



# *Therapeutic Cloning for Tissue Repair*

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16 September 1999

8.30 am – 4.00 pm

Becker House (The Dome)  
Canberra

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Australian Academy of Science

# *Background*

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The Australian Academy of Science, in pursuing its broader objective of promoting informed discussion on important scientific issues, is hosting a Forum on therapeutic cloning for tissue repair.

The Forum will explore present capabilities and future possibilities in advanced reproductive and genetic technologies. It will inform participants on the current and proposed regulatory and legislative framework in Australia.

The Academy has issued a Position Statement on Human Cloning, in which it considers

*reproductive cloning to produce human fetuses is unethical and unsafe and should be prohibited. However, human cells, whether derived from cloning techniques or from embryonic stem cells should not be precluded from use in approved research activities in cellular and developmental biology.*

The Forum will consider the exceptional circumstances that might permit scientists to seek Institutional Ethics Committee approval to derive human cells from cloning techniques or from embryos, with due regard to the highest standards in scientific merit, in safety issues and in the ethical acceptability of the research.

## *Organising Committee*

Professor John White, FAA (Chair)

Professor Sue Serjeantson (Consultant)

Professor Oliver Mayo, FAA

Professor Philip Pettit

Professor Roger Short, FAA

Professor John Hearn

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# Program

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- 8.30 am Registration
- 9.00 am **Welcome**  
Professor John White  
Australian Academy of Science

## *Plenary session*

- 9.05 am **Recent developments in human and animal cloning**  
Professor Neal First  
University of Wisconsin-Madison
- 9.35 am **The British response to cloning**  
Professor Martin Evans  
Cardiff University
- 10.00 am **Discussion**
- 10.15 am Morning tea

## *Update of the science*

- Chair:* Professor Roger Short  
*Royal Women's Hospital*
- 10.45 am **Primate embryonic stem (ES) cells**  
Professor John Hearn  
Australian National University
- 11.00 am **Human ES cell research in Australia**  
Professor Alan Trounson  
Monash Medical Centre
- 11.15 am **Directed differentiation of ES cells:  
implications for novel human therapies**  
Professor Peter Rathjen  
University of Adelaide
- 11.30 am **Application of cloning technology in domestic livestock**  
Professor Oliver Mayo  
CSIRO Animal Production
- 11.45 am **Discussion**
- 12.15 pm Lunch
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## *The legislative and regulatory environment for human embryonic stem cell research*

Chair: *Professor Philip Pettit*  
*Australian National University*

1.00 pm **Recommendations from the Australian Health Ethics Committee**  
Professor Don Chalmers  
Chair, AHEC

1.30 pm **Legal issues**  
Associate Professor Loane Skene  
University of Melbourne

1.45 pm **The legal situation in Western Australia and South Australia**  
Dr Sandra Webb  
Health Department of WA

2.00 pm **Should we clone human beings? The ethical issues**  
Professor Bob Williamson  
The Murdoch Institute for Research into Birth Defects Ltd

2.15 pm **Discussion**

2.30 pm Afternoon tea

2.45 pm ***Panel session: The way ahead***

Chair: *Professor John White*  
*Australian Academy of Science*

- Professor Don Chalmers, AHEC
- Reverend Dr Norman Ford  
Caroline Chisholm Centre for Health Ethics
- Professor Philip Pettit, ANU
- Dr Gregory Pike  
The Southern Cross Bioethics Institute
- Associate Professor Loane Skene, U. Melb.

3.45pm **Summing up & recommendations**

4.00 pm Close

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# *Speakers and Abstracts*

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## *Plenary session*

### **Recent developments in human and animal cloning**

#### **Professor Neal First**

Human cell transplantation therapies offer promise for restoration of functions of damaged or diseased organs, glands, and tissues. They also offer possibility for genetic engineering of the transplanted cells to prevent immune rejection or to resist loss or failed function of diseased cells.

None of this seemed possible until 1997 when the birth of Dolly from transfer of an adult mammary cell into an enucleated sheep oocyte and studies in several laboratories established that differentiated mammalian cells could be reprogrammed to become multipotential cells. The second milestone experiments were those of Thomson et al. In 1998 and 1999 establishing that non-human primate and human embryonic stem cells lines could be established cultured to large numbers and differentiated into all cell types of the body in a teratoma established by transplantation of the cells into a SCID mouse.

As a result of these exciting discoveries several companies, some hospitals, and government agencies are vigorously attempting to make human cell therapy a useful and commonly used procedure.

Recent research is focused on several questions.

1. Since the SCID mouse teratoma procedure is slow and inefficient, could embryonic stem cells be directly engineered down and maintained in lineage pathways by appropriate in vitro treatments to become a multiplying population of the cell type desired. For some cell types such as myocardial cells and for blood cell lineages, this is now possible.
2. Can cells of any lineage become cells of another lineage? It is also known that a lateral differentiation from cells of one lineage to cells of another lineage can occur at least in vivo. Mouse hematopoietic cells transplanted to the brain became neural cells.

It is also known from 1999 studies in the laboratory of Moshe Szyf that human cells contain a DNA demethylase that can demethylate both fully methylated and hemimethylated DNA. These studies provide the possibility that someday somatic cells of a patient's own body might be redifferentiated to be therapy for another cell type.

3. Will long term cultured cells from an aged patient fail to maintain telomeres, chromatin normalcy and have short lifespan after transplantation? Cells which have not passed through an early embryonic period may not. Cells resulting from nuclear transfer were inconclusive in the case of Dolly. However fetal cells at the University of Massachusetts which were cultured for 42 passages and considered aged, resulted, after nuclear transfer in fetuses who's cells remained normal through 42 passages of cell culture. The later suggests that the longevity of a cell is restored by nuclear transfer.
  4. How can immune rejection of cells foreign to the patient be prevented? This is a major problem for cell or organ transplantation. One commercial approach is to produce large numbers of ES cell derived cell lines, which can be antigen typed and matched to the patient as is done for blood transfer. Another approach is to use the patient's own cells through nuclear transfer to produce immune tolerant ES cells and differentiated cells for therapy.
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Nuclear transfer is a potential method for avoiding problems of aged cell lines and immune cell rejection. Embryonic or primordial germ cell lines and genetically engineered cell lines capable of becoming offspring have been established from fetal or somatic cell nuclear transfer in domestic animals and mice but not non human or human primates.

Although more than 150 offspring have been produced from nuclear transfer with fetal or adult mammalian cells, the efficiency of producing offspring or cell lines passing SCID mouse or offspring tests is low. Some of the failures are failures in cell programming others appear to be due to failed or inappropriate gene expression.

If therapy cells are to be produced from nuclear transfer a problem created by the inefficiency of the procedure will be where to obtain the large supply of human oocytes to used as recipient cells for transplantation of the cell to be cloned.

Our laboratory explored the possibility of using bovine oocytes as recipient cells for transfer of nuclei from adult cells of sheep, pigs, rats, and rhesus monkeys. A high frequency of blastocyst embryos showing evidence of nuclear reprogramming resulted. When transferred into females of the species of the nucleus in sheep and pig pregnancies were initiated but not maintained. Attempts to produce embryonic stem cell lines were successful for bovine x bovine embryos but unsuccessful for non human primate x bovine embryos. If eventually perfected this system could alleviate the problems of supply of human oocytes.

Overall, progress towards human cell therapies has been rapid. Examples of success such as skin, blood cells, and some brain cells when using cells within a lineage have reached clinical trials. The embryonic stem cell approaches discussed above are waiting perfection and clinical trials. The potential for a new era of disease therapy is evident.

**Neal First** holds the L.E. Cassida Chair of Reproductive Biology and Animal Biotechnology at the University of Wisconsin-Madison. He holds appointments in the Department of Animal Sciences and Obstetrics and Gynecology. He is a member of the United States Academy of Science and former member of the National Advisory Board on Ethics in Reproduction. He was the first director of the United States Department of Agriculture's National Animal Genome Program. Professor First has received the highest awards of two societies as well as the United States Von Humboldt Award and the International Wolf Prize for his pioneering research in *in vitro* production of cattle embryos and cloning of cattle. He is advisor to several animal biotechnology companies.

## The British response to cloning

### Professor Martin Evans

The Human Fertilisation and Embryology Act 1990 set up the Human Fertilisation and Embryology Authority to issue licences without which it is a criminal offence to carry out any manipulation, storage or research on human embryos or gametes outside the body. The act was sufficiently far-sighted to prohibit one cloning technique:

*"A licence cannot authorise –  
d) replacing a nucleus of a cell of an embryo with a nucleus taken from a cell of any person, embryo or subsequent development of an embryo."*

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When the “Dolly” furore broke therefore, the UK regulations were in a relatively secure position in banning reproductive cloning. Although unfertilised eggs are used this section of the act has been construed by Counsel’s opinion to include also these techniques.

The advent, however, of human embryonic stem cells derived both from embryos and from primordial germ cells raises anew questions of the possible use of nuclear transfer into embryos as a prelude to derivation of totipotent cells genetically matched to the nuclear donor. These should provide a route to cell replacement therapies. In addition at least one therapeutic purpose for nuclear transfer to create an embryo for reimplantation has been raised. A public consultation document was initiated the HFEA together with a non-statutory advisory body – the Human Genetics Advisory Commission and the report published in December 1998. This report recommended that the Government might like to strengthen the ban on reproductive cloning but to allow specifying that licences might be issued for *developing methods of therapy for mitochondrial diseases and for therapy for diseased or damaged tissues or organs*.

Despite widespread media opinion that the government would accept these recommendations it has not but has asked for further expert opinion. A new “Chief Medical Officer’s Expert Advisory Group on Therapeutic Cloning” has been set up.

**Martin Evans** is Professor of Mammalian Genetics and director of the School of Biosciences of Cardiff University.

*After graduating from Cambridge in 1963 he decided on a career studying the genetic control of vertebrate development and undertook research for his PhD at University College London in the department of Anatomy and Embryology. During this early research on changes of messenger RNA profile during neural induction in Xenopus he was using pioneering techniques of agarose gel electrophoresis and metabolic double labelling. These experiences led to a realisation of the need for a tractable experimental system to study development in isolation from the whole embryo and with the possibilities of genetic manipulation and he therefore chose to explore the use of cultures of mouse teratocarcinoma stem cells in tissue culture systems. He was the first to maintain these cells in tissue culture under conditions where their ability to differentiate was retained indefinitely. Studies from his laboratory showed extensive differentiation of these cells in culture and the means whereby this happened was shown to be that corresponding to organisation of a normal mouse embryo. Moreover these cells would participate extensively in normal development in combination with a normal embryo and give rise to adult mice.*

*These studies showed the close relationship between these “EC” cells and normal mouse embryos but it was not until 1981 after his return to Cambridge that together with Matt Kaufman he was able to isolate similar cells from normal mouse embryos. Subsequently they rapidly demonstrated, together with his student and post-doc Liz Robertson and student Allan Bradley, that these cells which became known as “Embryonic Stem Cells” (ES cells) were able to be used to fully regenerate fertile breeding mice from the tissue culture cells and that these could therefore carry mutations introduced and selected or screened for in culture. This is now the basis of all the mouse knockout and targeted genetic manipulation.*

*Since pioneering these fundamental developments which created new routes to experimental mammalian genetics and hence functional genomics, he has been exploiting them using gene knockout and gene trap methods both for novel discovery and to create animal models of human disease. From his laboratory came the first demonstration of gene therapy to cure the deficit in Cystic Fibrosis in the whole animal and recently, from a mutated mouse model, insights into the breast cancer gene BRCA2 function.*

*He has published 118 scientific papers. He is a Fellow of the Royal Society and a founder Fellow of the Academy of Medical Sciences, Doctor of Philosophy and Doctor of Science.*

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## *Update of the science*

### **Chair: Professor Roger Short**

*Professor Roger Short held a Personal Chair in Reproductive Biology at Monash University from 1982-1995. In 1996, he was appointed Wexler Professorial Fellow in the Department of Perinatal Medicine at the Royal Women's Hospital. Formerly he was the foundation Director of the Medical Research Council's Unit of Reproductive Biology in Edinburgh, Scotland from 1972-1982, and prior to that, he had been on the scientific staff of the Agricultural Research Council's Unit of Reproductive Physiology and Biochemistry in Cambridge, England from 1956-1972. He was also a Reader in Reproductive Biology in the School of Veterinary Medicine at the University of Cambridge, and a Fellow of Magdalene College.*

*One of Professor Short's major research interests has been the evolution of human reproduction. Professor Short has published over 300 scientific papers in a wide variety of scientific journals, and has just completed writing a book with Dr Malcolm Potts called, "Ever since Adam and Eve: the Evolution of Human Sexuality". It was published by Cambridge University Press in February 1999.*

*He holds US and EEC patents for the use of melatonin to control jet lag.*

### **Primate embryonic stem (ES) cells**

#### **Professor John Hearn**

The successful isolation of human embryonic stem cells (ES cells) in 1998 (1) followed similar isolation in the rhesus and marmoset monkeys in 1995/96 (2,3), fifteen years after the first isolation of ES cells in mice (4,5). A major reason for this long delay was the lack of availability of an experimental embryology system and the necessary reagents in primates.

As part of our broader research program on primate implantation, we focused from 1986 on the series of obstacles to be overcome in achieving stem cell isolation. These barriers included (i) non-surgical embryo recovery, to conserve primate numbers; (ii) individual culture of embryos to outgrowth stages in vitro; (iii) measurement of gonadotrophin releasing hormone and chorionic gonadotrophin secreted by individual embryos; (iv) confirmation of ES cell markers; (v) demonstration of prolonged undifferentiated cell proliferation, and (vi) stable potential to form derivatives of all three embryonic germ layers.

After the success with ES cells derived from hundreds of rhesus and marmoset blastocysts, Thompson derived ES cells from 5 of 14 inner cell masses from human embryos cultured to blastocyst stage after in vitro fertilisation. These embryos were donated by individuals after informed consent and after Institutional Review Board approval. Studies are continuing on the determinants of cell lineage choice in primate ES cells.

These findings open up a wide range of basic and strategic options in cell biology with significant applied therapeutic potential. Future challenges include the ability to regulate cell lineage choice; to isolate organ or tissue specific stem cells rather than depend on embryo derivation; and to remove ES cells for subsequent long term storage, as an individual transplant bank, without damage to the embryo. Informed debate on the scientific and ethical factors involved is absolutely necessary to achieve success.

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References: 1. Thomson et al (1998) PNAS 282, 1145; 2. Thomson, Hearn, et al (1995) PNAS 92, 7844; 3. Thomson, Hearn et al (1996) Biol. Reprod. 55, 254; 4. Evans & Kaufman, (1981) Nature 292, 154; 5. Martin (1981) PNAS 78, 7634.. 6. Hearn et al (1994) Marshall's Physiology of Reproduction 3, 535-676, Chapman & Hall, London.

**John Hearn**, Director of the Research School of Biological Sciences at the Australian National University, researches the reproduction and development of large mammals, specialising in embryo implantation in primates and marsupials. Before taking up his present post in 1998 he served as Senior Scientist and Consultant, Human Reproduction Program, WHO Geneva (1996-98); Director, NIH-Wisconsin Regional Primate Research Center USA (1990-96); Deputy CEO, Agriculture and Food Research Council UK (1987-90); Director of Science, Zoological Society of London (1979-87) and Scientist, MRC Reproductive Biology Unit, Edinburgh (1972-79). He was awarded his PhD at ANU (1972) for studies of embryonic diapause in the wallaby.

## Human ES cell research in Australia

### Professor Alan Trounson

Research aimed to develop human embryonic stem (ES) cells was initiated in 1994 as a joint initiative between Professors Alan Trounson and Ariff Bongso at Monash University and the National University of Singapore (NUS). With the full approval of the NUS Research and Ethics Committee and support of Singapore's Medical Research Council, embryos not needed by IVF patients were donated for research to develop ES cells.

Techniques developed to efficiently grow embryos to the blastocyst stage were used to culture donated embryos and the undifferentiated inner cell mass (ICM) cells mechanically or immunosurgically separated from trophectoderm cells and the ICM cell clusters grown on selected feeder cells in medium containing factors that aid the maintenance of the undifferentiated state at the NUS.

Cell lines transferred to the CEHD have been maintained in long-term cultures (> 40 passages) as undifferentiated cell types under the care of Drs. Ben Reubinoff and Martin Pera. They have shown that these putative ES cells will differentiate into a very wide range of cell and tissue types, spontaneously and in response to specific culture conditions and factors. These include neuronal ganglia, lung epithelia, gut tissue, muscle cells, bone, cartilage, etc..

The research priorities of the group are to identify the factors and conditions that maintain and expand the ES cell lines, and specify the lineage pathway decisions during cellular differentiation and development of tissue and primitive organs. The identification of controlling factors, proteins and genes in these transformations will have a very major impact on human medicine in the near future.

**Alan Trounson** is Director, Centre for Early Human Development and Deputy Director of the Monash Institute of Reproduction and Development. Prior to entering medicine, he developed embryo production, transfer and freezing procedures in sheep and cattle. At Monash University he pioneered human in vitro fertilization (IVF), embryo freezing and other techniques for assisted conception, genetic mutations in infertility and genetic diagnosis in embryos. Present research include transgenesis and cloning in cattle, sheep, mice and rats, and the development of human ES cells.

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## Directed differentiation of embryonic stem (ES) cells: implications for novel human therapies

### Professor Peter Rathjen

Recent developments in cloning and reproductive technologies form the basis of a novel, widely applicable approach to disease management through the use of cell and gene therapies. These technologies will exploit known advantages of pluripotent cells, the founder cells of the mammalian embryo which have the potential to give rise to all other cells of an animal. Pluripotent cells, often termed embryonic stem or ES cells, can be manipulated genetically with precision, can proliferate indefinitely in culture, and can differentiate into any other cell type normally found in a mammal. Combined manipulation, expansion and differentiation of these cells in vitro therefore heralds the possibility of an unlimited supply of cells that can be genetically modified to achieve useful therapeutic outcomes.

Much recent work has focussed on the isolation and maintenance of pluripotent cell populations from various species. While it has proven difficult to maintain pluripotent ES cells from species other than certain strains of mice, recent reports suggest that this can be achieved for a range of species including humans.

Therapeutic use of ES cells requires the development of protocols allowing regulated differentiation of these cells into medically useful populations. Unfortunately, little is known of the signals that direct this process during embryogenesis, although the cellular origin of some inductive signals has been deduced. ICM cells, the embryonic equivalent of ES cells, normally undergo a defined program of differentiation in the embryo leading to the formation of an obligatory intermediate pluripotent cell population, primitive ectoderm, followed by differentiation into the 3 germ layers of the animal, ectoderm, endoderm and mesoderm. All somatic cell populations in the animal trace their origin to one of these 3 germ layers.

We have applied knowledge gained from the study of early mouse embryogenesis to direct the differentiation of mouse ES cells into homogeneous populations of differentiated cells. Soluble, secreted signals implicated in early embryonic differentiation events convert ES cells homogeneously into primitive ectoderm, which in turn can be differentiated specifically into either ectoderm or mesoderm. These germlayer equivalents go on to form differentiated cell populations such as neural stem cells and neurons, and blood and muscle cell types respectively. Our ability to direct the differentiation of ES cells in a manner analogous to normal differentiation in vivo provides confidence that homogeneous populations of therapeutically useful cells derived from ES cells are a realistic prospect.

***Peter Rathjen** is currently professor and head of the Department of Biochemistry, University of Adelaide. The 1985 Rhodes Scholar for South Australia, he studied for his PhD at Oxford University from 1985-1988, and commenced work on embryonic stem cell differentiation as a postdoctoral fellow in the laboratory of Dr John Heath. He returned to the Department of Biochemistry in 1990 and has continued to pursue investigations into genes that regulate ES cell maintenance and differentiation. Since 1993 he has chaired the Scientific Advisory Board of BresaGen, a South Australia-based biotechnology company with interests in cell therapy.*

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## Cloning technology in domestic livestock production

### Dr Oliver Mayo

Cloning may be defined as production of a cell or organism with the same nuclear genome as another cell or organism. We can distinguish between reproductive cloning, which produces a new individual organism by nuclear replacement, and therapeutic cloning, which produces stem cells, tissues or organs.

Cloning thus includes the natural production, by embryo splitting, of identical twins in humans and other mammals.

Cloning includes deliberate embryo splitting, which is used routinely where individual animals are sufficiently valuable to warrant it, as in dairy cattle breeding, or for research purposes where multiple identical individuals are needed.

Cloning of some tissues, eg in medicine human skin for auto-transplant, is standard and unexceptionable. Cloning of other tissues, such as embryonic stem cells, is under widespread investigation for its potential benefits in research and tissue production.

Reproductive cloning of adult individuals by nuclear transfer was first demonstrated in sheep in 1997 and has subsequently been demonstrated in goats, cattle and rabbits. It is a potentially very valuable tool for research on differentiation, development and aging, and as such is of value in itself. It is also of considerable potential benefit as a path to the more reliable production of transgenic livestock.

Progress on all fronts relevant to livestock production will be discussed.

***Oliver Mayo** is Chief of CSIRO Animal Production. Before taking up this post about a decade ago, he was head of the Biometry Section at the Waite Agricultural Research Institute. He is a Fellow of the Australian Academy of Science and the Australian Academy of Technological Sciences and Engineering. CSIRO Animal Production is concerned with all aspects of livestock production, from fresh water aquaculture to wool, in temperate Australia. Dr Mayo's own research and interest include the efficiency of wool production and the application of gene technologies to animal improvement.*

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# *The legislative and regulatory environment for human embryonic stem cell research*

**Chair: Professor Philip Pettit**

*Philip Pettit is Professor of Social and Political Theory at the Research School of Social Sciences, Australian National University. He is a regular Visiting Professor at Columbia University, New York and has also held visiting positions in London, Paris, Oxford and Cambridge. Among his recent books are Three Methods of Ethics (with M. Baron and M. Slote, Routledge, 1997), Republicanism: A Theory of Freedom and Government (OUP 1997) and The Common Mind: An Essay on Psychology, Society and Politics (OUP 1993). He is a philosopher by discipline but works on a range of interdisciplinary issues, including constitutional and policy-related questions in law and politics and foundational questions that arise in psychology and economics.*

## **Recommendations from the Australian Health Ethics Committee**

**Professor Donald Chalmers**

There has been considerable international reactions to the report of the Dolly event. Most national governments have reacted by introducing bans on the intentional cloning of a whole human being. At the international level the UNESCO Declaration on Human Genome and Human Rights has stated that reproductive cloning of human beings is contrary to human dignity and shall not be permitted. This is consistent with declarations from the Council of Europe and the World Health Organisation.

Three states of Australia have specific legislation in relation to assisted reproductive techniques and, in particular, human cloning. The remaining states and territories observe the NHMRC, Ethical Guidelines on Assisted Reproductive Technology. These guidelines provide that embryo experimentation "... should be limited in ways which reflect the human nature of the embryo, acknowledging that there is a diversity of views on what constitutes the moral status of a human embryo..." There are substantial limits on embryo research under the state legislation and the NHMRC Ethical Guidelines. The Academy of Science Position Statement – on Human Cloning noted difficulties which may be created by the legislation and guidelines to investigations of possible therapeutic benefits which may be derived from some cloning techniques.

This paper considers the NHMRC Ethical Guidelines and the application of those guidelines to embryo research. The paper will also consider the AHEC Report on the Scientific, Ethical and Regulatory Considerations Relevant to Cloning of Human Beings, 16 December 1998.

**Don Chalmers** is Professor of Law at the University of Tasmania and also Chairperson of the Australian Health Ethics Committee. He is also a member of the National Health and Medical Research Council. He chaired the Commonwealth Ministerial Review of the National Institutional Ethics Committee system in 1995. He has represented the Australian Health Ethics Committee at the San Francisco and Tokyo World Summits of National Bioethics Commissions. He chaired the AHEC Working Party which prepared the Report entitled Scientific, Ethical and Regulatory Considerations Relevant to Cloning of Human Beings, December 1998 which was presented to the Commonwealth Minister for Health and Aged Care.

Professor Chalmers was Law Reform Commissioner in Tasmania from 1991 until 1997. He is currently a Board member of the Australian Institute of Family Studies. His major research interests include Health Law and Ethics, Trusts and Law Reform. He is also the author of seven books on PNG Law, Legal Studies, Trusts and Criminal

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*Law; major government reports and contributor to legal treatises such as Laws of Australia, Halsbury's International Encyclopaedia on Medical Law and articles on medical ethics.*

## **Legal issues**

### **Associate Professor Loane Skene**

Embryo splitting and nuclear transfer for the purpose of cloning human beings is prohibited by legislation in Victoria, South Australia and Western Australia; and the New South Wales government has indicated an intention to introduce similar legislation. These procedures are also prohibited by the National Health and Medical Research Council's *Ethical Guidelines on Assisted Reproductive Technology*. Although the NHMRC document distinguishes between cloning of humans and cloning of human parts, it does not advocate that the latter should be allowed. The NHMRC guidelines, like the Victorian and South Australian legislation, prohibit the production of embryonic stem cell lines.

Many other national and international instruments prohibit human cloning. Again, the intention is sometimes to ban cloning of humans but in some cases, the wording is so wide that it covers all types of cloning, even cloning of tissues and cells.

Insofar as embryos are required for cloning of stem cells, Australian legislation and guidelines limit the purposes for which embryos may be created and used. These provisions will need to be reviewed if cloning of cells for therapeutic purposes is to be permitted.

**Loane Skene** is Associate Professor and Reader in the Faculty of Law at The University of Melbourne; and Adjunct Associate Professor and Reader in the Faculty of Medicine, Dentistry and Health Sciences at The University of Melbourne. She holds the degrees of Bachelor of Laws with Honours from The University of Melbourne (1970) and Master of Laws from Monash University (1984). She is a Barrister and Solicitor of the Supreme Court of Victoria.

Loane is the author of two books: *Law and Medical Practice: Rights, Duties, Claims and Defences*, (Butterworths, 1998); and *You, Your Doctor and the Law* (OUP, 1990); and numerous chapters in books and journal articles. She is a member of the federal Genetic Manipulation Advisory Committee; the National Health and Medical Research Council's Gene Therapy Research Advisory Panel and Genetic Registers Committee; and the Genetics Ethics Committee of the Victorian Anti-Cancer Council.

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## The legal situation in Western Australia and South Australia

**Dr Sandra Webb**

The presentation will set out an overview of the likely effects of the relevant legislation in these two states. It will also suggest the legislative changes that would appear to be necessary to clearly prohibit reproductive cloning, but also allow potential for approval of therapeutic cloning in WA and SA within a comprehensive regulatory framework.

### RELEVANT LEGISLATION

- WA HUMAN REPRODUCTIVE TECHNOLOGY ACT 1991  
Subsidiary legislation: *Reproductive Technology (Licences and registers) regulations 1993*; *Reproductive Technology (Licences and registers) Amendment regulations 1995*; *Directions given by the Commissioner of Health to set the standards of practice under the HRT Act 1991*. WA Government Gazette 171, 3 October 1997.
- SA REPRODUCTIVE TECHNOLOGY ACT 1988  
Subsidiary legislation: *Reproductive Technology (Code of ethical research practice) regulations 1995*; *Reproductive Technology (Code of ethical clinical practice) regulations 1995*.

Both Acts seek to regulate human reproductive technology practices and both establish a statutory system of licensing of those who carry out these procedures. Both Acts establish an 11 member Council of diverse interests and expertise that advises on licensing and licensing standards, and approves research proposals or research licences. The WA Act contains a huge amount more detail than the SA Act, in the way of definitions, offences and principles to guide the setting of standards for licensees.

In Western Australia:

- 'Cloning' as defined in the WA Act clearly refers to reproductive cloning only, and is ruled out by an explicit offence.
- Therapeutic cloning is restricted or ruled out in many ways under the Act, whether as research or in clinical practice, although this is not by way of an explicit offence.
- The Parliamentary Select Committee that recently reviewed the WA Act recommended that the way should be left open for therapeutic cloning technology and that embryo research provisions in the WA Act should be brought in line with the NH MRC guidelines, but the prohibition on development of an embryo for other than for treatment should remain in place. The Government has not yet responded to these recommendations.

In South Australia:

- 'Cloning', defined in the *Reproductive Technology (Code of ethical research practice) regulations 1995* as a procedure 'directed at producing two or more genetically identical embryos from the division of one embryo', would be banned by the cloning prohibition in that Code, as would any research likely to harm an embryo. This would limit a number of research and clinical applications of both 'reproductive cloning', and 'therapeutic cloning'.
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- However, 'reproductive cloning' may not be fully prohibited under this Act. Research directed at 'reproductive cloning' using 'Dolly style' cloning techniques is not explicitly banned under the Act, and it appears that approval could also be granted in the future for the clinical use of some types of cloning technology for 'reproductive cloning', if no longer considered experimental.

However, to pass a law that would allow the potential for approval of the full range of therapeutic cloning technologies, with minimal absolute prohibitions in the Act, may be difficult for politicians, until the community has a better understanding of the issues involved. Effective communication by scientists will be needed to achieve this.

**Sandy Webb** is Executive Officer of the WA Reproductive Technology Council. Her roles are varied, relating predominantly to coordinating the implementation of the WA Human Reproductive Technology Act 1991 in all its aspects- legal, ethical, scientific, medical and social.

Her early career was in scientific/medical research in reproductive biology, and in 1991 she was awarded a PhD from Cambridge University, on the basis of her work in the evaluation of IVF and related procedures in WA.

She participated in the development of the 1996 guidelines on ethical issues in ART for the Australian Health Ethics Committee of the National Health and Medical Research Council, and is a member of the Working Party that is currently developing recommendations for the Commonwealth Minister for Health on 'National Data Collection on Assisted Reproductive Technology'.

## Should we clone human beings? The ethical issues

### Professors Robert Williamson and Julian Savulescu

Few issues have raised the public temperature as much as human reproductive cloning. Since Dolly the sheep, and her fellow cows and mice, have been cloned, by extension it is likely that humans also could be reproductively cloned. The "debate" about reproductive cloning has been marked by poor reasoning and an excess of rhetoric. Cloning may be politically dangerous, unseemly, or unlawful in terms of traditional rights of inheritance of property. It may be genetically disadvantageous to the species, or dangerous medically to the cloned individual. It is certainly less fun than sex. There is a "yuk factor". None of these make reproductive cloning unethical *per se*. We examine the ethics of reproductive cloning, and conclude that cloning replicas of adult genotype for reproductive purposes alone is unethical by constraining autonomy, but balance this against the ethical good that will come from developing this technology to achieve breakthroughs in transplantation and other medical areas. We propose a way to solve this conflict.

**Robert Williamson** (PhD, FRS, FRCPath (UK), FRCP (Edin), Hon MD Turku) has been Director of the Murdoch Institute and Professor of Medical Genetics of the University of Melbourne since April 1995. Before that he was Professor of Molecular Genetics at St Mary's Hospital, University of London from 1976. His early studies on globin protein synthesis and polysomes helped to establish the existence of mRNA in mammalian cells. He led research into the molecular genetics of thalassaemias, and was the first to clone the human globin genes as cDNAs in 1977. This led to gene mapping for muscular dystrophies and cystic fibrosis, and identifying mutations causing Alzheimer's disease and myotonic dystrophy. He has taken a major interest in gene therapy, using liposomes to introduce genes for CFTR in a clinical trial with cystic fibrosis patients in London and studying gene therapy for ataxia and thalassaemia in Melbourne. He has a major interest in education and ethics as applied to human genetics.

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## Panel session: *The way ahead*

### **Chair: Professor John White**

*John White is Science Policy Secretary of the Australian Academy of Science and a professor of Physical and Theoretical Chemistry in the Research School of Chemistry at the Australian National University where he has been since 1985. Previously he was Director of the international Institut Max von Laue-Paul Langevin, Grenoble, France and a Fellow of St John's College, Oxford. He is a Fellow of the Australian Academy of Science and a Fellow of the Royal Society. Professor White's research interests concern the use of neutron scattering and x-ray reflectometry methods for determining the structure and dynamics of molecular self assembly.*

- **Professor Donald Chalmers**

*Don Chalmers is Professor of Law at the University of Tasmania and also Chairperson of the Australian Health Ethics Committee. He is also a member of the National Health and Medical Research Council. He chaired the Commonwealth Ministerial Review of the National Institutional Ethics Committee system in 1995. He has represented the Australian Health Ethics Committee at the San Francisco and Tokyo World Summits of National Bioethics Commissions. He chaired the AHEC Working Party which prepared the Report entitled Scientific, Ethical and Regulatory Considerations Relevant to Cloning of Human Beings, December 1998 which was presented to the Commonwealth Minister for Health and Aged Care.*

*Professor Chalmers was Law Reform Commissioner in Tasmania from 1991 until 1997. He is currently a Board member of the Australian Institute of Family Studies. His major research interests include Health Law and Ethics, Trusts and Law Reform. He is also the author of seven books on PNG Law, Legal Studies, Trusts and Criminal Law; major government reports and contributor to legal treatises such as Laws of Australia, Halsbury's International Encyclopaedia on Medical Law and articles on medical ethics.*

- **Reverend Norman Ford**

*Norman Ford is the Foundation Director of the Caroline Chisholm Centre for Health Ethics, which is funded by Catholic Healthcare Institutions in Victoria. He is a Salesian priest and lectures in Ethics and Medical Ethics for the B.Theol. degree. He is a former Master of Catholic Theological and former President of the Melbourne College of Divinity. He is a member of several hospital ethics committees. He has published work on when the human individual begins and since his time as Visiting Fellow at Clare Hall, Cambridge (UK) in 1993-94 he has been researching practical ethical issues from conception to birth.*

- **Professor Philip Pettit**

*Philip Pettit is Professor of Social and Political Theory at the Research School of Social Sciences, Australian National University. He is a regular Visiting Professor at Columbia University, New York and has also held visiting positions in London, Paris, Oxford and Cambridge. Among his recent books are Three Methods of Ethics (with M. Baron and M. Slote, Routledge, 1997), Republicanism: A Theory of Freedom and Government (OUP 1997) and The Common Mind: An Essay on Psychology, Society and Politics (OUP 1993). He is a philosopher by discipline but works on a range of interdisciplinary issues, including constitutional and policy-related questions in law and politics and foundational questions that arise in psychology and economics.*

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- **Dr Gregory Pike**

*Dr Greg Pike is the Principal Research Officer at the Southern Cross Bioethics Institute in Adelaide. He holds a PhD in Physiology from Adelaide University and has worked in the fields of neurobiology and membrane biophysics both in Australia and overseas. In more recent years, he worked at the Royal Adelaide Hospital in the Department of Surgery on various clinical trials and research into methods in laparoscopic surgery.*

- **Associate Professor Loane Skene**

*Loane Skene is Associate Professor and Reader in the Faculty of Law at The University of Melbourne; and Adjunct Associate Professor and Reader in the Faculty of Medicine, Dentistry and Health Sciences at The University of Melbourne. She holds the degrees of Bachelor of Laws with Honours from The University of Melbourne (1970) and Master of Laws from Monash University (1984). She is a Barrister and Solicitor of the Supreme Court of Victoria.*

*Loane is the author of two books: Law and Medical Practice: Rights, Duties, Claims and Defences, (Butterworths, 1998); and You, Your Doctor and the Law (OUP, 1990); and numerous chapters in books and journal articles. She is a member of the federal Genetic Manipulation Advisory Committee; the National Health and Medical Research Council's Gene Therapy Research Advisory Panel and Genetic Registers Committee; and the Genetics Ethics Committee of the Victorian Anti-Cancer Council.*

## **Designing research in cellular and developmental biology that involves human stem cells**

The Panel is invited to comment on points of consideration that should engage scientists wishing to undertake research in cellular and developmental biology that involves human embryonic stem (ES) cells, whether these cells are derived from cloning techniques or from human embryos.

The United States National Bioethics Advisory Commission (NBAC) has identified a number of issues relating to scientific and research design considerations that would help ensure the research is "well-designed, important, feasible and timely".

The NBAC points of consideration are:

- A. The source from which the human stem cells will be obtained
    1. From existing cell lines (such as neuronal or hematopoietic stem cells)
    2. From aborted fetal tissue (following spontaneous or induced abortion or surgical termination of ectopic pregnancy)
    3. From stored/space embryos obtained from infertility treatment
    4. From embryos produced for research purposes (including somatic cell nuclear transfer)
  - B. Previous research involving animals
  - C. Alternatives to using human stem cells
  - D. Future plans and conservation of gametes, fetal tissue and embryos
    1. Will stem cells be produced and stored for later use?
    2. If a particular protocol is being proposed using stored embryos, does it use only the number of embryos necessary?
    3. What plans exist in the event that additional stem cells are needed?
  - E. The research setting
    1. Are the investigators scientifically qualified to carry out the proposed research?
    2. Is the research equipment (including facilities) appropriate for the conduct of research involving stem cells?
  - F. Ethical overview
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