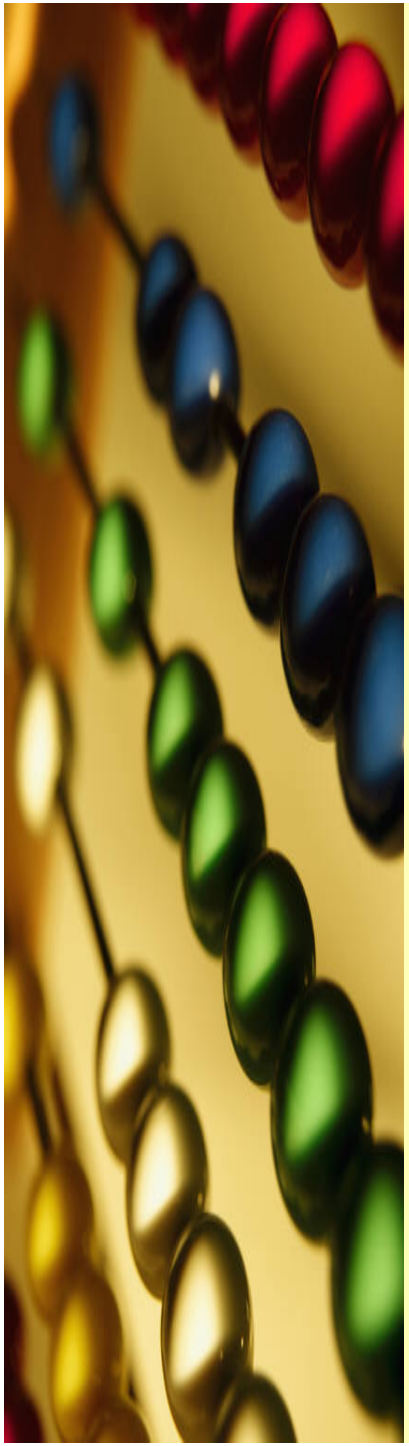

Purported Alternative Sources of Pluripotent Stem Cells

Genetics Policy Institute
Stanford University
June 10, 2006

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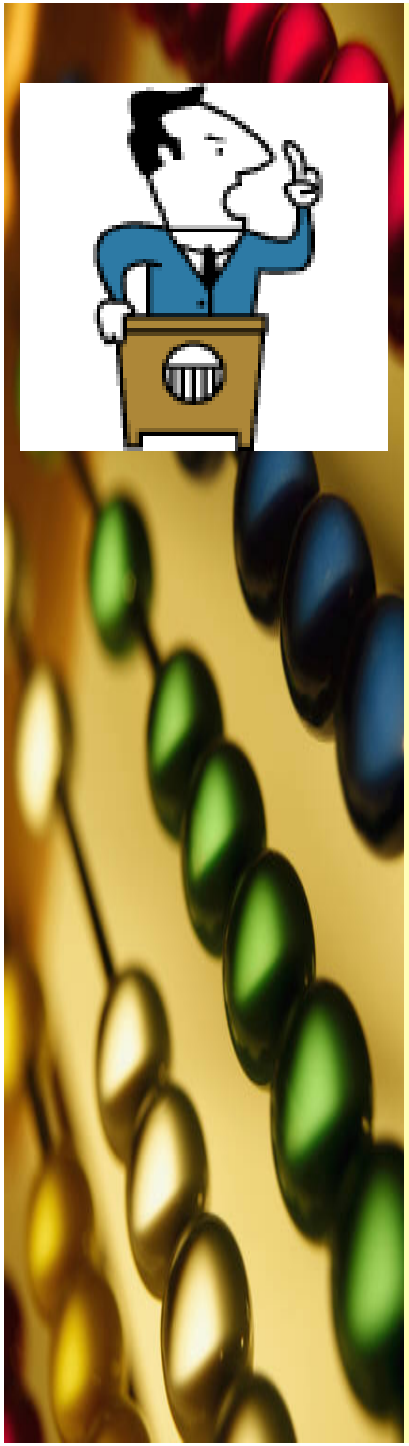
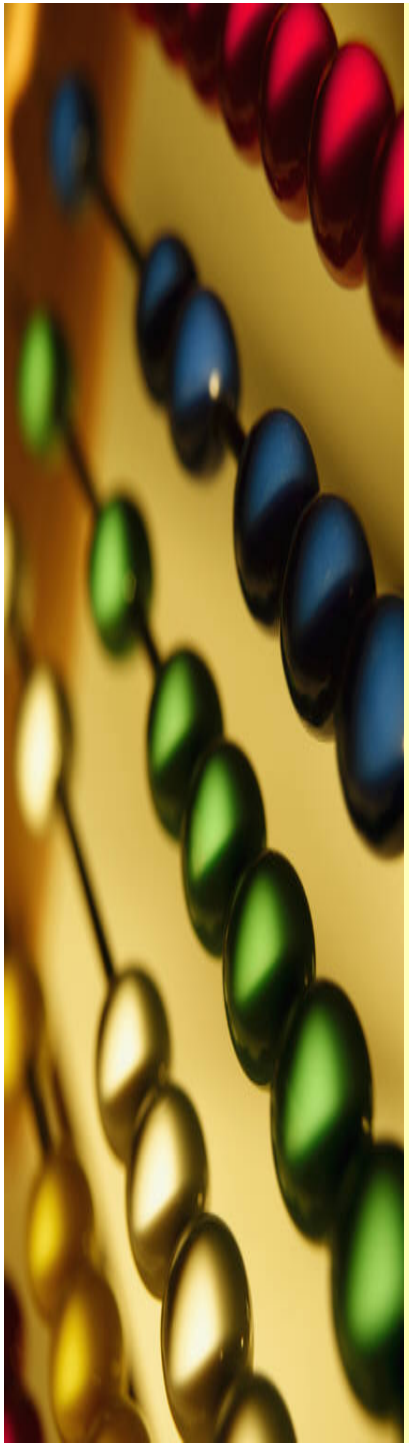


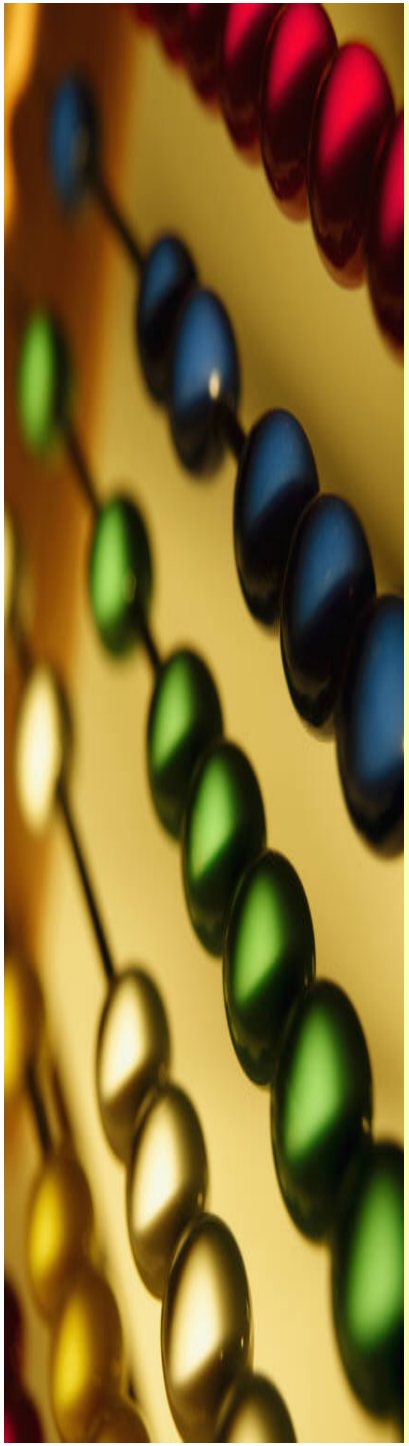
Claim: Seeking pluripotent stem cells ('PSC') from nonembryo sources is morally superior to embryo use

- Proponents
  - Concentrating on technical challenges
  - Less attentive to establishing claim of moral superiority
- In moral reasoning, as in scientific, we need rigor unclouded by wishful thinking
- Before a policymaker risks relief of suffering on "alternatives" to expanded hESC research
  - Should know whether claim of moral superiority is true



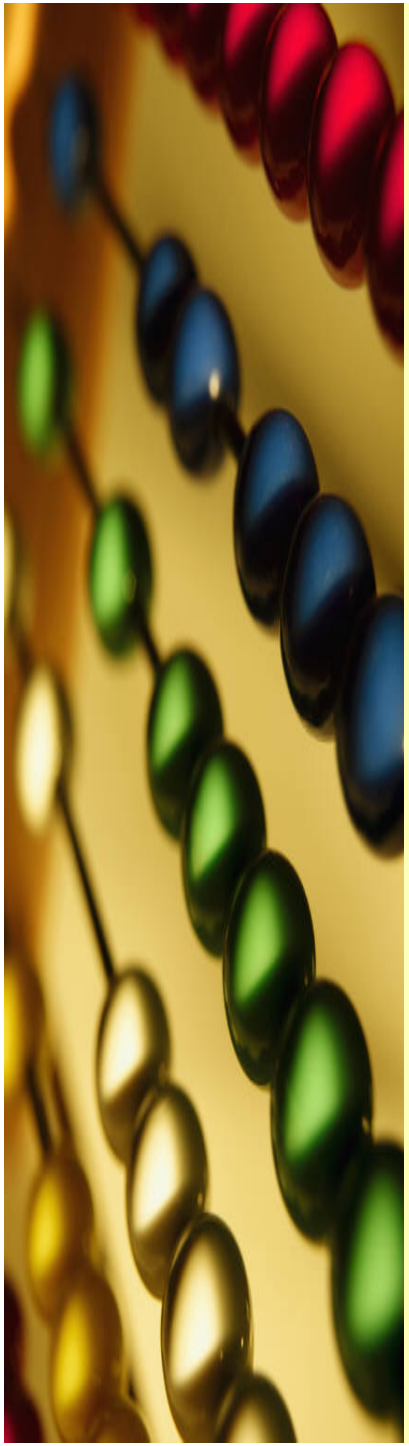
1a. Hurlclones

- Mutant clone (i) issues in PSC but (ii) is not an embryo
  - Why not an embryo?
    - "Mimics" fertilized eggs that die *in vivo*
    - "Mimics" teratomas, hydatidiform moles
      - Either these undergo embryogenesis, or they do not
        - If they do not, they differ from hurlclones
        - If they do, the process is deranged, and again they differ from hurlclones



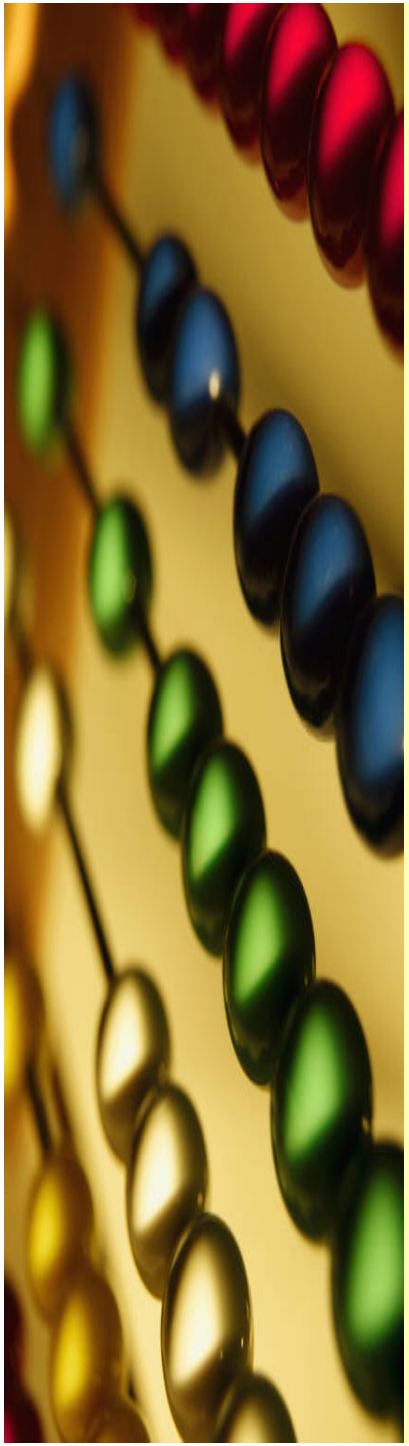
1b. Hurlclones

- Embryogenesis does not occur
  - Then what produces the ‘blastocyst’ from which PSC derived?
  - “The . . . embryo is not obviously abnormal before the onset of CDX2 expression” (Meissner and Jaenisch, *Nature* 439: 212-215 [2006])
- No moral argument offered for hurlclone use
  - Assumed that classification as ‘nonembryo’ suffices for moral defense of experiment
    - The naturalistic fallacy--offering a moral conclusion without adducing a moral premise



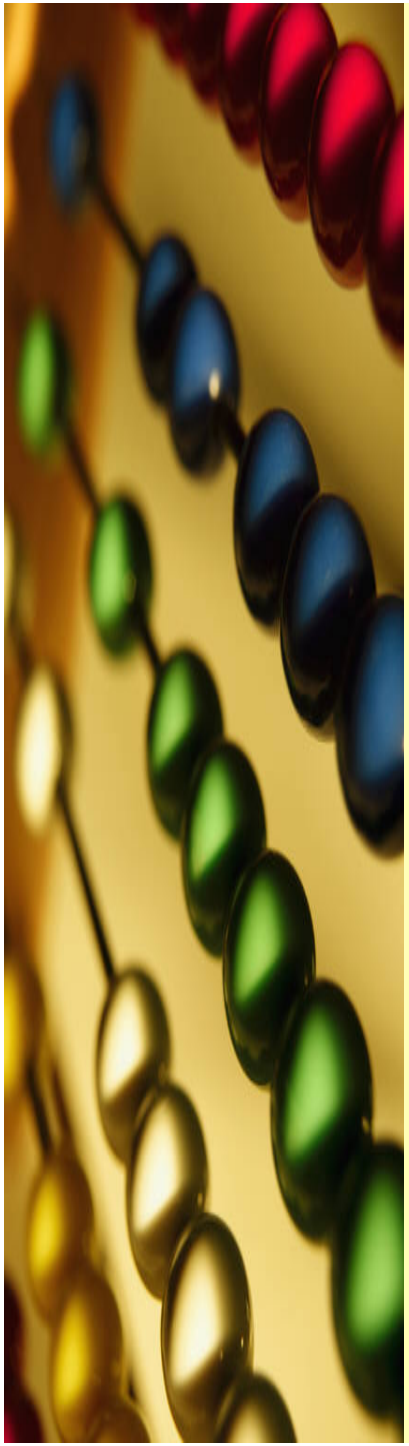
1c. Hurlclones

- Gestures at morality
  - Hurlclone lacks “the principle of life in it,” has “no inherent principle of unity, no coherent drive in the direction of the mature human form”
    - Implausible metaphysical posits
      - Compare ‘The Absolute enters into progress’
  - Hurlclone is disorganized
    - If nonintegration a justification for research, every early embryo is eligible
      - Fails to recognize that early embryo is a genomic individual
  - To gesture at morality is not to state a moral argument



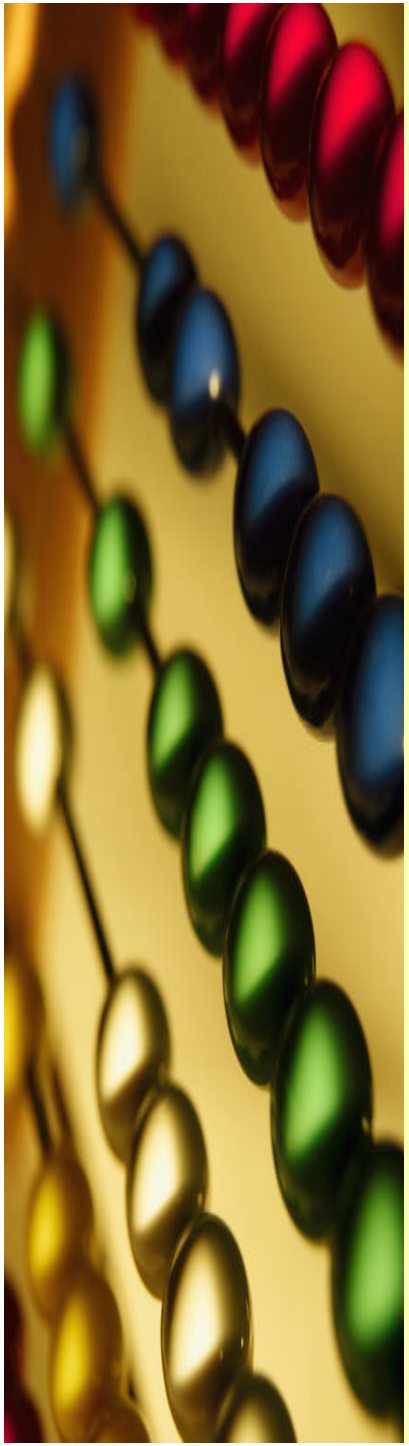
1d. Hurlclones

- Constructing a moral defense
  - Intrauterine transfer forbidden (the 'no-transfer premise')
    - Avoids charge of unsafe treatment of mother
    - Permits denial that any possible person corresponds
    - Negates duty to rescue
  - Permissible to use embryo-like being barred from the womb (a moral premise)
- **This defense justifies use of all donated embryos, surplus and clone**



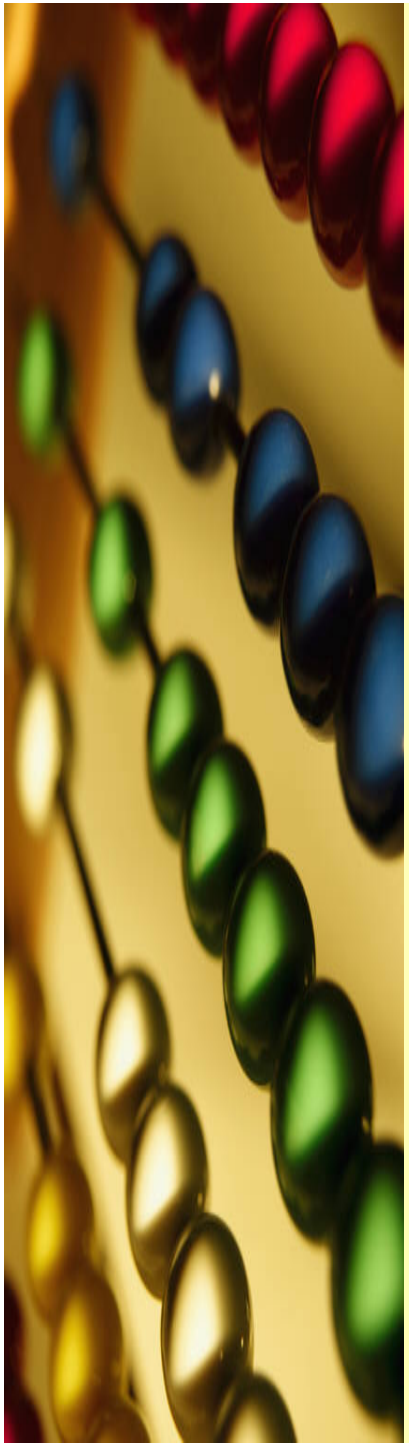
2. Cleavage-Arrested Embryos

- "Irreversibly arrested embryos" deemed dead
  - How to verify?
- Derived hESC likely abnormal
- Blastomeres recovered within first two days may be totipotent, i.e., embryos for moral purposes
  - To justify experiment, appeal to no transfer premise
    - From it, and companion moral premise, follows justification of using all donated embryos

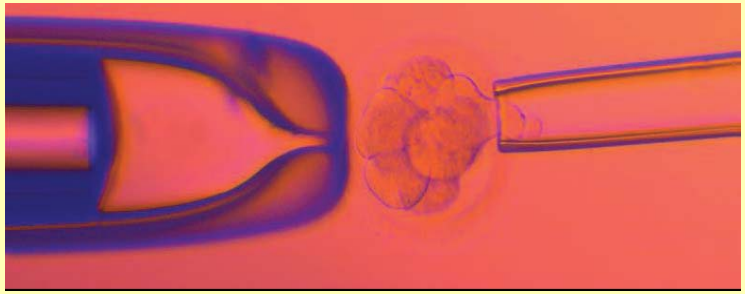


3. Parthenotes

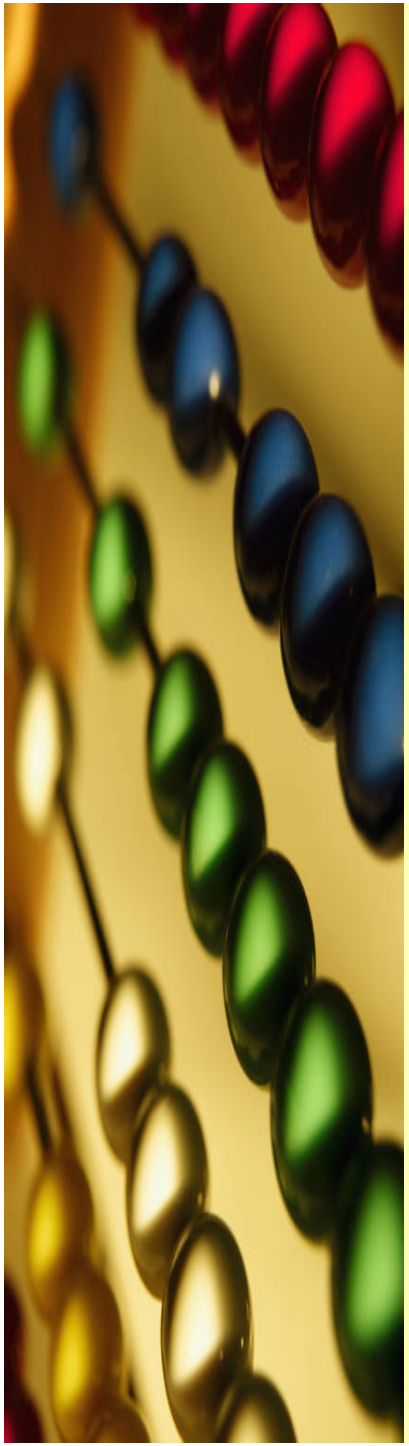
- Parthenogenesis: activation of oocyte without insertion of foreign DNA
- Parthenote a developing organism
  - At five days, called a 'blastocyst'
  - Moral concern attaches
    - Possibility of intervening genetically to overcome abnormalities in imprinting implicated in placental failure
  - Use requires appeal to no transfer premise
- Not known whether robust PSC derivable from parthenotes
  - Another special case for which we ought not settle given justification of the general case



4. Use of Embryo as PSC Source Prior To Intrauterine Transfer

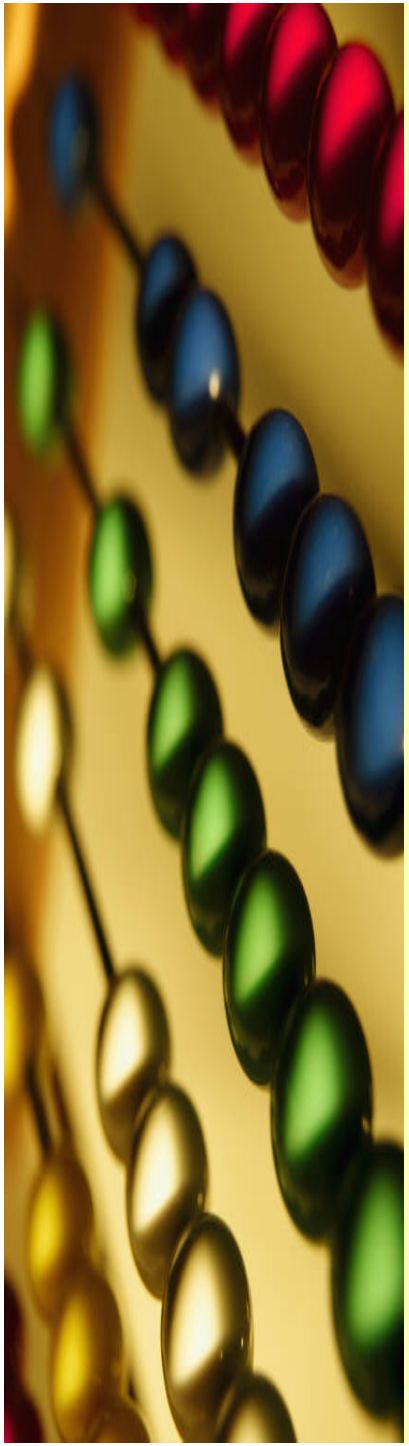


- (1) Derivation of hESC from removed blastomeres, (2) Preimplantation genetic diagnosis ('PGD')
- From cells removed, must grow more
  - Interposes *delay* of PGD, *delay* of transfer
    - For embryo, the less time outside the womb, the better
- Imposes risk to health of embryo, no benefit
  - Indefensible
  - Morally inferior to use of embryos barred from womb



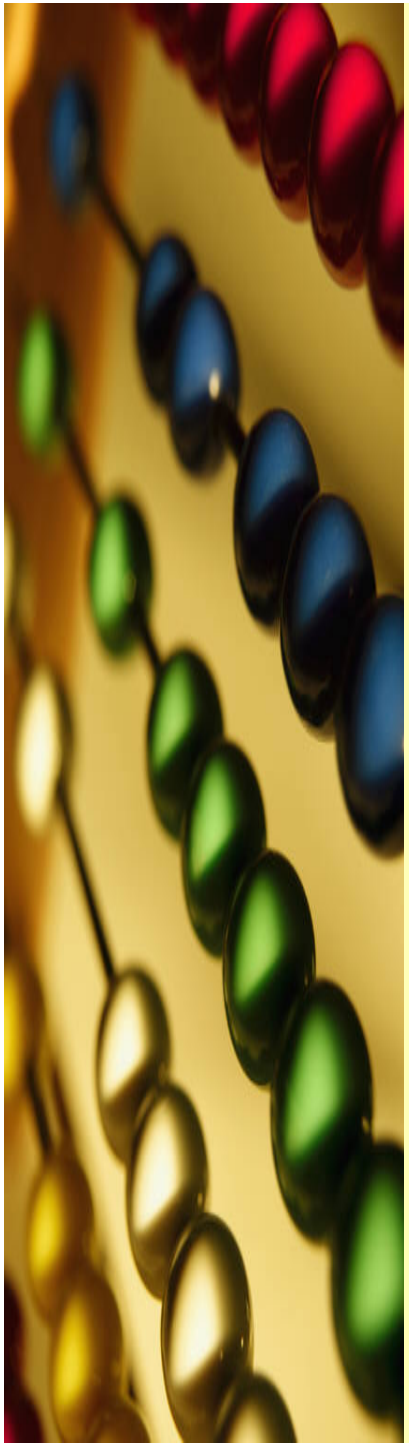
5. Transformation of Oocyte Into PSC Without Embryogenesis

- Fusion of oocyte and somatic cell to produce PSC
  - Engineering of overexpression of genes for pluripotency (e.g., *nanog*)
  - Experiments likely will create, sacrifice embryos
    - Back to the justification of hurlclones
  - Unknown
    - Whether it will produce human PSC
    - How its products will differ from hESC
- Variant: fusion of hESC and somatic cells
  - Requires embryos as sources of hESC



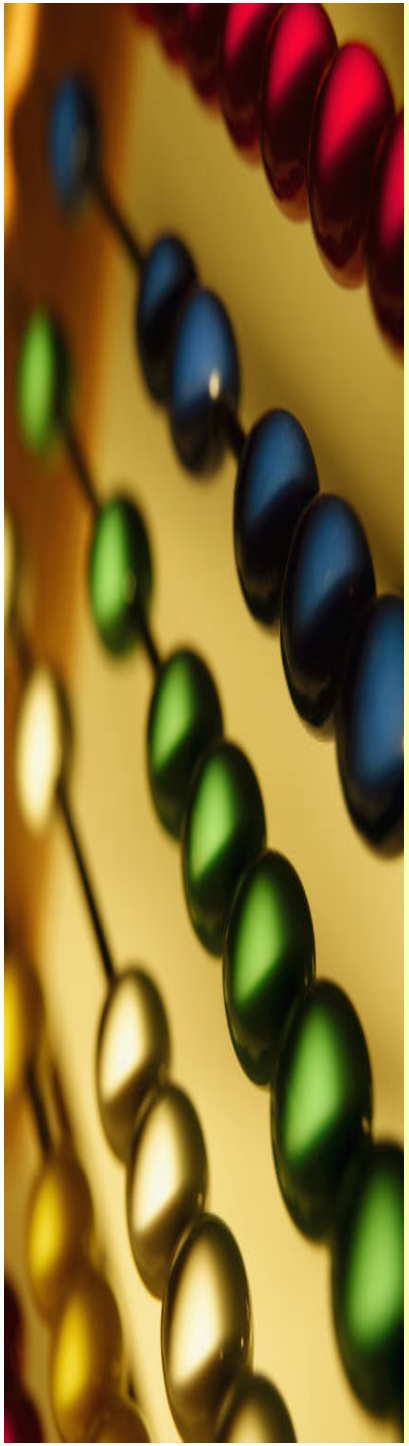
6. Dedifferentiation

- Cells dedifferentiate when they revert from specialization to multipotency or even pluripotency
  - Inducing dedifferentiation is the holy grail
- Posed as alternative to hESC research: accomplish dedifferentiation
  - Analogous to proposing to score a touchdown by dreaming rather than running a play
- Progress will be advanced by observing reprogramming in clones
  - But hESC could prove more reliably inducible
- Much of the work uses hESC
  - Experiments could produce totipotent cells



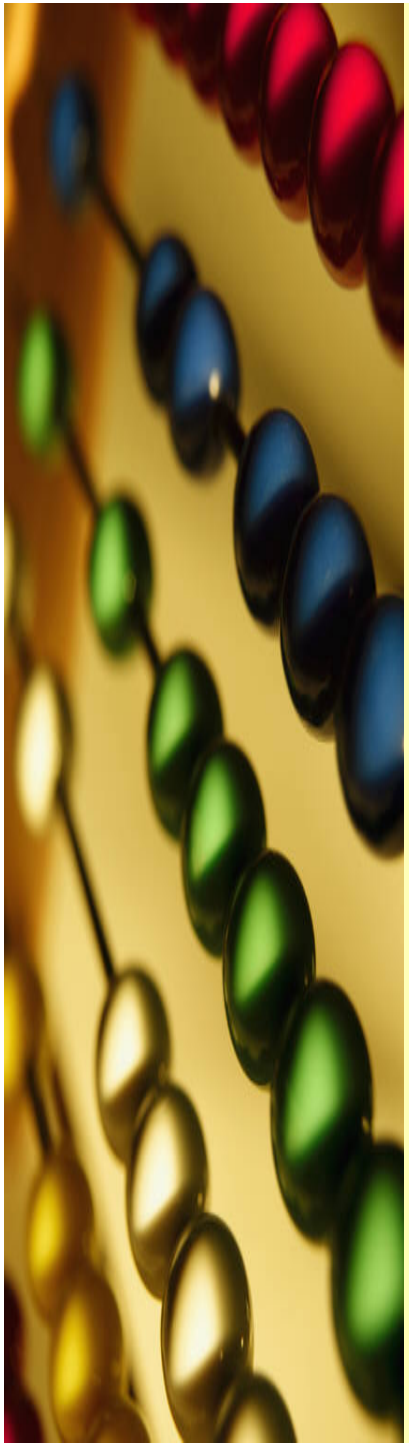
7. Amniotic Epithelial Cells

- "Significant plasticity" of cells available in placenta
  - Not self-renewing, hence not stem cells
  - Not clear whether pluripotent
- Burden to show functional equivalence to hESC



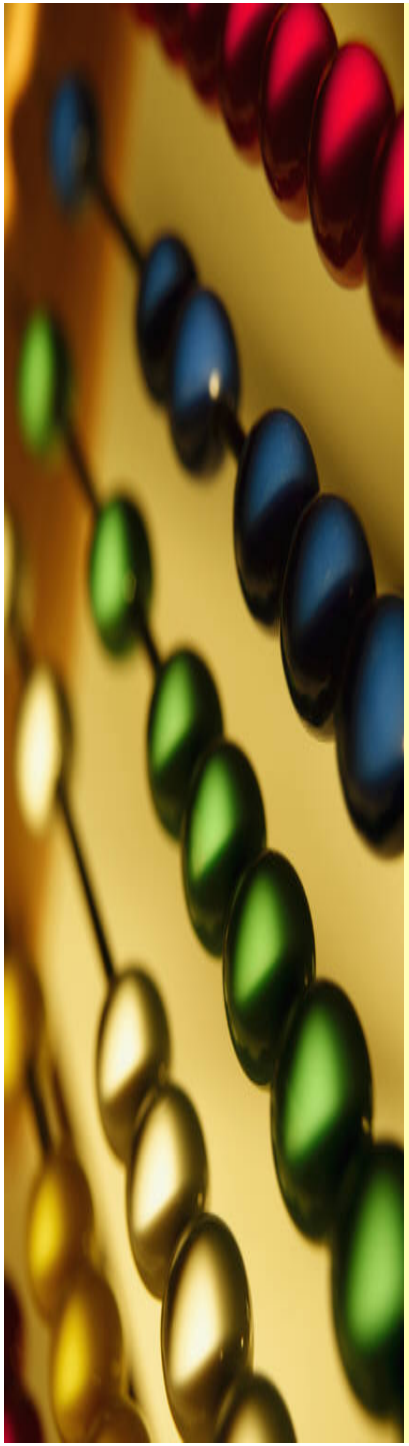
SUMMARY

1. Hurlclones	Defense justifies use of all donated embryos; derivatives compromised
2. Cleavage-arrested embryos	Defense justifies use of all donated embryos; derivatives likely abnormal
3. Parthenotes	Defense justifies use of all donated embryos; derivatives unknown



SUMMARY

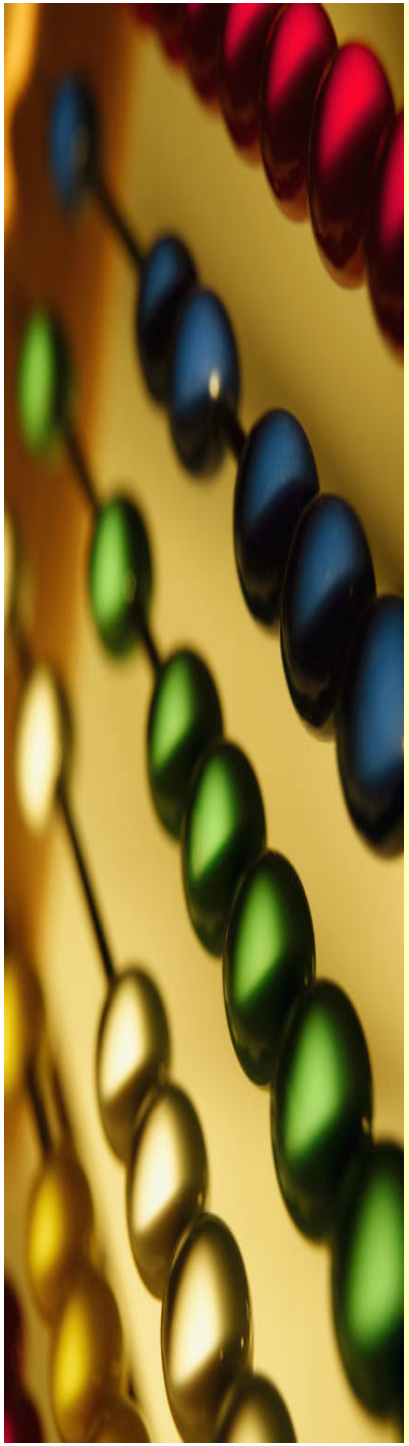
4. Use of embryo as PSC source prior to intrauterine transfer	Risks health of infant for no benefit to it. Indefensible.
5. Transformation of oocyte into PSC without embryogenesis	Will create, sacrifice embryos; defense justifies use of all donated embryos
6. Dedifferentiation	Experiments use embryos as sources of hESC
7. Amniotic epithelial cells	Not stem cells

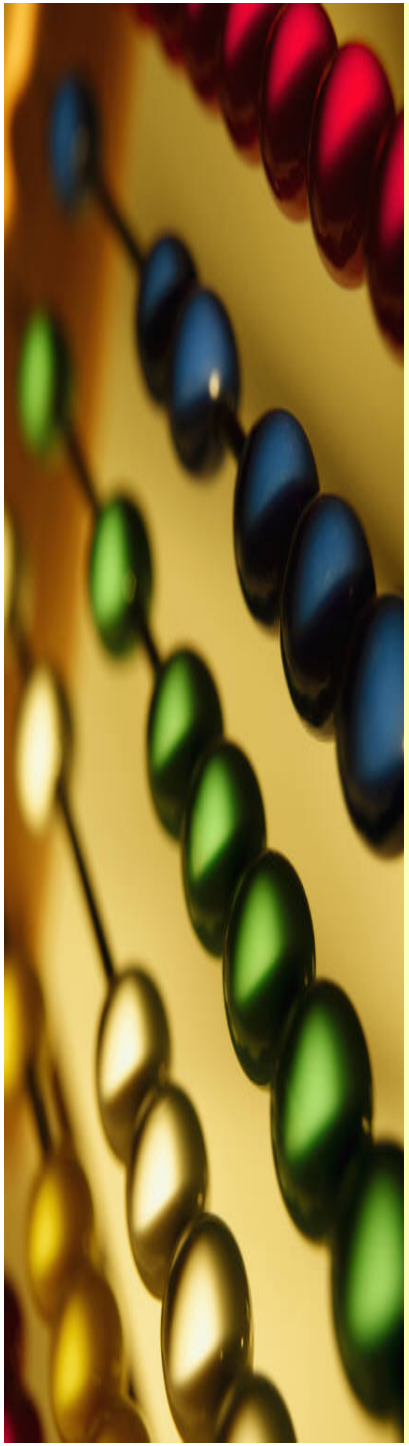


SUMMARY: No Present Moral Gain From "Alternatives"

- To the extent that "alternatives"
  - use or produce embryos,
  - lean on the justification of embryo use in general, or
  - fail to produce pluripotent cells,

  a choice to explore their peculiar products will not work a moral improvement



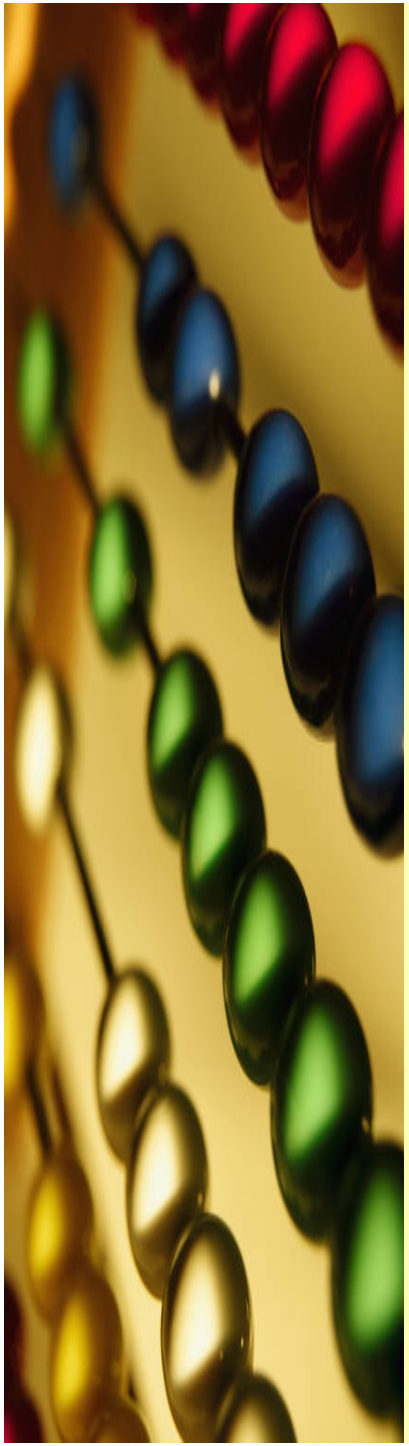


Inside The Trojan Horse

- Contents
  - <Castle-DeGette bill> *VETO*
  - Decoy bills as veto cover
    - Funding for "alternatives" (*Santorum-Specter et al.*)
    - Anticloning bill (*Brownback* or *Feinstein-Hatch*)
    - Antichimera bill (*Brownback*)
- This package would confine federally-funded regenerative medicine to
  - Five-year-old hESC lines
  - Inefficient methods
  - Malengineered clones
  - Abnormal cells

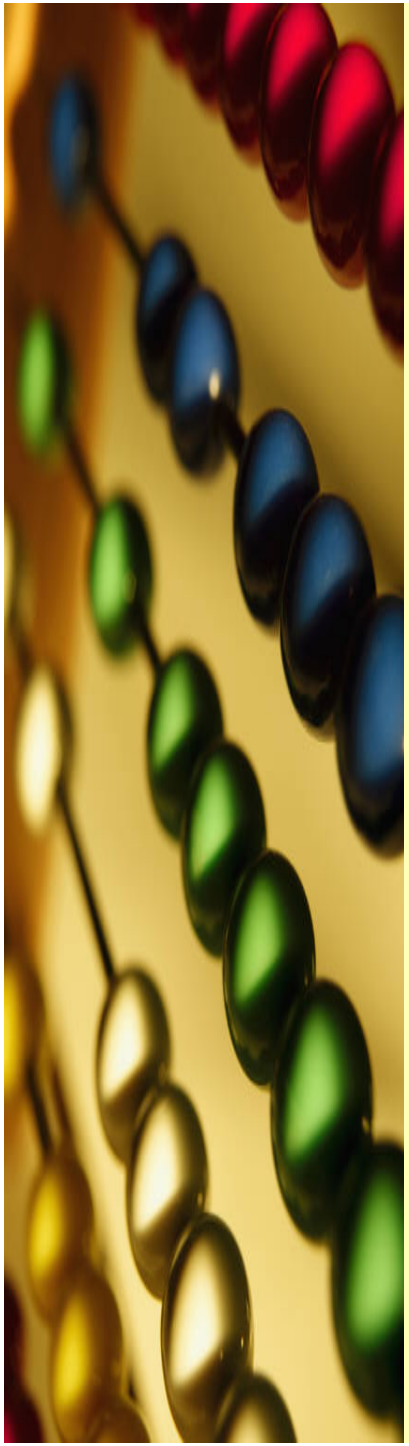
Redundant Anticloning Bills

- FDA interdiction of reproductive cloning
  - Since 1998
  - Risk of attempt: nil
- FDA jurisdiction
  - Four statutory grounds
  - Solidified in regulation on cells and cellular products (21 *C.F.R.* Part 1271, effective January 21, 2004)
- Legislation
  - Need: a figment of legislative imagination
  - Opportunity: ban nonreproductive cloning in research



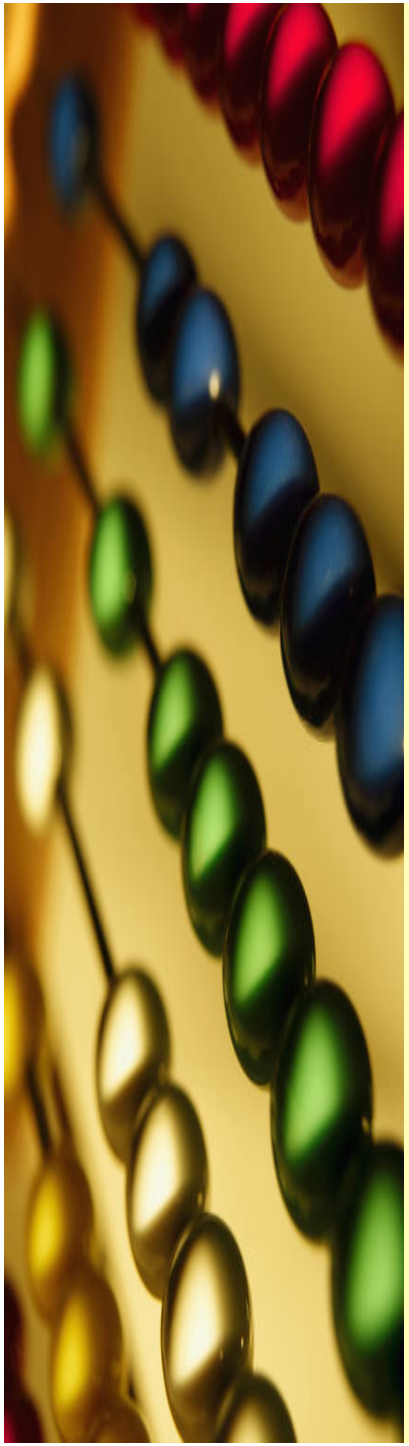
Brownback Antichimera Bill: There Goes the Family

- *Excerpt:* "The term `human chimera' means--
  - `(A) a human embryo into which a non-human cell, or any component part of a non-human cell, has been introduced;
  - `(B) ***a human embryo that consists of cells derived from more than one*** human embryo, fetus, or ***born individual***"
- *Impact:* IVF, which produces an embryo from gametes of two ***born individuals***, is a crime.



Conclusion

- We *lack*
  - in respect of embryo derivatives, functional equivalents procurable by means morally superior to use of embryos
- We *have*
  - compelling justification for medical use of donated embryos barred from the womb



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