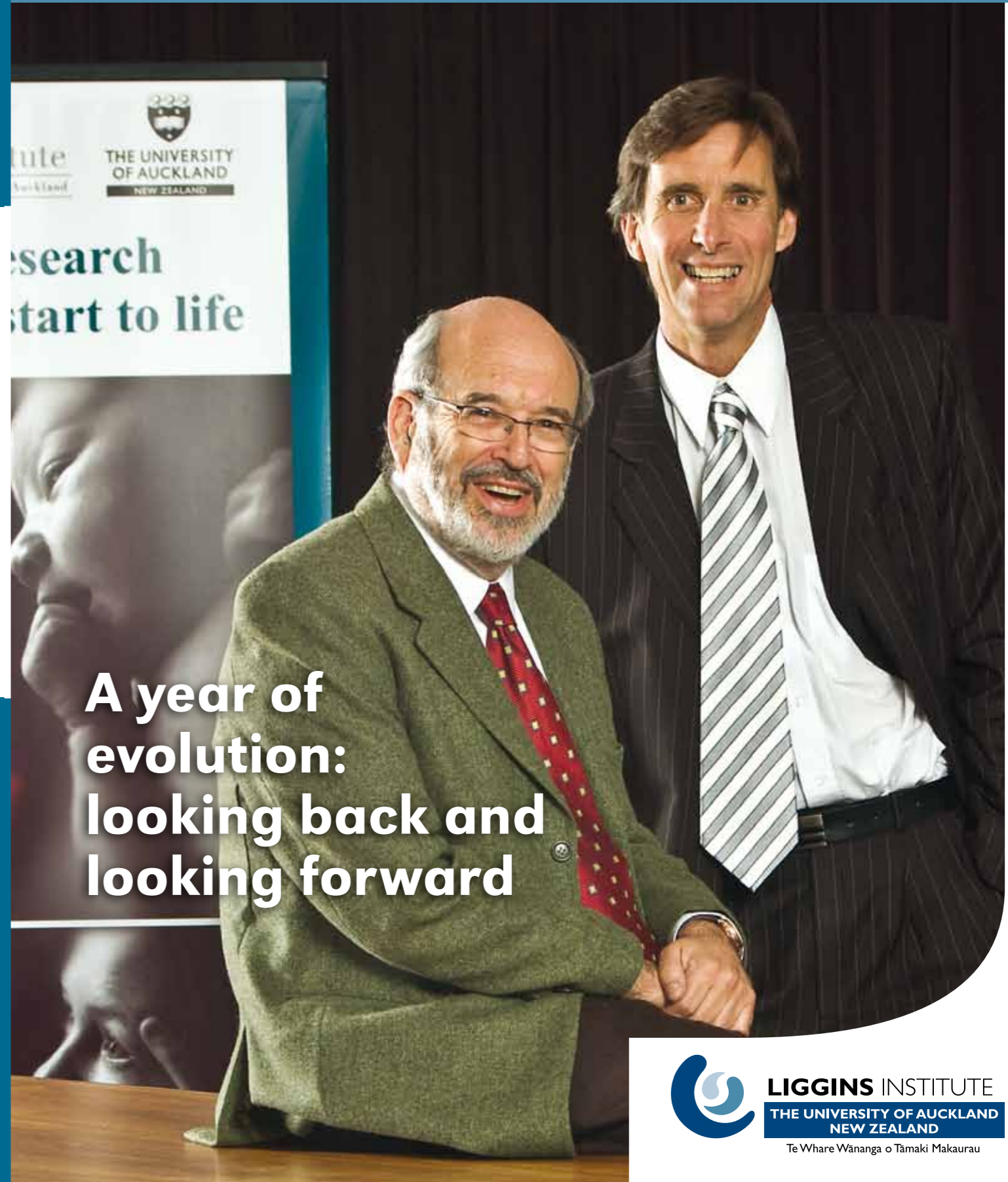


Dialogue

July 2009 | Issue 17



A year of evolution:
looking back and
looking forward

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Te Whare Wānanga o Tāmaki Makaurau

A year of evolution: looking back and looking forward

The year 2009 holds a special place in history; it moves from Charles Darwin's 200th birthday in February to the commemoration of 150 years since the publication of his landmark *On the Origin of Species* in November.

In this issue of Dialogue our stories highlight aspects of the Liggins Institute's central research theme which asks what makes us what we are. We introduce the Liggins' annual lecture series, which looks back at how evolution by natural selection has contributed to

our present: in our bodies, our health, our intellect and our philosophies. In a different time frame we consider how the more rapid processes of development during early life overlay our genetic inheritance to determine our future health and that of our children.

In a sense the Liggins Institute is also evolving as leadership passes to a new generation and its research focus on what makes a healthy start to life is strengthened through expanded national and international partnerships.



Evolution of an institute

The Liggins welcomes a new Director

Professor Wayne Cutfield has been appointed the second Director of the Liggins Institute following a competitive selection process led by The University of Auckland Vice Chancellor Professor Stuart McCutcheon.

Professor Cutfield succeeds founding Director Professor Peter Gluckman who resigned from his directorships of the Institute and the National Research Centre of Growth and Development (NRCGD) to avoid potential conflicts of interest in taking up his part time appointment as the first Chief Science Advisor to the Prime Minister of New Zealand from 01 July. Professor Gluckman will continue to be based at the Liggins Institute where he intends to be a very active member and researcher.

"After 21 years in academic management, this change in role will give me more time to do what I love best, developing research concepts and encouraging the Institute's emerging researchers," he says. "I shall continue to develop my current research portfolio focusing on what determines a healthy start to life, the interface between evolution and medicine and developmental biology at the human-agricultural interface, and at the same time

developing the Institute's international partnerships in epigenetic research.

Announcing the new appointment, the Vice Chancellor said he looked forward to the leadership that Professor Cutfield would bring to the Liggins. He acknowledged Professor Gluckman's contributions in establishing the Institute and the NRCGD, describing them as very important parts of the University's effort to grow its national and international contribution in research and postgraduate education.

"It is a sign of a healthy vibrant institute with a long term future that we can look to the next generation of leadership," adds Professor Gluckman. "I have always believed that no-one should lead an organisation for too long and it is indicative of the maturity of the Liggins Institute that we can find such excellent leadership within. I have every confidence that under the leadership of Professor Cutfield and his Deputy Director, Professor Murray Mitchell, the Institute will continue to grow and enhance its research reputation and its contributions to the public understanding of science."

For his part, Professor Cutfield relishes the opportunity to lead the Liggins Institute.

"In a short time the Liggins has achieved a commanding international reputation in biomedical research through its world class researchers and the strong leadership and research profile of its founder Peter Gluckman," he says.

"My mission is to provide an environment in which every Liggins researcher can deliver world class research. The range of skills and the cutting-edge technologies we have in the Institute give it a unique capacity to deliver high quality translational research that spans the full spectrum of basic laboratory-based science, through pre-clinical and clinical studies and on to health policy. It is the breadth of this translational research that really sets the Institute apart from other biomedical research institutes."

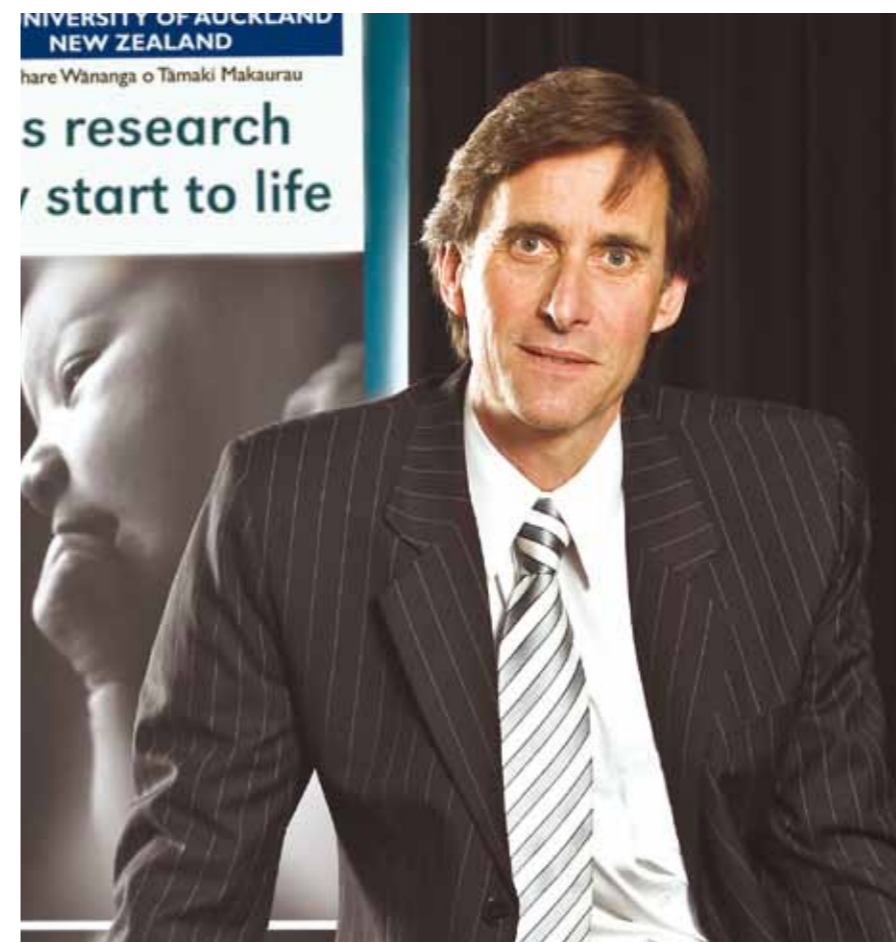
The Institute has a focused research theme of a 'healthy start to life'. Professor Cutfield says that within this theme he would like to see a greater strategic emphasis on discovering what is the full impact of nutrition during critical developmental phases, from before conception through to adolescence, on the health of New Zealanders throughout their lives.

"We are well positioned in this area with broad-based skills in nutrition research but we will need to strengthen our expertise further if we want to capture a leadership role in the field.

"Further, our interest in this field will extend beyond human health to the agricultural arena through collaborative strengthening of our relationship with AgResearch and other agricultural providers.

"At the same time, I see the Institute continuing to develop and refine its roles in the public understanding of science and the LENSscience programme for high school students."

A graduate of The University of Auckland's School of Medicine, Professor Cutfield has an international reputation for his clinical research in the discipline of paediatric endocrinology and as an academic leader. He is Chair of the New Zealand Growth Hormone Committee and Director of the Institute's Maurice and Agnes Paykel Clinical Research Unit - a specially designed children's research facility where he leads a highly productive research group focused on a broad range of clinical endocrine research topics.



Professor Wayne Cutfield

Contents

A year of evolution: looking back and looking forward	2
Evolution of an institute	3
Singapore collaboration brings mutual benefits	4
Singaporean partners join Epi Gen	4
New research centre will focus on foods for health	5
Darwin's legacy	6
Lessons from the past can enrich medical education	7
Team gets behind neonatal research	8
Growing old before you are born	10
Note to Friends	12
Gifts kick-start young careers	13
Seminars via satellite	14



Singapore collaboration brings mutual benefits pg4



Darwin's legacy pg6



Team gets behind neonatal research pg8



Gifts kick-start young careers pg13

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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.

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Singapore collaboration brings mutual benefits

Liggins Institute researchers are joining a major research effort to halt the escalating incidence of obesity and diabetes in Asian populations

Officials estimate that 300 million people world-wide will be diabetic by 2025 - and most of them will be in Asia. In an effort to reverse this trend Singaporean researchers have turned to scientists at the Liggins Institute. Professor Peter Gluckman now leads (on a part time basis) a new research programme in growth, development and metabolic diseases based at the Singapore Institute of Clinical Sciences (SICS). A number of senior staff at the Liggins are also contributing to the programme which covers basic science, clinical and population based studies.

"Coordinating activities between the Liggins and SICS gives us the ability to take cutting edge research and ideas to scale rapidly," says Professor Gluckman. "From the New Zealand perspective, this has provided access to technologies we could not otherwise afford and given us a high profile in what may be the most active and aggressive international centre of medical research."

The programme draws on the Liggins scientists' expertise in developmental epigenetics - understanding how the environment that the fetus and infant are exposed to influences the development of type II diabetes and obesity in adolescence and adulthood. However this focus has now broadened to include the effects on cognitive and emotional development.

The Singapore group has made rapid progress towards its target of over 100 staff since it began less than two years ago. It now has eight principal investigators, including a number with outstanding international reputations.



Professor Gluckman (top, second from left) with his research team at the Singapore Institute for Clinical Sciences

Professor Gluckman is also Chief Scientist for a related programme based at the National University of Singapore which focuses on the clinical and population based aspects of the research. The Translational Clinical Research (TCR) programme in metabolic disease (obesity and diabetes) is funded by the Biomedical Research Council of Singapore.

Liggins researcher Dr Susan Morton, who also heads the new longitudinal study of child development 'Growing up in New Zealand' based at The University of Auckland, has taken a major role in setting up a related study in Singapore. The Singapore project, which is part of the TCR programme, will follow 1200 children from before birth through to adulthood. It will chart their antenatal history and measure clinical markers that will

determine individual profiles of their genetic settings at the time of birth.

Professor Gluckman says that researchers will use these patterns to predict the children's future health. "This will help us find better ways to manage pregnancies and design interventions which might reduce their risks of developing obesity and diabetes," he says.

The TCR programme is administered through the National University of Singapore but involves some 12 different Singaporean partners. The Liggins Institute is an international partner and a number of Liggins investigators are involved as collaborators. "This has been particularly beneficial to the careers of some of our young and emergent investigators," adds Professor Gluckman.

human health," comments Professor Peter Gluckman, who is co-chair of the scientific consortium.

The group has already filed intellectual property claims and signed major research contracts with the food industry.

"The involvement of our Singaporean partners has been critical in opening access to companies that would not otherwise have committed to research in NZ," he adds.

New research centre will focus on foods for health

Partnership builds on common strengths in developmental biology

The Liggins Institute and AgResearch have put the official seal on a collaboration that will maximise the research capability of both organisations in the field of growth and development.

The Pastoral Foods for Human Health Research Centre has been established at the Liggins Institute, with scientists from AgResearch joining their Liggins colleagues in research that is applicable to the health and development of both humans and farm animals. The Centre is being led by Professor Peter Gluckman who sees the initiative as a new vision for using New Zealand's skills in biomedical and biological research to their maximum advantage.

"The Centre draws on the research strengths and resources of both organisations and formalises a collaboration which has in fact taken place for nearly 30 years," comments Dr Jimmy Suttie, Science and Technology General Manager for AgResearch's Applied Biotechnologies Group.

The team will explore fundamental aspects of mammalian biology such as the way the environment during early development determines how nutrients will be partitioned between growth and energy production throughout life. A fetus, human or animal, subjected to poor antenatal nutrition may predict that it will be born into a world where food is scarce. It therefore sets its metabolism to store energy as fat rather than build muscle, thus setting up a tendency towards obesity in humans and carcass fatness in animals.

"Improving our knowledge of these early life processes will give us the capacity to manipulate parameters, such as nutrition during pregnancy, to influence the settings of the genetic switches that children and animals are born with," says Professor Gluckman. "The idea is to improve the match between the pre-birth environment and the worlds that they will grow up in."

Armed with this knowledge, scientists in the Centre will work to develop better animal feeds, animal welfare products and practices and smart ways of handling and processing food products. In turn this will lead to a range of pastoral based foods with human health benefits.

The research programme places priority on scientific excellence and on delivering results which directly fulfil the needs of the pastoral, human health and human nutrition sectors.

"By combining our research effort we hope to make the best use of funding available from public-good and industry sources," says Dr Suttie.

The ultimate goal is to commercialise resulting research data, in turn benefitting local industry and enhancing economic returns.

"We believe that our combined capability across agriculture, nutrition, growth and health is unparalleled in New Zealand," adds Dr Suttie. "It has the potential to deliver considerable benefits to a food industry which is increasingly focused on products with health giving properties."



Dr Jimmy Suttie (left) and Professor Peter Gluckman will bring their knowledge of growth and development to The Pastoral Foods for Human Health Research Centre at the Liggins Institute.

Singaporean partners join Epi Gen

The Epi Gen Consortium, which was formed in 2006, brought together four of the world's leading research groups in the field of developmental epigenetics. This research partnership allowed the Liggins Institute, AgResearch, The University of Southampton and the Medical Research Council Epidemiology Resource Centre in Southampton to partner in their research, accelerate it and share intellectual property as they jointly developed their combined knowledge in the field.

As a result of their collaborations with the Liggins, the Singapore Institute of Clinical Sciences and the National University of Singapore joined Epi Gen in 2008.

Understanding epigenetic processes gives scientists the capacity to manipulate the nutritional and hormonal environment during the early stages of development and change the activity settings on certain genes.

"This has huge potential benefits for the agricultural and food industries and for

Darwin's legacy

From Devonian fishes to art, the Seasons of Life series takes a broad view of evolution

Celebrating a year of all things Darwin, the Liggins Institute's annual lecture series assembles five distinguished speakers to comment on Man's evolution - from the origins of the human body plan to our instinctive love of art.

22 July: Death, Sex and Evolution - 380 million year old fishes and the origins of the human body plan

Award winning Australian palaeontologist and author Dr John Long draws on his own discoveries to explain how perfectly preserved 3-dimensional fish fossils from Western Australia reveal the origins of vertebrate sex and an evolutionary pathway leading from pre-historic fishes to humans. Dr Long has been collecting fossils since the age of seven, his research interests and adventures have taken him to Antarctica, Africa, Asia, North America and Europe and every corner of Australia. His recent work has shed new light on the existence and fate of the dinosaurs of Australia and New Zealand. Currently Head of Sciences at Museum Victoria in Melbourne, he is author of many popular books, including ten for children, on evolution and pre-history.

29 July: The Cousin Marriage Controversy - from Darwin to the US and Modern Britain

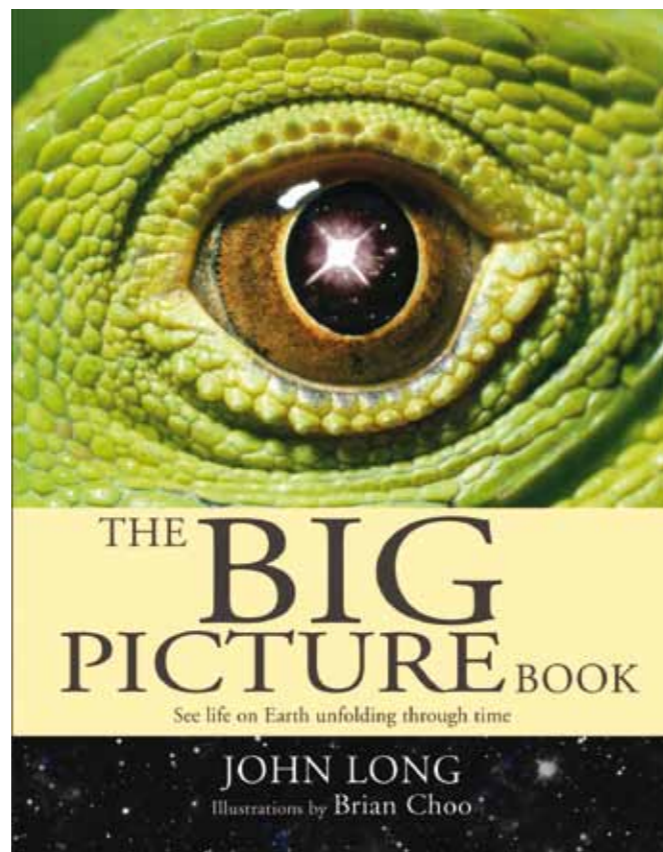
Charles Darwin worried that the early deaths of three of his ten children were attributable to intermarriage within successive generations of the Darwin and Wedgwood families; his wife Emma was his first cousin. Professor Hamish Spencer examines the genetic validity of controversial laws which ban marriage between cousins in some countries. Professor Spencer is an evolutionary biologist whose interests range from the history and theory of population genetics to elucidating fundamental evolutionary processes in groups of organisms, such as molluscs and birds. He is Head of Zoology at The University of Otago and a principal investigator in two of New Zealand's Centres of Research Excellence, the Allan Wilson Centre for Molecular Ecology and Evolution, and the National Research Centre for Growth and Development.

19 August: Evolution, Art, Science and Purpose

Does evolution by natural selection rob life of purpose? In our third lecture, Brian Boyd, University Distinguished Professor of English at The University of Auckland, argues the contrary view. He shows how evolutionary thinking has lately expanded from the biological to the human world, first into the social sciences and recently into the humanities and the arts. Darwin, he says, has made it possible to understand how purpose, like life, builds from small beginnings; in a very real sense, evolution creates purpose. Professor Boyd is an acknowledged expert on the Russian novelist Vladimir Nabokov but his current interests range through evolution, cognition and fiction, the philosophy of science and the relationship between evolution and the humanities. His book *On The Origin of Stories: Evolution, Art and Fiction* (Belknap Press of Harvard University Press, 2009) is described by psychologist Steven Pinker as "insightful, erudite, and thoroughly original."

16 September: Darwin and Medicine

Evolution is geared for survival of the species rather than for individuals to have long and healthy lives. University Distinguished Professor Peter Gluckman heads the Liggins Institute's Centre for Human Evolution, Adaptation and Disease and is the lead author of the first textbook for medical students on evolutionary medicine (*Principles of Evolutionary Medicine*, Oxford University Press, 2009). In this lecture he will explain the evolutionary origins and paradoxes of many problems in modern



The opening speaker, Dr John Long has written a number of books to introduce children to basic concepts in science. During his visit he will meet with teachers and educators as part of the National Research Centre for Growth and Development's community engagement programme.

medicine and how recent advances in science have led to a realisation that incorporating evolutionary thinking is essential for medicine to achieve its full potential.

6 October: The Art Instinct: why we evolved to love beauty

Pleasure in natural and artistic beauty is found across the globe and through history. In our final lecture philosopher Denis Dutton shows how Darwin explains why - from Homer of the Iliad to the Homer of The Simpsons, from the Lascaux caves to Carnegie Hall - human beings are enchanted by the arts. Professor Dutton is author of *The Art Instinct: Beauty, Pleasure, and Human Evolution* (Oxford University Press, 2009), widely regarded as the most important work of aesthetic theory of the new century. He is Professor of Philosophy at the University of Canterbury and editor of the website Arts and Letters Daily.

The Seasons of Life series is an established part of the Liggins Institute's programme to engage with its community to discuss issues which affect our health and society. The early evening lectures are designed for non-scientific audiences and questions are welcomed. They are free and open to the public but bookings are essential.

Refer to the Liggins website www.liggins.auckland.ac.nz for details, email friends@auckland.ac.nz or telephone (09) 303 5972 for bookings, updates or further information.

Lessons from the past can enrich medical education

Father of Darwinian medicine gives a lecture the Liggins Institute



Todd Smith (left) tells Professor Randolph Nesse about his research poster which was presented at BioEd 2009. The meeting, hosted by the Alan Wilson Centre, in Christchurch in February was one of a coordinated series of events celebrating 200 years since the birth of Charles Darwin.

Evolution is something of a passion for Todd Smith, a fourth year medical student at The University of Auckland, but he never dreamed that a Summer Studentship at the Liggins Institute would have him chatting with two leading figures in the exploding field of Darwinian medicine, Professors Randolph Nesse and Peter Gluckman.

"I've been interested in evolution for years," says Todd. "It educates on a scientific level and also has the power to speak to us philosophically." His surprise that his fellow students knew so little about it led him to write an article about it for the student magazine.

So it was an amazing coincidence when last year a classmate pointed out a student project at the Liggins Institute evaluating the teaching of evolutionary principles at medical schools around the world. "I put all my energy into getting it," says Todd.

Darwinian medicine applies the principles of evolutionary biology to problems in medicine. Professor Gluckman, with colleagues Dr Alan Beedle and Professor Mark Hanson (University of Southampton), had just written the first ever textbook of evolutionary medicine for medical students (*Principles of Evolutionary Medicine*,

Oxford University Press, July 2009) and wanted to see a course taught in Auckland.

During three months' research, under the direction of Liggins research fellows Dr Beedle and Dr Tatjana Buklijas, Todd discovered that while evolution was widely taught to biology students, there were only 16 evolutionary medicine courses taught worldwide - and of those only three were through medical schools.

He was able to discuss his findings with Professor Nesse when the latter visited the Liggins in February to deliver a public lecture 'Medicine without evolution is like engineering without physics'.

Professor Nesse is Professor of Psychiatry and Professor of Psychology at the University of Michigan, where he directs the Evolution and Human Adaptation Program. Considered one of the founders of the discipline, he collaborated with George Williams on several early works in Darwinian medicine, including *The Dawn of Darwinian Medicine* (1991) and *Why We Get Sick: the New Science of Darwinian Medicine* (1995).

"It is perfectly possible to practice medicine without understanding evolutionary biology;

millions of doctors do it every day," claimed Professor Nesse in his lecture. The question he posed was whether they could be more effective if they understood natural selection in more depth.

He described the human body not in terms of the popular 'machine' analogy but rather as a bundle of trade-offs shaped by natural selection to maximise reproductive success, often at the expense of individual health and longevity. He believes that asking evolutionary questions is crucial to understanding why natural selection has left the body vulnerable to so many diseases.

His explanations pointed to the mismatch between our bodies and aspects of the modern environment that give rise to chronic disease and our bodies' inability to keep up with the faster evolving pathogens.

He cited examples of where natural selection has shaped defence regulation systems to express responses, such as pain, fever, cough and anxiety, which may not always be necessary in today's world. However, as he explained, it was these very responses which ensured survival and thus reproduction at earlier points in Man's evolutionary past.

Team gets behind neonatal research

Project to improve baby ventilation procedures draws widespread support



Working to improve outcomes for pre-term babies (left to right), Sue McKnight, Dr Kitty Bach and Shirley Peachey.

Why would three senior nurses, already working long hours, spend their precious time-off supporting a research student?

"Because we believed in the project and wanted it to succeed," says Shirley Peachey, a Clinical Charge Nurse in Auckland City Hospital's neonatal intensive care unit.

Shirley, fellow Clinical Charge Nurse Sue McKnight and Nurse Educator Jean Bertram, have each devoted the equivalent of half a year's full time work to assist young paediatrician Dr Kitty Bach with her PhD project aimed at improving the clinical care of small, sick babies.

Kitty's PhD supervisor, Consultant Neonatologist and Principal Investigator at the Liggins Institute Associate Professor Frank Bloomfield, is more direct. "It's been a huge commitment on the nurses' part," he says. "Quite simply, the research would not have happened without their involvement."

The nurses were driven by a desire to improve clinical outcomes for newborn babies who sometimes face months of intensive care. Sue explains that throughout the unit the focus is on each child and its long term health. "Anything we do has to be the best. There is a culture of learning in the nursery and everyone

has been interested in what we were doing and trying to achieve. We all want to improve our clinical practice."

For nearly 50 years, Auckland's National Women's Hospital (now National Women's Health) has had a reputation for its pioneering research-based care of newborn babies. In the 1960s and 70s Sir William Liley and Sir Graham Liggins achieved international fame for clinical innovations which increased the survival of sick and preterm babies. More recent developments in technologies and understanding have improved the odds for even younger and smaller babies.

The innovations are not without cost, says Kitty. "Almost all babies born before 28 weeks' gestation need artificial ventilation to breathe, but we know that this causes lung injury and chronic disease."

Kitty's particular interest is in the shear stress injury caused when the pressurised ventilator gases create turbulence at the junctions of the babies' tiny airways. The ventilators require a certain gas flow to pressurise the system and these are based on standards that have been adopted in neonatal units throughout the world. She says they noticed that the babies seemed more comfortable if the machines were operated at lower flow rates, but without evidence that the procedures were still effective and did in fact reduce lung damage, it would not be ethical to make any changes.

Kitty is one of a growing number of qualified medical specialists taking time out from the clinic to undertake research at the Liggins Institute. The Liggins fetal and neonatal physiology research team has a focus on improving clinical care through laboratory based research. They have developed a model intensive care unit at the Institute's research farm outside Rotorua. Here Kitty, Sue, Shirley and Jean have been using clinical equipment, and a certain amount of ingenuity, to ventilate and care for preterm lambs and collect data to show whether lower gas flow rates cause less lung damage.

The project has taken three years to complete, frequently involving 24 hour monitoring of the lambs under conditions quite different from the hospital nursery. It has been a team effort, dependent on the nurses' clinical experience, which Shirley estimates at nearly a century between them all.

"They've been a huge help, not only in the unit and helping with the delicate surgeries, but to me personally," says Kitty, "boosting my morale and making sure I got to eat and sleep."

"They've turned their hands to anything and everything that needed doing - from chopping wood for the fire to doing the washing for the next day's surgeries," she adds.

But for the nurses it has also brought rewards. "We've learned new skills, it never seemed hard," says Sue.

"I really enjoyed it, I had never been exposed to basic research before," adds Shirley. "It was good to get out of the nursery and do something completely different."

The study showed that ventilation was still effective at lower gas flow rates. Furthermore,



Dr Kitty Bach came to Auckland from the Netherlands for a one year clinical fellowship in 2004. She has been supported through her PhD by a prestigious Clinical Research Training Fellowship from the Health Research Council of New Zealand, with research funding provided by the Auckland Medical Research Foundation, the National Research Centre for Growth and Development and Auckland City Hospital. Dräger Medical Infant Care and Fisher and Paykel Healthcare provided clinical equipment for the study.

laboratory examination of lung tissue, in collaboration with Associate Professor Stuart Hooper's team at Monash University in Melbourne, has revealed a marked reduction in physical damage and in the activity of genes known to be early indicators of lung cell damage, compared with samples from animals ventilated at higher flow rates.

Already, it has brought the team international recognition. Kitty won the New Investigator's Prize when she presented her preliminary results at the recent meeting of the Perinatal

Society of Australia and New Zealand and she received a rare invitation to make an oral presentation at the prestigious Paediatric Research Society meeting in Baltimore.

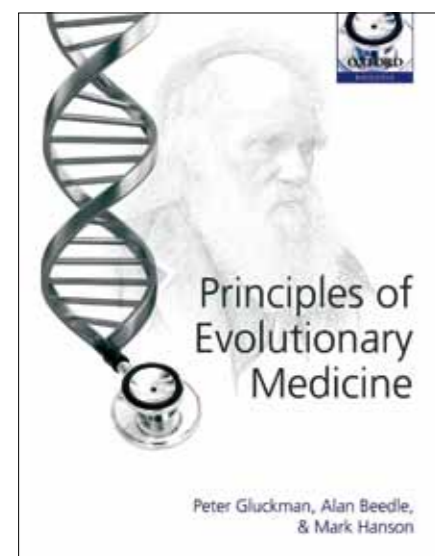
Once she has submitted her thesis, Kitty will seek approval for a pilot clinical trial of the improved procedures in the neonatal nursery. She already has financial backing for this from a philanthropic donor who supported an earlier Liggins based clinical research project and is keen to see on-going improvements in neonatal health.

Growing old before you are born

Professor Peter Gluckman discussed the far reaching impact of events at the beginning of life at The University of Auckland's Golden Graduates event in November 2008. We have received many requests for copies of this and present here an edited version.

This year is the 125th anniversary of the founding of the University; it is also 150 years since the most important day in biological history. On July 1, 1858 a joint paper was read at the Linnean Society in London. Sir Joseph Hooker read it on behalf of the two authors Alfred Russel Wallace and Charles Darwin, neither of whom was present. It was the first public description of the fundamental organising principle of biology, that of adaptation and natural selection. It is not really possible to understand how an organism works, how its parts fit together, without this integrating, organising principle. Yet despite this, medicine has been slow to recognise its importance. Indeed a textbook we have written, which will be published in July 2009, is the first organised summary of evolutionary medicine - 200 years after Darwin's birth.

Closely linked to evolution is the concept of heredity and genetics. Genes are made from DNA and it is through this that the biological instructions that make us what we are carried from generation to generation. At least that has been the dogma. For the last 100 years the whole of medicine has been focused on a simple dichotomy: genes and the environment - nature and nurture. Most people believe that the attributes we are born with are innate and fixed; attributes that develop after birth are due to nurture and can be changed. That mindset has been the dominant paradigm in science for the last three decades. The biological world has been dominated by the hunt for genes and clinical medicine has been



This textbook published in July 2009, 200 years after Darwin's birth, is the first organised summary of evolutionary medicine.

driven by magic bullet approaches or by trying to change adult life style.

That simple dichotomy is totally misleading and the concept that the gene is the only form of biological inheritance is flawed. The Liggins has been at the forefront of showing this to be so.

The question of what makes us what we are and will be is the most fundamental question in biology. Our research has revealed a further dimension: the process of development itself - arguably the most important determinant of our lives, and what we will be. Surprisingly, the impact of what happens at the very start of our lives is felt through the whole of our lives and into the next generation.

It is this work that has made the Liggins Institute world famous. Our Institute is unique in the way we have taken a very multidisciplinary approach: theoretical work, studies of genes and gene switches, studies in animals, clinical studies, population studies and even health economics studies. We direct research activities in seven countries, we even have a small branch based in Cambridge UK.

If a pregnancy is less than optimal, babies can be born small or premature and these babies can have lots of problems. They can be very frail, their brains can be damaged, their lungs may not work well. You will be aware that when infants are not properly fed, do not get adequate stimulation or are abused, they may have problems in childhood: impaired cognitive development, impaired stress responses and later emotional problems - it is also the case when fetuses have a poor environment inside the womb. Babies who have a poor start to life grow up to have more problems in adolescence, more obesity, more heart disease, more diabetes, more osteoporosis, more anxiety, more schizophrenia.

But the aging process is also changed: babies with a poor start to life grow older faster. A normal mouse lives about 700 days, if its mother had an inadequate diet during pregnancy it will only live 500 days - a forty per cent reduction in life span. Humans do the same. In Africa, where there is not the overlay of modern medicine, those born with a poor start to life have their life span shortened by an average of 15 years. So, we all started to age at different rates from before we were born. For those with a poor start to life, the impact is twofold: not only are they more likely to get diseases such as diabetes that will impair their

"The question of what makes us what we are and will be is the most fundamental question in biology."

quality of life, but the aging process itself is accelerated. They grow old faster.

How can this be? When crocodiles lay their eggs, whether the egg hatches into a male or female crocodile has nothing to do with their genes; crocodiles do not have sex chromosomes like we do. If the egg is laid in cool sand it becomes a female and if it is laid in warm sand it becomes a male. Simply put, the environment the embryo grew in radically changed aspects of the crocodile's biology for life - its behaviour, its genitalia, its growth. For the female bee, whether the larva turns into a queen or a worker depends solely on whether it is fed royal jelly. The worker and the queen have identical genes, but are very different. This is the new biology of gene switches - what we call epigenetics. Each gene has literally hundreds of switches that can be set like stops on an organ - but once they are set in early life many are essentially set for life.

We have shown, in animals and now in humans, that before birth these gene switches are set relative to the environment the mother creates for her embryo and fetus. We have learnt how to measure these switches, we have even shown how to shift these switches back to the proper set points after birth.

Why do fetuses have moveable switches on their genes? Well fetuses are just like us - we like to know about tomorrow's weather. They use whatever information they get from mother to predict the world they will be born into and set their gene switches accordingly, adapting their pattern of development to fit that world. If they predict a world where food will be short, they will shift their biology to deal with this. So they will prefer a high fat diet and take longer to be satiated so they can store fat when they can, just like a camel. They will slow their growth, make less muscle and change their metabolism. But if their forecast is wrong and they find a world rich in food, they are more likely to become obese and get diabetes. If they predict a stressful world because mother has been abused, their brains develop differently: they will have shorter attention spans, may be more aggressive, more anxious, their brain chemistry and hormones will be changed.



Professor Peter Gluckman addressing The University of Auckland's Golden Graduates

But fetuses are also like investment bankers (perhaps a dangerous analogy in these times) - they have to decide whether to invest for the short or the long term. If they think their world is going to be dangerous, they predict they are more likely to die early. The biological incentive of evolution is to reproduce, not to live forever. Our biology is designed to produce an optimal number of living offspring - think of salmon: mate once and die but be prolific in doing so.

If you do not think you are likely to live long, you are not going to take out an investment which has no payback for 50 years. Similarly, a fetus in that situation uses its limited energy and shifts its biological switches to accelerate its development. It invests less in the very energy consuming processes of repairing and maintaining its cellular systems against the damage caused by everyday exposure to ozone, toxins and radiation from the sun that eventually destroy our cells and lead to organ failure and death. It invests less in making spare cells, so we have fewer brain cells (making us more likely to have problems with our brains later in life), fewer kidney cells, fewer blood vessels. So babies who start life poorly are more likely to end life poorly: more heart disease, diabetes, osteoporosis and quicker degeneration.

But if we predict a world of plenty, we know we can get a better reproductive return by investing for the long term and a long life with more direct and indirect reproductive opportunities. I say indirect because we now know that in pre-modern societies

grandmothers were important components of child survival and that is why humans are unique in having a menopause and living beyond their own reproductive period. So the clock of aging is set early in life by shifts in these gene switches.

"The impact of what happens at the very start of our lives is felt through the whole of our lives and into the next generation."

What makes a poor start to life? The critical period extends from before conception through infancy; the major factors are nutrition and stress. These are the signals evolution has given the fetus tools to detect. Stress is easy to understand. But for nutrition it turns out that both extremes - not enough and too much - are bad. Nutrition has to be balanced and the most critical time is around the time of conception, when the embryo is most vulnerable, but it extends through infancy. Unfortunately people confuse a poor start to life with measures of birth weight; one can be of perfectly normal birth size yet have had signals of a dangerous future. Perhaps our highest research priority at the moment is to have a test that will allow us to tell who has had a poor start to life.

How important is this? Our data suggests that a poor start may contribute up to 30-50% of

the risk of the diseases of middle and old age. For all the hunting, genes only explain 10-15% of the risk of diabetes. This work is also important because it shifts the focus. We are currently doing an economic analysis, but all the preliminary work suggests that it is far more effective to intervene with good quality health education for young women and men (from primary school onwards) explaining how to drive those most important machines, their own bodies.

Can we do anything about it? Yes we can. In animals, we can already reverse the gene switches after birth. We shall soon be able to measure those switches in infants and I am certain we will be able to find ways, involving nutrition and early intervention programmes, to improve the destiny of at-risk children, as we have done in animals.

My goal has always been simple: to demonstrate that New Zealand can lead the world in an area of science; to show we can do it all - from the laboratory to the population; to show that we can be at the hub of an international research network. I think we have done that, but it is hard. It is only possible if we have a University that is intellectually strong and able to take intellectual risk. We cannot let the capacity to innovate slip, and sadly we live in a country which is yet to fully realise the critical role of research, knowledge and human capital as our only way ahead. We are struggling to survive. We cannot maintain these efforts and the standing of this University without your help.



Note to Friends

Since I wrote my first Note to Friends five years ago both the Liggins and its Friends have grown and flourished. The Liggins team of researchers, students and support staff has doubled in number, their international network of collaborations has grown and their research achievements have brought world fame.

This year marks a new milestone as Peter Gluckman steps down as Director in order to devote more time to his research and to serve part-time as the Prime Minister's Chief Science Advisor. It is wonderful to know that Peter is committed to expanding his research effort at the Liggins while taking on this critical role for New Zealand. I am delighted that Wayne Cutfield has been appointed Director and I have no doubt that the Institute will go from strength to strength under his leadership.

As the Liggins moves through this transition, and given the general climate, it is important that the Friends redouble their effort to support the Institute - their research is so important for the health of future generations.

The Friends of the Liggins Trust is also evolving and this year two new trustees have joined our Board. Former Principal of the Youth Court Judge Mick Brown is well known as an outspoken advocate for children and young people while Lyndy Sainsbury has outstanding credentials in community fundraising, most notably as Chair of the Museum Circle Foundation during the Auckland Museum's Grand Atrium Development project. Together we look forward to expanding our support for the Institute and developing the active involvement of our Friends.

I know that many of you enjoy the Institute's Seasons of Life lectures which have previously featured such international scientists as Lord Robert Winston and Professor Michael

Meaney. This year's series promises more treats as five distinguished speakers take the stage between July and October (see page 6 for details).

Our major fundraising event for 2009 is geared to the challenging economic times. On 10 September our friends and long time supporters Team McMillan BMW will open the doors of their Newmarket showroom for our Couture Car Boot Sale. All money raised will go to the Liggins Institute to assist their research into how events before birth and during infancy affect lifelong health.

You can help us by editing your wardrobe of all beautiful, but unwanted, New Zealand or international designer items and taking them to drop off points at the Liggins Institute 2-6 Broadway, Newmarket; or Regal Drycleaners 402 Broadway, Newmarket; or Regal Drycleaners 215 Kapa Road, Kohimarama. (Please let Regal know you are dropping off for the Liggins Institute).

Then go 'eco-chic' - come to our Couture Car Boot Sale and update your wardrobe with a gorgeous pre-loved frock. If you need any further information or would like to join our mailing list for updates and invitations please telephone (09) 303 5972 or email friends@liggins.auckland.ac.nz.

Warm regards

Roxane Horton
Chair, Friends of the Liggins Institute
Committee



Roxane Horton

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

Hon. Judge Michael Brown
Professor Peter Gluckman
Roxane Horton
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.

Gifts kick-start young careers

Two separate grants are funding innovative research projects

Research at the Liggins Institute depends on the contributions of bright young people from New Zealand and abroad. "We face intense competition from similar institutions to recruit students and post doctoral fellows of this calibre," says Deputy Director Professor Murray Mitchell, acknowledging the generosity of two organisations that are assisting Liggins research trainees.

Dr Steven Dodd, Account Manager for life sciences company Invitrogen, says that Invitrogen is delighted to see the far-reaching impact of the support they have provided for a post-doctoral fellowship in epigenetic research, awarded to Dr Anna Ponnampalam.

"Invitrogen has a particular interest in epigenetics research," he says, "and while the field is still in its infancy, we recognise that the work at the Liggins Institute has the potential to increase our understanding of the importance of epigenetic events in the world of life sciences."

Epigenetics is a term given to chemical changes that occur in DNA molecules without changing the genetic code. These changes are triggered by environmental factors and have the effect of regulating the activity of particular genes in the same way a dimmer switch regulates the intensity of a light.

Anna has been investigating epigenetic processes that take place in the endometrium (lining of the womb) during normal menstrual cycles. "We believe that this information will help us to understand some of the abnormal epigenetic processes that prevent successful implantation of a developing embryo or lead to early miscarriage," she says.

Anna won a President's Presenter's Award when she presented her research at the 2008 international meeting of the Society for Gynecologic Investigation. She has also secured a grant from the Liggins

Institute Development Fund for on-going research. Invitrogen's funding has indirectly helped three students who achieved Masters of Science degrees each with First Class Honours under Anna's supervision. They will now continue their research as Anna's first PhD students.

Meanwhile first year post-doctoral fellow Dr Kristin Connor and PhD student Luke Weaver-Mikaere have just learned they will benefit from the generosity of the Kelliher Charitable Trust. The Kelliher Trust has provided two awards for innovative research by young investigators at the Liggins Institute.

"These awards are intended to promote new ideas and collaborations that will catalyse further research opportunities," says Professor Mitchell. "They are unique to the Liggins and support our strong commitment to helping our young scientists develop their careers."

Kristin completed her PhD at the University of Toronto before joining the Liggins earlier this year. Her innovative project builds on work at the Liggins which shows that a poor start to life leads to later health problems such as obesity. But Kristin says that a poor start may not just be due to early under-nutrition, over-nutrition is also to blame. She will investigate how hormone pathways that regulate appetite develop in young brains and whether these change when mothers consume a high fat diet during pregnancy and lactation.

For his project, Luke will explore the cellular events that link inflammation caused by low-grade infection of the placenta and fetal membranes during pregnancy to brain damage in the unborn child and its preterm delivery. Luke also received a prestigious Māori Health PhD Scholarship from the Health Research Council of New Zealand to support him through his studies.



Professor Peter Gluckman (left), Dr Anna Ponnampalam and Dr Steven Dodd at a function marking the final instalment of Invitrogen's support for epigenetic research at the Liggins Institute.

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.

Seminars via satellite

School students quiz scientists on national television



Behind the scenes: The three seminar pilot series was co-presented by teachers and scientists, produced by Volt TV Productions (Auckland) with equipment provided by R2.CO.NZ (Wellington) and broadcast to five high schools in West Auckland, Gisborne, Tauranga and Kaitia that had been provided with a set-top box and satellite dish.

LENScience

Bringing schools and scientists together

The Liggins Institute is home to LENSscience, a unique education concept that was established in 2006 to provide links between secondary schools and biomedical science communities.

LENScience is based in the Institute's purpose designed Sir John Logan Campbell Classroom but is forging links with schools throughout New Zealand and inspiring programmes across the world.

Programmes, linked to current school curricula, are designed and delivered by senior school science teachers in collaboration with scientists.

Programmes target students at different levels of interest, background and achievement. They include day classes for Year 7 to 13 students, a mentor programme for high achieving students in Years 10 - 13 and initiatives specifically targeting Māori and Pasifika students as well as the interactive TV seminar series for senior biology students.

Programmes are backed up by contextualised learning resources, an interactive wikisite and professional development opportunities for teachers.

Schools are given free access to all LENSscience programmes but the Institute relies on the support of its community to make this possible.

LENSscience acknowledges the on-going support of the National Research Centre for Growth and Development, the Sir John Logan Campbell Residuary Estate, suppliers and other organisations.

<http://lens.auckland.ac.nz>

With all the tension and excitement that go with a live broadcast, LENS-TV hit New Zealand's national airwaves last October. The Liggins Institute's public areas were transformed into a television studio, complete with live audience, for three pilot seminars designed to give senior biology students an added boost in their preparations for end of year examinations.

This year the renamed LENSscience Connect will broadcast eight seminars to more than 1,000 students at 80 schools from Kaitia to Invercargill, Gisborne to Fiordland between May and November, on topics such as breast cancer, the effect of the environment on gene expression, climate change and human evolution. Students use a wiki (a collaborative website) to question presenters live during the seminars or to later add their ideas to an on-going, on-line discussion.

The programme is an extraordinary story of lateral thinking and cooperation. It is the realisation of the long-held ambitions of LENSscience Director, Jacquie Bay and Liggins founding Director Professor Peter Gluckman to unite students across the country in learning experiences that highlight the work of local scientists. They both believe that modern information communication technologies hold huge potential for connecting teachers and learners, not just in schools (or in science) but right across the community.

These seminars aim to challenge students focused on achieving excellence in NCEA level 3, NZ Scholarship and other examinations. "Even in our largest schools there are comparatively few working at this level but in smaller centres these students can feel very isolated," says Jacquie.

Her initial attempts to reach this widespread audience through traditional conferencing and internet technologies proved disappointingly unreliable. Solutions only evolved when she brainstormed with staff from The University of Auckland's Information Technology Services (ITS).

"We needed to think outside the square," says technology architect Robert Hamilton, who called upon his contacts at broadcast-telecommunications company Kordia™ to investigate the possibility of using their satellite technology.

"The project just took off from there," adds Jacquie. "Every one was keen to put theory into practice but it was nearly the end of the school year and we had only a few weeks to put it all together."

I would like to help the Liggins Institute and become a valued member of the Liggins community

Please enrol me as a friend

Single @ \$60 per year Double @ \$100 per year Lifetime Friend @ \$1000 each Business or organization @ \$2000 per year

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I enclose my donation \$ _____

My cheque is enclosed (Please make cheque payable to Friends of the Liggins Institute)

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Please Post To: Friends of the Liggins Institute, PO Box 110085, Auckland 1148, New Zealand

Further information: Telephone 64 9 303 5972, Facsimile 64 9 373 7497, Email friends@liggins.auckland.ac.nz

Thank you for supporting the Liggins Institute. Gifts and membership donations are tax deductible.

We would like to be able to cater to your interests. If you wish, please make a few comments below about what aspects of the Liggins Institute interest you and what you would like to know more about or see more of. You may also be willing to describe what motivates you to support the Institute. The information provided will be kept confidential, but we will use it to plan our programmes so that our supporters gain maximum benefit from their association with the Institute.

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

Please fold and tape closed. If you have enclosed a cheque you may prefer to place in an envelope using the FreePost number and address on the reverse of this form.

For Robert and the ITS team it was new territory, involving a huge commitment of time, resources and personnel to establish links to Kordia for the broadcasts and, at the same time, relaying the seminars live via the high speed Kiwi Advanced Research and Education Network (KAREN) and traditional internet.

The effort has been worthwhile and a lot of fun says Robert. "It's been amazing to have the live feed back from the schools and for the first time see the direct impact of our work."

The Kordia team immediately saw the long term potential of the collaboration and readily contributed resources to the project. Kordia CEO Geoff Hunt says that it fits in perfectly with the company's single organising idea - bringing people and technology together.

"This project is doing just that; delivering better technology into regional New Zealand in a way that can positively impact current educational resources," he says.

"The regions can often play second fiddle to the metropolitan areas, but Kordia is focused on delivering ubiquitous standards of technology to all New Zealanders. Kordia's work with the Liggins Institute is yet another example of this."

Over 300 students participated in the trial which proved a great success, rating highly amongst students and teachers for its relevance and usefulness. Of these students, 85% intend to study science, engineering or medicine at university. The feedback was summed up in the comments of one Year 13 student who said, "I found the seminar inspirational - the big picture of human evolution has never been expressed so clearly for me."

"Satellite technology gives schools right across the country direct access to the very latest scientific knowledge and ideas from world class researchers by simply turning on the TV," says Jacquie. "The interactive website and links allow students to form nationwide connections and facilitate conversations between our current thought leaders and those of tomorrow."