planted oocytes to develop properly was cell-cycle incompatibility between the donor nucleus and recipient oocyte, with chromosomal abnormalities arising in the transplanted nuclei once development was initiated[8]. In mammals, most of the early embryonic nuclei that are used as donors are in either the S or G2 (non-diploid) phases of the cell cycle. This is not compatible with the diploid metaphase-II-arrested oocytes — the preferred recipient stage. When nuclei in S or G2 are introduced into metaphase-II-arrested oocytes, they tend to undergo additional DNA replication and premature chromosomal condensation, resulting in aneuploidy (whereby the nucleus is not diploid), and abnormal development[8].

Wilmut *et al.* may have partially overcome this problem by transplanting nuclei from cells that have been arrested in the diploid G0 phase of the cell cycle by serum starvation. By arresting donor nuclei in G0, there should be better synchrony in the timing of DNA replication between the transplanted nucleus and the cytoplasm of the recipient oocyte once development is initiated, reducing the incidence of chromosomal abnormalities. It might also explain why it has been so difficult to clone mice: nuclei in the early preimplantation stages are mainly in S or G2, and it is very difficult (if not impossible) to arrest embryonic stem cells in G0 by serum starvation.

Other factors that may have contributed to the success of Wilmut *et al.* are increased access of chromatin from cells in G0 to oocyte 'remodelling factors' (presumably transcription factors and chromatin-binding proteins), and the fact that in sheep, transcription of the embryonic genome does not begin until the 8–16-cell stage, whereas in the mouse transcription occurs in the late 2-cell stage[9,10]. This would, in theory, allow the sheep embryo at least two rounds of the cell cycle to reprogramme or remodel the transplanted adult nucleus to an embryonic state. But if these aspects are significant, it may not be possible to reproduce the results in other mammalian species, as the onset of embryonic transcription varies between species.

So what of the future? Nuclear transplantation from somatic cells could be used to produce clones of sheep that have been selected for particular traits; however, this may not be easy given the seasonality of sheep reproduction and the complexity of embryo transfer. Although the number of successful transplants is still extremely low, technical improvements will no doubt be made. Could the technique eventually be used to introduce modified genes into the sheep germ line? Current hurdles to this include the targeting frequency of genes in somatic cell lines versus embryonic stem-cell lines, the availability of isogeneic genomic libraries, and the length of time that a normal karyotype can be maintained in cultured sheep cell lines. Nuclear transplantation should also prove useful in studying the consequences of ageing on the function of the genome, and the impact of telomere shortening on senescence. Moreover, similar results could perhaps be obtained from the nuclei of neurons, or other cell types that have permanently withdrawn from the cell cycle. The success of Wilmut *et al.* in deriving a viable lamb from an adult cell will no doubt stimulate work to adapt or modify the technique to other mammalian species. Maybe, in the future, the collective noun for sheep will no longer be a flock — but a clone. □

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Phototransduction

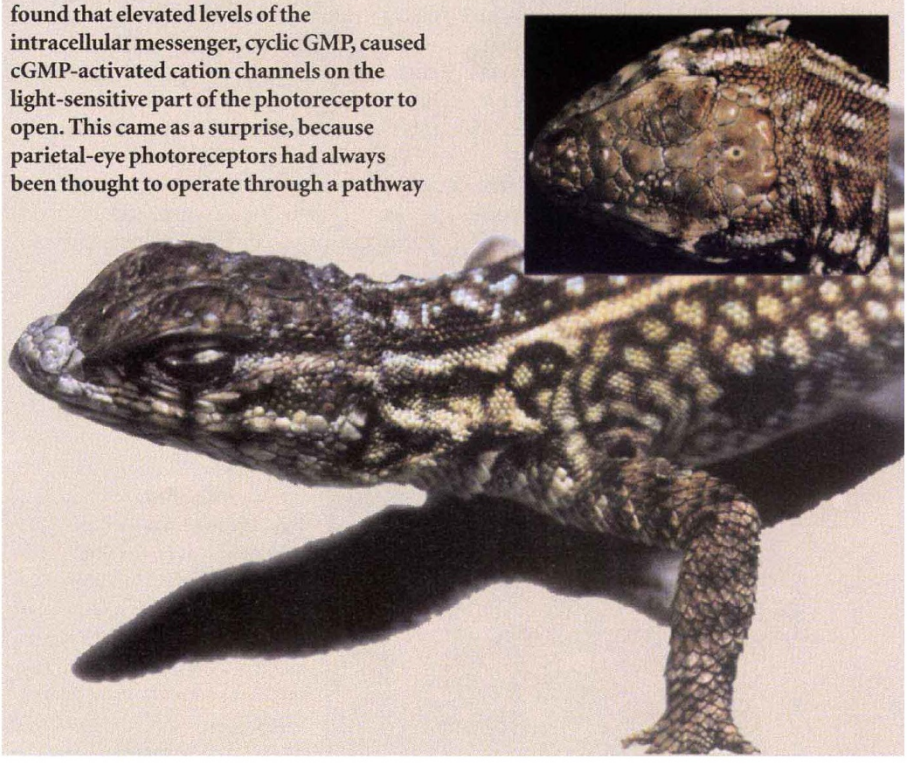
Why lizards can't turn a blind eye

Most mothers would agree that an extra eye on the back of the head could be a useful device for keeping watch over their children. What they may not know is that many lizards and other lower vertebrates already have exactly this modification, in the form of a third, or parietal, eye. In the side-blotched lizard, *Uta stansburiana*, the parietal eye can be seen as a small dark spot (about 200 μm in diameter) underneath a translucent patch of skin at the midline — just behind the lateral eyes. For many years, photoreceptors in the parietal eye were thought to respond to light through a different intracellular signalling pathway from that used by the rods and cones in the lateral eyes. But in this issue (*Nature* 385, 815–819; 1997), Finn *et al.* show that, in fact, the converse is true.

By recording the responses of parietal-eye photoreceptors to light, Finn *et al.* found that elevated levels of the intracellular messenger, cyclic GMP, caused cGMP-activated cation channels on the light-sensitive part of the photoreceptor to open. This came as a surprise, because parietal-eye photoreceptors had always been thought to operate through a pathway that involved a different intracellular messenger, inositol trisphosphate. The new results bring the parietal-eye photoreceptors into line with vertebrate rods and cones, which also use a cGMP-mediated signalling cascade. But in this case, the levels of cGMP decrease in response to light, so the cGMP-activated cation channels close.

Finn *et al.* believe that their work may be of evolutionary significance, as all of the so-called 'ciliary' photoreceptors (a group that includes rods, cones, parietal-eye photoreceptors and hyperpolarizing photoreceptors in scallops) use a cGMP-mediated signalling pathway — so the chances are that if humans did have a third eye, it would respond to light by essentially the same mechanism as the other two.

Alison Mitchell



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