HIGHLIGHTS

STEM CELLS

Taking new orders

Oct4
http://www.ncbi.nlm.nih.gov/locuslink/LocRpt.cgi?l=18999

Thy1
http://www.ncbi.nlm.nih.gov/locuslink/LocRpt.cgi?l=21838

Nuclei that are transplanted from differentiated somatic cells to enucleated eggs of frogs or mammals take on the properties of the acceptor eggs. The molecular mechanisms that underlie this process of nuclear reprogramming are poorly understood, but involve new transcriptional instructions. Now, reporting in *Current Biology*, John Gurdon and colleagues show that a stem-cell marker is expressed in the nuclei of differentiated adult mouse and human cells after transplantation, and that this reprogramming does not require DNA replication.

A major activity of eggs is to induce replication, so to study the transcriptional reprogramming activity in eggs, Gurdon and colleagues chose *Xenopus* oocytes (growing egg cells), as they are nonreplicating but have a high transcriptional activity. *Xenopus* oocytes were injected with the nuclei of mouse fetal fibroblasts, and tested for the presence of *Oct4* mRNA — a stem-cell marker — using reverse transcriptase (RT)-PCR. Mature, spliced *Oct4* transcripts could be detected in oocytes that had been cultured at 18°C. The level of the transcript was 5–10 times higher when nuclei were injected into the oocyte nucleus (germinal vesicle, GV) than when nuclei were deposited in the cytoplasm.

To see whether the reprogramming activity of *Xenopus* oocytes was also effective for nuclei of adult mouse cells, mouse thymocyte nuclei were injected into the GV of oocytes. Fully spliced *Oct4* transcripts could be detected in oocytes that had been incubated for less than 2 days at 18°C. As the levels of *Oct4* transcripts increased, the thymus-specific differentiation marker *Thy1* decreased and became undetectable by day 5.5. Crucially, the oocyte's reprogramming activity is highly efficient, as the number of *Oct4* transcripts in GV-injected oocytes after 5.5 days of incubation was comparable to that of cultured mouse embryonic-stem cells. The cross-species reprogramming activity of *Xenopus* oocytes even extended to differentiated adult human cells, as the human *OCT4* gene was activated in oocytes 4–6 days after GV injection with human lymphocyte nuclei.

It will be interesting to study the expression of other genes in this experimental system, and to further investigate the molecules and mechanisms of nuclear reprogramming. And, eventually, it might become possible to directly reprogramme human cells for cell-replacement therapy.

Arianne Heinrichs

References and links

ORIGINAL RESEARCH PAPER Byrne, J. A. *et al.* Nuclei of adult mammalian somatic cells are directly reprogrammed to *oct-4* stem cell gene expression. *Curr. Biol.* **13**, 1206–1213 (2003)

WEB SITE

John B. Gurdon's laboratory:
http://www.welc.cam.ac.uk/groups/gurdon.html