DOI:
10.1038/nrm2212

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CLONING

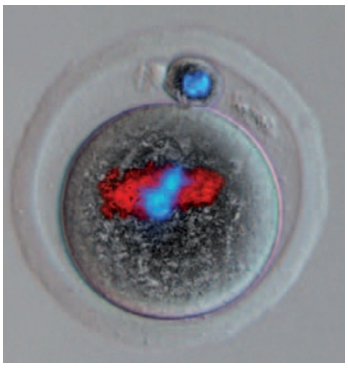
Taking technical and ethical hurdles

Embryonic stem (ES) cells are a promising source for regeneration therapies and, in the future, it may be possible that each of us will be able to use our own frozen pool of cells when in need. But, for the time being, stem-cell research is faced with tremendous challenges, including the problem of immune rejection of cells that have been transplanted for therapy and the ethical issues that are associated with the use of human embryos. Now, Egli and colleagues describe a different approach for the production of ES-cell lines.

It has long been believed in the cloning field that successful somatic-cell nuclear transfer (SCNT) — a way to make ES-cell lines — requires the use of unfertilized eggs. However, this study reports a solution that overcomes this problem and shows that fertilized eggs can also be used, at least in mice. The authors used condensed chromosomes from nocodazole-arrested donor zygotes and two- and eight-celled embryos. The chromosomes were injected into the cytoplasm of treated recipient zygotes, and the resulting blastocysts were returned to foster mothers. Donors from all three stages of development led to some live births.

But can ES cells also be used as donors? Genetic material from mouse ES cells was used, which led to nine live births or the creation of new ES-cell lines. By injecting these ES-cell lines into normal host blastocysts, Egli *et al.* showed that these cells had the full range of developmental potencies that would be expected from bona fide mouse ES cells. Although all nine animals died due to various defects, which indicated that there were problems in nuclear reprogramming, this method shows that early fertilized eggs or cells taken from them might prove useful in creating patient-derived human ES cells.

To test this hypothesis further, Egli *et al.* also used mouse skin cells to make donor-specific SCNT-derived ES cells. However, the most interesting finding came from the use of defective zygotes that contained three sets of chromosomes. These zygotes were used as recipients to produce ES cells. Although these embryos never develop normally, replacement of the three chromosome sets with one set from an ES cell led to a normally developing embryo. These findings indicate that defective human zygotes that are available from *in vitro* fertilization clinics could be useful, thereby eliminating the need for oocyte donation.



In the first embryonic cell division, condensed chromosomes (blue) assemble in a spindle (red) in the centre of the zygote. This time point provides an opportunity to replace the genome, allowing the production of cloned animals and stem-cell lines. Image courtesy of D. Egli, Department of Molecular and Cellular Biology, Harvard University, Cambridge, Massachusetts, USA.

The health of the cloned animals is clearly a problem, but this study indicates that non-viable fertilized eggs may eventually prove useful in creating patient-derived human ES cells. This is particularly important given the paucity of eggs that are available for cloning research and the controversy that surrounds egg donation.

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ORIGINAL RESEARCH PAPER Egli, D. *et al.* Developmental reprogramming after chromosome transfer into mitotic mouse zygotes. *Nature* **447**, 679–685 (2007)
FURTHER READING Colman, A. & Burley, J. Recycling the abnormal. *Nature* **447**, 649–650 (2007)