Terminology Related to the Debate on “Cloning”: Two Recommendations

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IBC conclusion

- The terminology used in the bioethical debates is misleading and does not adequately describe the technical procedures used (or potentially to be used) today. An in-depth analysis aiming at re-defining this terminology according to the new developments in human embryo research would be highly beneficial.

ELEMENTS OF THE PROBLEM

- Subject is intrinsically emotional, with perceived potential to spill into other domains (what is life; when does life begin; tension between maternal and embryonic/fetal rights; abortion debate; etc)
- Drama of announcement of Dolly
- Interesting science and technology but confusing to non-experts; always shifting
- Potential medical applications and understanding of biology
- Different perspectives of religions, politics, culture
- Armchair bioethicists, and excited but poorly informed journalists
- Imperfect terminology became fixed too early
- UN initiative was premature and tried to do too much

Problems with the Terminology

- "Reproductive cloning" is still only theoretical in humans
- "Therapeutic cloning" through somatic cell nuclear transfer (SCNT) also misleading: few therapies; much of the research is for understanding physiology; does not reflect several new technologies e.g. iPS cells; piPS cells
- SCNT involves only one nuclear DNA component (diploid, from a somatic cell), so
  - Technically there is no fertilization (sexual union of gametes) is involved
  - So some people question if the resulting entity is really an embryo
  - So the definition of an embryo becomes linked to potential to develop into a baby
  - But problem is that now even somatic cells also have this potential

Further Issues

- When does life begin?
  - Is this is a biological, medical, religious or philosophical question?
- When do moral rights accrue/ begin? An event or a process?
  - Different perspectives, especially religious
    - At fertilization? (but SCNT does not involve fertilization)
    - Is fertilization same as conception? (some apply this term after implantation)
    - When clump of cells develop polarity? (14 day rule)
    - When ensoulment occurs?
    - At birth?
- Are embryonic rights the same as human rights?
- What about personhood; and when does that begin?

Dictionary Definitions of an Embryo

- The young of a viviparous animal, esp. of a mammal, in the early stages of development within the womb, in humans up to the end of the second month.
- a. An organism in its early stages of development, especially before it has reached a distinctively recognizable form.
- b. An organism at any time before full development, birth, or hatching.

- 2.a. The fertilized egg of a vertebrate animal following cleavage.
- b. In humans, the prefetal product of conception from implantation through the eighth week of development.

- The organism in the early stages of growth and differentiation from fertilization to, in humans, the beginning of the third month of pregnancy. After that point in time, it is termed a fetus.
- A young animal that is developing from a sexually fertilized or parthenogenetically activated ovum and that is contained within egg membranes or within the maternal body. The embryonic stage ends at the hatching or birth of the young animal.

Definitions of an Embryo From Two Major Reports: a Group of Cells or an Organism?

- From NAS report: A **group of cells** arising from the egg that has the potential to develop into a complete organism. In medical terms, **embryo** usually refers to the developing human from **fertilization** (the **zygote** stage) until the end of the eighth week of gestation when the beginnings of the major organ systems have been established
- From (Bush) Council on Bioethics: 1. The developing **organism** from the time of fertilization until significant differentiation has occurred, when the organism becomes known as a fetus. 2. An organism in the early stages of development.

Problems with Defining a Human Embryo in the Context of SCNT

- Traditionally, an embryo is the result of the fusion of a sperm and an egg
- The single-celled entity that results from the fusion of a sperm and an egg is a "zygote.” After it divides, it is an embryo.
- If an embryo is defined as the entity resulting from the sexual union of a sperm and an egg, then the entity resulting from SCNT is not an embryo
- Other terms used include blastocyst; pre-embryo; pre-implantation embryo

Questions re a Biological Definition of Human Embryo

1. Should the potential to produce a live birth form part of the biological definition of a human embryo?
2. Should fertilization and/or syngamy form part of the biological definition of human embryo?
3. Should the biological definition of human embryo exclude techniques combining DNA from more than one species?
4. Should the biological definition of human embryo include a developmental time point?

Human embryo: a biological definition

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- *A human embryo is a discrete entity that has arisen from either:*
- *the first mitotic division when fertilization of a human oocyte by a human sperm is complete or*
- *any other process that initiates organized development of a biological entity with a human nuclear genome or altered human nuclear genome that has the **potential** to develop up to, or beyond, the stage at which the primitive streak appears,*
- *and has not yet reached 8 weeks of development since the first mitotic division.*
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Crux of the debate: Cosmic Biological "Singularity" (Daar and Sheremeta, 2002; 2003)

- We suggest that the beginnings of an appropriate distinction between somatic cells and zygotes….. lie in the act of sexual union of the sperm and egg. Perhaps it is the sexual conjugation of these two gametes, with the resultant admixture of DNA and the crucial event of genetic recombination, with its unpredictability in terms of the resultant new phenotype, that imparts the specific moral boundary--a kind of cosmic biological "singularity"--that is afforded to the zygote and its subsequent developmental forms.
- This, and the further issues of whether **full** "human life," and indeed "personhood," with all their moral considerations and interests, begin at the moment of fertilization, whether the "singularity" comes at a later stage, or whether moral considerations, interests and personhood accrue gradually with embryonic/fetal development, are thorny issues that are at the crux of this debate.

But....

- The entity resulting from SCNT, or from re-programing somatic cells, has not undergone this cosmic bio-sexual singularity
- **So, does the entity resulting from SCNT, which is not intended for reproduction, have the same moral rights as an ordinary embryo?**
- **Is the issue now one of intention?**

Somatic Cells are Potential Embryos?

- It is now no longer necessary that a sperm initiate the division of an egg to become an entity (blastocyst) from which human pluripotent stem cells can be derived. A somatic cell nucleus can be re-programmed in SCNT to achieve essentially the same end
- Ergo, any somatic cell has the "potential" to initiate life. The zygote is indeed "totipotent," but its totipotency arises from a non-totipotent cell somatic cell.
- Can we therefore argue that the somatic cell, which can participate in SCNT or be re-programmed genetically or by other means, is a potential embryo (if one insists that (sexual) fertilization is not needed to define an embryo) ?
- Should we therefore extend moral consideration to all somatic cells? Is it unethical to destroy somatic cells? They do after all have life and that life is human

"14 Day Rule"

- The UK Human Fertilisation and Embryology Act (and others) permits experimentation on human embryos up to the 14-days post-fertilization stage. The justification for this 14-day rule is that it is immediately after this stage (i.e. on day 15) that the "primitive streak" is formed. Up until that point the embryo is simply a symmetrical cluster of cells. The primitive streak gives the embryo a body axis such that head, tail, left and right can be defined and physically orientated in relation to each other. Additional reasons proffered for the 14-day cutoff point are that up to that point: (1) implantation into the womb has not yet been completed; and (2) the embryo still has the potential to split to form identical twins (i.e. its potential personhood has not been fixed)

New Problems with New Advances

- A number of new scientific developments may have an impact on future development of international governance of cloning. On one hand, the work carried out since 2006 on induced Pluripotent Stem (iPS) cells and their possible uses has created more technical possibilities for reproductive manipulation of human embryos and hence brings new problems into the debate. Since it has been demonstrated that functional germ cells may be created from embryonic stem cells, this raises the possibility of creating germ cells from somatic cells (via iPS cells) which further blurs the borders between different stages of human development and reproduction.

Recommendation 1. Focus Any New UN Initiative Only on Artificial Human Reproductive Cloning.

- Retain the term “human cloning” only to reproductive cloning
- Define it
- Make the definition wide enough to include any new technological developments, but keep the end result clear i.e. the *artificial* production of a baby that has essentially the same nuclear DNA as that of an existing or previous existing human being (i.e. derived from nuclear genes from a diploid cell)
- Stick to this focus on reproduction no matter what; don’t complicate it

Recommendation 2. Stop Using the Terms "Therapeutic" and "Research" Cloning to Obtain Stem Cells

Instead of therapeutic or research cloning I propose using the following:

- Derivation of pluripotent cells by
  - Somatic cell nuclear transfer
  - Re-programming (iPS; piPS, etc)
  - Any other (new) technology
- This is descriptive, technically accurate, simple, easily understandable, and capable of incorporating any future scientific and technological developments. It also allows more nuanced and differentiated ethical analyses, depending on what technology is under scrutiny. It takes away ideological orientations, and provides more light than heat

Can IBC do this?

I hold that as IBC is the only globally mandated ethics committee, we do have an opportunity to provide leadership on this issue. And it is not too late. The terms currently used are misleading and confusing to the public, and the public will appreciate some clarity.