



Dialogue



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 Postdoctoral Fellow
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Liggins researchers discover clue to breast cancer malignancy



Associate Professor Peter Lobie (right) and research fellow Dr Farhad Shafiei examine breast cancer cells using a fluorescence microscope.

Research led by an associate director of the Institute may save lives

Liggins Institute scientists have discovered a switch that makes breast cancer cells become invasive and therefore deadly. The finding may lead to new ways to stop the disease spreading and therefore reduce the number of women who die from it.

Breast cancer, one of the leading forms of cancer in women from western countries, becomes deadly when it metastasises, spreading from the breast to other organs

such as the brain, lung and liver. If it does not metastasise and remains as a tumour within the breast, it can be cured.

The new research suggests tumours metastasise in response to growth hormone produced in the breast.

Associate Professor Peter Lobie and his colleagues increased the amount of growth hormone produced by a breast cancer cell, and found that the previously non-invasive

cancer cells changed, becoming invasive.

These results suggest that blocking locally produced growth hormone may improve breast cancer prognoses. Liggins

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THE UNIVERSITY OF AUCKLAND
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 HEALTH SCIENCES

New Postdoctoral Fellow examines beginnings of life

A Maurice Paykel Postdoctoral Fellow will spend the term of his fellowship at the Liggins Institute



Maurice Paykel Postdoctoral Fellow Dr Mark Green is a reproductive biologist whose research focuses on the embryo during the first days after conception.

Dr Mark Green is an inaugural recipient of one of the two Maurice Paykel Postdoctoral Fellowships awarded at The University of Auckland. With its support he has embarked on two years at the Liggins Institute working with Professor Jane Harding on the relationship between maternal nutrition and early fetal development.

“This is a fantastic opportunity for me and hopefully I will be able to bring some skills that will add to the vast knowledge and expertise already at the Liggins,” says Dr Green. “I’m very pleased to be at the Liggins Institute – Professor Harding’s well known internationally in this area of research and I feel lucky to be able to work as part of her research team.”

The fellowship is intended for a developing researcher of the highest potential.

Dr Green is from the United Kingdom, and spent the last two years doing post-doctoral research on the influence of nutrition on sex ratio in cattle and sheep, as well as the regulation of bovine embryo growth and maternal recognition of pregnancy, at the University of Missouri in the United States. Whilst there he became an expert at in vitro fertilisation techniques for ruminants, and studied how glucose and dietary fat concentrations around the time of fertilisation affect embryos.

“Glucose concentrations are critical to

the development of embryos,” he says. “The optimal amount of glucose that they need varies during development and between different species. If cattle embryos are cultured with the same concentration of glucose as human embryos, their development can be hindered and many don’t survive.”

His research in Missouri led to some discoveries of how maternal nutrition can skew the sex ratio of offspring.

“The theory of nutritional influences on sex ratio is controversial. The relationship is apparent in many polygynous species such as deer but it is not as obvious in humans.

“Scientists from Missouri had previously shown that when glucose is too high in IVF cultures, more female than male embryos were lost. We then made a surprising discovery - that female embryos produce twice as much of the hormone that tells their mothers to maintain the pregnancy.”

“This helped us discover that the increased production by females of this hormone was to compensate for her susceptibility to high glucose concentrations. Compared to males, females are exposed to twice the level of glucose metabolism, as the genes involved in glucose metabolism are located on the X chromosome – females have two X chromosomes, and males only one.”

“This only happens for a few days, until one of the X chromosomes gets naturally

inactivated later in development.”

Dr Green’s background and skills in this area of reproductive biology are a valuable addition to Liggins research, says Professor Jane Harding, Deputy Director of the Institute.

“Our work has been focussed on how maternal nutrition around the time of conception can influence the way the fetus grows and develops in late gestation. Dr Green’s research experience in studying the embryo very early after conception will be enormously valuable and complementary to our existing research programme.”

During his time at the Liggins Institute Dr Green will examine how a mother’s nutrition around the time of conception affects the development of her embryo and influences its growth trajectory. This follows the finding by Liggins scientists that undernutrition around the time of conception can lead to premature birth and altered growth and development of the fetus.

He plans to do some collaborative work with the Liggins’ partners in the National Research Centre for Growth and Development (one of New Zealand’s seven centres of research excellence), particularly those at Massey University.

“One of the things I find most exciting about this research area is that it is not only important to human health, but it is also directly useful to agriculture.”

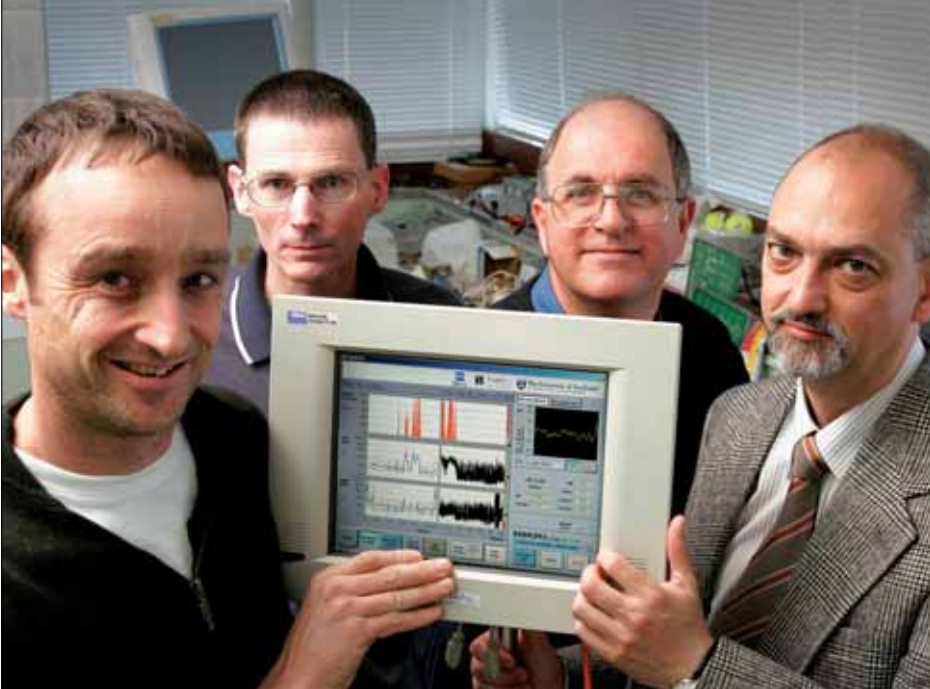
The Fellowship he holds is funded by the Maurice and Phyllis Paykel Trust and awarded jointly with the Woolf Fisher Trust, and was launched following Mr Paykel’s death in 2002.

Mr Paykel co-founded the company Fisher and Paykel with his brother-in-law Mr Woolf Fisher. Throughout his career he pioneered and supported engineering and biomedical advances and their commercial application in New Zealand, and was a major philanthropist to The University of Auckland.

The fellowships will be awarded every two years to Fellows who will work in the University’s Faculties of Medical and Health Sciences, and Engineering. The other inaugural fellowship is held by Dr Merryn Tawhai who works at the Bioengineering Institute modelling pulmonary function.

The brain rescue monitor moves forward

The monitor has become standard in Australasian nurseries



Associate Professor Chris Williams, Mark Gunning, Sued Emmanuel and Dr Michael Navakatikyan have poured their collective effort into developing the brain rescue monitor.

The brain rescue monitor developed by Liggins Institute scientists is proving to be a valuable addition to every hospital nursery in Australasia.

“The device is now appearing in nurseries in the United States,” says neuroscientist Associate Professor Chris Williams, the ‘father’ of the monitor.

The monitor picks up normal and abnormal function on each side of a baby’s brain, revealing not only when injury occurs, but approximately where. Until it became available last year, medical staff who suspected brain injury in a baby had to summon a specialist technician who would take a reading of brain activity and then leave.

Now, nurses and neonatologists can apply the monitor and get a constant, easy to read, on-line display of brain function.

“It’s very clear that the monitor can pick up injury reliably and accurately at an early stage in near term infants,” says Dr Williams. “We’ve had seven or eight scientific papers reporting positive trial results. One of these is published, there are more in press, and there are several conference abstracts.

“As a result, the monitor is becoming

useful as a clinical management tool to assist with decisions on treatment aimed at preventing permanent brain damage.”

It has been commercialised and is being marketed by BrainZ Instruments Ltd.

Dr Williams is quick to credit the unsung heroes behind the monitor. “Mark Gunning, Christina Parra, Sued Emmanuel and Michael Navakatikyan are the ones who have brought the plans to life.”

The monitor is also proving to be a valuable tool for research into brain injuries. An example is joint Auckland-Melbourne studies into brain injury in extreme preterm babies - those born at 24 to 25 weeks of gestation weighing only a few hundred grams.

“Claire West (a clinical fellow doing a PhD at the Liggins) and Dr Malcolm Battin (an associate member of the Institute and neonatologist at National Women’s Hospital) have found that the brain function of these tiny babies deteriorates in the first few days after birth,” explains Dr Williams. “In these babies the plumbing in their hearts that lets them access oxygen from air doesn’t establish properly at birth. The study is using the monitor to examine

whether the injury is caused by a resulting oxygen shortage.

“The monitor can pick up any injury as it happens. Later on it is verified using magnetic resonance imaging (MRI) and neurological outcome.”

Another big issue for neonatal intensive care is the best way to diagnose and monitor seizures. The monitor is being used in seizure studies.

Sometimes seizures produce no observable outward signs, especially if the baby is on a ventilator. But because the monitor can pick up brain activity patterns that come with seizures, doctors are now able to recognise such ‘silent’ seizures and treat them with anticonvulsants.

“Some anticonvulsants don’t work reliably in babies, and sometimes medical staff need to try two or three different kinds,” explains Dr Williams. “With the monitor right there, they have an instant way to tell when they’ve found one that is working.”

The centralising of Auckland hospitals at the Grafton site is a positive thing for research associated with the monitor, believes Dr Williams, because the Institute is located only a hundred or so metres away. “It will really boost the Liggins’ collaborations,” he says.

Collaborative research with Starship Children’s Hospital into the problem of infant brain injury during cardiac surgery is already underway.

“At present nobody knows that the injury has occurred until it’s too late to do anything,” says Dr Williams.

“We’re collaborating with Dr John Beca, a paediatric intensivist based at Starship, to use the monitor during the surgery and afterwards in intensive care. Our feasibility study is complete, and the next step is the proper trial.

“The ideal outcome will be to have the monitor being used during all cardiac surgery and reporting when injury starts to occur. Treatment decisions could be made instantly to counter that. It would make a huge difference to the quality of the rest of that child’s life – brain damage is something to be dreaded.”

The team are now working on versions of the monitor for full term infants, very premature babies and adults.

New honorary professor for the Liggins Institute

A distinguished professor and author has joined the Liggins Institute



Perinatal physiologist Professor Mark Hanson will carry out collaborative research with Liggins Institute scientists.

Professor Mark Hanson knows more about unborn babies than do most people in the world. He has an international reputation in developmental physiology, leading for 20 years one of the few research groups investigating both pre and postnatal physiology. He is Director of the Centre for Developmental Origins of Health and Disease at the University of Southampton, a ground-breaking author, and now an honorary professor at the Liggins Institute.

“Professor Hanson is an expert on how fetal development sets aspects of a baby’s physiology for the rest of its life - indeed he is the United Kingdom’s most distinguished perinatal physiologist,” says Liggins Director Professor Peter Gluckman. “His honorary appointment with us adds significantly to Liggins Institute research.”

Professor Hanson’s particular expertise in cardiovascular physiology is reflected in his being awarded a Chair in Cardiovascular Science by the British Heart Foundation in 2002. He also directs research into the development of the placenta and the way maternal and fetal nutrition affect the function of neural, endocrine and cardiovascular systems throughout life.

Professor Gluckman is delighted to have accepted a reciprocal post as honorary

professor at the University of Southampton’s Centre for Developmental Origins of Health and Disease. “The capacity for developing new knowledge is vastly increased by the new insights that spring from high quality collaborations,” says Professor Gluckman. “The Southampton scientists are amongst the best in the world in this area, and the exchange is bound to be fruitful.”

Professors Hanson and Gluckman joined forces to co-author a paper in the prestigious journal ‘Science’ in September this year, entitled ‘Living with the past: Evolution, development, and patterns of disease.’ In it they introduce the concept of fetal programming as a dimension of evolution, describing how genes and the environment interact to prepare offspring for the environment into which they are born.

They have also written a book for non-scientific audiences on the same topic. The Fetal Matrix: Evolution, Development & Disease will be published in November by Cambridge University Press. It describes in detail how humans and animals adjust their growth and development in the womb according to the physiological cues they receive from their mothers.

The authors explain how this ‘predictive adaptation’ has evolved over time. It is a

faster way to adapt humans and animals to their environment than classical evolution, they write, because it doesn’t rely on altering the genetic code, which generally takes many generations to respond to a changed environment.

However, it is a tactic that can backfire in today’s world, when people do not eat the diet that their bodies were led to expect during their development in the womb. The results are obesity, heart disease and other diseases of affluence. This is particularly so in the third world, where people born to undernourished mothers often grow up to eat diets that are far richer and more concentrated than those of their parents and grandparents.

The ensuing global health problems are one of the main points of focus of the International Society for Developmental Origins of Health and Disease. Professor Hanson is Secretary of the Society, and Professor Gluckman its Chair.

Professor Hanson will spend a significant amount of time at the Liggins Institute carrying out collaborative research with Liggins Institute scientists. Professor Gluckman will do the same at the University of Southampton.

Become Part of Our Vision

If you are committed to advancing healthcare and improving quality of life, and want to see New Zealand take greater strides in the knowledge society, then you may wish to consider supporting the Institute. Please contact us at:

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Lord Winston draws Artworks crowds

A charity auction, dinner and public lectures were boosted by the presence of Lord Robert Winston

For the second year running, the Liggins Institute has been the beneficiary of the Artworks Black Tie Dinner and Charity Auction at the Hilton hotel, Auckland.

Seats were sold out well in advance of the early September event, which was organised by the Rotary Club of Ellerslie Sunrise. It featured charismatic speaker, television presenter and eminent scientist Lord Robert Winston. Radio personality Max Cryer presided as MC.

Lord Winston spoke about the value of the Liggins Institute's work to society, and encouraged the audience to lend it their philanthropic support.

The evening saw spirited bidding for donated auction items. These included works of art, jewellery, travel packages and autographed 'Lord of the Rings' memorabilia.

Laughter erupted when Lord Winston leapt onto the podium during the bidding for a set of books authored by him. "Tea at the House of Lords" was to be thrown in for the successful bidder, he announced.

Lord Winston is a member of the United Kingdom's House of Lords, where he comments on a wide range of medical,

ethical and scientific issues.

He attracted large crowds to the two fundraising public lectures he gave at the Hilton during the Artworks week. One lecture was titled 'Creating humans', and the other 'Can the public trust scientists?'

The audience emerged from the former lecture thoroughly entertained and knowing a lot more about the process of creating humans. Lord Winston focussed on assisted reproductive technologies – his own area of research – but his lecture ranged from pronucleate eggs and ethics to the first microscopes and the agony of infertile couples.

A 17th century scientist observed a sperm in a very early version of a microscope, he explained. In it the scientist observed a little human, complete with arms and legs. The published report was widely regarded, and fulfilled the common belief that females were just incubators, and everything important came from the male.

"The message is that scientists see what they want to," he said. "Nothing in science is absolute. But that doesn't mean that science is less valuable – in fact

science is more valuable if we understand its limitations."

Had the early scientist been correct, our beliefs about when life starts would be quite different, pointed out Lord Winston.

"Our ethics depend entirely on our understanding of the natural world. Purely *ad hoc* decisions not based on biology cannot make good ethical decisions."

Lord Winston also fascinated 600 high school students from around Auckland when he spoke at St Kentigern's College during his visit.

At a one day workshop on the biology of the period around conception, he led discussion between scientists from the National Research Centre for Growth and Development. The Liggins Institute is the Centre's leading partner and Lord Winston a member of its scientific advisory board.

Lord Winston is a scientific patron of the Liggins Institute.

Liggins staff members are making plans to attract another international personality to feature at next year's fundraising events. The Institute is grateful to the Rotary Club of Ellerslie Sunrise for organising Artworks.



Lord Robert Winston (left) is welcomed by Professor Peter Gluckman to a National Research Centre for Growth and Development workshop day.

New support for Liggins Institute

'Friends' throw weight behind the Liggins



Roxane Horton is the Chair of the Friends of the Liggins Institute committee.

A group of Aucklanders has formed a charitable trust, 'Friends of the Liggins Institute'.

"The Friends will raise funds for the Institute and boost awareness of its work," says Friends Chair Roxane Horton. "Many people, especially parents, are interested in the Institute's work but have no other simple way of supporting it.

"I am filled with admiration for the Institute's work and excited by the commitment of the researchers. They focus single-mindedly on applying their research to improving the health of our babies and

get groundbreaking results. They deserve our support."

Liggins Institute Director, Professor Peter Gluckman, has welcomed the launch of the Friends.

"New Zealand's investment in medical research is low compared with other countries," he said. "I am delighted that the Trust has been established to support our work. I hope people will be inspired to join our voyage of discovery and help us make a difference."

Friends will be kept up to date with the work of the Liggins through the Friends' newsletter, 'Hand in Hand'. They will also have the opportunity to meet Liggins scientists, see their research in action, and attend lectures and social events with distinguished visitors.

The first Friends event was an exclusive pre-dinner drinks hour with Lord Robert Winston before the Artworks dinner in September (see page 5). Friends were also able to purchase reduced price tickets to the two lectures given by Lord Winston. The Friends committee recently launched a spring lecture series covering subjects such as 'Childhood obesity' and 'The importance of grandmothers'. The lectures, which are open to all Friends and their guests, are given by researchers at the Institute and are presented in a fashion that will inform and entertain non-scientists.

To become a Friend (\$60 per person or \$100 per couple for a year), contact the Friends of the Liggins on 09 303 5972, or e-mail friends@liggins.auckland.ac.nz.

Liggins Director honoured

Liggins Director Professor Peter Gluckman has been made a Foreign Associate Member of the Institute of Medicine (IOM), a component of the National Academy of Sciences of the USA. He is the first New Zealander ever to be elected and one of only 60 non-Americans who are members of the Institute.

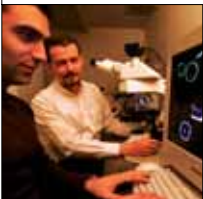
Election is considered one of the highest honours in the fields of medicine and health.

Members are elected on the basis of their professional achievement and contributions to research. The process is highly selective, and recognises those who have made major contributions to the advancement of the medical sciences, health care, and public health.

The IOM provides objective, scientifically sound advice concerning health and science policy to American policy-makers, professionals, society leaders and the public.

Professor Gluckman was obviously thrilled by the recognition. "It demonstrates the high regard in which the Institute's focus of research is held internationally," he said.

New IOM members are nominated and selected by existing members. Professor Gluckman's election to membership was announced in October at the IOM's annual general meeting.



Continued from front page...

scientists are working to develop medications to block the hormone.

The results were published by the prestigious American journal 'Proceedings of the National Academy of Sciences' in September.

Previous research by Dr Lobie has shown that there is a direct relationship between the level of locally produced growth hormone and the status of the breast cancer cell activity. The present study shows that this kind of growth hormone is responsible for the conversion to the invasive form.

Growth hormone made by the breast has

different properties from growth hormone made by the pituitary gland and the synthetic hormone that is used therapeutically. Dr Lobie has shown in other studies that the medical use of growth hormone by injection has no effect on breast tumours.

Dr Lobie came to the Liggins Institute last year, and is Associate Director (Biotechnology) of the Institute. He was recently awarded a sought-after grant from the Marsden Fund, administered by the Royal Society of New Zealand, to fund research into the details of how growth hormone produced in the breast has its

effect on breast cancer cells.

His associate investigator in the Marsden-funded research is Dr Starling Emerald, who came with Dr Lobie to the Liggins Institute from the Institute of Molecular and Cell Biology in Singapore.

Their expertise in the way growth hormone communicates with other cells is part of a wider programme of Liggins Institute research into growth and development. Other areas of the Institute's focus include the hormonal control of growth, insulin resistance, appetite regulation and the central nervous system effects of growth hormone.

Fetus or foetus?

Oe no, fetus is not an Americanisation

Regular Dialogue readers may have noticed an apparent spelling inconsistency in this newsletter. American spelling seems to have been used for the word 'fetus', yet English versions of words otherwise predominate: scientists specialise, oestrogen circulates, and women go into premature labour.

In fact, we always adopt the English version of words, as is the convention in New Zealand. But in the case of the unborn baby, the English spelling is incorrect. The 'oe' makes the word appear to come from ancient Greek, but there is no evidence for that.

Words that contain 'oe' have their origins in the ancient Greek language. They were borrowed from Greek by Latin, with 'oe' being the Latin alphabet's representation of the Greek vowel. It used to be written as a ligature, 'Œ'. English in turn borrowed the words that contain it from Latin.

Many such words have since had their Greek origins obscured by American spelling - foetid becomes fetid, for example. On the other side of the Atlantic, even the English have occasionally lapsed - foeminine has become feminine, and foederal is now federal.

Yet the ancient Greeks would not have known what a foetus was. Instead they would have used the term 'brephos', a uniquely Greek word that denotes an unborn or newborn baby.

Neither would the Romans have used the word foetus. They wrote fetus, and the word is purely Latin.



Leonardo da Vinci 'The fetus in the womb'

The pseudo-Greek spelling has been around for many centuries. St Isidore, Archbishop of Seville, made the mistake in his *circa* 620 AD book commonly known as the *Etymologiae*. He incorrectly wrote that foetus was derived from the verb 'foveo', to keep warm.

The Oxford Latin Dictionary (1982) gives three meanings for fetus. The first is the bringing forth of young, and the second is

'that which is born'. The final definition, 'the young while still in the womb', is its modern usage.

So fetus is not an Americanisation, but a true reflection of its Latin roots.

Thanks to Dr Paul McKechnie from the Department of Classics and Ancient History at The University of Auckland for his help with this article.



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Professor Peter Gluckman FRS Director

Professor Peter Gluckman is a world renowned Professor of Paediatric and Perinatal Biology. He is one of only two New Zealand doctors, and one of two paediatricians worldwide, to be elected a Fellow of the British Royal Society. His work has focused on understanding the basic mechanisms of two major obstetric and perinatal problems – infant brain injury resulting from oxygen deprivation and intrauterine growth retardation.



Professor Jane Harding Deputy Director

Professor Jane Harding is internationally recognised as an academic neonatologist. Her research spans both clinical and biomedical studies. She is an authority on placental function, the regulation of fetal growth and the consequences of poor fetal growth.



Professor Murray Mitchell Research Director

Professor Murray Mitchell is Professor of Pharmacology and Clinical Pharmacology at The University of Auckland. He has a worldwide reputation for his research into the biology of premature labour and the biochemistry of hormones related to this.



Assoc. Prof. Bernhard H. Breier Associate Director

Associate Professor Bernhard H. Breier is an international authority on the endocrinology and physiology of fetal programming and the regulation of growth and metabolism by the somatotrophic axis. His research focuses on the physiological mechanisms that regulate pre- and postnatal growth and metabolism, and how these interact with nutrition and environmental factors.



Assoc. Prof. Wayne Cutfield Associate Director

Associate Professor Wayne Cutfield is an expert on insulin sensitivity and action in children. In addition to clinical work at Auckland's Starship Hospital where he is Director of Endocrinology, he conducts both experimental and clinical research into aspects of growth and insulin resistance.



Associate Professor Peter Lobie Associate Director

Associate Professor Peter Lobie has worked at two of the world's most prestigious research centres: the Karolinska Institute in Stockholm, and the Institute of Molecular and Cell Biology in Singapore. A specific area of his most recent research is the production of human growth hormone in the mammary gland, and its possible role in the development of breast cancer.



Mr Mark Shepherd Associate Director

Mark Shepherd is the Institute's Chief Operating Officer. A multi-lingual science graduate, he made a career in change management consultancy and has worked across Europe and India for some of the world's largest companies. At the Liggins he ensures sound financial control, transparent policies and service contracts, efficient infrastructure and clear communication.

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The Liggins Institute is the leading partner
in the National Research Centre for Growth
and Development, one of New Zealand's
Centres of Research Excellence.

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 Chief Operating Officer or the University Registrar for further information.

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