

insight

PRINCE HENRY'S INSTITUTE OF MEDICAL RESEARCH Newsletter Autumn 2004

Director's message



Dear Friends,

Welcome to the Autumn 2004 issue of *Insight*.

Over the past few months, Prince Henry's Institute has been successful in receiving grants from a range of sources including the National Health and Medical Research Council, Schering AG and Diabetes Australia.

These grants enable our scientists to tackle the health problem of male infertility, to investigate the link between body weight and fertility, and to continue our research into diabetes. All of which, you can read about in this issue.

Happy reading!

Regards
Professor Evan Simpson

Insight Prince Henry's Newsletter

Prince Henry's Institute of Medical Research
PO Box 5152 Clayton VIC 3168 Australia
Tel (03) 9594 4372
Fax (03) 9594 6125
www.phimr.monash.edu.au

Male infertility research leads to estrogen

The problem of male infertility is a complex issue. Four per cent of Australian men suffer this condition. With half of these men, the cause of the problem is unknown.

A recent discovery at Prince Henry's Institute sheds light on the problem of male infertility by proving that estrogen is not only crucial in female fertility but also essential for males.

Current research by Dr Colin Clyne has found that a protein called LRH-1, which is a key factor in estrogen production in females, also regulates estrogen production in the male testis.

Utilising the previous work of Professor Evan Simpson, who showed that human male patients unable to synthesise estrogens are infertile, Dr Clyne will investigate LRH-1 presence in the testes and its exact function.

Using new funds received from the National Health and Research Council over the next three years, Dr Clyne hopes to identify the genes regulated by LRH-1 and the proteins with which it interacts.



Dr Colin Clyne investigates the protein LRH-1 found in the testis.

These studies may help to identify new genes associated with male infertility and to develop more effective treatments for this common health problem.

This work was published in the January 2004 issue of *Endocrinology*.

For more information visit
www.phimr.monash.edu.au

Inside

- 2 Schering deal signed for prostate, infertility, contraceptive research
- 3 Estrogen deficient eggs survive to fertilisation
- 3 Prince Henry's features in *Nature* and *Science*
- 4 Linking fertility to bodyweight
- 4 Minister praises research on World Diabetes Day

Schering deal signed for prostate, infertility, contraceptive research

A major collaborative research and licensing agreement with pharmaceutical company Schering AG will expand current research into male reproductive health



Above: (from left) Prof Evan Simpson, Director of PHIMR and David de Kretser, Director of Monash Institute, will combine their research expertise to improve men's health.

Above right: (from left) Dr Moira O'Bryan, Prof Gail Risbridger (MIRD) and Assoc Prof Rob McLachlan (PHIMR) working together on men's health under the Schering agreement.

New therapies for prostate disease, male infertility and male contraceptives are the focus of a major collaborative research and licensing agreement between Schering AG (a leading German pharmaceutical company), Prince Henry's Institute of Medical Research and the Monash Institute of Reproduction and Development.

Prince Henry's Institute and Monash Institute will combine their men's health research expertise with Schering AG in this exciting research and development program.

This expanded collaborative network – called "The Melbourne Male Network" arose from an existing collaboration between Schering AG, Monash Institute and PHIMR.

"This agreement reinforces the value of basic research in the development of new approaches to the treatment of prostate cancer and disease", says Professor Gail Risbridger, Head of the Centre for Urological Research at Monash Institute.

"Scientists at the Centre, in collaboration with Professor Evan Simpson, Director of Prince Henry's Institute, will look at the hormonal control of

the prostate in an effort to develop new treatment options," she said.

The male infertility component to be conducted at PHIMR will be led by Associate Professor Rob McLachlan and Dr Liza O'Donnell. Sperm production will be a focus of the team with the aim of identifying new targets for male-based contraceptives.

The male infertility team at Monash Institute will focus on genes implicated in male fertility and will be led by Institute Director Professor David de Kretser with Dr Moira O'Bryan.

"This alliance recognises the globally significant research expertise of Prince Henry's Institute and Monash Institute in the fields of prostate disease and male reproductive health and ensures a long term commitment to improving men's health overall," said Professor Simpson.

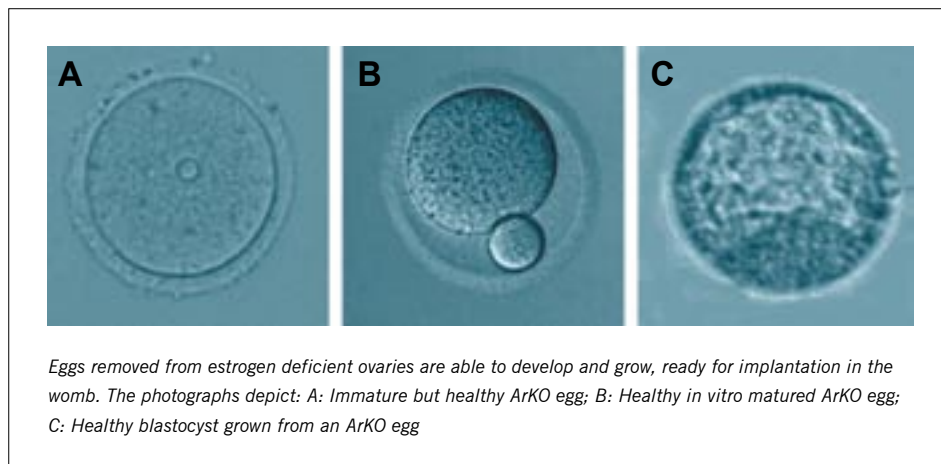
Estrogen deficient eggs survive to fertilisation

Estrogen has long been thought to be crucial in the developing life of an egg, for fertilisation and embryo development. Scientists have now shown that this is no longer the case.

Research led by Dr Margaret Jones of Prince Henry's Institute and Dr Gayle Jones from the Monash Institute of Reproduction and Development has shown that estrogen is not necessary for eggs to be matured or fertilised.

In previous studies using the ArKO mouse (deficient in estrogen) conducted by Kara Britt, the Young Australian of the Year in Science and Technology in 2002, it was found that with a lack of estrogen, the mice ovaries underwent progressive degeneration and the females were subsequently infertile. At the time, it was thought that the actual egg would not be intact.

Further studies in the young female ArKO mice, led by Dr Margaret Jones



and Dr Gayle Jones, have established that the developmental potential of the egg is saved by removal from the estrogen deficient ovary.

The eggs removed from these ovaries matured in vitro, could be fertilised in vitro and developed through to the blastocyst stage, ready for implantation in the womb.

"This research is significant because it demonstrates that estrogen is not required for the eggs to be healthy, fertilised and undergo development," said Dr Margaret Jones.

"At this early stage, we are yet to determine whether the embryos produced from estrogen-deficient eggs are viable when transferred to foster mothers," said Dr Gayle Jones.

"Although estrogen deficiency is not a common condition in humans, our research contributes to the overall knowledge of reproductive health and we hope will have implications for improving infertility treatments in the future," she said.

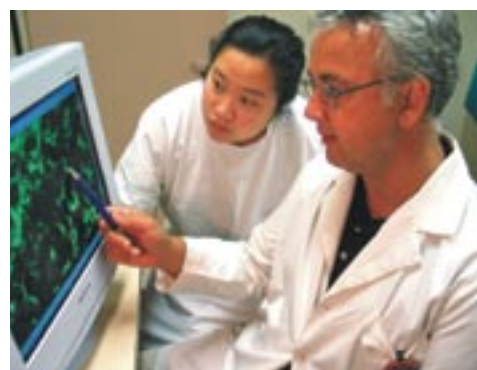
This research is available on line in the journal *Biology of Reproduction*.

Prince Henry's featured in *Nature* and *Science*

Associate Professor Vincent Harley and his team at Prince Henry's Institute have been recognised in the internationally renowned scientific journals *Nature* and *Science* with features on intersex research and studies on transsexualism.

Both articles are available on line. Visit www.sciencemag.org Dec 19, 2003 issue - News of the Week for the article *Sex Reversal, Protein Deterred by Nuclear Barrier* and www.nature.com, Jan 29, 2004 issue - News Feature *The Most Important Sexual Organ*.

For more information about articles in *Insight* call Rebecca Scott (03) 9594 4391 or email rebecca.scott@phimr.monash.edu.au



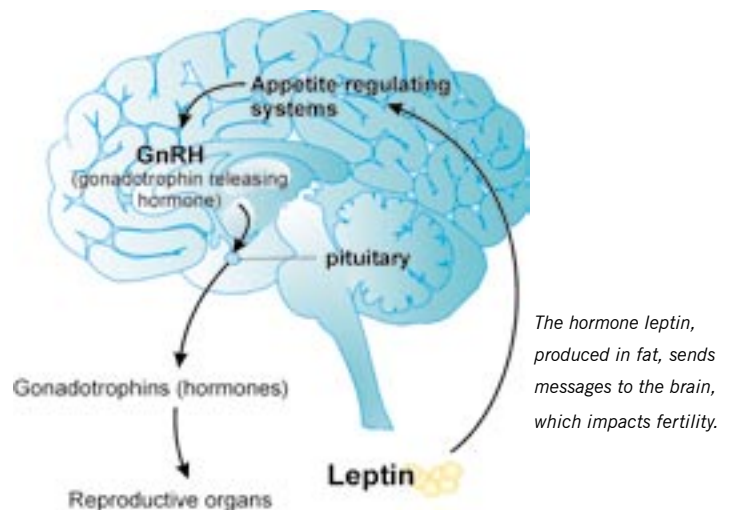
Associate Professor Vincent Harley with Dr Helena Sim.

Linking fertility to bodyweight

Scientists at Prince Henry's Institute are investigating the link between fertility and body weight.

Reproduction is driven from the brain. The brain 'senses' a reduction in body weight and responds by ceasing to secrete gonadotrophin-releasing hormone (GnRH) that drives the reproductive process.

Research led by Professor Iain Clarke at Prince Henry's Institute has shown that animals that are underweight have reduced reproductive function because the brain 'senses' the differences in the body composition, by detecting the levels of the hormone leptin which is produced by fat. In this way, leptin informs the brain of our body weight.



Research shows that by administering leptin, under-nourished animals believe they are fat, which in turn reactivates the reproductive process.

The mechanisms within the brain that allow leptin to trigger the reproductive system in animals of low body weight are not clearly understood.

Professor Clarke has recently received a three-year grant from the National Health and Medical Research Council to explain these mechanisms.

"This research grant will help improve our understanding of the way the brain regulates body weight and reproduction and may pave the way for leptin to be used as a therapeutic treatment for some significant health problems," said Professor Clarke.

More information can be found at: www.phimr.monash.edu.au/neuroendocrinology.html

Minister praises research on World Diabetes Day 2003

The new Minister for Health and Ageing, the Hon. Tony Abbott praised Australian medical research institutes including Prince Henry's Institute for their efforts into diabetes research.

Several hundred people attended the World Diabetes Day breakfast on November 14th, 2003 at the Hotel Windsor in Melbourne, to hear about diabetes research.

Associate Professor Vincent Harley and Dr Helen Kasimiotis from Prince Henry's Institute were recipients of grants from Diabetes Australia, for their discovery of the gene SOX 13 and its potential role in replacing insulin production in type1 diabetes.



Scientists at the World Diabetes Day Breakfast included: (**back row**) Helen Kasimiotis and Vincent Harley - Prince Henry's Institute, Malcolm Gray, Director - Diabetes Australia Research Limited and the Hon Tony Abbott, Minister for Health and Ageing, (**front row**): Gordon Bunyan, Vice Chair - International Diabetes Federation, Western Pacific Region Council, and John Townend, Chair - Diabetes Australia Research Limited.