EMBRYONIC STEM CELLS FROM NON-DESTRUCTIVE SOURCES: A WAY OUT OF THE ETHICAL QUAGMIRE?

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Cameron: “The Biotech Century”

Signs of this modern era:
- ART techniques
- Excess frozen embryos
- Stem cell research
- Cloning
Ethics v. Scientific Progress  
(According to Calvin & Hobbes)

OK, Hobbes, press the button and duplicate me.

Are you sure this is such a good idea?

Brother! You doubting Thomases get in the way of more scientific advances with your stupid ethical questions! This is a Brilliant idea! Hit the button, will ya?

I'd hate to be accused of inhibiting scientific progress...

Here you go.

Boink

Button
Calvin and Hobbes (continued)
Human embryonic stem cells

- Pluripotent cells: not yet differentiated into mature cells
- Advantages of using stem cells:
  - Can be programmed along one developmental pathway
  - Not likely to be rejected immunologically (fewer surface markers)
  - May perhaps grow into new nerve or muscle cells
The Medical Case

- Chronic diseases that might be helped:
  - Diabetes mellitus
  - Spinal cord or brain injury
    - Replace neurons
    - Replace glial cells
  - Parkinson’s disease
  - Heart disease (heart muscle does not regenerate)
- Frozen embryos are available (though no proven benefit of this research yet)
- SCNT (“cloning” techniques): may provide additional embryos to meet the demand
Day 3
Ethical Objections to Destructive Embryo Research

- Sanctity of life concerns
  - Conception view of human personhood
  - Objections similar to those regarding abortion

- Utilitarian rationale
  - "Since frozen embryos are going to be destroyed anyway"
  - Assumes as given that which may not come true
  - Concerns about moral complicity
  - Frozen embryos will never meet the demand, must resort to cloning

- Somatic sources have demonstrated great benefit:
  - Umbilical cord
  - Bone marrow
  - Epithelial cells
  - Amniotic fluid
  - 72+ somatic cell treatments now in clinical use
  - Animal studies show great promise for the near future
Human stem cells may be produced without embryos ‘within months’

Report: Amniotic fluid yields stem cells
Technique doesn't harm embryos; called 'giant step forward' for research

Japan’s leading genetic researcher could be “a couple of months” from reaching the Holy Grail of biotechnology – producing an “ethical” human stem cell without using an embryo, he has said.

But in an exclusive interview with The Times, Shinya Yamanaka, who has pioneered the field, urged the scientific community not to stop stem-cell research so early.

‘Do not stop stem-cell research if the patients will die if you don’t do it,' he said. ‘The field is growing fast.'
Public Policy Initiatives:
- New Jersey: state budget includes $9.5 million for Stem Cell Institute
- California: Proposition 71 sets aside $3 billion for embryonic stem-cell research over 10 years
- Illinois: Gov. Rod Blagojevich creates a stem-cell research institute by executive order
- Maryland: Stem Cell Research Act allocates $15 million for embryonic stem-cell research grants.
- Missouri voters back a constitutional amendment that safeguards embryonic stem-cell research in the state
- Iowa eases limits on some types of stem-cell research.

June 20, 2007: President Bush vetoes legislation that would have eased federal restraints on stem-cell research.
Can We Block the Juggernaut?
(Calvin and Hobbes)

CALVIN, I'M LATE FOR WORK!
Are There Ethical Alternatives?

- The PGD Proposal
- The Non-Viable Embryo Proposal
- The Altered Nuclear Transfer Proposal
PGD: an established method of genetically screening embryos during IVF attempts

Samples a single blastomere of the 3-day morula

Embryos with single gene defects discarded:
- Duchenne muscular dystrophy
- Hemophilia A
- Fragile X syndrome
- Retinitis pigmentosa
- Tay Sach's disease
- Others
Using PGD Techniques for Stem Cell Research

- Technique:
  - Use PGD methods to remove a single blastomere
  - Replicate this cell in culture to produce a stem cell line

- The embryo:
  - Now minus one cell
  - Can be implanted into a woman’s uterus
  - Such implanted embryos can develop normally
Ethical Concerns

- This may not be practical
  - Normally, cells taken at a later (blastocyst) stage
  - Stem cell lines may require 100s of cells
  - Robt. Lanza (ACT) claims to have done this:
    - Controversial paper in *Nature*
    - Paper was “proof of concept” only

- Violates long-held traditions of human experimentation
  - Embryo derives no benefit
  - Informed consent not possible
Why not use “non-viable” embryos?

Only destroy embryos whose further development has arrested.

Analogous with “brain death” criteria for organ transplantation.
Ethical Concerns

- Could the derived cells be useful as stem cells?
  - The cause of developmental arrest may be within the component cells
  - This may make such cells inappropriate for stem cell cultures

- No real ethical warrant
  - Are such embryos truly “dead?”
  - “Brain Death” in adults well established
  - No parallel criteria for embryos
#3: ALTERED NUCLEAR TRANSFER (ANT)
This commissioned working paper was discussed at the Council's December 2004 meeting. The views expressed here do not represent the official views of the Council or of the United States Government.

**Altered Nuclear Transfer as a Morally Acceptable Means for the Procurement of Human Embryonic Stem Cells**

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**Introduction**

With the sequencing of the human genome and our increasing knowledge of the molecular mechanisms of basic cell functions, we are entering an era of rapid advance in the field of developmental biology. Current scientific interest in embryonic stem cells is a logical step in the progress of these studies and holds the hope of providing important research tools as well as possible therapeutic applications.

http://www.bioethics.gov/background/hurlbut.html
The Hurlbut Proposal:

- SCNT technique
- **Prior** to transfer of diploid DNA into ooplast:
  - RNA interference used to block expression of cdx2 protein
  - Prevents development of trophoblast
- **After** nuclear transfer:
  - Resulting entities incapable of implantation
  - Called by Hurlbut “biological artifacts”
  - Can be disaggregated after formation of inner cell mass
  - Resulting cells can then be used for stem cell cultures
  - Technical aspects already partially confirmed in a mouse model
**Ethical Concerns**

- **Key question:**
  - Are such “biological artifacts” non-embryos or disabled embryos?
  - There are natural biological precedents:
    - Germ cell tumors (teratomas)
    - Hydatidiform moles

- **ANT-OAR:**
  - Variation of Hurlbut idea
  - **Direct** creation of pluripotent stem cells
  - Modification of epigenetic state so that no embryo-like aggregation possible (no inner cell mass)
  - Not yet tested in an animal model
Proposals: Good News or Bad News?

- For those who hold to personhood at conception:
  - These proposals may not pass ethical muster
  - ANT-OAR still only theoretical

- For the scientific community at large:
  - The desire for destructive embryo research continues unabated
  - Current stem cell researchers in the private sector will not bother with additional constraints

- On the other hand:
  - Limited research has been performed based on ethical concerns alone
  - Ethically, this is good news for everyone.
References

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