HUMAN STEM CELL RESEARCH CONSULTATION PAPER
BIOETHICS ADVISORY COMMITTEE
SINGAPORE

INTRODUCTION

Recent developments in human stem cell research have raised hopes of discovering new cures for debilitating and fatal illnesses and to alleviate human suffering. At the same time, these developments raise important issues about the ethics of such research. As such, in December 2000, the Bioethics Advisory Committee (BAC) was established and charged by the Government with the task of addressing the ethical, legal and social issues arising from human stem cell research, as well as to consider the related issues of human reproductive and human therapeutic cloning. The BAC will make policy recommendations on these issues to the Ministerial Committee for Life Sciences.

There are essentially two competing ethical commitments: to protect human life and to advance human life by curing disease. The BAC's fundamental approach in addressing these issues is to protect the rights and welfare of individuals, while allowing the biomedical sciences to develop and realise their potential for the benefit of mankind.

This consultation paper invites serious public discussion on these ethical issues. It seeks the views of the community, especially organisations with medical, religious, scientific, ethical and legal interests.

The paper sets out, in brief, relevant basic scientific information, the potential benefits of research, and the main ethical issues that arise. In preparing this consultation paper, the BAC considered various positions adopted by other countries including the United Kingdom, the United States of America, Australia, New Zealand, Israel and Japan. The Committee has also reviewed the relevant scientific literature, the views held by the major religions, and of local experts in this field.

SCIENTIFIC CONSIDERATIONS: HUMAN STEM CELLS

Stem cells are unspecialised cells. They are able to proliferate or continually reproduce themselves and also serve to renew tissues throughout an individual's life. Their uniqueness lies in the fact that they are able to differentiate into other types of cells with specialised functions, e.g. heart, muscle, blood, or brain cells.

The three recognised types of human stem cells are embryonic stem cells derived from early embryos ('ES cells'), embryonic germ cells derived from foetuses ('EG cells') and adult stem cells derived from tissues such as the bone marrow, umbilical cord blood and brain ('AS cells').

The level of ability to specialise into different types of cells appears to vary for ES cells, EG cells and AS cells. At present, ES cells appear to have the greatest potential to develop into nearly any cell type, followed by EG cells and to a much lesser extent, AS cells. In addition, ES cells appear to be highly proliferative, both in the embryo as well as in culture, while AS cells may be more difficult to maintain and expand in culture.

TREATMENT POSSIBILITIES

Research into human stem cells, especially ES cells, holds the promise for tremendous benefits to mankind in three major areas, namely: (i) new therapies, (ii) pharmaceutical development and (iii) human developmental biology.

In the long term, it is believed that there is considerable potential for human stem cells to be used to treat a wide range of disorders by replacing damaged or diseased cells. For example, it is possible that ES cells can be used to generate specialised cells, tissues and organs, for the treatment of diseased organs in various illnesses, for example heart failure, Alzheimer's disease, Parkinson's disease and certain other neurodegenerative diseases.

In addition, ES cells provide unique opportunities for scientists to better understand the fundamental mechanisms of embryonic development, tissue differentiation and repair. Such knowledge holds the promise for improved treatments of fertility disorders, the prevention of premature pregnancy loss, as well as the diagnosis and prevention of birth defects.

As a result of the differences in the properties and the research potential of ES cells, EG cells and AS cells, the full benefits of human stem cell research are likely to require the use of all three types of cells. ES cells are understood to be the most fundamental and extraordinary of the stem cells.

SINGAPORE'S RESEARCH IN STEM CELLS

Researchers in Singapore, in collaboration with researchers in Australia and Israel, were instrumental in developing 6 embryonic stem-cell lines for research. The ES cell lines originate from ES cells derived from 5-day-old frozen embryos which were in excess of requirements for clinical use, donated with informed consent of the donors for research.

From the ES cells extracted, the ES cells have been serially propagated, to date, at least 200 times, to form the ES cell lines. There is however concern in the scientific community that the existing ES cell lines may not be adequate to deal with issues such as immunological rejection at the stage of clinical application.

ETHICAL AND SOCIAL CONSIDERATIONS

It is recognised that that the fundamental ethical concern of human stem cell research is that of deriving ES cells from human embryos. As mentioned earlier, there are two important ethical commitments: to protect human life and to advance human life by curing disease.

Some argue that the human embryo requires no particular moral attention whatsoever. However, most would agree that human embryos deserve respect as a form of human life; disagreements arise regarding both what form such respect should take and what level of protection is required at different stages of embryonic development.

Within the latter view, some hold that, as a moral principle, the use of any embryo for research purposes is unethical and unacceptable on the grounds that an embryo should be accorded full human status from the moment of its creation. Others accept the special status of an embryo as a potential human being, yet hold that the respect due to the embryo increases as it develops

and that this respect, in the early stages in particular, may properly be weighed against the potential benefits arising from the proposed research. They recognise an essential need for careful regulation of the proposed research, with clear principles to govern the development and use of the techniques of such research together with barriers that must not be crossed, some limits fixed, beyond which such research must not be allowed to go.

The British current restrictions and controls on embryo research reflect this latter view, providing the human embryo with a degree of protection in law but allowing the benefits of the proposed research to be weighed against the respect due to the embryo. In UK, the Human Fertilisation and Embryology Act 1990 ('the 1990 Act') allows the creation and use of human embryos up to 14 days old for research purposes. Such research is subject to a licence being issued by the Human Fertilisation and Embryology Authority ('HFEA') with other strict conditions under the 1990 Act. Under the 1990 Act, research on human embryos was restricted to areas relating to fertility, reproduction and congenital diseases. However, the Human Fertilisation and Embryology (Research Purposes) Regulations 2001 have widened the scope of permitted research to include research into (a) increasing knowledge about the development of embryos; (b) increasing knowledge about serious disease; and (c) enabling any such knowledge to be applied in developing treatments for serious disease.

The position in the United States of America, effective 10 August 2001, supports limited public funding for research on human embryonic stem cells obtained from established cell lines. Privately funded human stem cell research remains free from control.

In Singapore today, human embryos of less than 14 days old, which are created through in-vitro fertilisation (IVF) techniques but not used in assisted reproduction treatments, can be used for research provided they meet the stringent regulatory stipulations under the 'Guidelines for Private Healthcare Institutions Providing Assisted Reproduction Services' issued under Regulation 4 of the Private Hospitals and Medical Clinics Act (1990). The use of these embryos does not alter their final disposition.

Human embryos which are less than 14 days old have no pain or sentience since only at the 14th day does a primitive streak appear and develop into the nervous system.

THE BAC'S CURRENT VIEWS

There is a need to find a proper public policy balance between the opportunities that biomedical science offers to improve human welfare and the limits set by important ethical obligations.

Based on the foregoing, the BAC does not foresee any fundamental ethical objections to research with AS cells.

Similarly, for EG cells, the BAC is of the view that there are no new ethical issues arising from the use of such cells, so long as the decision taken to abort is taken separately and independently from the decision and consent to extract the EG cells.

The BAC recognises that ethical opinion on the use of embryos no longer needed for infertility treatment as a source of stem cells is divided. The BAC does not agree with the view that the human embryo deserves no particular moral attention whatsoever. However, while the BAC recognises the special status of an embryo as a potential human being, it accepts that it is justified to use early embryos, not more than 14 days old, for serious research, which may benefit others.

The BAC is of the view that reproductive cloning of human beings should not be permitted. Human reproductive cloning goes against the moral idea that a human being is not to be treated as a means to an end, but only as an end. With reproductive cloning, a human being may be brought into existence for a utilitarian purpose. The primary purpose of existence is demeaned, and there is a loss of human dignity. The social, religious and legal implications are very serious and wide ranging, for example, those relating to identity and responsibilty. There is also the reduction of bio-diversity. While reproductive cloning could potentially provide a treatment option for infertility, nevertheless this possible benefit is greatly outweighed by ethical concerns and safety issues, such as the high risk of foetal abnormalities.

The BAC is also concerned with what has been termed human 'therapeutic cloning'. This is research which involves the creation of embryos by cell nuclear transfer. Human therapeutic cloning has the potential of creating a human embryo for reproductive cloning. This potential must <u>not</u> be allowed

to be realised under any circumstances. Scientists believe that research involving the creation of embryos by cell nuclear transfer would have the potential benefit of discovering the mechanism for reprogramming adult cells and provide compatible tissues for treatment. Therapeutic cloning appears to be an essential part of human stem cell research. The BAC notes that in UK, therapeutic cloning is permitted under strict conditions. Provided that the necessity of using embryos created by cell nuclear transfer is clearly demonstrated, on a case to case basis, with proper consent of the donors and under appropriate governmental oversight, the BAC is prepared to support it. Again, the embryos used must not be more than 14 days old. The same rationale, rigorous conditions, and stringent control apply to the use of embryos created by fertilization for the purpose of research.

The BAC is strongly of the view that there must be a well-established and effective framework for the control of research involving embryos in Singapore. This oversight must include the ethical and scientific review of proposed research involving the derivation or use of human stem cells. There must also be mechanisms for such research to be monitored for adherence to ethical guidelines and standards and to highlight any currently unforeseen concerns which may arise.

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