

POSTGRADUATE RESEARCH OPPORTUNITIES

# LIGGINS INSTITUTE



2012–2013





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The Liggins Institute is the host partner in the National Research Centre for Growth and Development, a Centre of Research Excellence hosted by The University of Auckland.

# Welcome



Welcome to the Liggins Institute, I am delighted that you are considering a postgraduate research programme with us. Whether your aim is to establish a career in biomedical research or cultivate skills that will complement further study or clinical practice, I am confident that you will find it a rich and rewarding experience.

"The Liggins" was the first of The University of Auckland's Large-Scale Research Institutes, established to focus primarily on world-class research and postgraduate teaching. In just 10 years

we have established an outstanding reputation for research on maternal, fetal and child health and unravelling the science that drives it. Related research includes the impact of nutrition on health throughout the lifecourse; epigenetic regulation of growth and development; perinatal and degenerative neuroscience; breast cancer; and evolutionary medicine.

Our strength lies in our capacity to perform and deliver high-quality translational research that moves ideas from basic laboratory science, through pre-clinical testing in physiological models to clinical and population-based studies that can influence medical practice and health policy. Postgraduate projects frequently include two or more stages of the translational process allowing students to progress and test experimental findings in live situations.

As a Liggins student you will work with internationally recognised research leaders and have opportunities to collaborate with research groups at first-class overseas universities. Many of our graduates have received international awards and obtained positions at premier research organisations and universities.

In the second half of 2012 we shall move into new, state-of-the-art facilities alongside staff and students of the Faculty of Medical and Health Sciences.

As Director of the Liggins Institute, my mission is to foster an environment in which every Liggins researcher can deliver world-class research. Our students are an integral part of that effort.

I invite you to read about our major research themes and the particular opportunities available within each of our research groups. Then contact us to find out how you can achieve your career goals with us.

A handwritten signature in black ink, appearing to read 'Wayne Cutfield', with a stylized flourish at the end.

**Professor Wayne Cutfield MBChB, DCH, FRACP**  
Director, Liggins Institute



# Research themes

Our research demonstrates the importance of children having a healthy start to life and the on-going importance of nutrition in promoting and supporting optimal health throughout life.

**We have a number of broad, overlapping research themes exploring**

- **Maternal, fetal and child health**
  - the lifelong legacy of early life events
- **What makes us what we are**
  - genetic and molecular mechanisms
- **Nutrition throughout life**
  - its role in development and optimal health
- **Evolution, adaptation and disease**
  - influences of the past on our future health
- **Perinatal and later life brain damage**
  - how can we help?
- **Breast cancer**
  - developing new treatment strategies



## The Liggins legacy

The Liggins Institute is named after one of New Zealand's most eminent medical scientists Professor Sir Graham Liggins.

Professor Liggins (often referred to by his nickname "Mont") demonstrated the power of a brilliant mind to recognise the unexpected, to perform fundamental biomedical research and to rapidly translate it into clinical research, followed by clinical application.

He showed that giving steroids to women experiencing early labour could accelerate

infant lung development enough to enable premature newborn babies to breathe independently. His work, which led to a much deeper understanding of the birth process, transformed the practice of neonatology and led to dramatically improved survival rates among premature babies all over the world. His technique is now standard obstetric practice.



*Professor Sir Graham Liggins FRS (1926 – 2010)*



# About the Liggins Institute

A world-class centre for postgraduate research and study

The Liggins Institute provides an ideal environment in which to explore one of life's most fundamental questions: what makes us what we are?

Liggins students have access to some of the best laboratory and clinical research facilities in New Zealand and academic staff recognised as leaders in their fields of biomedical and clinical research and a wide range of other disciplines.

## Graduate and postgraduate programmes

Courses: doctorates, masters, postgraduate diplomas, BSc (Hons) projects.

Subjects: Biomedical Science, Medical Science, Health Science, Māori Health and Science.

Masters, diploma and BSc (Hons) courses are coordinated through the Faculty of Medical and Health Sciences or the School of Biological Sciences in the Faculty of Science.

Doctoral students enrol directly with the Liggins Institute.

You will find more information about these courses in the section for future postgraduates on the Liggins Institute website.  
[www.liggins.auckland.ac.nz/postgrad](http://www.liggins.auckland.ac.nz/postgrad)

## Students at the Liggins Institute

There are currently around 45 students at the Liggins Institute, including more than 30 PhD students. They come from many different backgrounds and disciplines and cover a wide range of ages and over 20 different nationalities.

## Support and facilities available to postgraduate students

Each student is assigned at least two supervisors who are responsible for the student's research training and support. Supervisors are trained by the University to provide students with top level supervision. The Liggins has established provisional and annual review processes for PhD students which ensure that project goals are achieved and high quality degrees are completed on time.

International students are supported both within the Liggins Institute and through the University's international student support programme.

All Liggins students are allocated their own desk and computer and have access to state-of-the-art research facilities and equipment. These include cell culture facilities, a research farm, a clinical research unit, confocal microscopy, flow cytometry, mass spectrometry, DEXA scanning, Real-time PCR analysis, and SNP, methylation and expression analysis using a Sequenom Epityper.

## Convenient location

The Liggins Institute is centrally located alongside the Faculty of Medical and Health Sciences on The University of Auckland's Grafton campus. This is within 15 minutes' walk of the city centre and the shopping districts of Newmarket, Karangahape Rd and Ponsonby, while the University's main campus is just 10 minutes away. Across the road is Auckland City Hospital and Auckland Domain, one of Auckland's largest public parks. The area is well served by public transport including buses and trains.

## Accommodation

A wide range of options is provided on The University of Auckland website.  
[www.accommodation.auckland.ac.nz](http://www.accommodation.auckland.ac.nz)

## PhD student scholarships

There is a wide range of postdoctoral scholarships available. Please visit The University of Auckland website to search the database of scholarships to find one that fits your criteria. [www.auckland.ac.nz/scholarships](http://www.auckland.ac.nz/scholarships)

## Find a project and a supervisor for your study at the Liggins

Research at The Liggins Institute is conducted by a number of research groups, each of which includes world-class scientists. The groups and their research areas are introduced in the following pages. Each profile includes research projects that are currently being undertaken by postgraduate students or are available for new students.

For further information please contact any of the named investigators whose projects interest you.

To find out more about enrolling in our doctoral programmes, visit [www.liggins.auckland.ac.nz/doctoralentry](http://www.liggins.auckland.ac.nz/doctoralentry)



**Dr Mhoyra Fraser**

*The Liggins Institute's Academic Director Dr Mhoyra Fraser heads the Perinatal Neuroscience research programme. She is also responsible for ensuring that postgraduate students are appropriately enrolled and receive quality supervision and support.*

*"The Institute provides excellent facilities for graduate and postgraduate research training," she says, "and we have an outstanding track record in achieving top quality PhD graduations."*

*"Our academic staff have international reputations in a wide range of fields and are able to devote significant time to supporting and training students in research, manuscript preparation and thesis writing."*

# ★ LiFePATH Group

\*Liggins Fetal, Perinatal and Maternal Translational Research for Lifelong Health – investigating how perinatal events and the perinatal environment affect long term growth and development

## Investigators

Associate Professor Frank Bloomfield  
Distinguished Professor Jane Harding  
Professor Caroline Crowther  
Dr Anne Jaquiere  
Dr Jane Alsweiler  
Dr Mark Oliver

## Research focus

Our programme investigates the ways in which maternal, fetal and neonatal nutrition and the intrauterine environment affect fetal and postnatal growth, development and long term health. We are also working to understand the causes and consequences of preterm birth and intrauterine growth restriction (IUGR). These conditions have long term implications including neonatal and on-going illness, compromised growth and cognitive development, and increased risk of chronic adult conditions such as obesity, cardiovascular disease and diabetes.

Visit [www.liggins.auckland.ac.nz/fetusandnewborn](http://www.liggins.auckland.ac.nz/fetusandnewborn)

Our multidisciplinary team includes scientists and clinicians conducting translational research that examines clinical problems at a molecular level, through whole animal physiology to clinical trial and application. We have an excellent track record of training clinicians and scientists in research, with more than ten completing PhDs in Obstetrics and Paediatrics.

## Student research

We offer students trained in clinical and biomedical science disciplines a wide range of stimulating postgraduate research opportunities covering

- Clinical trials in perinatal care, including trials of maternal and neonatal interventions to improve perinatal outcomes and child health
- Clinical follow-up studies on the impact of neonatal conditions on child development and long term health
- Animal physiological research, including causes and complications of preterm birth in a large animal model
- Laboratory-based research into mechanisms underlying observed physiology
- Research synthesis and translation, including Cochrane systematic reviews, clinical guidelines, and implementation to practice

## Research projects

- The CHYLD study: A large multi-disciplinary prospective cohort study investigating the development of young children who were at risk of developing neonatal hypoglycaemia [see box this page].
- Anaemia study: Anaemia is very common in preterm babies and anaemia in fetal life alters development of the coronary artery tree. We are investigating the effects of anaemia in the preterm neonatal lamb on development of the coronary artery tree.
- The long term consequences of being conceived a twin: We have shown that being conceived as a twin is associated with increased adiposity in adulthood. We are studying the effects of twin conception on adult glucose tolerance, insulin sensitivity and hypothalamic-pituitary-adrenal axis function in sheep.

- Postnatal consequences of intrauterine treatment of the growth restricted fetus: We developed the first intrauterine treatment for IUGR, demonstrating that intra-amniotic treatment with insulin-like growth factor 1 increases fetal growth. We are now studying the postnatal consequences of this treatment, investigating aspects of adult physiology following this treatment.
- Is an unpredictable food supply bad for your health? This project investigates the effects of an unpredictable food supply on weight gain, metabolism and appetite regulation in juvenile lambs.
- Nutrition of shift workers: Workers on rotating shifts have higher rates of metabolic diseases than their non-shift working colleagues. This study will investigate the effect of eating patterns on markers of metabolic disease in shift workers as a potentially remediable factor.

## Contacts

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**Deborah Harris**

*"I want my research to help the patients I care for," says Deborah Harris a nurse practitioner in the neonatal intensive care unit at Waikato Hospital.*

*Deborah is just completing her PhD, researching the effects of low blood glucose concentrations in newborn babies. The condition, known as hypoglycaemia, sometimes leads to brain damage. "At present we don't know which babies will have problems or how severe or frequent the hypoglycaemia needs to be to cause damage," she says.*

*During her PhD research, Deborah trialled a new device that continuously monitors glucose concentrations in babies who were thought to be at risk. She is now a member of the Steering Group for the CHYLD study, a large clinical trial following the children in her study and assessing their health, vision and physical and cognitive development at two and four and a half years of age.*

*The CHYLD study provides excellent opportunities for doctoral research in a range of clinical and science disciplines. We are currently recruiting potential PhD candidates with backgrounds in paediatrics, nursing, developmental psychology and related disciplines.*

*For more information about joining the team, email [CHYLD@auckland.ac.nz](mailto:CHYLD@auckland.ac.nz).*



# Clinical Endocrinology Research Group

We are investigating how early life events, particularly nutrition, alter the risk of children and young people developing obesity, diabetes, metabolic and cardiovascular diseases.

## Investigators

Professor Wayne Cutfield  
Associate Professor Paul Hofman

## Research focus

### Conception through to adolescence

- How does altered nutrition during this time impact on adult health?
- What are the mechanisms mediating these effects?

This knowledge will enable us to manipulate nutrition to improve the long term health of at-risk individuals.

We are also investigating the long term effects of early nutritional environments in children conceived through *in vitro* fertilisation or ovulation induction; born small for gestational age, preterm or post-term, born to older mothers, and twins.

We aim to understand the molecular and epigenetic mechanisms driving these changes, so we can develop targeted interventions to prevent or minimise adverse health effects in later life.

### Adolescence

We are assessing cardiovascular function in adolescents with obesity and diabetes mellitus, and working to develop interventions to prevent and reduce obesity.

### Adulthood

We are examining the impact of changes in micronutrients on metabolism, body composition and cardiovascular status in adults, as well as the mechanisms underpinning these effects.

Visit [www.liggins.auckland.ac.nz/clinendo](http://www.liggins.auckland.ac.nz/clinendo)

## Student research projects

- The impact of changes in micronutrients on body composition, metabolism and cardiovascular status in children and adults, and the underlying mechanisms of these effects
- The impact of post-term birth on body composition and metabolism in childhood
- The capacity to exploit non-exercise activity thermogenesis as a mechanism to prevent weight gain and promote weight loss in adolescents and adults

*In these projects students may be involved in any step of translational research, from laboratory to animal models, and then on to clinical assessment and treatment studies.*

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### Dr Tim Savage

*Dr Tim Savage is one of the Liggins Institute's clinical research fellows. Tim comes from Ireland where he obtained his medical degree, then trained and worked as a general paediatrician.*

*In Auckland he is balancing the busy demands of tertiary training in paediatric endocrinology and diabetes at Starship Children's Hospital with research for a PhD at the Liggins Institute. His research is investigating the impact of fertility treatment and maternal age on children's growth and metabolism.*

*Clinical researchers at the Institute are investigating the effects of assisted reproductive technologies on children's growth and development. They have shown that, while children conceived through in vitro fertilisation (IVF) are just as healthy as their normally conceived peers, there are some subtle physical and metabolic differences between the two groups.*

*Tim says that although IVF receives a lot of attention, more than twice as many children are conceived following treatment with drugs that stimulate ovulation. His research has also turned up some slight differences in the growth of these otherwise healthy children.*

*"At present we don't know what causes these differences. Fertility drugs lead to changes in the ovary and uterus around the time of conception, so it may be that the course of development is influenced by the environment in which conception occurs. We will need to follow these children as they grow up to see if there are any long term effects.*

*"My time at the Liggins has given me an appreciation of the benefits of research, and the skills to critically evaluate the results of clinical research. Not only will it broaden my career opportunities, it will enhance my future clinical practice and benefit my patients," says Tim.*

# Human Nutrition Research Group

Our multidisciplinary research programme is focused on identifying the key genetic and cellular mechanisms that link good nutrition to long-lasting health.

## Principal Investigator

Professor David Cameron-Smith

## Research focus

Across the lifespan food is a major determinant of health. Food contains a complex array of chemicals that directly affect genes, cell signalling and metabolic pathways within the body.

### Nutritional strategies for healthy ageing

Ageing leads to the loss of muscle increasing the risk of falls, fractures and frailty. Our aim is to understand what causes muscle loss by examining the genetic and cell signalling mechanisms that are central to muscle growth and repair. Knowledge of the key mechanisms is translated into clinical research focused on identifying effective dietary and lifestyle strategies to reduce muscle loss.

### Molecular nutrition and non-communicable disease (NCD) prevention

Nutrients control the programming and expression of many thousands of genes. Focusing on adipose tissue and muscle, we are investigating the mechanisms by which nutrients control genes. Current projects include examining the molecular actions of bioactive lipids, including omega-3 fatty acids and phospholipids, on tissue growth, inflammation and insulin sensitivity.

### Dynamic responses to meals

With each meal nutrients enter into the body, activating genetic and molecular responses required for nutrient storage, metabolism and immunity. We are building comprehensive profiles of the genes and signalling responses in circulating immune cells, adipose tissue and

muscle. Current investigations include the dynamic post-meal gene, inflammation and metabolomic responses to different fats and proteins.

Visit [www.liggins.auckland.ac.nz/nutrition](http://www.liggins.auckland.ac.nz/nutrition)

## Student research projects

- Understanding the origins of suppressed protein synthetic response to ingested nutrients in older individuals
- Integrating the metabolomic and transcriptomic responses to ingested nutrients in human adipose and skeletal muscle
- Defining the absorption and impact novel lipids exert on post-meal inflammatory responses
- The metabolomics and transcriptomics of skeletal muscle in responses to altered physical demands, including exercise and inactivity
- The epigenetics of muscle mass gain in humans

## Contacts

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### Professor David Cameron-Smith

Professor David Cameron-Smith is the Liggins Institute's Deputy Director and Research Director.

"My passion," he says, "is unravelling the genetic and biochemical mechanisms that determine how the food we eat shapes our future health and wellbeing."

"The Liggins Institute is a world leader in establishing how nutrition from conception to early adulthood influences disease risk throughout the lifecourse. I want to apply some of that knowledge to improving the health of our ageing population."

As Professor of Nutrition at The University of Auckland he is developing research relationships in nutrition and health sciences across the University and promoting collaborations with external research organisations and industry.

"In my brief time here I've discovered a huge depth and breadth of knowledge, from professors through to early career postdoctoral researchers. This creates a fantastic environment for postgraduate students and an ideal place to nurture a research career," he says.



# Developmental Programming Group

Understanding the role of altered maternal nutrition on the growth and development of offspring

## Principal Investigator

Dr Mark Vickers

## Research focus

The incidence of obesity and related metabolic disorders (such as diabetes and cardiovascular disease) is increasing at an alarming rate and represents a major public health issue for the 21st century.

Metabolic disease results from a complex interaction of genetic, physiologic, behavioural and environmental factors. Numerous hypotheses have been advanced to explain its current dramatic increase, including increased food availability and reduced energy expenditure associated with changing work habits. The recent rate of increase suggests that environmental and behavioural influences, rather than genetic causes, are fuelling the present epidemic.

In this context, epidemiological and experimental evidence suggests that alterations in early life nutrition have a major impact on the health and wellbeing of offspring.

Our work focuses on the role of altered maternal nutrition (including undernutrition and high fat diets) on the growth and development of offspring. We are particularly interested in how nutrition affects obesity, the regulation of the metabolic hormones insulin and leptin, and reproductive function. We are also investigating possible intervention strategies (pharmacologic and nutritional) aimed at reversing this "programming" of adult disease. Our work spans *in vitro* methodology, molecular biology, immunohistochemistry and epigenetics through to whole animal physiology.

Visit [www.liggins.auckland.ac.nz/devprogram](http://www.liggins.auckland.ac.nz/devprogram)

## Student research projects

- The impact of altered maternal nutrition on health and wellbeing of offspring
- The role of leptin in reversing metabolic disorders induced by developmental programming
- The role of altered maternal nutrition on fetal and placental metabolism
- Maternal nutrition and reproductive fitness
- Developmental epigenetics
- The effect of maternal exercise on body composition in offspring

## Contacts

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### Dr Graham Howie

*The career of one recent graduate shows there are many pathways to postgraduate research at the Liggins Institute.*

*Over 16 years in the ambulance service, Graham Howie enjoyed the wide variety of people and situations that were part of his daily life. But Graham decided he wanted to know more about what really made people tick.*

*He launched into part time university study – first a BA in psychology and then a master's in neuro-anatomy. Eventually, his quest to find out why people are what they are led him to doctoral study at the Liggins Institute, attracted by its reputation as a world leader in research focused on the long term consequences of early life development.*

*His research followed the effects of a mother's nutrition during pregnancy on her offspring. Using the rat as an experimental model, he showed that mothers on a high fat diet before and during pregnancy have offspring who are likely to become obese and develop cardiovascular disease, hypertension and diabetes.*

*"Our research has been cutting-edge," he says, "my supervisor Dr Mark Vickers is a world leader in this field. It is tremendously exciting to do an experiment and then see the results come in – results that have real relevance to the society we live in."*

*Graham says that what he most enjoyed about being a student at the Liggins was the intellectual stimulation and freedom to develop his own ideas in an intellectually secure environment – and having opportunities to discuss them with experts in the field.*

*Graham is now able to put that research to good use. He is a Senior Lecturer in Paramedicine and Emergency Management at the Auckland University of Technology. His role includes designing and teaching postgraduate courses for paramedics and community health workers that will enrich their professional practice with new knowledge based on the very latest biomedical and clinical research.*

# Pregnancy Complications Research Group

Understanding the role of altered maternal nutrition on the growth and development of offspring

## Principal Investigator

Professor Philip Baker

Professor Baker is moving to Auckland later in 2012 to take up joint appointments as Director of the National Research Centre for Growth and Development and Professor of Maternal and Fetal Health at the Liggins Institute.

## Research focus

Preeclampsia is the leading cause of maternal and perinatal morbidity and mortality internationally with 50,000 – 100,000 maternal deaths annually, while two in three stillbirths and one in four neonatal deaths occur in small babies. Both conditions are associated with long term health problems such as cardiovascular disease and metabolic abnormalities.

## Current research programmes include:

- Using murine models to identify novel potential therapies for preeclampsia and intrauterine growth restriction
- Using metabolomics to develop screening tests for major pregnancy complications

Other interests have included: vascular adaptation to pregnancy, placental cell invasion, placental cell turnover, endothelial progenitor cells (EPCs), adverse pregnancy outcome in teenage pregnancies, fetal origins of adult disease (such as schizophrenia) and the effect of

maternal stress on pregnancy outcome, and MRI imaging in pregnancy.

Further details and research publications, visit <http://scholar.google.com/citations?user=WsNhHqIAAAAJ&hl=en>

National Research Centre for Growth and Development  
[www.nrcgd.org.nz](http://www.nrcgd.org.nz)

## Student research projects

- Investigation of potential new therapies for fetal growth restriction and preeclampsia
- Determination of the “pregnancy exposome”: exposure to environmental agents in pregnancy
- Characterisation of the fetal growth restriction (FGR) placenta in both the developed and developing worlds, with emphasis on placental epigenetics

In these projects students may be involved in any facet of translational research, from cellular studies, to *in vitro*/animal models and clinical assessment/treatment studies.

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# Reproductive and Developmental Biology Group

Investigating fetal and placental growth and development, embryo implantation, pregnancy and parturition

## Investigator

Dr Anna Ponnampalam

## Research focus

Our current research includes

- The mechanisms of major complications of pregnancy such as preterm birth, gestational diabetes, preeclampsia and spontaneous recurrent miscarriage
- Epigenetic regulation of embryo implantation and parturition
- Gene expression and regulation of the human endometrium during the menstrual cycle

Visit [www.liggins.auckland.ac.nz/reprodev](http://www.liggins.auckland.ac.nz/reprodev)

## Student research projects

- Adverse effects of endocrine disruptors on human reproductive health
- Epigenetic regulation of embryo implantation
- The role of the endometrial epithelium in embryo implantation
- Epigenetic regulation of parturition

## Contacts

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*Dr Anna Ponnampalam (centre) supervising summer research students*

# Epigenetics and Genome Organisation Group

DNA is packed into cells in a way that affects how genes are turned on and off. Its overall organisation ultimately affects the characteristics of a particular cell. This apparently simple observation gives rise to a multitude of questions.

## Principal Investigator

Dr Justin O'Sullivan

## Research focus

DNA is packed into cells in a way that affects how genes are turned on and off. The spatial organisation of DNA within a cell is heritable, correlates with transcription levels, moves, and rearranges in response to the cell-cycle, development and transcriptional memory. Thus the overall organisation of DNA ultimately affects the characteristics of a particular cell. There are a multitude of questions that arise from this apparently simple observation.

## We are investigating how the 3-dimensional organisation of a genome is formed and regulated.

What role does epigenetics have in shaping this organisation? How does the organisation relate and respond to developmental and environmental changes? We are also investigating how genome organisation is related to symbiotic and pathogenic relationships.

## Our studies are designed to advance our understanding of the complex inter-relationships between what a cell's DNA codes for (the genotype) and the result of the genotype's conditional expression (the phenotype).

In particular we are interested in how the expression of the genotype is epigenetically and spatially controlled (epigenomics). We are investigating these problems using a holistic systems biology approach to understand genome structure formation, function and inheritance. This approach integrates cutting edge methods and technologies from molecular biology, bioinformatics and computational biology.

## Our work will enhance our ability to predict how distant genetic locations, hosts and pathogens communicate.

It will impact on a wide range of endeavours including our ability to predict how genetic modifications affect genome function in biotechnological and therapeutic applications. Moreover, it will pave the way to a greater understanding of the dynamics that underpin developmental pathways and genome evolution.

## Student research projects

- How are bacterial genomes organised? Are there general principles that can be extended to higher systems?
- Can we combine biophysics and experimental data to create predictive 3-dimensional models of genome organisation? What do these models tell us about how organisms respond to their environment?
- Do mitochondria control the development of human cells by directly "talking" to the host genome with their own DNA?

## Contacts

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# Developmental Epigenetics Group

We are investigating the molecular mechanisms through which factors in the early life environment determine an individual's phenotype, physiology and health profile. Knowledge from this emerging field of science holds potential benefits for both human health and agriculture.

## Principal Investigator

Dr Allan Sheppard

## Associates

We work in close collaboration researchers at the Liggins Institute, elsewhere in New Zealand and internationally, including Professor Sir Peter Gluckman, Professor Wayne Cutfield (Liggins Institute); Tony Pleasants (AgResearch); Professor Graeme Wake (Massey University); Professor Mark Hanson and Dr Keith Godfrey (UK); Professor Terrence Forrester (Jamaica) and Associate Professor Michael Raghunath (Singapore).

## Research focus

"Epigenetics" refers to the molecular mechanisms that cause changes in gene expression without direct alteration to the DNA sequence. It includes DNA methylation (the potentially reversible addition of a methyl group to specific DNA sites) and reversible modifications of the histone proteins that package DNA within chromosomes. Collectively, these epigenetic changes can control how actively genes are expressed.

During early life, the environment in which an organism develops influences the activity of genes through modulation of the epigenetic structure of the genome. Developmental epigenetics explains how the same genetic sequence can be functionally translated selectively in different cells at different times as a result of different environmental influences that occur during development. It explains why children with a comparable genetic heritage can grow up with their own individual phenotype which includes body composition and health risks.

Improving our knowledge of these early life processes will give us the capacity to manipulate parameters, such as nutrition during pregnancy and in the early postnatal period, to influence the activity levels of key metabolic genes.

The developmental epigenetics group brings together Liggins scientists with scientists at AgResearch on research that is applicable to both humans and farm animals.

The team is exploring developmental plasticity, the process through which the environment can have a profound influence on fundamental aspects of early mammalian development. Acting through maternal sensing of environment (particularly nutrition), the physiology of a fetus (human or animal) becomes adapted in expectation of its future postnatal environment. This process serves to increase postnatal survival and evolutionary success.

Visit [www.liggins.auckland.ac.nz/devepigen](http://www.liggins.auckland.ac.nz/devepigen)

## Student research projects

- Epigenetic mechanisms underpinning life history outcomes and the developmental origins of health and disease hypothesis
- Development of early life epigenetic markers to provide prognostic tools for prediction of adult disease
- Functional validation of epigenetic mechanisms contributing to phenotype variance
- Computational biology and mathematical modelling of epigenetic regulation of phenotype

## Contacts

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# Centre for Human Evolution, Adaptation and Disease

Exploring the interface between evolutionary theory and medicine and public health

## Investigators

Professor Sir Peter Gluckman  
Dr Alan Beedle  
Dr Tatjana Buklijas  
Dr Felicia Low

## Associates

We work in collaboration with leading NZ and international researchers including: Professor Hamish Spencer (University of Otago); Professor David Raubenheimer (Massey University); Dr Allan Sheppard (Liggins Institute); Associate Professor Peter Dearden (University of Otago); Professor Mark Hanson (Liggins Institute and University of Southampton); Professor Terrence Forrester (Liggins Institute and University of West Indies).

## Research focus

Our main interest is in evolutionary medicine: the interface between evolutionary theory and medicine/public health. We use concepts from evolutionary and developmental biology to inform and interpret experimental and clinical research performed by the Liggins Institute and its international collaborators. We are developing a research agenda and teaching curriculum for evolutionary medicine.

One particular focus is the role of developmental plasticity in shaping adult human health. Developmental plasticity occurs early in life when an organism is able to take signals from its environment, make predictions about the world it will grow up in and adapt its development to suit. Thus, babies that grow in a pre-birth environment where nutrient supplies are scarce adapt their development for what they perceive as a poor future. Problems arise, however, when this turns out not to be the case and they find themselves in a world of fast and fatty foods.

We apply the idea of “the plastic human” to interpret the increasing prevalence of metabolic disorders such as obesity and type 2 diabetes, and to encourage policy-makers to take a life course approach to prevention of these diseases. In turn, we also use insights from experimental studies to explore theoretical issues in evolutionary and developmental biology, such as how developing organisms can show both plasticity and robustness (insensitivity to the environment).

Read:

1. Gluckman, Beedle and Hanson, *Principles of Evolutionary Medicine*, OUP, 2009
2. Gluckman PD et al., How evolutionary applications improve the understanding of human health and disease. *Evol Appl* 2011; 4: 249-63

Visit [www.liggins.auckland.ac.nz/chead](http://www.liggins.auckland.ac.nz/chead)

## Student research projects

- Evolutionary medicine
- Early life epigenetic markers as prognostic tools for adult disease
- Animal models as empirical tests of the developmental origins of health and disease hypothesis

## Contacts

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**Sir Peter Gluckman**

*The Centre for Human Evolution, Adaptation and Disease at the Liggins Institute is headed by one of New Zealand's most recognised scientists, Sir Peter Gluckman.*

*Sir Peter is a Distinguished Professor and Professor of Paediatric and Perinatal Biology at The University of Auckland and was Director of the Liggins Institute from its foundation in 2001 until he stepped down in 2009 to take up a part time position as the first Chief Science Advisor to the Prime Minister of New Zealand.*

*Sir Peter's contributions to the global understanding of how events during development and in our evolutionary past interact with our environment to shape our health has brought him a string of highly prized international awards including: Fellowships of The Royal Society (London), the Institutes of Medicine of the National Academies of Science (USA) and the Academy of Medical Sciences of Great Britain.*

*He is passionate about communicating a better understanding of science within the community and, with colleague Mark Hanson of The University of Southampton, has co-authored popular science books: The Fetal Matrix (2004), Mismatch – why our world no longer fits our bodies (2006) and Fate, Fat and Disease – why exercise and diet are not enough (2012).*



# Perinatal Neuroscience Group

Investigating perinatal brain development and strategies to prevent or treat brain damage in vulnerable newborns

## Principal Investigator

Dr Mhoyra Fraser

## Research focus

### Studies investigating how fetal stress during development can alter fetal stress steroid hormone action

Being born small, even within the normal range, is significantly associated with increased risks of developing hypertension, coronary heart disease and type 2 diabetes. Research shows that adverse events before birth, such as poor maternal nutrition and stress, and fetal hypoxia (oxygen deprivation), alter the development and function of organs and display some degree of sex bias. Such adaptations may safeguard fetal survival during these challenges but become permanent with pathological consequences in adult life.

Exposure to inappropriate levels of cortisol during fetal life may lead to a resetting of hippocampal-hypothalamo-pituitary adrenal axis (HHPA) reactivity. Fetal stress and altered stress steroid hormone activity reduce growth and result in permanent hypertension, hyperglycaemia, hyperinsulinaemia and altered behaviour and hyperactivity of the HHPA axis.

### Studies to advance our understanding of the complex mechanisms which link preterm brain injury to infection/inflammation

Being born too early and too small is associated with severe and debilitating consequences. At least half the survivors have neurodevelopmental problems that affect their daily life while 15% develop severe problems such as cerebral palsy. The cause of this injury

is unclear and there is no current treatment. However, brain injury is very strongly associated with low-grade infection of the placenta and fetal membranes. We are investigating how infection damages the brain, with the goal of preventing or alleviating damage in these vulnerable babies.

A characteristic of the developing brain, in particular the preterm brain, is its limited capacity to repair brain cells following injury. We are therefore investigating the potential for stem cell therapy to prevent or alleviate white matter injury and/or neuronal loss in the immature brain.

Visit [www.liggins.auckland.ac.nz/perinatalbrain](http://www.liggins.auckland.ac.nz/perinatalbrain)

## Student research projects

- Preterm brain injury and the role of intrauterine infection
- Stem cell therapy: is this a viable therapeutic option for preterm brain injury?
- Effects of fetal stress on the long term regulation of the fetal hippocampal-hypothalamo-pituitary adrenal axis
- Prenatal neuroendocrine mechanisms that may contribute to susceptibility to diet-induced obesity in adult life

## Contacts

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### Luke Weaver-Mikaere

Luke Weaver-Mikaere is currently in a PhD biomedical research programme under the supervision of the Liggins Institute's Academic Director Dr Mhoyra Fraser. In his research project he is investigating some of the pathways through which intrauterine infections can lead to fetal brain injury.

*"If we can understand more about the molecular mechanisms that link infection to preterm injury, we will have a better chance to develop strategies to improve clinical outcomes for vulnerable, preterm babies," says Luke.*

Luke has received a Health Research Council of New Zealand Māori Health Research Career Development Scholarship and a Kelliher Charitable Trust Research Innovation Award to support his studies.

# Brain Degeneration and Repair Group

Investigating the origins and mechanisms of degenerative neurological conditions

## Principal Investigator

Dr Jian Guan

## Research focus

Our research investigates the pathology, pathogenesis and underlying mechanisms of degenerative neurological conditions such as Parkinson disease and late-life dementia. We have recently discovered a potential endocrine regulatory pathway of growth factors. Using animal models, we are studying changes in learning, memory, social behaviours and other cognitive functions. We are also examining associated changes in morphology, biological lesions and genetic modifications in the brains, using histology, immunochemistry, cell culture and RT-PCR.

Visit [www.liggins.auckland.ac.nz/brainrepair](http://www.liggins.auckland.ac.nz/brainrepair)

## Student research projects

- Autocrine regulation of growth factors
- The effects and mechanisms of small neuropeptides on neuronal and synaptic plasticity

- Vascular degeneration in Parkinson Disease
- The role for endogenous neuro-genesis and plasticity in functional recovery from Parkinson disease
- Vascular origins of dementia
- Age-related cognitive decline
- Nutrition and age-related memory decline

## Contacts

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**Dr Jian Guan**

*Dr Jian Guan is a Senior Research Fellow at the Liggins Institute. Her research has focused on understanding the biological function of growth factors following brain injury and in chronic neurological conditions in neonatal, infant, young adult and aging brains.*

*More recently she has been investigating the effects of nutrition on brain development, premature aging and cognitive function. Her experience includes designing animal based experiments and models, behavioural testing, neuronal anatomy, neurobiology and pharmacology.*



# Breast Cancer Research Group

We have a particular interest in developing targeted therapies to block tumour growth and progression.

## Investigators

Dr Jo Perry  
Dr Dongxu Liu

## Research focus

New Zealand has one of the highest rates of breast cancer in the world. It is the leading cause of cancer deaths among New Zealand women and one in nine women will be affected during their lifetime. Over the last 20 years there has been significant progress in the way breast cancer is treated and the mortality rate has been steadily declining. However, a significant number of New Zealand women still die from breast cancer or suffer from recurrent disease. It is therefore important to identify new strategies for treating the disease.

One of the most active areas of cancer drug development is “targeted therapies”. These are treatments which block tumour growth and progression by interfering with specific molecules or signalling pathways required for the survival, growth and spread of cancer cells.

Our current research is focused on identifying new therapeutic targets for the treatment of breast cancer. In particular, we are interested in the contribution of secreted growth factors to cancer progression and resistance to therapy. We have identified several potential therapeutic targets which are currently under investigation as part of our cancer research program.

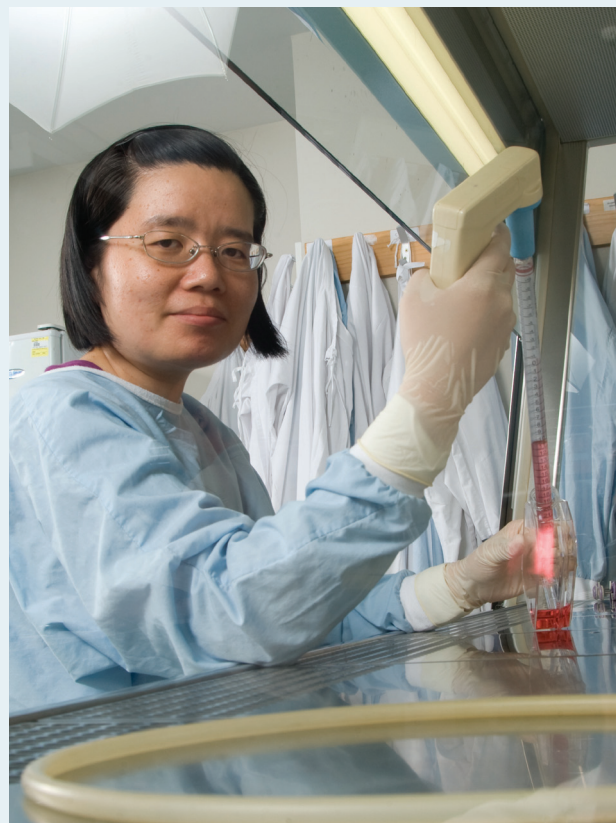
Visit [www.liggins.auckland.ac.nz/breastcancer](http://www.liggins.auckland.ac.nz/breastcancer)

## Student research projects

- Characterisation of novel secreted oncogenes
- The role of human growth hormone in neoplasia
- Inhibiting the function of trefoil factor family members to treat breast cancer
- Characterisation of glial cell line-derived neurotrophic factor family members in human breast cancer
- The role of secreted growth factors in the development of resistance to therapies used in the treatment of breast cancer

## Contacts

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	Dr Dongxu Liu	Investigator	dx.liu@auckland.ac.nz	
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### Dr Jian Kang

*Dr Jian Kang is just one of the high achieving PhD graduates who began their research careers in the Institute's Breast Cancer Research programme.*

*Following a BSc with first class honours, which included a research project with the group, she stayed on to investigate why some breast tumours become resistant to endocrine therapy.*

*Jian became the first recipient of the Merck Young Achiever Award, established in 2010 to recognise excellence in research presentation by emerging scientists at The University of Auckland. She won the award for her paper published in the prestigious cancer research journal Oncogene. It described the role of artemin (a protein which 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. The paper's other authors included Jian's PhD supervisor Dr Jo Perry and co-supervisors Professor Peter Lobie and Dr Dongxu Liu.*

*After completing of her PhD, Jian took up a position as a research officer at the prestigious Garvan Institute of Medical Research in Sydney, Australia. Other graduates from the programme have moved on to postdoctoral positions in leading international cancer research laboratories in Canada, the United States, Europe, Singapore and Australia.*











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