TOOLBOX

Induced stem cells retain traces of their former state

BY **MARISSA FESSENDEN**

30 JULY 2014

Fresh start: Stem cells created through nuclear transfer — a technique that replaces the nucleus of an egg cell with a nucleus from an adult cell — carry fewer reprogramming errors.

Reprogrammed stem cells carry remnants of their previous cell states in the form of chemical cues that alter gene expression, reports a paper published 10 July in *Nature*[1]. An alternative method that creates so-called nuclear transfer embryonic stem cells produces fewer errors.

Working with stem cells offers tantalizing opportunities to study the genetic basis of complex diseases **such as autism**. Stem cells that are pluripotent, meaning that they can develop into any cell type, can come from several different sources.

Embryonic stem cells are harvested directly from an embryo created through *in vitro* fertilization. **Induced pluripotent stem cells**, or iPS cells, are adult cells reprogrammed to an undeveloped state through chemical manipulation. Nuclear transfer embryonic stem cells (NT ES cells) are created by replacing the nucleus of an egg cell with the nucleus of an adult cell.

NT ES and iPS cells both retain the unique genetic signature of the adult cell donor, so they can be used to study diseases such as autism and to test therapies. iPS cells also skirt the ethical challenges of using embryos.

Some earlier research indicated that iPS cells **sometimes carry large deletions or duplications**

of DNA called **copy number variations**. It was **unclear** whether those variations are introduced during the reprogramming process or represent an incomplete reversion to an undeveloped cell.

The new study directly compared NT ES cells and iPS cells with embryonic cells with the same genetic background, produced through *in vitro* fertilization. The three cell types all carry small numbers of copy number variants. However, when the researchers examined chemical tags on the DNA — epigenetic marks — they found that iPS cells retain tags harking back to their previous state.

These altered epigenetic patterns also affect how the marked genes are transcribed into RNA. The differences indicate that iPS cells are incompletely reprogrammed, the researchers suggest, whereas the chemical environment of the egg, even *in vitro*, reprograms NT ES cells more faithfully. Further work with NT ES cells may reveal what kind of chemical cues the egg relies on and whether scientists could use them to create better iPS cells.

References:

1. **Ma H.** *et al. Nature* **511**,177-183 (2014) **PubMed**