In the news

OF COWS AND MEN

Researchers in the UK have requested permission to generate embryos by inserting human nuclei into cow eggs that have been depleted of their own nuclei. These embryos, which would not be allowed to develop for longer than 14 days, would be used for stem-cell research aimed at treating neurological disorders such as Alzheimer's and Parkinson's disease. Another team of researchers wants to use a similar technique to study how eggs can reprogramme adult cells into stem cells (*BBC News*, 7 Nov 2006).

"We are concerned that the current state of the technology means that hundreds of eggs from young woman will be required to generate a single human embryonic stem cell line. Therefore, we consider it more appropriate to use non-human eggs from livestock as a surrogate", says Stephen Minger, one of the researchers (*Telegraph*, 7 Nov 2006).

Although not an entirely new technique, mixing human and animal eggs and sperm is prohibited in the UK by the Human Fertilisation and Embryology Act 1990. But, the applicants are hopeful that this could change within a few months, opening up a new range of research possibilities.

Unsurprisingly, some members of the public are critical. Calum MacKellar of the Scottish Council on Human Bioethics is concerned that these studies "might also undermine human dignity and human rights" (*BBC News*, 7 Nov 2006).

However, Evan Harris, a member of parliament and a member of the Commons Science and Technology Select Committee, raises an opposing point: "If human benefits can be derived by perfecting therapeutic cloning techniques or from research into subsequently-derived stem cells, then it would actually be immoral to prevent it just because of a 'yuck' factor" (*BBC News*, 7 Nov 2006).

Asher Mullard

DNA DAMAGE

The road of death

> "…CDK2-mediated phosphorylation of the transcription factor FOXO1 regulates apoptosis following DNA damage."

DNA damage activates checkpoint pathways that induce cell-cycle arrest and subsequent DNA repair or cell death. Cyclin-dependent kinase-2 (CDK2) is inhibited by DNA damage, but whether CDK2 has a role in DNA-damage-induced cell death has been unknown. Donald Tindall and colleagues have addressed this question and found that CDK2-mediated phosphorylation of the transcription factor FOXO1 regulates apoptosis following DNA damage.

Given that FOXO transcription factors control a number of cell-death genes, Tindall and co-workers investigated a possible connection between CDK2 and the activity of FOXO proteins. They found that endogenous CDK2 phosphorylates FOXO1 at residue Ser249, and to a lesser degree residue Ser298, *in vitro*. This effect was abolished by a CDK inhibitor. The authors developed a phosphorylation-specific antibody and provided *in vivo* evidence for the CDK2-dependent phosphorylation of FOXO1. The antibody recognized wild-type FOXO1, but not a Ser249 to Ala249 (S249A) mutant of FOXO1. Small-interfering RNA (siRNA)-mediated silencing of CDK2 led to a decrease in FOXO1 phosphorylation, whereas FOXO1 phosphorylation was increased in cells that had been transfected with a constitutively active CDK2 mutant.

The transcriptional activity of FOXO1 was decreased in the presence of ectopically expressed CDK2 and its regulator cyclin E. By contrast, its transcriptional activity was increased

METASTASIS

Contract and move

The regulated assembly and disassembly of cell–extracellular matrix junctions (focal adhesions) contributes to cell motility and tumour invasion. Rho–ROCK signalling promotes focal adhesion disassembly at the rear of the cell by inducing contractile forces that are dependent on the phosphorylation of myosin light chain-2 (MLC2). Isacke and colleagues now show that the Rho–ROCK–MLC2 signalling pathway is activated to generate contractile forces at distinct subcellular locations through endosomal trafficking.

Using human cancer cell lines the authors compared the small interfering RNA (siRNA)-mediated depletion of the promigratory transmembrane receptor ENDO180 (also known as CD280) and two other endocytic receptors. ENDO180 is constitutively recruited into clathrin-coated pits on the cell surface, which are then internalized into intracellular endosomes. Only the depletion of ENDO180 induced tail-retraction defects, indicative of reduced Rho–ROCK–MLC2-mediated contractile forces. This phenotype