How do stem cells work? Scientists aren’t sure

Eggs and sperm do it when they combine to make an embryo. John Gurdon did it in the 1960s, when he used intestinal cells from tadpoles to generate genetically identical frogs. Ian Wilmut did it too, when he used an adult mammalian cell to make Dolly the sheep in 1996. Reprogramming — reverting differentiated cells back to an embryonic state, with the extraordinary ability to create all the cells in the body — has been going on for a very long time.

Scientific interest in reprogramming rocketed after 2006, when scientists showed that adult mouse cells could be reprogrammed by the introduction of just four genes, creating what they called induced pluripotent stem (iPS) cells[1]. The method was simple enough for almost any lab to attempt, and now it accounts for more than a thousand papers per year. The hope is that pluripotent cells could be used to repair damaged or diseased tissue — something that moved closer to reality this year, when retinal cells derived from iPS cells were transplanted into a woman with eye disease, marking the first time that reprogrammed cells were transplanted into humans.

There is just one hitch. No one, not even the dozen or so groups of scientists who intensively study reprogramming, knows how it happens. They understand that differentiated cells go in, and pluripotent cells come out the other end, but what happens in between is one of biology’s impenetrable black boxes. “We’re throwing everything we’ve got at it,” says molecular biologist Knut Woltjen of the Center for iPS Cell Research and Application at Kyoto University in Japan. “It’s still a really confusing process. It’s very complicated, what we’re doing.”

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