Derivation of human embryonic stem cell lines from single cells of 4-cell stage embryos: be aware of the risks

Sir,

Most of the human embryonic stem cell (hESC) lines have been derived from the inner mass of blastocyst stage embryos, some from 8-cell stage morula (Streclchenko *et al.*, 2004) and some from isolated blastomeres from morulae (Chung *et al.*, 2008).

In a very recent abstract, a Belgian team (Van de Velde *et al.*, 2008) elegantly established an embryonic stem cell line from a single blastomere isolated from a 4-cell stage embryo (from 1 out of 12 embryos). This team had a unique opportunity to establish good quality embryos from donated oocytes and sperm. By deriving a line from one blastomere, they gave evidence for the totipotency of single cells at 4-cell stage in human embryo. The resulting hESC line was, however, chromosomally abnormal with a deletion in chromosome 18 and a duplication in chromosome 7.

In Switzerland, the embryo research law is very strict, and obtaining good quality embryos for hESC derivation is virtually impossible, even though the law allows hESC derivation and culture. Our team recently derived a hESC line (Ch-ES1) from a frozen-thawed 4-cell stage embryo, in which only one blastomere survived thawing. The surviving cell grew on human foreskin feeders (Hovatta *et al.*, 2003) and formed a hESC-like colony which has since then been passaged and cultured as a hESC line for over a year (Feki *et al.*, 2008). This line proved to be chromosomally very abnormal, with triploidies and several deletions and duplications. It forms malignant teratocarcinoma-like tumors when injected into SCID mice.

The Belgian team has now an excellent opportunity to show how often such lines are abnormal, a type of study still very difficult in many other countries. It is not new that poor quality embryos often have chromosomal abnormalities (Hardarson *et al.*, 2003), but on the other hand, we do not know yet how much culture conditions affect the chromosomes of early lines, even though culture adaptation is well known (Draper *et al.*, 2004).

In this light, the interpretation of many media that derivation of lines from single blastomeres is ethically a more acceptable method of derivation of hESC lines than destroying whole embryos cannot be supported by the scientific community. It appears that sometimes even the scientists themselves provoke such ideas (Chung *et al.*, 2008). The Belgian team has just been revealing very important biological mechanisms, but some media changed even their message to that direction. Also in Switzerland, we have to make clear that we now have an important tool to solve some problems in cancer development, but it does not offer solutions for any ethical questions in hECS derivation. The fact that hESC lines can be obtained from cells without destroying the embryo, or from cells of a 'dead' embryo, does not make such lines ethically more acceptable. Abnormality issues should not be underestimated.

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Impact of hyperglycemia on early embryo development and embryopathy: *in vitro* experiments using a mouse model

Sir,

Fraser *et al.* (2007) identify the media they used in their work as mKSOM and KSOM, and characterize them as a 'synthetic oviductal medium enriched with potassium'. We wish to point out that his characterization is erroneous. A medium called SOM was developed by Lawitts and Biggers (1991) using the experimental strategy called 'sequential simplex optimization' (hence SOM). SOM medium was not designed to imitate the composition of oviductal secretions. It was developed to overcome the 2-cell block which, at the time, interfered with many studies on the developmental biology of the mouse embryo. KSOM was later modified by raising the potassium concentration in SOM (Lawitts and Biggers, 1993) based on