CHAPTER 2

STEM CELL RESEARCH AND HUMAN CLONING: AN OVERVIEW OF SCIENTIFIC ASPECTS

Introduction

2.1 The fields of stem cell research and cloning are complex and rapidly developing areas of scientific endeavour.

2.2 There are a number of detailed and accessible accounts available of the science involved in these fields. In particular, the report of the Australian Parliament's House of Representatives Standing Committee on Legal and Constitutional Affairs, *Human cloning: scientific, ethical and regulatory aspects of human cloning and stem cell research*, August 2001,[1] provides a comprehensive introduction to human reproductive processes as well as to the specific technologies involved in stem cell research and human cloning.

2.3 Other sources of information for non-specialists are the National Health and Medical Research Council's (NHMRC) fact sheets,[2] and the National Institutes of Health (NIH), *Stem Cells: Scientific Progress and Future Research Directions*, June 2001.[3]

2.4 The Committee will not repeat in detail the information available from these sources. It seeks in this chapter to provide an overview of the technologies pertaining to stem cell research and human cloning, before outlining a range of the scientific concerns raised in evidence in relation to them.

Defining terms

2.5 In this section, the Committee seeks to define the terms and to outline the main areas of possible future scientific development in stem cell research and human cloning in such a way that the provisions of the Bills before the Senate and the ethical issues provoked by them can be properly considered.[4]

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1 House of Representatives Standing Committee on Legal and Constitutional Affairs, *Human cloning: scientific, ethical and regulatory aspects of human cloning and stem cell research*, August 2001 [hereafter *Human cloning*].

2 These are available at http://www.nhmrc.gov.au

3 See US Department of Health and Human Services website, http://www.nih.gov/news/stemcell/scireport.htm (23 August 2002).

4 Department of the Parliamentary Library, Bills Digest No.17 2002-03, *Research Involving Embryos and Prohibition of Human Cloning Bill 2002*, p.4.

Stem cells

2.6 There are two types of cell which form 'the building blocks of the body'. They are called 'germ' cells and 'somatic' cells.

2.7 Germ cells are located in the ovary and testis, and are the cells from which sperm and eggs arise. All other cells types in the body are somatic cells. They are usually specialised for their roles as, for example, muscle cells or nerve cells in particular tissues or organs.[5]

2.8 The House of Representatives Human cloning report explained that 'all cells form initially from unspecialised cells. In the embryo, stem cells form the early tissues and organs. Under the influence of unknown genetic and chemical signals, cells become specialised and differentiated. Some stem cells are retained in most tissues or organs throughout life to participate in regeneration and repair'.[6]

Embryonic stem cells

2.9 After fertilisation of the human egg by sperm, the process of cell division in the embryo commences. By about the fourth day, the embryo consists of a ball of 32-64 cells, known as a 'morula'.[7]

2.10 By day five or six, the morula has developed into a 'blastocyst'. The blastocyst consists of an outer casing of cells and an inner cell mass.[8] The cells of the 'outer casing' are already committed to becoming placental tissue and have lost the ability to develop into other tissues and organs. The 'inner cell mass', however, is composed of embryonic stem cells and they become many or all of the specialised cells or tissues of the body.[9]

2.11 Embryonic stem cells can be removed from the blastocyst with a thin glass needle, or by a biochemical dissociation of the cells.[10] The removal of the embryonic stem cells from the blastocyst entails the destruction of the embryo.

2.12 The embryonic stem cells can be placed into a culture medium, where they can replicate and remain undifferentiated indefinitely. They can also be frozen and

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5 *Human cloning*, pp.16-17.

6 *Human cloning*, p.16; see also National Institutes of Health (NIH), *Stem Cells: Scientific Progress and Future Research Directions*, http://www.nih.gov/news/stemcell/scireport.htm (23 August 2002), p.ES-2.

7 *Human cloning*, p.13.

8 *Human cloning*, p.13.

9 *Human cloning*, p.20.

10 *Human cloning*, p.20.

stored, or grown in culture to differentiate into a wide range of specialised cell types or 'lineages'.[11]

2.13 Stem cells that have differentiated into specialised types, either spontaneously or in response to specific culture conditions, are called 'stem cell lines'. The Academy of Science has noted that:

> The research challenges are to identify and characterise the factors and conditions that maintain, expand and direct the lineages of the cell lines, to drive exclusive differentiation of cells into desired tissue types.[12]

Adult stem cells

2.14 An adult stem cell is an undifferentiated or unspecialised cell that occurs in differentiated tissue and is responsible for normal repair and replacement of that tissue.[13] Adult stem cells have been found in sources including bone marrow, blood, the brain, skeletal muscle, the pancreas, fetal tissue and tissue from the umbilical cord.[14]

2.15 Adult stem cells are able to make identical copies of themselves, or to 'self-renew', for the lifetime of the organism.[15]

2.16 It has been difficult so far routinely to identify adult stem cells from the majority of organs. They are also not easy to grow or maintain in an undifferentiated state in culture, because 'they naturally incline to become one or other more specialised cell type such as muscle, nerve or skin'.[16] However, in the past three years, there has been a major expansion in research on adult stem cells and there is a new understanding of their flexibility.[17] In particular, some evidence suggests that, given the right environment, some adult stem cells are capable of being 'genetically reprogrammed' to generate specialised cells that are characteristic of different tissues.[18]

Embryonic germ cells

2.17 An embryonic germ cell is derived from fetal tissue. As noted earlier, germ cells are located in the ovary and testis, and are the cells from which sperm and eggs

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11 *Human cloning*, pp.20-21; Australian Academy of Science, *Human Stem Cell Research*, 18 April 2001, p.12.

12 Australian Academy of Science, *Human Stem Cell Research*, 18 April 2001, p.12.

13 *Human cloning*, p.21; *Stem Cells: Scientific Progress and Future Research Directions* (NIH), p.ES-2.

14 *Stem Cells: Scientific Progress and Future Research Directions* (NIH), p.ES-2.

15 *Stem Cells: Scientific Progress and Future Research Directions* (NIH), p.ES-2.

16 *Human cloning*, p.21.

17 *Human cloning*, p.22.

18 *Stem Cells: Scientific Progress and Future Research Directions* (NIH), p.ES-3.

arise. Embryonic germ cells are isolated 'from the primordial germ cells of the gonadal ridge of the 5- to 10-week foetus'.[19]

2.18 Embryonic germ cells are like embryonic stem cells in that they have the capacity to differentiate into many or all of the tissues in the body. They are not, however, identical in their properties and characteristics.[20]

Embryonic stem cells and germ cells - The Trounson debate

2.19 The differentiation between different cell types, their derivation and properties (including developmental potential) is complex. That difficulties arise can be seen in the debate that arose following Professor Alan Trounson's presentation of the rat with a motor neurone lesion.

2.20 In a presentation to the Liberal/National parties that received widespread publicity, Professor Trounson referred to experimentation on a paralysed rat as an example to demonstrate that 'embryonic stem cells have been used to derive tissue for transplantation for the following major diseases/pathologies':

> Human ES cells directed into neural stem cells and motor neurone cells – when injected into the spinal column of rats with a motor neurone lesion (viral induced) – no muscle control at all below C6 (lower body) – were completely reversed (animals walked again and had control of bowel and bladder function) – potential application for human Motor Neurone Disease.[21]

A similar presentation was made in a Parliamentary briefing for National Science Week on Thursday, 22 August 2002.

2.21 Subsequent to the presentation it was established that the paralysed rat had been treated with 'differentiated germ cells from the early sex gland of a two month old aborted foetus'.[22] This led to much criticism of Professor Trounson for misrepresenting the science involved and misleading the politicians with the presentation. The Committee received many general comments echoing these views. A number of witnesses did provide specific comments relating to the Trounson presentation and the science involved.

2.22 Professor Peter Silburn, a clinical neurologist, told the Committee:

> The issue was used, and it was portrayed that this was an embryonic stem cell line from a human that was used to treat and cure–the word 'cure' was used–an animal with motor neurone disease. We have subsequently learnt

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19 *Stem Cells: Scientific Progress and Future Research Directions* (NIH), p.ES-2.

20 *Stem Cells: Scientific Progress and Future Research Directions* (NIH), p.ES-2.

21 The Case for Embryonic Stem Cells, notes for the presentation by Alan Trounson, p.5. The example is referenced to Kerr et al. Nature Medicine – On Line: August 2002.

22 *Submission* 1042, p.6 (Do No Harm – Dr van Gend).

> that when you actually look at that evidence, look at that statement, indeed they were not human embryonic stem cell lines. We also found out that these in fact were not published…We also found out that in fact it was not motor neurone disease and that the animal was not cured.[23]

2.23 The point of difference between a germ cell and an embryonic stem cell was commented upon by Dr Amin Abboud, a lecturer in medical ethics and health law:

> Listening to [Professor Trounson's] explanation of the differentiation between germ cells and embryonic stem cells reminded me–and I am not trying to be cynical–of what medieval theologians are often accused of: questioning how many angels can dance on a pinhead. There is a fundamental difference between a differentiated germ cell–it was a gonadal germ cell–and an embryonic stem cell, and I feel his explanation is wanting scientifically.[24]

2.24 Professor Trounson provided an explanation at the hearing of the terminology used in the presentation and the provenance of the research he quoted. He disputed that there is a 'fundamental difference' between the two types of cell:

> I use the term embryonic stem cells to describe embryonic germ cells. In doing so, I did not mislead members of parliament because the terms 'embryonic stem cells' and 'embryonic germ cells' are often used interchangeably…
>
> Embryonic stem cells from embryos are functionally indistinguishable from embryonic germ cells and will do everything that embryonic germ cells can do in terms of differentiation and tissue colonisation. Both represent human pluripotential stem cells derived from embryos and are quite distinct from adult tissue stem cells.
>
> Given the time available and the need to make several points about the potential benefits of embryonic stem cells, rather than give an extended lesson in cell biology, I used the term 'human embryonic stem cells' in a generic sense. This is not incorrect. It is perfectly reasonable to use a study on embryonic germ cells to support the argument for further research using embryonic stem cell lines derived from IVF embryos for treatment of some motor neurone disorders…
>
> I do not believe that I had any intention to mislead you or any other members of the parliament during that period of time. If I did, I apologise; it was certainly not my intention. I was trying to make an argument that this was the first time I had ever seen 'human embryonic stem cells' generically used in an animal in that way.[25]

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23 *Committee Hansard* 17.9.02, p.52 (Professor Silburn); see also *Committee Hansard* 24.9.02, pp.176-7 (Dr van Gend).

24 *Committee Hansard* 24.9.02, p.173 (Dr Abboud).

25 *Committee Hansard* 24.9.02, pp.136, 147.

2.25 Senator Jacinta Collins did not accept Professor Trounson's explanation:

> The public record shows quite clearly that in the question I asked you…I sought to understand the distinction between embryonic stem cells and those used in the particular case. Your response reiterated three times: 'No, they were embryonic stem cells.' This is what has given the media and others cause to believe that perhaps they were deliberately misled.[26]

2.26 Professor Trounson did however receive international support for his view. Professor Marilyn Monk, from the Institute of Child Health in London, submitted:

> His "error" was that he was not exact in that he did not make clear the derivation of the stem cell. The stem cells originally came from the gonads of an aborted post-implantation fetus rather than from the sub-population of cells of the pre-implantation embryo mentioned above. The point is that they are the same lineage of cells - the embryonic stem cells - just further 'down the line'. Both types of cells behave in similar ways in terms of their developmental potential.[27]

Properties of cells

2.27 For the purposes of this inquiry, the properties of cells that are of interest are those related to their capacity to 'differentiate' or 'specialise' into particular kinds of tissue.

2.28 'Differentiation' is the process by which an unspecialised cell, such as a stem cell, becomes specialised into one of the cells that make up the body. During differentiation, certain genes become activated and other genes become inactivated, meaning that the cell develops specific structures and performs specific functions.[28] For example, a mature, differentiated nerve cell has thin, fibre-like projections that send and receive the electrochemical signals that permit the nerve cell to communicate with other nerve cells.

2.29 In the laboratory, stem cells can be manipulated to become specialised or partially specialised cells and this is known as directed differentiation.[29] However, most of the cellular triggers and signals that determine how cells are differentiated to become, say, muscle, nerve or skin cells, are not understood.[30] Much of the research in

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26 *Committee Hansard*, 24.09.02, p.146 (Senator Collins).

27 *Submission* 1021, p.2 (Professor Monk). Dr Michael West who organised the collaboration in the US that led to the isolation of human embryonic stem cells made similar comments and advised that 'the terms were and continue to be used interchangably by some scientists' *Submission* 1083, p.1 (Dr West).

28 *Stem Cells: Scientific Progress and Future Research Directions* (NIH), p.ES-2.

29 *Stem Cells: Scientific Progress and Future Research Directions* (NIH), p.ES-2.

30 *Human cloning*, p.17.

this area is directed towards understanding how to control and direct cell differentiation or to identify the factors responsible for doing so.[31]

2.30 The kind of capacity that cells possess to differentiate into different kinds of cell is described by the concept of 'potency' or potential.

2.31 Totipotent cells can develop into a whole individual. The cells that possess this capacity are fertilised eggs and the individual cells of the embryo up to the 16-32 cell stage.[32]

2.32 Pluripotent cells have the capacity to develop into many or all the cells of the body, but cannot develop into whole individuals. The only known sources of human pluripotent cells are embryonic stem cells and embryonic germ cells.[33]

2.33 Recent research on adult stem cells indicates that they have the capacity to generate not only the tissue in which they are found, but to generate the specialised cell type of another tissue.[34] It is thought, however, that adult stem cells can differentiate into a more restricted range of tissues or organs than embryonic stem cells. They are thus described as 'multipotent' rather than 'pluripotent'.[35]

Cloning technologies

2.34 The Australian Academy of Science has defined 'cloning' as:

> the production of a cell or organism with the same nuclear genome as another cell or organism.[36]

2.35 As this definition makes plain and as the report into human cloning of the House of Representatives Standing Committee on Legal and Constitutional Affairs emphasised, cloning does not necessarily mean the replication of an entire individual.[37] It can mean simply the replication of a cell or group of cells.

2.36 Cloning occurs naturally in the 'asexual reproduction of plants, the budding of yeast in beer, the formation of identical twins and the multiplication of cells to repair damaged tissue in the normal process of healing'.[38] Cloning may also be achieved

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31 *Human cloning*, p.23.

32 *Human cloning*, p.17.

33 *Human cloning*, p.17; *Stem Cells: Scientific Progress and Future Research Directions* (NIH), p.ES-2.

34 *Stem Cells: Scientific Progress and Future Research Directions* (NIH), p.ES-3.

35 *Human cloning*, p.17.

36 *Human cloning*, p.19.

37 *Human cloning*, p.18.

38 *Human cloning*, p.18.

artificially.[39] At present, there are two artificial cloning technologies: embryo splitting; and nuclear transplantation, also known as 'somatic cell nuclear transfer'.[40]

Embryo splitting

2.37 The technology of embryo splitting involves fertilising an egg with sperm, and dividing the newly formed embryo into two or more individuals. In cases of identical twins this is the mechanism that occurs naturally, but it can also be performed in the laboratory. The individuals that result from this process, which is also known as 'fission', will be genetically identical to one another but not a clone of either parent.[41]

Somatic cell nuclear transfer

2.38 This technique was used to create 'Dolly' the sheep, and may be a technique used in developing stem cell therapies.[42] It involves removing the nucleus of an egg cell, which contains almost all of the genetic material in the cell, and replacing it with another cell nucleus. This second nucleus may be taken from any somatic cell, such as a skin cell or liver cell. In the case of Dolly, the cell was taken from the sheep's mammary gland.[43]

2.39 The enucleated egg and its new nucleus are fused using an electric current, and it forms a new embryo which is 'substantially' genetically identical to the organism from which the somatic cell was taken. In addition to the DNA from the somatic cell, this 'cloned' embryo would also possess very small amount of DNA attributable to the mitochondria in the egg cell.[44]

2.40 In theory, the cloned embryo may either be transplanted into a gestational mother and allowed to develop until birth, or it may be allowed to develop to the blastocyst stage when the inner cell mass or embryonic stem cells could be harvested, resulting in the destruction of the cloned embryo. In practice:

> the success of the somatic cell nuclear transfer procedure to form a viable blastocyst is approximately 1-2% of attempts made. The success of cloned embryos transferred to the uterus [of non-human mammals] resulting in live births is also of this order. The reasons for the many failures have yet to be fully defined. The efficiency of the procedure must be improved greatly

39 *Human cloning*, p.18.

40 Department of the Parliamentary Library Bills Digest No.17 2002-03, p.2.

41 Department of the Parliamentary Library Bills Digest No.17 2002-03, p.3.

42 *Human cloning*, pp.19, 23.

43 Department of the Parliamentary Library Bills Digest No.17 2002-03, p.2.

44 Department of the Parliamentary Library Bills Digest No.17 2002-03, p.2.

> before it becomes a viable technique, either for animal husbandry or for cell manipulation.[45]

2.41 Where the new embryo produced by a cloning technology is allowed to develop until birth, the term 'reproductive cloning' applies.

2.42 Where the new embryo is allowed to develop only so that its embryonic stem cells may be extracted, the term 'therapeutic cloning' has been applied. There is some dispute over the application of this term.

2.43 The term 'therapeutic cloning' derives from the potential application of the technology to the development of therapies. For example, through somatic cell nuclear transfer it is at least theoretically possible to create an embryo using the nucleus of a somatic cell from a patient. The stem cells that are subsequently extracted from that embryo are clones of the patient's own cells, and thus have the potential to grow into 'matching' or compatible tissue for the treatment of particular diseases. In other words, the purpose for which the cloned embryo is created is 'therapeutic' rather than 'reproductive'.

2.44 However, some have objected to the term 'therapeutic cloning' on the grounds that the relevant contrasting term should not be 'reproductive' but 'non-therapeutic'.[46]

2.45 The distinction between 'therapeutic' and 'non-therapeutic' scientific or medical research was made in the 1964 Declaration of Helsinki, and revised in Tokyo in 1975. This declaration was confirmed by the World Health Organisation and the Council for International Organisations of Medical Sciences as the basis for international guidelines for biomedical research involving human subjects.[47]

2.46 According to that distinction, 'therapeutic' research is research or practice carried out where the procedure is or is expected to be of benefit to the subject of the research. 'Non-therapeutic' research does not directly benefit the subject of the research, although it may be of benefit to others or to scientific understanding in general.[48]

2.47 The distinction was more recently affirmed by the Australian Health Ethics Committee in a statement by the Committee's chair, Dr Kerry Breen:

> Therapeutic interventions are interventions directed towards the wellbeing of the individual embryo involved and non-therapeutic interventions are interventions that are not directed towards the benefit of the individual

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45 *Human cloning*, p.22.

46 See, for example, *Submissions* 899, 981, and 987; *Committee Hansard*, 17.9.02, p.34 (Dr Juttner); *Committee Hansard*, 26.9.02, p.226 (Professor Tate).

47 See Senate Select Committee on Human Embryo Experimentation Bill 1985, *Human Embryo Experimentation in Australia*, September 1986, p.14 and Appendix VII.

48 See Senate Select Committee on Human Embryo Experimentation Bill 1985, *Human Embryo Experimentation in Australia*, September 1986, pp.14-16.

> embryo but rather towards improving scientific knowledge or technical application. Non-therapeutic experimentation includes both non-destructive procedures (which include observation) and destructive procedures…
>
> The more-recently-coined term `therapeutic cloning' collapses both (a) the distinction between therapeutic and non-therapeutic research on embryos and (b) the distinction between destructive and non-destructive experimentation on embryos. The creation of embryos specifically for research purposes, experimentation on those embryos and their subsequent destruction, etc. all fall under this term. It was because of the lack of transparency of the term `therapeutic cloning', because the term concealed rather than revealed these ethically-significant differences, that AHEC rejected its use.[49]

2.48 The cloning of an embryo in order to extract its stem cells for therapeutic application to others does not constitute a procedure 'of benefit' to the embryo.

2.49 The Reverend Professor Michael Tate, former Chair of the Senate Select Committee on Human Embryo Experimentation, observed:

> Language has now changed, and in a dangerous way that confuses the permissible ways in which to advance science in this area. Recently, 'therapeutic' has been simply opposed to 'reproductive'. This is because the question of cloning has become significant, and 'therapeutic', said to be advancing some knowledge that can have clinical or medical benefits immediately on the subject or, prospectively, on other embryos or human lives, is said to be undeniably good, whilst 'reproductive' experimentation is said to be still the subject of debate.
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> I believe we need to emphasize again that the term 'therapeutic' is misused if applied to the intentional and deliberate destruction of the subject of the experiment. However, if this definitional argument has been lost by the media's contrasting of therapeutic with reproductive, nevertheless, within 'therapeutic', distinctions clearly need to be made.[50]

2.50 The Academy of Science supports therapeutic cloning as 'a possible way ahead for the production of appropriate stem cell lines if that turns out to be what is needed to produce them'. The Academy also supports a moratorium on therapeutic cloning advising that 'at the moment the position of the Academy is that it is unwise to close [therapeutic cloning] off as a possibility in the future'.[51] Professor Robert Jansen indicated that he was not opposed to what he described as 'somatic cell nuclear transfer, sometimes referred to as therapeutic cloning' saying 'no, not as a matter of principle. I accept that, because of perhaps incomplete understanding of the issues, a suspension of activity in that area for three years might be reasonable. I do not have

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49 AHEC/NHMRC: Position on Cloning and Related Technologies, dated 15 December 2000, *Senate Hansard,* 7.02.01, p.21477.

50 *Submission* 899, p.2.

51 *Committee Hansard* 19.9.02, p.14 (Professor White, Academy of Science).

strong views.'[52] The Juvenile Diabetes Research Foundation was opposed to a permanent ban on the practice, recognising 'that there is quite a considerable amount of research that has to be done before we get to the stage where therapeutic cloning may or may not be useful'.[53]

Potential applications of stem cell research

2.51 There are two broad two areas of research with possible clinical applications enabled by stem cell technologies. They are:

- research into cell therapies; and
- 'spin-offs' from that research including research into early embryo development.

Stem cell therapies

2.52 The potential applications of stem cell therapies, whose development may or may not make use of cloning technologies, are said to be wide-ranging and revolutionary. The House of Representatives Human cloning report stated that:

> The ability to control and direct cell differentiation or to identify the factors responsible for doing so, has enormous potential for new therapies in medicine and for new biomedical industries…The potential benefits include a complete revolution in the ability to treat acute and chronic diseases, including Alzheimer's, Parkinson's, diabetes and many others.[54]

2.53 There are two main types of cell therapy currently envisaged as potentially arising from stem cell research. The first involves replacing or transplanting damaged or diseased cells by tissue developed either from embryonic stem cells or from adult stem cells. The second involves developing drugs or other therapies that may trigger tissue to repair itself or prevent tissue degeneration.

2.54 Professor Alan Trounson, Monash Institute of Reproduction and Development and CEO (Designate), National Stem Cell Centre, told the Committee that:

> Future research with embryonic stem cells will allow us, firstly, to discover factors that influence and regulate tissue formation. This knowledge may be used to develop pharmaceuticals for tissue repair in the future. Secondly, it will help us understand the role of genes in development and tissue function and why some of those genes lose their regulators and are associated with cancer later in life. Thirdly, research will help us produce cells in abundance that may be used to regain tissue function in people suffering from diseases such as diabetes, Parkinson's disease, cardiovascular disease and cystic

52 *Committee Hansard* 26.9.02, p.208 (Professor Jansen).

53 *Committee Hansard* 17.9.02, p.76 (Ms Royles, JDRF).

54 *Human cloning*, p.23.

> fibrosis. Fourthly, research will help us develop new drugs using some specific cell types such as hepatocytes in the liver.[55]

2.55 Professor Trounson spoke of these developments as contributing to 'a new era of medicine', with a combination of cell therapies and conventional medicine available to treat disease.[56] Mr Robert Moses, Chairman of the Board, National Stem Cell Centre, spoke on the potential of stem cell research as 'identified throughout the world as one of the three or four new bioscience endeavours most likely to yield major advances in the development of medicines during the next 10 to 15 years'.[57]

2.56 Other evidence to the inquiry, however, seriously questioned these claims, saying that they were overblown and premature.[58] Professor Colin Masters, Professor of Pathology at the University of Melbourne with expertise in the study of brain diseases, Alzheimer's and other neurodegenerative disorders, questioned claims made about the potential of research with embryos to create therapies:

> My observations on the current stem cell debate relate to the misrepresentation which has occurred over the potential therapeutic benefits of stem cell therapies, especially in the areas of Alzheimer's disease, Parkinson's disease, motor neurone diseases and other causes (traumatic and non-traumatic) of spinal cord paralysis.
>
> I have been concerned that advocates of embryonic stem cells as a therapy have created false expectations in the mind of the general community. The difficulties in developing these cells for therapeutic purposes in the brain pose immense scientific difficulties which require much more developmental research. The real value of stem cells for drug discovery has been almost overlooked in the public debate.[59]

2.57 Dr Peter McCullagh advised the Committee that his career was spent studying immunological tolerance in the area of experimental transplantation. He said:

> I am appalled at the meretricious arguments and claims that have been presented for what can be done in relation to transplantation if this bill goes through and if the research that is foreshadowed by people appearing in favour of the bill proceeds…In fact, when one looks at the claims made for transplantation based on embryonic stem cell research, I suspect that you will not find a single published paper on transplantation by any of the main protagonists.[60]

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55 *Committee Hansard*, 24.9.02, p.135 (Professor Trounson).

56 *Committee Hansard*, 24.9.02, p.135 (Professor Trounson).

57 *Committee Hansard*, 24.9.02, p.137 (Mr Moses).

58 See *Submissions* 84, 87, 162, 614; *Committee Hansard*, 17.9.02, p.53 (Professor Silburn) and 19.9.02, p.95 (Professor Rowe).

59 *Submission* 87 p.1 (Professor Masters).

60 *Committee Hansard*, 24.9.02, p.156 (Dr McCullagh).

2.58 Dr David van Gend, a general practitioner and the Queensland spokesperson for Do No Harm, expressed the view that proponents of embryonic stem cell research in particular have misrepresented both the prospects of that research and the proven therapeutic success of adult cells.[61]

2.59 Professor Peter Rowe, Director, Children's Medical Research Institute, Westmead, Sydney, stated that he had been interested for the past 38 years in the prospects of genetic or cell therapy, particularly for the treatment of childhood inherited disease and developmental abnormalities. Nevertheless, he considered that 'at this stage, human embryonic stem cells have very little to offer'. Professor Rowe said that:

> I think the public…has been grossly misinformed as to the potential…I feel that there is a lot of work that could be done on human embryonic stem cells, but to what end? Because I do not think we are ever going to use them in any form of treatment, not in the next foreseeable 20 or 30 years, if even then.[62]

2.60 Professor Michael Good, an immunologist and Director, Queensland Institute of Medical Research, argued that there will be major difficulties with the therapeutic application of tissue grown from embryonic stem cells because of the problems of immunological rejection. He also claimed that there is no established 'proof of concept' or 'proof of principle' that human embryonic stem cells can be used clinically, and that successful therapies derived from adult stem cells are being overlooked in the 'hype' about embryonic stem cells.[63]

2.61 Professor Good agreed that embryonic stem cell research should go ahead in animals, in order to establish any 'proof of principle', but that in the meantime:

> when there is a limited amount of money for research in this country…why would we waste it on putting something into human embryonic stem cell research that, in my estimation, will never make it into a therapy.[64]

2.62 The Committee asked the proponents of embryonic stem cell research to respond to these criticisms. In general terms, the proponents agreed that it is unrealistic to expect 'overnight' or 'miracle' cures from either embryonic or adult stem cell research, but disputed the claim that there is insufficient 'proof of principle' to justify undertaking research into human embryonic stem cells.

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61 *Committee Hansard*, 24.9.02, p.177 (Dr van Gend).

62 *Committee Hansard*, 19.9.02, p.95 (Professor Rowe).

63 *Committee Hansard*, 19.9.02, pp.89-91 (Professor Good).

64 *Committee Hansard*, 19.9.02, p.97, 102 (Professor Good); on the need to establish 'proof of concept' in animal models, see also *Committee Hansard*, 19.9.02, p.99 (Professor Rowe) and p.100 (Professor Bartlett).

2.63 For example, Professor John Shine, Secretary, Biological Sciences, Australian Academy of Science, stated that:

> we all realise that, in this particular area, the goal at the end of the day is to take one of our own cells, a skin cell or a blood cell, put it into culture, multiply it up, add the appropriate growth factors and transfer it or reprogram it into a nerve cell to treat Parkinson's or a pancreatic cell to treat diabetes. That is the goal at the end of the day.[65]

2.64 'To get there', he acknowledged:

> the academy, and all of us as scientists, recognise that we have an enormous amount of information that we have yet to gain - a lot of knowledge we have to learn - about what triggers cells and how they reprogram themselves in this situation…[66]

2.65 Professor John Hearn, a developmental biologist and Deputy Vice-Chancellor, Research, ANU, supported research in human embryonic stem cells, but agreed that 'embryonic stem cells are still a very long way off application to therapy'. He said that:

> it is unhelpful to have unqualified statements and sometimes emotional statements about the promise of this field, where we are at a very early stage …It is quite wrong to expect…that in the next five to 10 years, in the normal course of science and the normal progress of clinical trials, there is going to be anything that resolves those problems.[67]

2.66 Nevertheless, Professor Hearn submitted that the study of human embryonic stem cells will be important for understanding how cells 'choose' to develop into different types of lineage and that this understanding will have the potential to underpin major new therapies and possibly major new drugs.[68] Professor Hearn also disputed the claim that proof of principle sufficient to justify proceeding had not yet been established in relation to this research.[69]

2.67 Associate Professor Martin Pera, Co-Director, Centre for Early Human Development, Monash Institute of Reproduction and Development, similarly agreed that this is a rapidly evolving area of research and that 'it would be very wrong for anyone in the scientific community to promise cures in a certain time frame'.[70]

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65 *Committee Hansard*, 19.9.02, p.115 (Professor Shine).

66 *Committee Hansard*, 19.9.02, pp.115-116 (Professor Shine).

67 *Committee Hansard*, 19.9.02, pp.114-115 (Professor Hearn).

68 *Committee Hansard*, 19.9.02, p.114 (Professor Hearn).

69 *Committee Hansard*, 19.9.02, p.122 (Professor Hearn).

70 *Committee Hansard*, 24.9.02, p.143 (Professor Pera).

2.68 He also, however, disputed the claim that there is no proof of principle underpinning the research. He said:

> In recent years we have seen proof of concept of treatment in animal models, using mouse embryonic stem cells in Parkinson's disease, diabetes, stroke, demyelination, severe combined immune deficiency and myocardial infarcation.[71]

2.69 Proof of concept studies using human embryonic stem cells or embryonic germ cells transplanted into mouse models are, according to Professor Pera, 'probably taking place in labs around the world now. It will certainly be taking place in ours within the coming year'.[72]

2.70 Dr Andrew Elefanty, Senior Research Fellow and Laboratory Head, Centre for Early Human Development, Monash Institute of Reproduction and Development, argued that, in any case, there are limitations on the extent to which proof of concept studies in animal models can validate human stem cell research. He stated:

> Whilst human and mouse embryonic stem cells do have many similarities, there are many differences in the growth and differentiation of these two species of cells. Although we strongly believe in the use of mouse embryonic stem cells as a complementary system…it is evident that the differences between the biology of mouse and human embryonic stem cells will limit the degree to which results in the mouse system can be extrapolated to humans.[73]

2.71 Very similar points were made by Dr Edouard Stanley, joint head of the embryonic stem cell differentiation laboratory at the Centre for Early Human Development, Monash Institute of Reproduction and Development.[74] In view of this argument, Dr Stanley concluded that 'there is no valid scientific justification for restrictions to be placed on the work using or generating human ES cell lines'.[75]

2.72 However, in addition to their general concerns about allegedly exaggerated claims and about the lack of proof of principle, critics raised a number of more specific questions about the likely feasibility and effectiveness of potential therapies deriving from human embryonic stem cell research.

2.73 In what follows the Committee outlines the scientific issues that arise from three key questions:

- feasibility of tissue transplantation;

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71 *Committee Hansard*, 24.9.02, p.144 (Professor Pera).

72 *Committee Hansard*, 24.9.02, p.144 (Professor Pera).

73 *Committee Hansard*, 24.9.02, p.138 (Dr Elefanty).

74 *Committee Hansard*, 24.9.02, p.139 (Dr Stanley).

75 *Committee Hansard*, 24.9.02, p.139 (Dr Stanley).

- the relative therapeutic effectiveness of adult compared to embryonic stem cells; and
- the relationship between cell therapies and disease processes.

Feasibility of tissue transplantation

2.74 The House of Representatives report on human cloning discussed two hypothetical cases designed to illustrate tissue transplantation therapies that might arise from stem cell research.

2.75 The first involved the treatment of Type 1 diabetes:

> Using somatic cell nuclear transfer, the nucleus of a somatic cell from a patient with the disease could be fused with an enucleated donor egg. The cell would develop into a blastocyst from which inner cell mass cells could be isolated and grown in culture with growth factors, as yet unknown, to develop into pancreatic islet cells that produce insulin. Because these cells came from and are genetically identical to the patient…they would not be rejected when transplanted back into the patient. There would be little or no need for immune-suppressing drugs, with their often unpleasant and serious side effects.[76]

2.76 The second envisaged that it may be possible to identify and isolate adult stem cells from a particular tissue or organ type, multiply and grow them in culture, manipulate them to repair any genetic or metabolic deficiency, and then transplant them back into the damaged organ with a view to its repair.[77]

2.77 The great advantage of the hypothetical cell therapies outlined above is that they seem to overcome the problems of immune rejection which are currently associated with the transplantation of donated organs. New tissue is grown either from an embryo created by somatic cell nuclear transfer using the patient's own somatic cell, or directly from the patient's adult stem cells. It thus already matches the tissue of the patient for whom it is intended.

2.78 In practice, however, there are a significant number of difficulties to be overcome before these hypothetical therapies can become a reality.

2.79 First, if the tissue is grown from embryonic stem cells, then it is only directly compatible with the patient's own tissue if the embryo is the product of a somatic nuclear cell transfer in which a somatic cell from the prospective patient is fused with an enucleated egg. Even leaving aside the fact that this technique is prohibited by the current Bill, it is unclear that it would be viable in any case.

2.80 As noted earlier, the rate of success in forming viable blastocysts from somatic cell nuclear transfer is in the range of 1-2% of attempts made. The

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76 *Human cloning*, p.23.

77 *Human cloning*, p.23.

inefficiency of this procedure would mean that a very large number of human eggs would need to be available for every treatment.

2.81 One concern raised in relation to this technology was that, because of the number of eggs required, any clinical application of this practice would necessarily be exploitative of women, for example that women may possibly be coerced in some way into providing their eggs for such purposes.[78]

2.82 A second concern focused on the impracticality of the therapeutic application of the technology. For example, the Caroline Chisholm Centre for Health Ethics submitted that:

> A large supply of human eggs will be required as this procedure is very inefficient; and, unlike preimplantation embryos, eggs are in very short supply…Treatments involving therapeutic cloning therefore, will not be readily available, will be very time consuming, labor intensive and, as are result, expensive. Thus, apart from ethical considerations, therapeutic cloning is, and will remain, problematic.[79]

2.83 The leader of the scientific team that first isolated embryonic stem cells at the University of Wisconsin-Madison has been reported as saying that therapeutic cloning would be 'astronomically expensive'.[80] Likewise, Dr Christopher Juttner, Medical and Executive Director, BresaGen Ltd,[81] told the Committee that his company:

> felt from the beginning that therapeutic cloning using human eggs as the recipients of an adult nucleus was never going to be possible because the success rates are so low that you would have to hyperovulate 10 women to get enough cells - say 100 eggs - to have a chance of getting one matching cell line. So that was practically impossible. We felt it was ethically unacceptable because these would be egg donors and it would not be reasonable to ask anyone to do that.[82]

2.84 If the problem of rejection of tissue grown from embryonic stem cells cannot be overcome by the method of somatic cell nuclear transfer, then other options need to be investigated.

2.85 One such option involves the creation of a multitude of stem cell lines, from which tissue can be derived. However, there are significant differences in scientific opinion about how many such stem cell lines would be required in order to 'match' the needs of all possible patients.

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78 See, for example, *Submissions* 211, 882, 981 and 1036.

79 *Submission* 280, p.4 (Caroline Chisholm Centre for Health Ethics).

80 *Human cloning*, p.39.

81 BresaGen Ltd describes itself as 'a publicly listed Australian company acknowledged as one of the three world leaders in the therapeutic application of human ESC [embryonic stem cell] technology'. *Submission* 1030, p.2 (BresaGen Ltd).

82 *Committee Hansard*, 17.9.02, p.34 (Dr Juttner).

2.86 BresaGen Ltd informed the Committee that, in its view, '600-1000 such therapeutic ESC [embryonic stem cell] lines will provide adequate immunological tissue matching for 90-95% of humanity across racial/ethnic groups'.[83] Professor Michael Good, by contrast, estimated that 'millions' of stem cell lines would be required for such matching. According to Professor Good:

> This is because we all possess near-unique tissue types and it is extremely rare to find stem cells with the identical tissue type to ourselves. In humans, the tissue typing molecules are encoded by 'HLA' genes and there are 5 main types…Each gene has multiple 'alleles' or variants…The number of different HLA alleles in a population, however, is thought now to be about 500 and the different alleles can be found in different permutations and combinations. There are literally millions of ways to mix and match the different genes. Collectively, these different 'HLA' genes determine our 'tissue type'.[84]

2.87 A second potential solution to the problem of immune rejection was also proposed in evidence by BresaGen Ltd. Dr Juttner told the Committee that BresaGen had been experimenting with the somatic cell nuclear transfer technique. Rather than putting an adult somatic cell into an enucleated egg, they had tried 'putting adult cells into an embryonic stem cell that had had its nucleus removed'. He said:

> It is not easy. We have worked on that for three years in mice. We have had the beginnings of some success.[85]

2.88 Dr Juttner noted that this technique produced cloned embryonic stem cells, but not cloned embryos. For that reason, he believed that it would not be prohibited by the current Bill and that 'it is likely, I think, that the Biotechnology Centre of Excellence will take up and expand this if it does indeed go ahead'.[86]

2.89 In terms of the feasibility of tissue transplantation, tissue cultivated directly from adult stem cells does not present problems of immune system rejection. Many submissions to the inquiry thus argued that research should focus on adult stem cells, because of the ready therapeutic applicability of tissue so derived.[87] However, other evidence indicated that the cultivation of tissue from adult stem cells presents its own difficulties.

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83 *Submission* 1030, p.1 (BresaGen Ltd).

84 *Submission* 614, p.2 (Professor Good).

85 *Committee Hansard*, 17.9.02, p.34 (Dr Juttner).

86 *Committee Hansard*, 17.9.02, p.34 (Dr Juttner).

87 See, for example, *Submissions* 86, 280, 359, 614, 866, 876, 880, 1042.

Therapeutic effectiveness of adult compared to embryonic stem cells

2.90 Adult and embryonic stem cells have different properties. These affect both their presumed effectiveness in different situations, and the ease with which they can be studied and used.

2.91 There was extensive debate in evidence about the relative therapeutic prospects of research into embryonic and adult stem cells. A number of submissions provided extensive bibliographies of research published in scientific and medical journals supporting the use of either adult or embryonic stem cells.

2.92 Proponents of adult stem cell research referred to their successful use in therapies including using brain precursor cells to treat stroke, the patient's own stem cells to treat cancer and to treat bone defects, and bone marrow cells to treat muscle, gut and retina. Experiments with animal models have led to published accounts of adult stem cell success in the treatment of conditions such as Diabetes, Parkinson's and spinal injury.[88] Proponents of embryonic stem cell research noted studies indicating their potential for treatment of a range of diseases including neurological, cardiac, cancer and other conditions.[89] Embryonic stem cell research is still in its infancy, whereas adult stem cell research has been performed for a number of years.

2.93 Professor Martin Pera told the Committee that:

> The excitement over the potential for human embryonic stem cell research relates to the unique properties of stem cells…These [embryonic] cells may be grown in the laboratory indefinitely in the primitive embryonic state, and they retain the key property of embryo cells from which they originate – pluripotentiality or the ability to give rise to any type of adult body cell. This combination of properties has not been documented in any type of adult tissue stem cell isolated to date.[90]

2.94 According to Professor Pera, these two properties mean that embryonic stem cells 'in principle represent a potentially indefinite renewable source of human tissue for use in research or in transplantation therapy to correct a range of debilitating and currently intractable medical conditions'.[91]

2.95 By contrast, adult stem cells are generally rare in the tissues in which they have been discovered, and they have not been discovered to exist in all tissue types. They are difficult to isolate and extract.[92] Finally, while some types of adult stem cell can be grown successfully in culture, there are others that cannot be. Associate Professor Paul Simmons, head of the stem cell program, Peter MacCallum Cancer

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88 *Submissions* 86, 480, 614, 1042, 1571.

89 *Submissions* 23 Ad info 13.9.02, 871 Ad info 17.9.02, 895, 1030 Ad info 24.9.02, 1292

90 *Committee Hansard*, 24.9.02, p.135 (Professor Pera).

91 *Committee Hansard*, 24.9.02, p.135 (Professor Pera).

92 *Stem Cells: Scientific Progress and Future Research Directions* (NIH), p.ES-3.

Institute, told the Committee that, for example, haemotopoietic stem cells cannot be grown in culture. He said:

> When one attempts to grow haematopoietic stem cells in culture, they actually lose their stem cell properties – they differentiate. Try as we might, we have not – and I have been actively engaged in this form of research for at least 10 years – found ways to retain their stem cell properties. They differentiate.[93]

2.96 Although, Dr Simmons said, he is 'a passionate, fervent believer in the use of adult stem cells':

> [t]here are limited numbers, and we cannot grow all the adult stem cell populations we would like. These I think are two important limitations of adult stem cells which, in fairness, the committee needs to take on board if it is to engage in a rational debate on the relative merits of embryonic and adult.[94]

2.97 Arguments raised in opposition to research on embryonic stem cells include that embryonic stem cells are not the only stem cell alternative, that they are undesirable from the point of view of therapeutic application, and that adult stem cells have already been used in a large number of successful therapies while embryonic stem cells have not – although embryonic stem cells have not yet been the subject of the same level of extensive research.

2.98 In support of the view that the identified properties are undesirable in the clinical setting, Dr Peter McCullagh observed that the judgement that a cell's capacity to differentiate into a wide range of tissue is advantageous 'is completely context-dependent':

> When one is contemplating the use of cells from any source for the purpose of clinical transplantation, it is essential that their capacity for differentiation after their introduction into a recipient patient has been reliably defined and that this capacity is confined to cells of a type which are normally present in the anatomical location into which it is proposed that they be introduced…The moral is that toenails are fine, in their place, but are not an asset in one's brain. If the end use of cells is to be transplantation to a sensitive location, an unrestrained capacity for differentiation is not an advantage.[95]

2.99 Evidence given to the Committee by Professor Good also suggested that pluripotency may not be an advantage:

> The embryonic stem cells are all called totipotent. They have enormous proliferative potential and they can differentiate into every single cell of

93 *Committee Hansard*, 19.9.02, p.92 (Dr Simmons).

94 *Committee Hansard*, 19.9.02, p.92 (Dr Simmons).

95 *Submission* 480, p.2 (Dr McCullagh).

> 200-odd tissues of the body. That is not an advantage; it is a disadvantage. Why would you want to put cells into a person which have the potential to change into other cell types that are not required? Those particular cells, due to their totipotential, can give rise to teratomas; that is, tumours formed by cells which can give rise to multiple tissues.[96]

2.100 Similarly, Dr Megan Best, representing the Archbishop's Social Executive Committee, Sydney Diocese, Anglican Church, described embryonic stem cells as 'wild stallions and adult stem cells as more like domestic horses'.[97] She spoke of experiments with embryonic stem cells showing that they have 'a very disconcerting tendency…to form tumours, which has not been seen to the same degree in adult stem cells'. She noted:

> that, even though stallions may be able to run faster, it was easier to bridle a horse; and that, even if adult stem cells were not shown to be quite as plastic as the embryonic stem cells, this may in fact be an advantage.[98]

2.101 In support of the argument that embryonic stem cells may not really be unique in terms of their pluripotentiality, witnesses cited two developments in recent research into adult stem cells.

2.102 The first of these involves the observation 'made in many laboratories' of the 'plasticity' of adult stem cells.[99] The term 'plasticity' refers to the previously unsuspected capacity of adult stem cells to give rise, not just to their tissues of origin, but to 'completely unrelated cell types and tissues'.[100] For example, it has apparently been shown that stem cells from neural tissue can differentiate into bone or muscle tissue, that stem cells from bone marrow can differentiate into neural, liver, or epithelial tissues, and into skeletal muscle and myocardium, and that skeletal muscle tissue can differentiate into bone marrow.[101]

2.103 The second research development used to support the argument that embryonic stem cells may not really be unique in terms of their pluripotentiality is found in the work of Professor Catherine Verfaillie, University of Minnesota.[102] This research was paraphrased for the Committee in the following terms by Dr Simmons:

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96 *Committee Hansard*, 19.09.02, p.91 (Professor Good).

97 Dr Best said that she was reporting the analogy used by Dr William Hurlbut, Stanford University, *Committee Hansard*, 24.9.02, p.159 (Dr Best).

98 *Committee Hansard*, 24.9.02, p.159 (Dr Best).

99 *Committee Hansard*, 19.9.02, p.92 (Dr Simmons).

100 *Submission* 1292. The submission provides journal references to articles in which these findings have been published. See also *Submission* 1030, Additional information 24.9.02.

101 *Submission* 1292 (Peter MacCallum Cancer Institute).

102 Catherine Verfaillie et al., 'Pluripotency of mesenchymal stem cells derived from adult bone marrow', *Nature* AOP, published online 20 June 2002, doi:10.1038/nature00870.

> It demonstrated the presence in adult human bone marrow of what appeared to be a population of adult pluripotent stem cells. They are cells that ostensibly have characteristics very similar to embryonic stem cells. That is, they could give rise to cells of all three germ lands - endoderm, mesoderm and ectoderm. They had the apparent advantage over embryonic stem cells in that they did not form tumours in the animal models these investigators were using.[103]

2.104 A number of submissions to the Committee referred to these recent research findings to justify the claim that research using embryonic stem cells is unnecessary, and that any therapeutic applications needed can be derived from adult stem cells.[104]

2.105 However, Dr Simmons expressed serious reservations about that line of argument. He noted, first, that many of the experiments purporting to demonstrate adult stem cell plasticity had not been able to be replicated by reputable researchers, and that the results of the studies have come to be challenged on scientific grounds.

2.106 In particular, he wrote:

> Some reported phenomena have been shown to be artifacts due to contamination of transplanted cells while other examples of conversion to other cell types appear to be due to *fusion* of different adult stem cell types leading to the generation of potentially unstable hybrid cells with shared properties of each founder cell type.[105]

2.107 According to Dr Simmons, then, 'it is to my mind not appropriate to use stem cell plasticity as an argument to not study embryonic stem cells. It is looking very much like adult stem cells are not as plastic in their developmental properties as was initially suggested by publications'.[106]

2.108 Similarly, while Dr Simmons agreed that Professor Verfaillie's research involved 'a very amazing observation', it has yet to be reproduced by any other laboratory. In any case, he said that he did not accept that it made research into embryonic stem cells redundant, and he noted that Professor Verfaillie herself had urged that research into embryonic stem cells needed to continue.[107]

2.109 In an interview in Melbourne on 28 August 2002, Professor Verfaillie reiterated that point, saying that:

> My message has always been, even though we're excited about the adult cells, that it's too early to say that they will replace embryonic stem cells to

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103 *Committee Hansard*, 19.9.02, p.93 (Dr Simmons).

104 See, for example, *Submissions* 86, 156, 280, 876, 880, 1046.

105 *Submission* 1292 p.2 (Peter MacCallum Cancer Institute).

106 *Committee Hansard*, 19.9.02, p.92 (Dr Simmons).

107 *Submission* 1292; see also *Committee Hansard*, 17.9.02, p.32 (Dr Juttner), *Submission* 477 and 1043.

> the point that our institution, the Stem Cell Institute, we actually recruited and investigated who has extensive experience in human embryonic stem cell work, so we're now in a position to do exactly what you mentioned, which is to parallel research and comparing and contrasting the two cell types.[108]

2.110 As intimated by Professor Verfaillie's remarks, there are two main reasons given by scientists for the need to continue research into both adult and embryonic stem cells.

2.111 First, it is too early to determine fully just what the potential applications of the two sets of stem cells are. Professor John Hearn emphasised that the focus on embryonic stem cells in humans is only four years old, and on adult stem cells even less than that.

> So our knowledge of whether adult stem cells or embryonic stem cells are going to deliver the best benefit, either in advancing knowledge or in advancing potential therapies, is still open to major question.[109]

2.112 In a similar vein, Professor Sue Serjeantson, Executive Secretary, Australian Academy of Science, stated that the Academy:

> considers that research is warranted across a range of sources of stem cells in the hope of developing tissue for use in repair of damaged tissues. We would all be very happy if we thought that scattered adult stem cells could be used for tissue repair. The ethical dilemma would then go away, with it being set aside. But we think, it is unlikely at this time that the different types of stem cells - whether derived from germ cells, blood cells, adult tissues or embryonic stem cells - will all have the same characteristics; we think it is unlikely that they will all have the same potential to develop into particular tissues.[110]

2.113 The second reason given in support of continuing research into both adult and embryonic stem cells relates to the possibility that advances in one field will spur advances in the other.

2.114 Dr Simmons, for example, referred to recent research done in laboratories at Harvard and Princeton which compares two adult stem cell populations with embryonic stem cells. The comparisons show that there are 'genes that are uniquely expressed in each stem cell population and there are genes that are expressed in all three populations'. Dr Simmons noted that this 'commonality of gene expression' may

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108 Transcript of interview with Professor Catherine Verfaillie, The World Today, 22 August 2002, http://www.abc.net.au/worldtoday/s656192.htm (30 September 2002).

109 *Committee Hansard*, 19.9.02, p.114 (Professor Hearn).

110 *Committee Hansard*, 19.9.02, p.120 (Professor Serjeantson).

imply that there are 'fundamental aspects in terms of stem cell biology that we could approach only through studying all three types of stem cell'.[111]

2.115 Given, he continued, that the heart of the matter is 'to understand and define pathways with differentiation that are responsible for derivation of the matured cell types that stem cells give rise to', then the comparison of completely undifferentiated cells such as embryonic stem cells with adult stem cells 'will inevitably yield secrets as to how adult stem cells work'.[112]

2.116 Another example of the possible complementarity of work in adult and embryonic stem cells was provided by Dr Andrew Elefanty. He noted that 'the recent very rare bone marrow derived multipotential adult stem cells', isolated in the mouse, grow only in the presence of 'the growth factor lift'. This growth factor, however, 'was identified and isolated because it works on mouse embryonic stem cells'. Dr Elefanty commented that:

> there is, if you like, an example already of the cross-fertilisation of those ideas, and that is part of the reason why we feel so strongly that both lines of research have to proceed in parallel.[113]

2.117 Professor Bob Williamson, Director, Murdoch Childrens Research Institute, and Professor of Medical Genetics, University of Melbourne said that:

> Many, including me, are primarily interested in 'adult' stem cell research because for the diseases we hope to treat (such as cystic fibrosis or thalassaemia), avoiding rejection is a very important issue. However, we need to learn how to use adult stem cells, and to treat them so that they become more 'pluripotent' and can grow more easily (that is, more like embryonic stem cells). In a sense, we need to learn from embryonic stem cells how to use adult stem cells better. There is also a chance that new developments in immunology may make embryonic stem cells less likely to be rejected, and if this is true, they may become more useful for childhood diseases. What I believe to be absolutely certain is that there are real benefits in allowing adult and embryonic stem cell research to proceed side by side in the same laboratories, so the experiments cross-refer and so that lessons can be learnt by comparing the two systems.[114]

2.118 This body of scientific opinion was echoed by Ms Sheila Royles, Spokesperson, Coalition for Advancement of Medical Research Australia and Chief Executive Officer, Juvenile Diabetes Research Foundation. She asked the Committee 'to support the pursuit of both adult and embryonic stem cell research', saying:

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111 *Committee Hansard*, 19.9.02, p.93 (Dr Simmons).

112 *Committee Hansard*, 19.9.02, p.93 (Dr Simmons).

113 *Committee Hansard*, 24.9.02, p.154 (Dr Elefanty).

114 *Submission* 1002, p.2 (Professor Williamson).

> We are at the start of the marathon; we have two strong runners, embryonic and adult stem cells. As yet we do not know which one is going to be capable of finishing or whether in fact they will cross the line together. Let's not make the decision to eliminate one of our strongest runners before we even start. There are many, many scientific questions yet to be answered. I urge you to support legislation and give our researchers the opportunity to see whether this area of research really can deliver the benefits that we hope…[115]

Relationship between cell therapies and disease processes

2.119 A third set of questions surrounding the clinical applicability of stem cell therapies raises the issue of the relationship between cell damage and disease processes.

2.120 In crude terms, the problem is that even if you were able to introduce compatible 'new' tissue to replace degenerated or damaged cells, the disease processes which caused the damage to the original cells might just turn on the 'new' tissue.

2.121 For example, Professor Bernard Tuch, Director, Diabetes Transplant Unit, Prince of Wales Hospital, spoke of the problems associated with the attempted transplantation of healthy pancreatic tissue into diabetics. He told the Committee of an experimental study involving twins:

> This is not stem cell work, but perhaps it can be used to explain. They did take half a pancreas from the twin that did not have diabetes and transplanted it into the person with diabetes. And of course the person with diabetes was no longer diabetic for two weeks, and then their diabetes recurred because of the self-destruct mechanism which causes type 1 diabetes.[116]

2.122 Professor Michael Pender, a neuroimmunologist, made a similar point in relation to Alzheimer's disease, saying that it 'is a global disorder of the brain and is highly unlikely to be amenable to any form of cell therapy at any time in the future'.[117]

2.123 Similarly, Professor Peter Rowe argued that:

> It is not even sure that Parkinson's disease is primarily caused by specific self-generated damage within the particular part of the brain which is responsible for producing the symptoms. It may well arise from a systemic

115 *Committee Hansard*, 17.9.02, p.71 (Ms Royles).

116 *Committee Hansard*, 17.9.02, p.41 (Professor Tuch).

117 *Submission* 84, p.3 (Professor Pender).

> disorder, and work has been done to suggest that that is the case. In which case, you put cells in and you get the same process occurring again.[118]

2.124 Nevertheless, evidence suggested that even if direct transplantation of new tissue is unlikely to cure certain diseases or conditions, research into stem cells may lead to other therapies. In other words, the concerns just outlined may constitute arguments against the prospects of the successful transplantation of tissue derived from stem cells, but not an argument against stem cell research per se.

2.125 For example, Professor Perry Bartlett, Head, Development and Neurobiology Group, Walter and Eliza Hall Institute of Medical Research, Melbourne, described research he has recently undertaken to isolate and purify neural stem cells, which are adult stem cells, in the adult brain. He then said:

> The reason that we went on to purify and find these cells was not to be able to transplant them but to be able to finally discover what molecules regulate these stem cells in you and me to make nerve cells, because the $64 million question – and the $64 billion therapy – is to have a drug that is able to stimulate those cells that reside in our own brains and that can make nerve cells to replace those cells lost in stroke, Alzheimer's disease, et cetera.[119]

2.126 Professor Tuch explained that research into a promising approach to treating diabetes is currently being undertaken on embryonic stem cell lines.[120] It involves not tissue transplantation but learning how to direct the patient's own cells, by developing genes or other agents that might turn non-insulin-producing pancreatic cells into insulin-producing cells.[121]

Other applications of stem cell research

2.127 Although most of the evidence to the Committee focused on the issue of cell therapies and tissue transplantation, some witnesses drew attention to other applications of stem cell research.

2.128 For example, Professor David de Kretser, Director, Monash Institute of Reproduction and Development, noted that significant advances in knowledge will necessarily arise from the process of developing tissue for transplantation. He said:

> Researchers seeking to define the conditions necessary to enable an embryonic stem cell to proceed down a selected pathway of development will identify numerous products with the capacity to create markets for new drugs or specific fluids and substrates to enable these cell types to be grown.

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118 *Committee Hansard*, 19.9.02, p.95 (Professor Rowe).

119 *Committee Hansard*, 19.9.02, p.94 (Professor Bartlett).

120 *Committee Hansard*, 17.9.02, p.37 (Professor Tuch).

121 *Committee Hansard*, 17.9.02, p.41 (Professor Tuch).

> Each of these has the potential to develop small but important industries to underpin Australia's future role in biotechnology.[122]

2.129 Professor de Kretser also expressed the view that this research would also greatly expand knowledge of the 'normal development' of a human embryo, and hence increase understanding of developmental birth defects.[123]

2.130 A large number of submissions to the inquiry expressed grave concern that 'other research' undertaken as a result of the passage of the Bill would include other destructive research on embryos, including the use of human embryos for drug or toxicology testing, and even for the testing of cosmetics.[124]

2.131 The Southern Cross Bioethics Institute detailed the possible range of embryo research and observed the majority of the research would not be related to stem cells:

> The broad range of uses to which embryos will be subjected are described, in part, in the *Explanatory Guide to the Human Cloning and Research Involving Embryos Bill 2002*…the following categories for the use of excess Assisted Reproductive Technology (ART) embryos were identified:
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> - for the derivation of stem cells;
> - for examining the effectiveness of new culture media used in ART practice;
> - for better understanding embryonic development and fertilisation;
> - to train clinicians in micro-surgical ART techniques;
> - to examine gene expression patterns of developing embryos; and
> - for improving ART techniques.
>
> To this list may be added:
>
> - toxicology studies on live human embryos, and
> - testing new drugs on humans rather than animals.
>
> Therefore, even within the context of the Bill it is recognised that human embryos will be used for purposes other than ES cell extraction, even though these uses have been largely ignored in the debate. The promotion of ES cell research in the emotive context of human suffering is being used as a beach-head to gain generalised access to human embryos, most of which will be destroyed for purposes like ART research, toxicology and drug testing.[125]

2.132 Professor Bartlett commented on the commercial motivation for some of the embryo research that would be allowed by this Bill:

> In fairness to companies like BresaGen, they are aware that therapy is 10 to 20 years away. Stem Cell International's CEO has said publicly that

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122 *Submission* 1041, p.4 (Professor de Kretser).

123 *Submission* 1041, pp.4-5 (Professor de Kretser).

124 See, for example, *Submissions* 419, 672, 765, 876, 880, 892, 987, 1015, 1020 and 1040.

125 *Submission* 892, Attachment pp.8-9 (SCBI). See also *Submission* 282 (National Civic Council WA).

> therapy, in their eyes, is 10 to 20 years away. So they have to generate some form of income along the way. To use stem cells for screening and diagnostic purposes is a perfectly understandable use of such cells.[126]

2.133 The Committee notes that the uses of embryos in ART practice and research which are allowed by the Bill are not new uses. The Bill brings under a national regulatory system uses and practices which are currently regulated under State legislation, in the case of Victoria, South Australia and Western Australia, and by NHMRC/AHEC guidelines and the requirements of the Reproductive Technology Accreditation Committee.[127]

2.134 In relation to the use of embryos in toxicology or drug testing, the Committee notes that a distinction needs to be drawn between testing on live embryos and testing on embryonic stem cells which have been derived in the first instance from an embryo and then grown into stem cells lines.

2.135 Dr Juttner, Medical and Executive Director, BresaGen Ltd endorsed the use of embryonic stem cell lines for that purpose, saying that 'I think [it] is actually a proper activity if it saves patients from being exposed to testing of new drugs'.[128] Dr Juttner noted, however, that he 'absolutely rejected' the concept of using embryos as such for drug testing.

2.136 The NHMRC advised that the Bill does not prohibit the use of embryos or embryonic stem cells for toxicology testing. In the case of testing on embryos, however, any such proposed use would require a licence from the NHMRC Licensing Committee.[129]

Summary

2.137 Research involving stem cell and cloning technologies is in its infancy.

2.138 Most scientists would agree that there is as yet insufficient experimental data to be certain either just how important research into stem cells is likely to be, or to be certain about the relative value of embryonic and adult stem cells for that research.

2.139 However, many agree that therapies derived from stem cell research have at least the potential to ameliorate currently incurable conditions, ranging from diabetes to spinal cord injuries to motor neurone, Parkinson's and Alzheimer's diseases.

2.140 In the next chapter, the Committee considers the nature of the ethical issues that arise in relation to this research.

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126 Committee Hansard, 19.09.02, p.99 (Professor Bartlett).

127 *Submission* 23, pp.16-17 (NHMRC).

128 *Committee Hansard*, 17.9.02, p.40 (Dr Juttner).

129 *Committee Hansard*, 26.9.02, p.257 and *Submission* 23, Additional information 18.10.02, p.5 (NHMRC).