children who were born at the normal time," says Liggins Director Professor Wayne Cutfield who supervised the study. "Almost half of the teenage boys were overweight or obese."

The baton has now been handed to Dr Ahila Ayyavoo, a paediatric endocrinologist from India.

For her PhD, Dr Ayyavoo is testing New Zealand children born post-term and comparing them to children born at the normal time. "The Swedish children had their height and weight measured, and now I am looking for any deeper physiological changes – their blood pressure, the way they metabolise glucose and their body composition."

Dr Ayyavoo will also look for any differences in children born to mothers with severe nausea and vomiting during pregnancy.

"Whereas post-term babies have compromised nutrition at the end of their gestation, nausea and vomiting theoretically reduce nutrition early in gestation – and nobody's ever looked at the long term effects of that before," she says.



Dr Jacques Beltrand assesses body composition scans.

It was the attitude of Dr Ayyavoo's Liggins Institute supervisors that attracted her to the Institute, she says. "Professor Wayne Cutfield and Associate Professor Paul Hofman have extensive expertise, but what struck me most when I met them at a conference was the caring way they guide upcoming researchers."

Dr Ayyavoo has won a grant from pharmaceutical company Eli Lilly, and she is seeking further funding.

Young achiever award recognises Liggins student

Liggins Institute PhD student wins achievement award.



Jian Kiang

Liggins Institute PhD student Jian Kiang has become the first recipient of the Merck Young Achiever Award.

The award, worth \$6000 and sponsored by specialist chemicals company Merck Ltd, was established to recognise excellence in research presentation by emerging scientists at The University of Auckland.

It was open to graduate students and post doctoral research fellows who had a paper published or accepted for publication in a well reputed, peer reviewed international journal during the last 12 months.

Jian, who recently submitted her thesis, won the award for her paper published in the prestigious cancer research journal *Oncogene*. It describes the role of artemin (a protein that is involved in the growth and development of

brain cells) in making breast cancer cells resistant to endocrine therapy that uses anti-estrogenic drugs such as tamoxifen.

Scientists in the Liggins Breast Cancer Research Group were the first to demonstrate an association between artemin secretion and poor clinical outcomes in breast cancer patients.

The paper's other authors include Jian's PhD supervisor Dr Jo Perry and co-supervisors Professor Peter Lobie and Dr Dongxu Liu.

Jian has recently taken up a position as a research officer in the Cancer Research programme at the Garvan Institute of Medical Research in Sydney, Australia.

Research Day – showcasing student achievement

An annual event helps young researchers learn presentation skills and provides fascinating snapshots of research at the Institute.

In August The Liggins Institute held its second annual Research Day for trainees. The late Professor Sir Graham (Mont) Liggins presented the prizes at the inaugural event in 2009; sadly it was the last time that his failing health allowed him to visit the Institute. Mont attached great importance to encouraging young researchers, and over the course of his career supervised many PhD and Masters students.

The day provides an opportunity for research students to present a snapshot of their work to peers, Institute staff and a panel of expert judges.

“The Liggins Research Day is designed to help our young scientists develop the presentation skills required for international careers in biomedical research,” says Dr Mhoya Fraser, the Institute’s Academic Director who spearheaded the event.

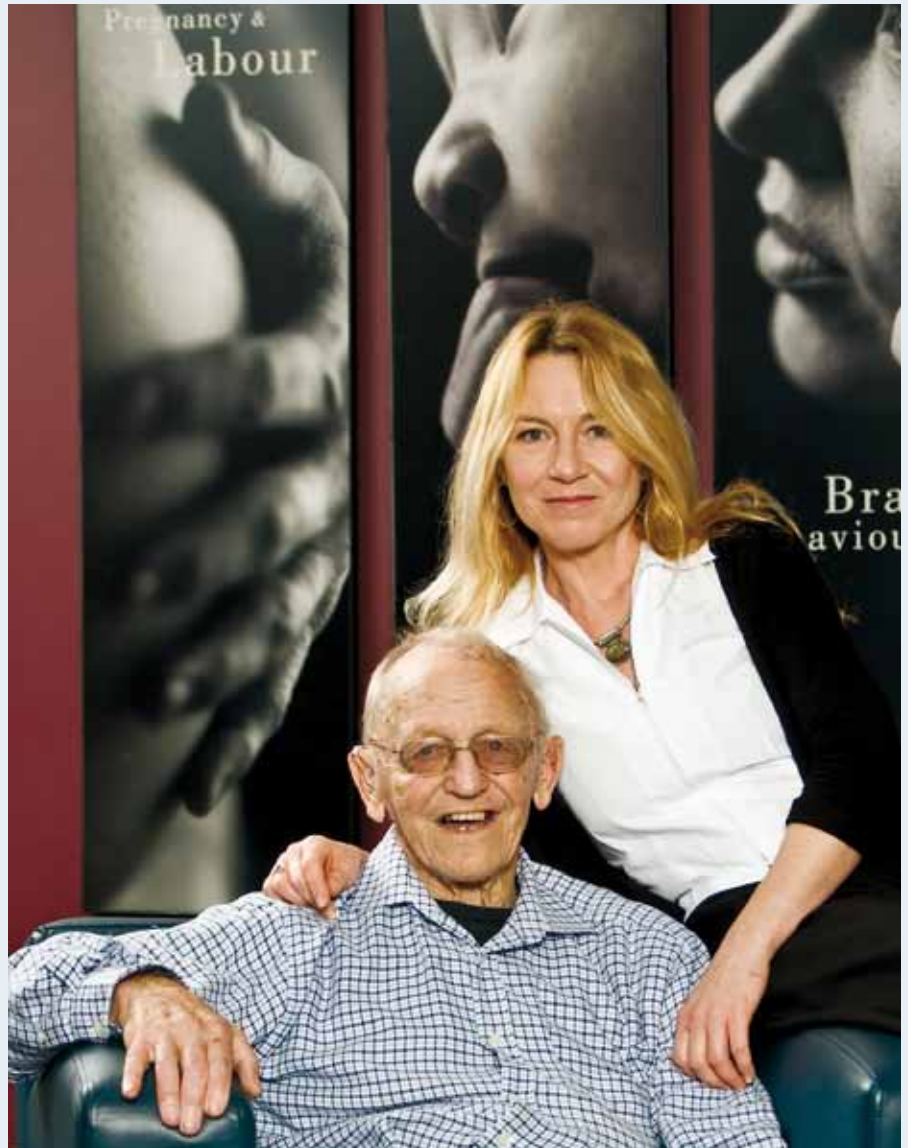
Last year, 34 students presented their work, either in oral or poster format. The group included nine Year 13 students from Auckland secondary schools who were participating in the LENSscience Junior Scientist Award programme (see page 10 for more).

The Liggins-based postgraduate students presented topics spanning the full range of clinical and biomedical research at the Institute.

Some students are already qualified and practising in clinical medicine. Attracted by the Institute’s focus on translating discoveries in basic science into clinical applications, they aim to improve their practice by taking time out to investigate a related topic in depth.

As an example, paediatrician Dr Martin de Bock presented his investigation into how increasing the amount of fibre teenage boys eat affects the action of their glucose-regulating hormone insulin. His subjects, from Auckland’s Onehunga High School and Tamaki College, are volunteers from a group of students within both schools whose science learning last year was linked to the work of the Institute’s Diabetes Research Group.

Students with science backgrounds outlined projects ranging from investigations of gene activity in isolated cells through to developmental programming in physiological models. Masters student Angelica Bernal won



The Liggins Institute Academic Director Dr Mhoya Fraser with her former PhD supervisor Emeritus Professor Sir Graham Liggins at the inaugural Liggins Research Day.

the graduate student section, presenting evidence that poor fetal and neonatal nutrition might affect later reproductive capacity (see page 9). In the PhD section, Luke Weaver-Mikaere won joint first place with his presentation on how infection of the placental and fetal membranes triggers the release of chemicals that can damage the fetal brain.

First place also went to PhD student Deborah Harris, a nurse practitioner in the neonatal intensive care unit at Waikato Hospital. Deborah is evaluating methods that could

reliably detect episodes in which newborn babies’ blood glucose reaches dangerously low concentrations likely to cause brain damage (see page 8 for more).

“Research Day celebrates the achievements and determination of our young trainees,” says Dr Fraser. “It helps enhance the international reputation of the Liggins Institute, and continuation of this event will enable it to grow further.”

Sweet success

Prize winning presentation carries warning about effect of fructose on fetal development.

Master of Science student Cassandra Yap won an award for her presentation at last year's Liggins Institute Research Day on how fructose intake affects developing fetuses.

She is doing the research with fellow student Zöe Clayton under the supervision of Research Fellows Drs Deborah Sloboda and Mark Vickers, who have a particular interest in how maternal nutrition affects the health and well-being of offspring.

Cassandra and Zöe became interested in the topic during lectures given by Dr Vickers to Postgraduate Diploma in Science students. Then, as summer students working with the Liggins team, they learned the techniques they needed for their Masters' research, where they are investigating how increased fructose in a pregnant mother's diet affects development before and after birth.

Fructose was chosen because it has been blamed as a major contributor to the obesity epidemic. Fructose occurs in honey, fruit and some vegetables, but it is widely used as a sweetener in processed foods and soft drinks, resulting in a massive increase in its consumption that is raising concern.

For example, people now drink five times more sweetened beverages than 50 years ago, and these beverages are now the leading source of

added sugars in the diet. OECD data ranks our soft drink consumption as ninth in the developed world, and places us third for obesity, with more than a quarter of the population obese.

"Despite our current high sugar intake, nobody has previously looked specifically at how fructose added to the diets of pregnant mothers affects the growth and development of the placenta, fetus and newborn," says Dr Vickers.

The researchers added fructose to pregnant rats' drinking water in amounts equivalent to human mothers consuming two cans of soft drink per day. While they saw no change in maternal weight or body composition (compared with rats fed a normal diet), mothers had impaired sensitivity to insulin – a key problem in type 2 diabetes. There were also marked differences in the development of their offspring – but only the females.

The placentas supplying nutrients to female fetuses were significantly smaller than those of males, even though there were no observed weight differences between the fetuses or newborns. In addition, the metabolism of the female fetuses appeared less able to keep pace with the increased amount of fructose they were receiving from their mothers.

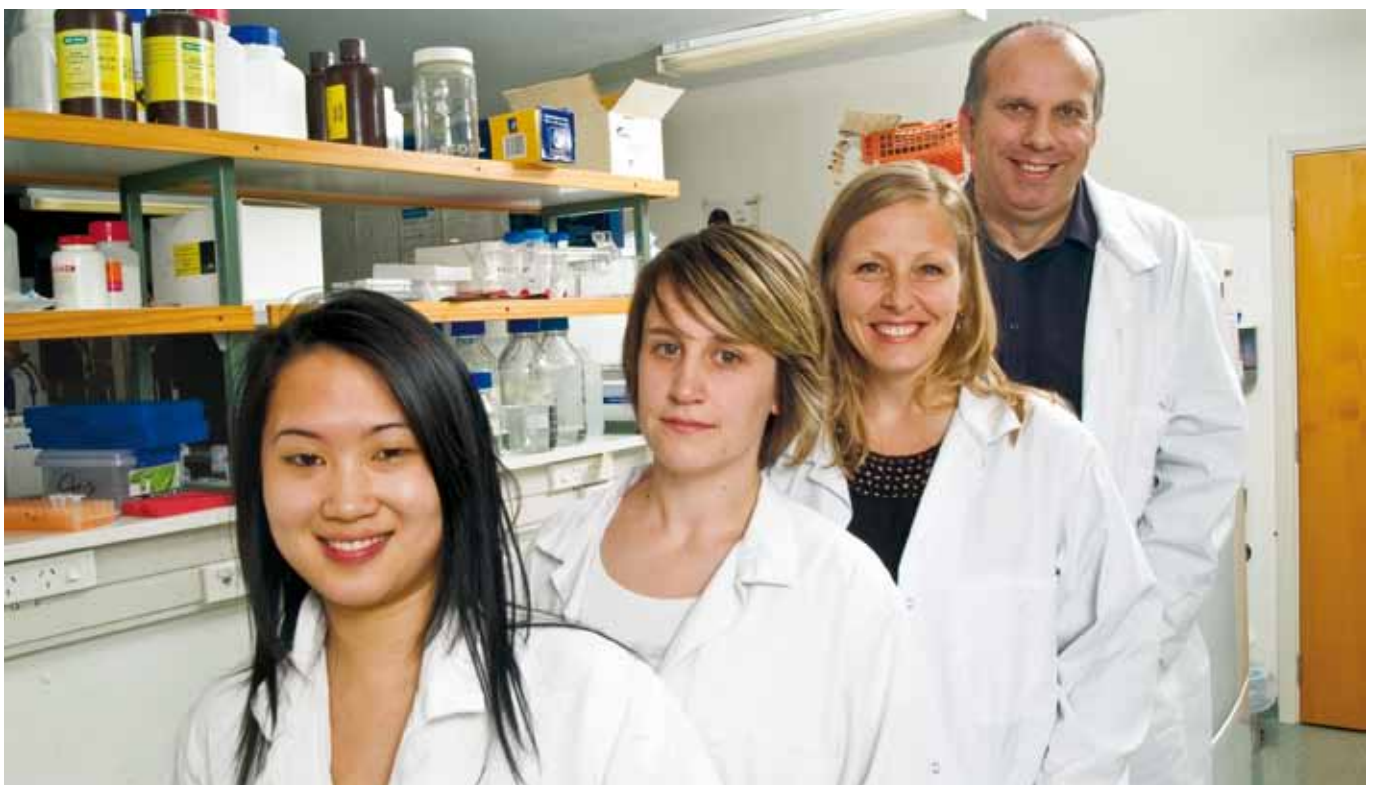
Dr Vickers notes that these results are quite different from when rats had high fat diets during pregnancy. "The mothers on the high fat diets put on noticeable amounts of weight, and placental weight was reduced for both sexes.

"The results demonstrate a very fine balance between maternal nutrition and fetal development. While the mothers in our fructose study showed no outward sign of their higher sugar intake in terms of body weight, the development of their female offspring was clearly compromised."

Cassandra is currently investigating the mechanisms that mediate the sex-specific effects that fructose has on placental development, while Zöe looks at how it affects the activity and regulation of the liver's metabolic enzymes.

The team is also planning follow-up studies to see if increased fructose has long term consequences for the offspring's health, and whether it affects a second generation.

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



The research team, from left: Cassandra Yap, Zöe Clayton, Dr Deborah Sloboda and Dr Mark Vickers.

Student publication highlighted

A paper by a Liggins Institute PhD student earned editorial comment.



Deborah Harris

A research paper by PhD student Deborah Harris and her supervisors was singled out for editorial comment when it was published in the *Journal of Pediatrics* last year. The paper

describes a method she has been trialling in the neonatal intensive care unit at Waikato Hospital to monitor glucose concentrations in newborn babies.

Deborah, a nurse practitioner, says that babies' blood glucose concentrations tend to fluctuate as they adapt to life outside the womb. Babies who are born preterm or to diabetic mothers, and those who are small or large for their gestational age, frequently suffer periods of hypoglycaemia (low blood glucose), which increases their risk of brain damage.

Glucose concentrations are routinely measured in blood samples obtained by intermittent 'heel pricks'. This makes it difficult to know exactly when and for how long the concentrations fall to potentially dangerous levels.

The paper reports her trial of a device which uses a sensor inserted under the baby's skin to provide continuous measurements of glucose around the cells. It showed that this method was convenient, accurate and reliable and picked up many more episodes of low glucose concentrations than intermittent blood sampling.

However, the authors cautioned that further research is needed before they can predict how long and how severe hypoglycaemia needs to be to cause brain damage in any particular baby, and that there is danger of treating babies unnecessarily.

This concern was reiterated by the journal's editors, who also noted that it should be balanced against the fact that the technology has the potential to detect a number of serious neonatal disorders.

Deborah and her PhD supervisor and co-author Professor Jane Harding are members of the steering group for a large study aimed at discovering which aspects of hypoglycaemia lead to brain damage. The CHYLD (Children with Hypoglycaemia and their Later Development) study will examine a group of two year old children who had continuous glucose monitoring in the first few days after birth. Researchers will assess the children's mental and physical development, memory, vision and general health and relate these outcomes to episodes of hypoglycaemia they may have experienced as newborns.

IVF and the beginning of life

In vitro fertilisation research puts spotlight on earliest development.



Dr Mark Green and colleague Dr Sarah Hopkins with a poster describing their research group's findings.

Many Liggins Institute scientists are driven to discover more about how very early stages of life affect long term health. In collaboration with Fertility Associates Ltd, the focus of interest has become earlier than ever.

The researchers are comparing children implanted in their mothers' wombs via IVF with naturally conceived children, and finding intriguing differences.

Led by Liggins Institute Director Professor Wayne Cutfield, the team showed that IVF-conceived children are taller, slimmer and have healthier blood lipid profiles than naturally conceived children.

"We are unsure of the cause, but suspect that the difference is related to the drugs used to stimulate the ovary in IVF and their indirect effects on the uterus," says Professor Cutfield.

With their interest aroused by the significance of the effect, the researchers launched another study to include a comparison of children implanted as fresh embryos with those implanted as previously frozen embryos.

It is the first study ever to separate and

investigate the impact of whether the embryo was fresh or thawed.

The researchers looked at the children's birth weight, height, hormones associated with growth, and blood lipids (which can indicate potential heart disease).

"We were particularly interested to find subtle differences between the children in the two IVF groups at six years of age," notes Liggins reproductive physiologist Dr Mark Green.

However, the investigators emphasise that their data represent only one time point in the children's development. Longer term follow-up studies are needed before they can draw conclusions about whether different environments at the time of conception impact adult health.

Sir William Liley: Following up fetal transfusion

Recipients of a life-saving blood transfusion are being sought.

In another pioneering baby treatment follow-up, researchers are looking for people who received a blood transfusion before birth to treat anaemia caused by rhesus disease. They want to check whether having anaemia as a fetus alters heart development.

Nearly 50 years ago, Sir William Liley developed the transfusion technique to stop babies dying or being born disabled as a result of rhesus haemolytic disease. This is caused by an incompatibility between mothers' and babies' blood types that destroys the babies' red blood cells, forcing their hearts to work harder.

Liley, working from the Postgraduate School of Obstetrics and Gynaecology at Auckland's National Women's Hospital, transfused the fetus through the mother's abdominal wall

with healthy red blood cells matching the mother's blood type. He first performed the procedure successfully in 1963, launching its use internationally.

"It was a major achievement that saved the lives of countless babies around the world," says Dr Alexandra Wallace, a paediatrician who is conducting the research for her PhD at the Liggins Institute.

"The study is being carried out because there are hints that early anaemia can change the development of the arteries that supply blood to the heart, but this needs to be checked in humans," she says.

She believes that information from the study may help babies in the future by indicating the

level of anaemia at which they should be transfused. This includes unborn babies and, more commonly, premature newborns who become anaemic.

Fetal transfusion is less common today because anaemia is usually prevented by giving at-risk pregnant women antibody injections.

The research team led by Professor Jane Harding would like to make contact with anyone who received blood transfusions before birth for fetal anaemia. Please contact Dr Wallace on 0800 500 194 or email fetalanaemiastudy@auckland.ac.nz.

The research is funded by the Health Research Council of New Zealand and the New Zealand Lottery Grant Board.

Mont Liggins was a contemporary of Liley and assisted him in developing the transfusion technique. Mont followed Liley's lead in his research career: "Bill had told me that he had decided on his line of research by looking for an important obstetric disorder which had the potential to be prevented and came up with haemolytic disease. I took up his philosophy and came up with premature birth..." he wrote in an autobiography.

A good year

2010 brought a number of memorable 'firsts' for high achieving Liggins Institute graduate Angelica Bernal.

The 24 year old student, who moved to New Zealand from The Philippines eight years ago, graduated from The University of Auckland with a Master of Science degree, with First Class Honours in Biomedical Science. Her research project, which investigated how maternal undernutrition affects female offspring's later reproductive capacity, was supervised by Dr Deborah Sloboda with co-supervision by Dr Mark Vickers and University of Otago researcher Dr Mark Hampton.

She was awarded first place in her section when she presented her findings at the Liggins Research Day in August.

"After meeting Deb Sloboda and learning about her research work, I was immediately fascinated that a baby's environment before

birth determines its life-long health," she says. "I knew the Liggins Institute would provide an excellent research base for exploring this area of science and was keen to be a part of it."

As well as her research at the Institute, Angelica spent part of her time in Christchurch with the University of Otago's Free Radical Research Group learning techniques to assess whether the changes she had observed in the ovaries of adult rat offspring (following maternal undernutrition) were caused by increased oxidative stress.

Her paper describing the results of her study has been accepted for publication in the on-line journal *PLoS ONE*. She will also have the opportunity to learn more about the long term effects of the early life environment when



Angelica Bernal

she takes up a position as a research technician at the Liggins Institute in January.

Science education explodes with achievement

Extraordinary accomplishments in bringing schools and scientists together have been made by the Liggins Institute's LENSscience programme.

Stretching learning around New Zealand

LENScience Director Jacquie Bay has harnessed information communication technologies to create a special kind of learning event called LenScience Connect. Collaborating with the University's Information Technologies Services (ITS) division and broadcast telecommunications company Kordia, she led the development of this innovative method to create learning environments for students and teachers nationwide.

The venture began in 2008 when three trial seminars by Ms Bay and Liggins Institute scientists were broadcast live via satellite TV and high speed broadband to senior biology students at five high schools. The seminars were supported by Web2.0 tools (wiki and live chat), enabling interactivity before, during and after the seminars.

In 2009 the programme was expanded to eight seminars and broadcast to more than 1000 students nationally. It won the Telecommunications Users Association of New Zealand award for innovation in education.

The current programme includes professional development for biology teachers and seminars to expand younger students' scientific horizons.

In November, the technology was used outside science. The University's Faculty of Education used the LENSscience Connect platform to broadcast a professional development seminar on literacy to teachers at 450 schools.

Ms Bay attributes the programme's success to LENSscience's collaboration with ITS, Kordia and production company VoltTV.

"Their support and belief in us has been amazing," says Ms Bay. "The ITS team led by Robert Hamilton has put hundreds of hours into the project, while Kordia has contributed significant support and resources including the satellite time required for these seminars to reach schools that do not have high speed internet connections."

ITS Enterprise Architecture Manager Tim Chaffe is delighted to see the concept adopted by other University departments. "We have

worked to simplify the technology to create a proven and portable platform that can be used in wider applications. We are now developing a studio facility that can be used by faculties and groups across the University to broadcast similar learning events."

LENSscience Connect is currently funded by the National Research Centre for Growth and Development.

Eager school scientists blossom

Over the past two years, groups of high school students with a strong interest in science have been extended by the LENSscience Junior Scientist Award.

Linking directly to the school science curriculum, the Junior Scientist Award programme provides challenges extending beyond the Year 13 level. Participating students, either from the science fair entry scheme or the Māori and Pacific entry stream, have demonstrated the potential for successful careers in science.

The programme opens students' eyes to science's possibilities, explains LENSscience senior educator Helen Mora. "Importantly, students who come from less academically focused backgrounds now realise they have a place in the University and realistic prospects of careers in science.

"They also gain valuable skills in goal setting and critical analysis that will stand them in good stead as they move into tertiary education and beyond," she says.

The first group of nine students graduated from the demanding programme last year. They completed an original, in-depth scientific research project, communicated their research results to a range of audiences, contributed 20 hours of science-linked community service and attended events where scientists were presenting their work.

Their final task was to defend their research findings before a panel of scientists and educators.

The students were assigned scientific mentors and received on-going teaching and support from LENSscience educators. Their research topics ranged from the effects of plastic contaminants on genes in the placenta to environmental effects on seaweed distribution in the Manukau Harbour.

All the graduating students will begin University studies next year, with some assisted by prestigious scholarships.

"The students won three of the 20 places at the Royal Society of New Zealand's 'Realise the Dream' event for high achieving students," explains Jacquie Bay. "In addition, five of the nine have had major conference opportunities based on the quality of their research.

"What Helen has achieved with these students is quite incredible," says Ms Bay of her colleague.



Junior scientists at work.

LENSscience Director Jacquie Bay was last year awarded the prestigious Peter Spratt Medal by the New Zealand Association of Science Educators. The award recognises sustained and innovative contributions to science education at a national and regional level.

Working it out

Research into the exercise capacity of teenage diabetics yields novel outcomes.

When exercise physiologist Silmara Gusso needed to examine the hearts of diabetic teenagers during a workout, a normal exercise bicycle was of no use. Silmara wanted to assess her subjects using a magnetic resonance imaging (MRI) scanner, which is incompatible with ferromagnetic metal and requires patients to lie down.

Seeking to develop a specially designed bike for use in the MRI scanner, she and Associate Professor Paul Hofman turned to the Auckland Bioengineering Institute at The University of Auckland.

The result was a fruitful collaboration involving the creative and technical ability of engineers and their students. Project leaders Associate Professor Poul Nielsen and Dr Andrew Taberner saw it as an opportunity to create a custom ergometer that was cheaper and better than the commercial models.

"It was an interesting new problem to tackle: we had to overcome the way the MRI scanner's magnetic field and radio frequency interfere with some key electronics," says Dr Nielsen.

The electronics measured how hard the patients were working, and allowed Silmara to

instruct them to change the effort required.

The engineering pair hold honorary appointments at the Liggins Institute and have collaborated on several bioinstrumentation projects.

Silmara was carrying out the research for her PhD, supervised by Dr Hofman and Professor Wayne Cutfield of the Liggins Institute.

In a study that was the first of its kind in the world, she examined how type 1 diabetic teenagers' hearts respond to exercise training. She drove all over Auckland for two years to supervise 75 teenagers' gym workouts, and exercised them in an MRI scanner before and after five months of training.

"We knew that diabetic teenagers have impaired exercise capacity due to their cardiovascular systems being affected by the disease. But nobody had previously established the details of this impairment and MRI is absolutely the best way to discover such things," she explains.

"We showed that, with training, diabetics do have the capacity to improve their cardiovascular function and minimise their impairments. Their improvement wasn't as

large as the non-diabetics in our study, but their quality of life was better."

One boy told her how he hated always being the last one in running at school. After his training he was delighted to be "in the front pack of guys in my PE class". The teenagers' parents also commented on their children's improvement in glucose control and mood.

The MRI Silmara used is at the Faculty of Medical and Health Sciences, where other scientists are now using the bicycle to learn more about how the heart changes during exercise. The engineers are working on an improved version which could potentially be commercialised in the future.

Silmara came to the Liggins Institute from The University of Auckland's Department of Sport and Exercise Science at the Tamaki Campus. Previously she was a physical education teacher in Brazil, her home country.

Her research was funded by the National Heart Foundation, the Maurice and Phyllis Paykel Trust and the Australian Paediatric Endocrinology Group.



Silmara Gusso supervises one of her research subjects exercising on a custom-designed exercise bicycle.



Friends of the **LIGGINS** INSTITUTE Charitable Trust

News for and about our supporters

Although 2010 disappeared fast, it was a good one for the Friends of the Liggins Trust and we are looking forward to 2011.

During the year a number of new members joined our Liggins Community Group, headed by Cecilia Lambie. All with young children, they appreciate the relevance of the Liggins Institute's research to their lives and those of their children.

Building on their own successful careers, they brought their creativity and organising skills to their first project, the second Couture Car Boot Sale at Team MacMillan BMW in September. The evening had a real buzz as more than 350 guests shopped for designer clothes at bargain prices - all generously gifted by designers, stores, manufactures and other Liggins supporters. The Group is already planning this year's event.

The Liggins Community Group, which is based mainly in Auckland's Eastern suburbs, would welcome new members keen to be involved in events and activities supporting and promoting

the work of the Liggins Institute. Alternatively, you may feel inspired by the exciting challenge of beginning a Group in your own community. If either of these possibilities appeals to you, then please do not hesitate to get in touch with me or the Liggins' Advancement Manager Graeme Woodside, using the contact details on this page.

Annual appeal

Our second annual appeal to Friends and supporters is currently underway. The generous response to the 2009 appeal enabled us to provide seed funding for two innovative research projects. One project is exploring links between early life nutrition and breast cancer, while the second is investigating a novel way to prevent childhood obesity.

In addition, we are supporting upcoming young researchers through a summer studentship and a postdoctoral fellowship. We hope to fund further projects from the proceeds of this appeal.



Image by Photographers Inc

Lyndy Sainsbury - Chair of the Friends of the Liggins Institute Charitable Trust Board.

If you have not been contacted and would like to contribute to our appeal, please use the coupon inside the back cover of this issue of *Dialogue*.

We appreciate your support

Our Trustees join me in thanking all our Friends for their interest in and support of the work of the Liggins Institute during 2010. With a successful signature event and an increasing team of supporters and donors, the Trust has a growing capacity to fund research that in time will result in new knowledge and solutions for challenging medical questions.

Best wishes,

Lyndy Sainsbury

Friends of the Liggins Institute Charitable Trust

An independent charitable trust was formed in 2004 by a group of people enthusiastic about supporting the Institute's work.

Trustees

Professor Sir Peter Gluckman
Kaaren Goodall
Professor Alastair MacCormick
Lyndy Sainsbury (Chair)
Harry White

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Friends of the Liggins Institute Charitable Trust Board has been registered by the Charities Commission (registration number CC26321) and donations are eligible for tax deductions.

Disclosure

The Liggins Institute is committed to maximising the benefit of its research for New Zealand and, where appropriate, seeing its research translated into effective therapies. Accordingly, in some areas it has licensed its intellectual property to the pharmaceutical industry or to start-up companies associated with the Institute. The terms of these arrangements provide funds which can be committed to public good (ie non-commercial and cutting-edge) research within the University. In accordance with University policy and international practice in developing start-up companies, some staff will, or could, personally benefit from interest in these start-up initiatives. The University and, therefore, the Institute have taken this approach with the aim over time of increasing the capacity of the University and the Institute to undertake novel and leading-edge fundamental research. Most of the research within the Institute is, and will always be, of this nature and can never attract commercial investment. The University and Institute are mindful of the need to ensure that donated funds are applied only to the public good research components of the Institute's activities and cannot be applied (unless requested by the donor) to projects where commercial arrangements have been entered into. Specific procedures have been developed to ensure this, and potential donors are invited to contact the Institute's Advancement Manager or the University Registrar for further information.

A continuing partnership

Commitment to excellence is at the heart of an evolving relationship.

Since 2004 *Dialogue* has included on its back cover the caption “a partnership of excellence”. The words refer to the very special partnership between the Liggins Institute and Team McMillan BMW and MINI. The relationship between the two organisations has grown and developed in many ways, exemplifying the commitment that each partner has to recognising and promoting the highest levels of achievement, professionalism and leadership in their respective fields.

Since that time Team McMillan has generously funded *Dialogue*'s production costs. “We are very proud of *Dialogue*,” says Liggins Institute Director Professor Wayne Cutfield. “Each issue consistently brings positive feedback from readers throughout New Zealand and overseas. I am sure that this reflects not only the content but the high production values that we are able to maintain thanks to the support of Team McMillan.”

One of the Institute's most successful fundraising events, the 2007 Celebrating Creative Connections dinner and charity auction held at the Auckland Museum, was the result of Team McMillan's generosity. They donated the Art Bonnets from their BMW Art Awards to the Institute for auction at the spectacular event which raised more than \$70,000 to benefit Liggins research and education programmes.

In 2009 the former Chair of the Friends of Liggins Community Group, Roxane Horton, brought a new concept to the Auckland charity scene: the unique and now 'trademark'

TEAM MCMILLAN AND THE LIGGINS INSTITUTE

A partnership of excellence

Team McMillan BMW and MINI support the Liggins Institute's quest for a healthy start to life. They fund the production costs of this newsletter, and will donate \$500 to the Institute every time a friend or associate of the Institute purchases a new or approved used BMW or MINI; please mention *Dialogue* at the time of purchase.

Liggins Couture Car Boot Sale. She and her team immediately saw Team McMillan's sophisticated new car show room as the perfect setting for the event. The result was a car boot sale with a difference. Hundreds of pieces of exquisite New Zealand and international designer clothing sourced from the wardrobes of Auckland's most stylish women were displayed amongst luxury cars for fashionable shoppers to seek out bargains – while feasting on canapés and French champagne.

So successful was the evening that the incoming committee immediately started planning a reprise for 2010. Months of work by the Community Group led by Cecilia Lambie went into acquiring sponsors, selling tickets and assembling many hundreds of new and pre-loved fashion garments and accessories.

The resulting fashion frenzy far exceeded the Group's expectations and raised more than \$32,000, which the Friends of the Liggins Institute Charitable Trust will donate to the Institute as seed funding for innovative new research projects led by talented

young researchers.

“We are really grateful to our many sponsors and supporters who provided garments to sell and hospitality to enjoy, not to mention everyone who bought clothes and accessories on sale,” says Cecilia.

The Group extends sincere thanks to everyone who supported their cause and contributed to the event's success, especially the major sponsors: Team McMillan BMW, Nicholas Feuillatte Champagne, Wither Hills Wines, Regal Drycleaners, Elizabeth Arden Prevage, and ViaductNZ EFTPOS.

“We are delighted to support the Friends of Liggins event,” said Team McMillan BMW and MINI Director, Bob McMillan. “It is a natural fit exemplifying our commitment to supporting excellence in design and research which, together with innovation and professionalism, are core values of the Liggins Institute and Team McMillan.”



Bargain hunting at the 2010 Liggins Couture Car Boot Sale in Team McMillan BMW's showroom.

The Director comments

Despite the excellent and innovative research produced by the Liggins Institute, research funding is increasingly hard to secure. We need to become more entrepreneurial in order to survive and grow.

The problem comes partly from our field of expertise: OECD figures show that biomedical research is the most competitive field in which to obtain funding, and this trend is increasing.

The other challenge is our location. In New Zealand, funding success has fallen to less than 10% of applications. Competition amongst researchers far outstrips the modest annual budget increases to research organisations.

Our public good research funding agencies acknowledge that they are able to fund only a portion of high quality fundable research. Several of these agencies have revised their funding priorities, reducing the pool of funding available for this country's biomedical research.

We cannot, therefore, assume that the Liggins Institute's increasingly innovative grant applications will lead to a major increase in our research funding.

Our approach to these challenges is creative. We are sending greater numbers of our grant applications to funding agencies in the USA, Europe and Australia. International collaborations are being strengthened, enabling us to access a broader range of funding.

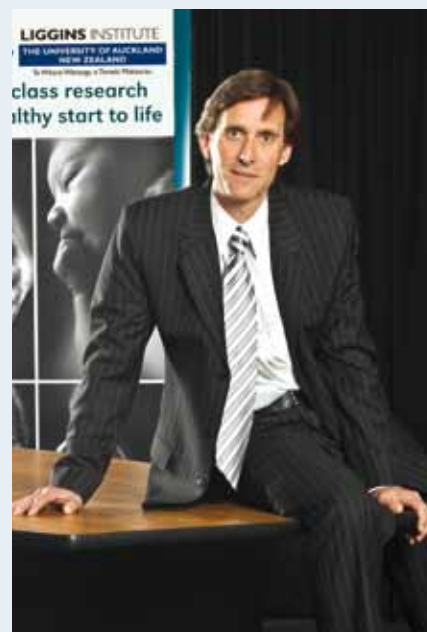
In addition, we are well-placed to benefit from this year's Government Budget incentives for businesses to invest in research and development. The incentives include new technology grants and transfer vouchers.

Although the transfer voucher budget of \$20 million over four years is modest, my impression is that many New Zealand companies in the nutrition field are thinking harder about the role of research institutions in their growth and development.

One reason for this is that New Zealanders are becoming more critical and discerning of the purported health benefits of nutritional products. To successfully grow, these companies need scientific evidence showing that health benefits are real, and to demonstrate the mechanisms through which they occur.

The Liggins Institute's expertise in nutrition during pregnancy and early life and in clinical trials places us in an ideal position to engage with local industry-funded research. Already we have a number of local and international nutrition research contracts being developed with nutrition industry partners, and we expect these opportunities to increase markedly.

Despite the constrained public good research funding environment, I believe these new initiatives will enable the Liggins Institute to grow research activities over the next five years.



*Professor Wayne Cutfield,
Director of the Liggins Institute.*

Professor Wayne Cutfield

From laboratory to hospital

Translating discoveries into clinical practice is a rigorous process.

Within five years of Mont Liggins discovering that cortisol helps prepare fetal lungs for life after birth, the treatment was helping preterm babies breathe, thus saving lives.

Rapid translation of basic science into clinical practice is a major theme of the Liggins Institute. What needs to be done to achieve this?

The process is now longer and tougher than in Mont's heyday because tests for safety and effectiveness have become more rigorous. The medical tragedy of thalidomide was an impetus for such rigour.

When it comes to developing new drugs, the process may take more than a decade, cost

millions of dollars and have a tiny chance of success.

Each potential drug must be tested in animals for effectiveness and safety. It is then tested in a small number of healthy people, then in patients with the disease that the drug aims to treat, and then finally in a large clinical trial. At each phase, many drugs fail to meet the required standards.

For new management procedures – such as ventilation techniques in newborns, for example – or using an existing medication for a new treatment, the barriers are lower. Firstly a small pilot trial is often performed to check for safety and as a marker of effectiveness. A

clinical trial follows, preferably in a number of different centres or hospitals (see 'Superb design, slow acceptance' on page 15 for more on what makes a clinical trial convincing).

These tests are approved and overseen by committees. Clinical trial results are checked as the trials proceed, and trials can be stopped if the effect is overwhelmingly positive, negative or absent.

The high standard of evidence required for new treatments and procedures is central to the modern goal of evidence-based medicine. In the past, the opinion of experienced physicians strongly influenced the treatment used, but today more substantial proof is required.

I would like to support research projects at the Liggins Institute.

Please enrol me as a Friend of the Liggins Institute:

- Supporter (up to \$75) Friend (\$75+) Benefactor (\$250+) Patron, or Trust or Corporate Partner (\$5000+)

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Email friends@liggins.auckland.ac.nz

Thank you for supporting the Liggins Institute.

Friends of the Liggins Institute Charitable Trust Board has been registered by the Charities Commission (registration number CC26321) and donations are eligible for tax deductions.

When the time is right, after you have provided for your family and friends, you might consider making a gift (sometimes called a legacy or bequest) to the Liggins Institute in your will. Please tick here if you would like further information about this option

If you no longer wish to receive information about the Liggins Institute please tick here

Superb design, slow acceptance

Designing a first-rate trial was one matter, but convincing clinicians quite another.

When Mont Liggins and Ross Howie came to test the effect of steroids on human babies, they knew that their study needed certain characteristics if the results were to be objective and credible.

It had to be controlled, meaning that half the women were injected with the steroid betamethasone, and half given an identical-looking control, or placebo. It also had to be randomised, so that whether a woman received the real treatment or the placebo was determined at random. In addition, it needed to be double blind, so neither the patients nor the medical staff looking after them knew who received the treatment and who the placebo. Finally, it had to include many participants to maximise the chances of finding even a small benefit if it did exist.

They did their job well. They recruited 1142 women to their superbly designed randomised controlled clinical trial, which is recognised as

the best way to provide evidence on a treatment's effectiveness.

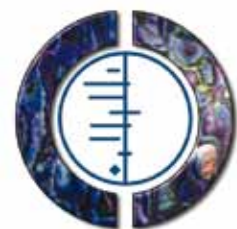
The resulting paper was rejected by the prestigious journal *The Lancet* on the grounds that it lacked general interest. But it caused a storm of excitement when *Pediatrics* published it in 1972, and remains one of that journal's most cited papers.

In spite of the impeccable study design, the treatment's impressive halving of the death rate and the replication of results in other centres, it was more than 20 years before the treatment was routinely implemented outside New Zealand and Australia.

Many premature babies certainly died due to the delay, which Mont Liggins and Ross Howie believed was partly due to a belief that "nothing good could come from the colonies".

The human cost of ignoring such robust evidence was one of the driving forces behind

the establishment of the esteemed Cochrane Collaboration, which promotes the use of evidence-based medicine by combining clinical trial results into a form which is easy to interpret for clinical use. The significance of the Liggins and Howie trial is such that the Collaboration uses as its logo a graph of results from early trials of antenatal steroids to prevent preterm death.



The logo of the Cochrane Collaboration. The lines represent seven studies of antenatal steroids to prevent preterm death. The small horizontal line at the top represents the Liggins and Howie trial - the largest and most influential of these trials.

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