The Science, Ethics and Politics of hESC Research

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hESC research involves:

- The derivation of hESC lines
  - Basic research
- The use of hESC lines
  - Basic research
  - Applied medical research
- With both basic and applied medical research there are ethical concerns regarding the sourcing of stem cell lines from human embryos

To permit or prohibit?

- Using which mechanism?
  - Legislation, regulation, research guidelines
- If some embryo research is permitted, under what constraints?
  - Nature, scope, duration
  - Created vs. 'spare' embryos
  - Fresh vs. frozen-thawed embryos
  - Purchased (exchanged) vs. altruistic embryos
  - Healthy volunteers vs. IVF patients
- Will the 'rules' apply to all or some embryo research?
  - Public or private funding

Informed consent for human embryo research

- From whom?
  - Gamete providers
  - Embryo providers
- For what?
  - Nature, scope of proposed research
- Voluntariness
  - IVF providers (undue deference)
  - Paid providers (financial inducements)
- Right to withdraw

All of this presumes we 'know one when we see one'

- What is a human embryo?
- From the perspectives of
  - Science
  - Ethics
  - Politics (law and policy)

Science

- The term 'embryo' technically applies after implantation is complete (approximately 14 days after fertilization) until eight weeks of development
- Prior to implantation, the proper scientific terms for the product of conception at different developmental stages are: zygote, morula and blastocyst

Science

- Human embryo research typically limited to 14 days
- So research involves pre-embryos, not embryos
- *An attempt to finesse the moral issue*
- Those who are concerned about the killing of human embryos don't care about a name – they care about moral status of the developing human

Ethics

- *"Is the human embryo 'protectable' life'?*
- "Is it truly human?"
- "Is it a person?"
- "Does it have a right to life, or is it merely due respect?"
- "Can it be destroyed with impunity, or is its destruction intrinsically wrong?"

Ethics

- *The ends of the spectrum*
- Human embryo has full moral status at conception when it receives its genetic code (Noonan 1976) *and so warrants protection from invasive and destructive research*
- Human embryo has no intrinsic value (and no right to life), and as such it *can be used for research* provided there is informed consent (Singer and Kuhse 1986)

Ethics

- *Between these extremes*
- Human embryo is "entitled to profound respect, but this respect does not necessarily encompass the full legal and moral rights attributed to persons" (Ethics Advisory Board 1979: 101)
- Research is ethically permissible when:
  - the research is in pursuit of important therapeutic goals
  - these goals cannot be achieved by less ethically controversial means
  - there is informed consent.

Ethics

- From a utilitarian perspective, embryo research should be permitted to (i) realize the benefits of increased knowledge, and (ii) secure therapeutic advances in reproductive, genetic and stem cell treatments.
  - Increased understanding of normal cell development
  - Ability to screen new drugs in vitro
  - Tissue for cell-based regenerative medicine
- To date, some jurisdictions have formally sanctioned human embryo research, others have not.

Law: UK, HFEA Act 1990

- *Human embryo defined with reference to fertilization*

1.—(l) In this Act, except where otherwise stated—
(a) embryo means a live human embryo where fertilisation is complete, and
(b) references to an embryo include an egg in the process of fertilisation,
and, for this purpose, fertilisation is not complete until the appearance of a two cell zygote.

Law: Germany Embryo Protection Act 1990

- *Human embryo defined with reference to fertilization, and capacity (totipotency)*
- "the human egg cell, fertilised and capable of developing, from the time of fusion of the nuclei, and further, each totipotent cell removed from an embryo that is assumed to be able to divide and to develop into an individual under the appropriate conditions for that."
- *Act* prohibits any interventions on, or manipulations of, the human embryo "for a purpose not serving its preservation."

Law: US Dickey Amendment (since 1996)

- *Human embryo defined with reference to what it is not (i.e., a human fetus, neonate, child, or adult)*
- "For purposes of this section, the term 'human embryo or embryos' includes any organism, not protected as a human subject under 45 CFR 46 as of the date of the enactment of this Act, that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes or human diploid cells."

Law: Canada, AHR Act 2004

- *Human embryo defined with reference to species membership and time*
- "embryo" means a human organism during the first 56 days of its development following fertilization or creation, excluding any time during which its development has been suspended, and includes any cell derived from such an organism that is used for the purpose of creating a human being

Law: New Zealand, HART Act 2004

- *Human embryo defined with reference to biological term and capacity*
- "Embryo includes a zygote and cell or a group of cells that has the capacity to develop into an individual; but does not include stem cells derived from an embryo."

Guidelines: US, National Research Council (2005)

- *Human embryo defined with reference to biological development (implantation to eight weeks)*
- "An animal in the early stages of growth and differentiation that are characterized by cleavage, laying down of fundamental tissues, and the formation of primitive organs and organ systems; especially the developing human individual from the time of implantation to the end of the eighth week after conception, after which stage it becomes known as a foetus."

Law: UK, HFEA Act 2008

- *Definition amended to recognize that a human embryo could be created by means other than fertilization*:

1(1)—In this Act (except in section 4A or in the term "human admixed embryo")—

(a) embryo means a live human embryo and does not include a human admixed embryo (as defined by section 4A(6)), and

(b) references to an embryo include an egg that is in the process of fertilisation or is undergoing any other process capable of resulting in an embryo"

The troubled word *'embryo'*

- A brief comparison of the different legal definitions of the term 'embryo' as entrenched in different jurisdictions (whether they permit or prohibit human embryo research) reveals the absence of agreement on what a human embryo is.
- Do we "know one when we see one"?

The human embryo

- UK: 'What key features describe the human embryo?'
  - "live", "human", and not "admixed", able to be created by fertilization or any other process
- US: 'Where does the human embryo come from?'
  - "fertilization, parthenogenesis, cloning, or any other means from one or more human gametes or human diploid cells."
- Germany: 'What can the human embryo do?'
  - "develop into an individual under the appropriate conditions," and "develop into a human being if the necessary conditions prevail."
  - what matters is the organism's or cell's potential to become a fully developed human being (however created and regardless of the conditions necessary for the potential to be expressed)

Science: Alternatives …

- Attempts to assuage moral reservations:
  - Parthenogenesis
  - Cloning by somatic cell nuclear transfer
  - Single-cell embryo biopsy,
  - Altered nuclear transfer,
  - Discarded poor quality IVF embryos
  - Humanesque hybrid embryos (transferring a nucleus from a human somatic cell into an enucleated nonhuman egg)
  - Reprogramming of somatic nuclei

Baylis 2008; Green 2007; President`s Council on Bioethics 2005

Ethical objections

- Parthenogenetic embryos might have moral status because of their developmental potential
- Cloned embryos (clonotes) might have moral status because of their developmental potential.
- Single-cell embryo biopsy -- single cells removed from embryo might be totipotent, and thus might have moral status because of their developmental potential

Ethical objections

- Altered nuclear transfer
- Discarded poor quality IVF embryos
- Humanesque hybrid embryos (transferring a nucleus from a human somatic cell into an enucleated nonhuman egg)
- iPS cells reprogramming of somatic nuclei

iPS cells (2007)

- Successful genetic reprogramming of adult cells to create human induced pluripotent stem cells (Takahashi et al., 2007; Yu et al., 2007)
- "Only time will tell, but I know where I'm going. . . If you can't tell the difference between iPS cells and embryonic stem cells, the embryonic stem cells will turn out to be a [sic] historical anomaly" (cited in Cyranoski 2008)

iPS cells (2007)

- Even a scientist who cares not a whit about the morality of embryo destruction will adopt this technique because it is so simple and powerful. The embryonic stem cell debate is over . . . scientific reasons alone will now incline even the most willful researchers to leave the human embryo alone
(Krauthammer2007, A23)

iPS cells (2007)

- Opponents of hESC research insist that cell-based regenerative medicine could be pursued without destroying human embryos.
- Others suggest that iPS cells might just be another kind of embryo (Kaebnick 2008).
- SO – what is an embryo?

A way forward?

- The human embryo (however it is defined) is an entity of moral concern.
- There is no integrity-preserving compromise for those who believe:
  - Research to derive hESC kills human embryos
  - Killing human embryos is wrong
  - Therefore, research to derive hESC is wrong
- It is against this backdrop that the policy decision to permit or prohibit hESC research must be made

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