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Oocytes direct from embryonic stem cells

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Cathy Holding
Email: cholding@hgmp.mrc.ac.uk

The technique of cloning in animals currently requires that a single diploid nucleus be introduced into an enucleated oocyte, which is then stimulated to restart the embryonic development program. Recent evidence suggests that the source of the diploid nucleus governs the success of the technique, such that nuclei that have a lower level of epigenetic imprinting are more likely to achieve a successful clone because this low level of imprinting is easier to erase, aiding the 'restart' of development. In the May issue of Sciencexpress, Karin Hubner and colleagues at the Center for Animal Transgenesis and Germ Cell Research at the University of Pennsylvania, USA, attempt to produce oocytes directly from embryonic stem cells, bypassing the need for nuclear transfer (*Sciencexpress* 2003, 10.1126/science.1083452).

Hubner *et al.* previously showed that only one of two different enhancers that govern expression of the Oct4 gene, a gene controlling pluripotency in embryos and germ cells, is used depending on whether it is in the lineage that will derive the embryo, or the lineage that will derive the germ cells. By knocking out the embryo-specific enhancer, and using the germ cell enhancer to drive expression of green fluorescent protein instead of Oct4, they were able to provide a marker to follow the development of 'germ cells' in a culture of embryonic stem cells. They also followed in these cells the expression of several genes that mark the maturation of germ cells and successively selected out the marker-expressing cells. These then developed into oocyte-like structures before progressing on, presumably through parthenogenesis, to blastocyst-like structures. If proven to produce viable offspring, this technique could provide a highly efficient means of cloning in animals by side-stepping the problems associated with erasure of epigenetic imprint when diploid nuclei are transferred.

References

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2. *Sciencexpress*, [http://www.sciencexpress.org]

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4. Comparative analysis of human, bovine, and murine Oct-4 upstream promoter sequences.