Ethical aspects of pluripotent stem cell research

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ESHRE Campus, Valancia, 8 November 2010

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Main ethical problem: the moral status of the embryo

3 positions:

- The embryo has the same moral status as a person
- The embryo has the same moral status as a bundle of cells
- The moral status of the embryo increases the more it grows = gradualistic position

Main ethical problem: the moral status of the embryo

iPS cells: the end of all ethical troubles!

iPS cells are equivalent to ES cells but do not generate any ethical problems.

Enjoy this illusion for a minute

Is the entity an embryo?

The answer will depend on the definition AND on the implications of the definition.

Example: a cell or coherent whole of cells that has the potential to grow into a human.

Potentiality argument: a cell or group of cells has a special moral status because it has the potential to develop into a human being.

Is it an embryo?

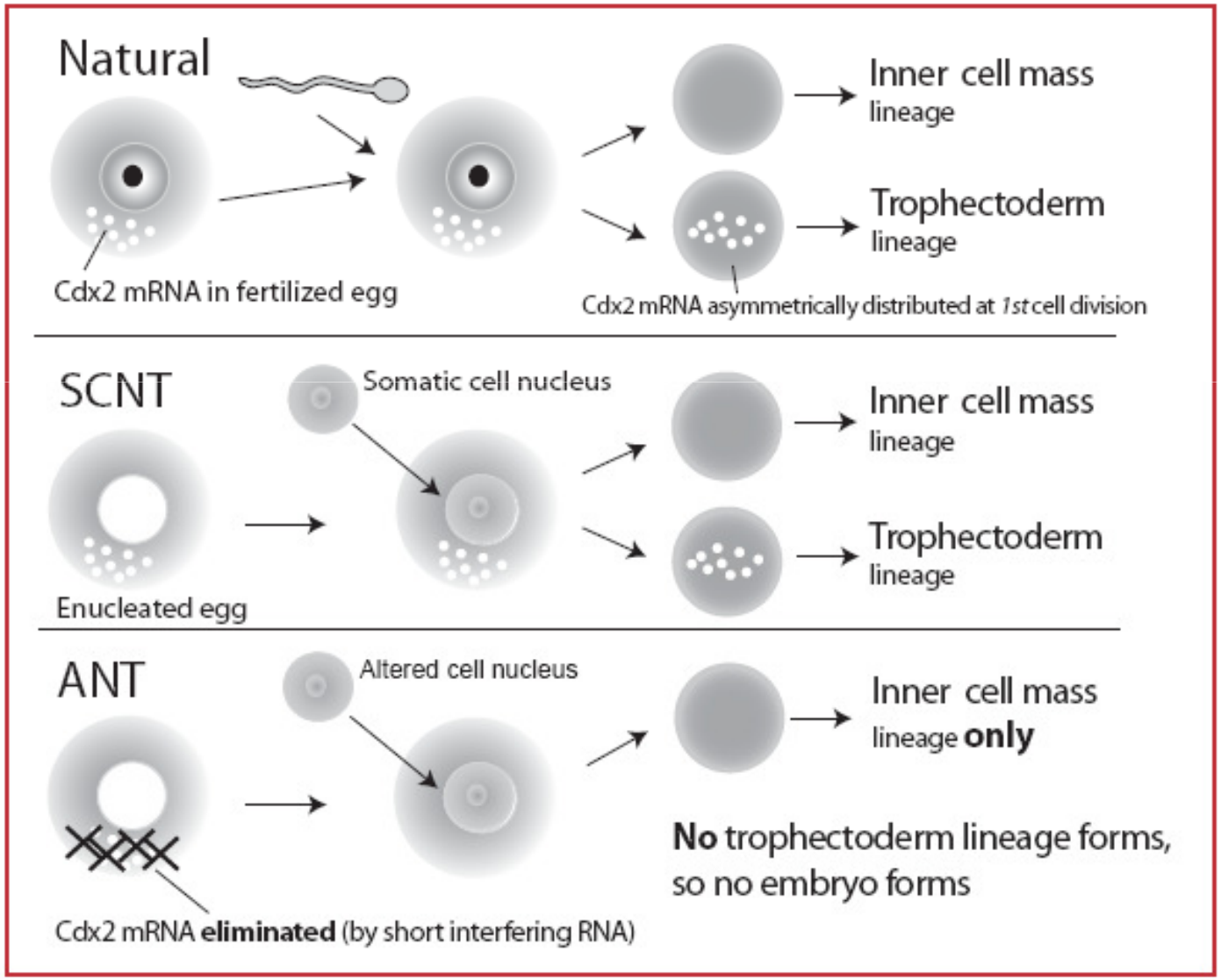
Different ways of defining an embryo:

- Method of creation: fertilisation, SCNT, parthenogenesis ...
- Certain characteristics or capacities: potentiality, totipotency ...

If the entity is not an embryo, than all problems are solved.

Two examples: - Altered Nuclear Transfer
- parthenotes

Altered Nuclear Transfer



Is it an embryo?

Altered Nuclear Transfer (Hurlbut): embryo-like entity

Two criteria to distinguish an embryo from an embryo-like entity:

1. The entity should have an integrated organismic structure.
2. The genetic alteration should be made ab initio.

Such entity has the same moral status as a teratoma, mole, cyst or parthenote.

Main problem: how do we distinguish an embryo-like entity from a defective embryo? E.g., aneuploidic embryo.

Technical interventions and modifications

Problem: how much technical intervention is included in the definition of an embryo?

- If no intervention is allowed, then a normal embryo in vitro would not be an embryo.
- If all interventions are allowed, then every somatic cell would be an embryo.

Example: parthenote: this entity never leads to a new organism in mammals . Conclusion: it is not an embryo.
However, if certain (paternal) genes are inserted, a parthenote can become a living mammal. Example: mouse Kayuga. Conclusion: should we treat every parthenote like an embryo?

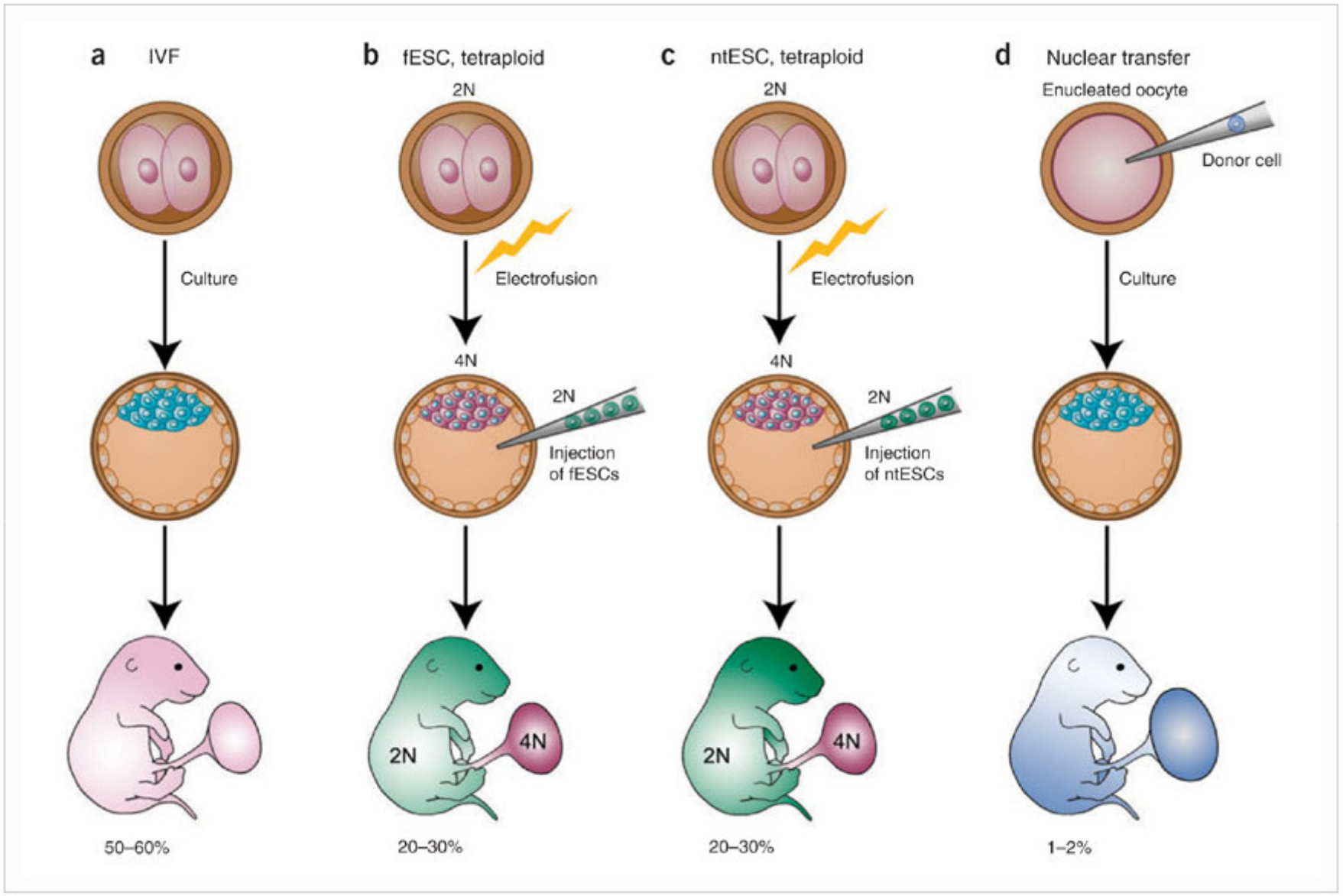
Technical interventions and modifications

Problem: pluripotency of iPS cells is tested by tetraploid complementation.

July 2009: generation of viable mice from iPS cells (Kang et al., 2009; Zhao et al., 2009)

Most common argument to defend that iPS cells are not embryos: they alone cannot give rise to a full-grown organism. They require a surrogate trophoblast given by the tetraploid cells.

But: this trophoblast does not become part of the proper embryo (inner cell mass).
Conclusion: these cells have the inherent capacity to grow into a new organism when placed in the appropriate environment.


a
IVF
Culture
50–60%
b
fESC, tetraploid
2N
Electrofusion
4N
2N
Injection
of fESCs
2N
4N
20–30%
c
ntESC, tetraploid
2N
Electrofusion
4N
2N
Injection
of ntESCs
2N
4N
20–30%
d
Nuclear transfer
Enucleated oocyte
Donor cell
Culture
1–2%

iPS cells versus ES cells

People seem to believe that iPS cells are a separate category while they are adult stem cells. The same problem as with the adult stem cells remain: are they equivalent with ES cells (and how to prove it)?

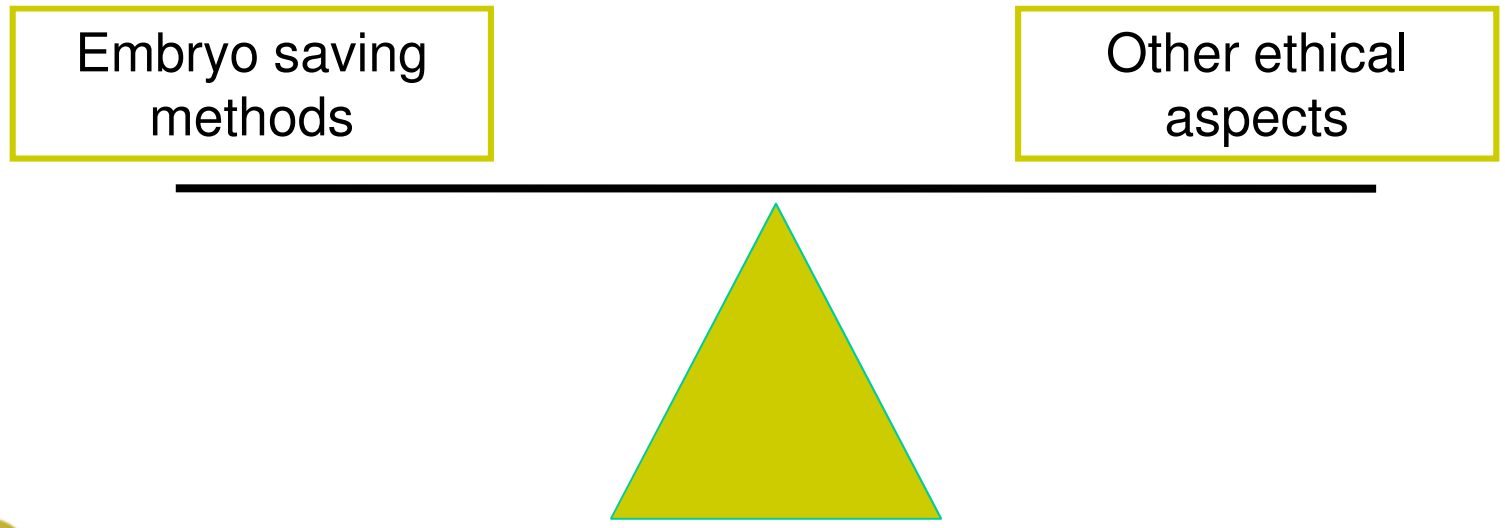
The opponents of research on ES cells argue that there are enough indications that adult stem cells (including iPS cells) can do the job. The proponents of ES cell research want to continue parallel lines of research.

Important point: if iPS cells turn out NOT to work, we will have lost years (with all the avoidable casualties).

The ethical balance

The opponents of embryo research want to convince us that any method which does not use and destroy embryos is morally superior regardless of the possible other disadvantages.

A clear case of **ethical overselling**: grossly exagerating the ethical advantages before one even knows whether or not these cells will do the job.



iPS cells

Other relevant elements to put in the balance:

- the fastest path to therapy?
- the safest way?
- the most cost-effective method?
- the most widely applicable method?

All these elements are morally relevant and should be taken into account in deciding which cells to use in research and therapy.

Other ethical problems

General problem: ethical principles that work fine in general research lead to problems in pluripotent SC research

- confidentiality of genetic information of the donor
- consent and withdrawal of consent
    - problem: specificity of information. Future use in research (see biobanking)
    - broad / blanket / generic consent: problematic for specific uses such as: derivation of human gametes; producing human animal chimeras; use for transplantation. Solution: cover common uses and recontact if unanticipated uses are planned.
    - right to withdraw: destruction of the cell line? Anonymity?
    - feedback of incidental findings to the donor

Other ethical problems

- intellectual property rights and patenting (for donor and for scientific progress)
- new ES cell research is needed to test safety
- embryonic SC derived gametes: embryo creation is needed to test the functionality
- safety concerns in clinical applications
    - in vivo properties of immortal cell types
    - genetically manipulated cell types

Increasing commercial pressure to move (prematurely) to therapy: when to move from bench to bed.

Conclusions

The respect owed to the embryo is but one element in the ethical balance to decide about the justifiability of scientific research. The good that might be generated by the research in terms of knowledge and/of therapy is a powerful argument against those who oppose all embryo research.

As long as there is insufficient knowledge about the characteristics of the different cell types, research should be conducted in parallel.

More effort should be put in the practical problems encountered when working with pluripotent stem cells in order to arrive at internationally agreed guidelines and procedures.