CLONING

I smell a rat

The sweet smell of success in the form of the long-awaited arrival of cloned rats recently wafted from the online version of *Science*.

Despite numerous attempts, cloning researchers were previously unable to clone rats using somatic cell nuclear transfer (SCNT). The problem has been that rat oocytes spontaneously but abortively activate within 60 minutes of being removed from the oviducts, before researchers can transfer a somatic cell nucleus into the enucleated oocyte.

To circumvent this problem, Qi Zhou and colleagues have developed a quick one-step SCNT procedure: the somatic nucleus is injected into the oocyte with a micropipette, which is only withdrawn after it has sucked up the endogenous meiotic chromosomes.

But even this dextrous technical feat was not enough to solve the problem of premature activation of the oocyte: two separate sets of chromatids at opposite poles were still apparent in 40% of the oocytes selected for SCNT, which indicated that these oocytes were already activated. Also, despite the transfer of hundreds of reconstructed embryos into many foster mothers, in no case did a fetus start to develop. Clearly, most oocytes were not suitable for cloning, even using the authors' impressively rapid manipulation.

So, as well as the change to the SCNT procedure, Zhou and colleagues used a protease inhibitor (MG132) to block the first meiotic metaphase–anaphase transition in the rat oocytes while they were being collected. This reversible blockade of oocyte activation did the trick: from a large number of attempts, 16 fetuses started to develop in 4 females before they were sacrificed.

The next series of experiments used the same approach but with smaller numbers of embryos and foster mothers. The result: one pregnant female and the 'eureka' moment of the birth of three cloned rats. The two clones that survived to sexual maturity happily proved their fertility by producing the next generation in the old-fashioned way.

The cloning of the rat, which is an important model for the study of many human diseases, is a big step forward for those that study it. However, even more exciting is the encouragement that this study might give those working on other hard-to-clone species: maybe a little species-specific technical tweaking is all that is needed to clone these species too?

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References and links

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FURTHER READING Rhind, S. *et al.* Human cloning: can it be made safe? *Nature Rev. Genet*. **4**, 855–864 (2003) | Jacob, H. J. & Kwitek, A. Rat genetics: attaching physiology and pharmacology to the genome *Nature Rev. Genet*. **3**, 33–42 (2002)
WEB SITE
Jean-Paul Renard's laboratory:
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