STEM CELLS

A well-preserved program

Genes that restore pluripotency to mature mouse cells can initiate similar reprogramming in more distantly related species.

Scientists working with rodents should reflect on how good they have it. With well-defined strategies for isolating and engineering embryonic stem cells, the sky is essentially the limit for performing sophisticated genetic modifications in mice and rats. For other animal models—such as the songbirds studied by Duke University's Erich Jarvis—this option remains out of reach. Thus, when his colleague Ute Hochgeschwender passed along a paper by Japanese researcher Shinya Yamanaka describing genetic reprogramming of mature mouse cells to yield embryonic stem cell–like induced pluripotent stem cells (iPSCs), Jarvis immediately recognized the promise of this technology.

He, Hochgeschwender and former postdoc Ricardo Rosselló dove right in. "Instead of trying to clone the bird transcription factors, we just took the mammalian genes and decided to transfect bird cells with them and see if we get a similar result," says Jarvis. "And the amazing thing is, we did." After introducing the four mouse genes and carefully fine-tuning the culture conditions, the researchers obtained chicken and zebra finch cells that recapitulate many of the core features of mouse iPSCs. These 'partial iPSCs' began to express their own endogenous pluripotency genes and could form tissues from all three embryonic germ layers in implantation experiments—a critical test of *in vivo* pluripotency. Inspired by this success, Rosselló tested the same approach on other species such as zebrafish, which also yielded partial iPSCs with pluripotent characteristics. Although less successful overall, even reprogrammed fruit fly cells exhibited some features of adult stem cells.

Jarvis notes that some critics have focused on the phenotypic differences between these cells and 'standard' iPSCs. He believes that some of these may disappear with improved cultivation and the use of endogenous reprogramming genes, but others may be species specific. "The field is heavily mired in defining stem cells from a 'mouse-centric' point of view," he says. To his thinking, both the similarities and differences are interesting, and the fact that mouse genes can even partially reprogram cells from distantly related species speaks to remarkable evolutionary conservation. "I'd like to see other people repeat this and find out whether stem cell induction genes have more conserved functions across the vertebrate kingdom than some other genes," he says.

Michael Eisenstein

RESEARCH PAPERS

Rosselló, R.A. *et al.* Mammalian genes induce partially reprogrammed pluripotent stem cells in non-mammalian vertebrate and invertebrate species. *eLife* **2**, e00036 (2013).