NEURAL INDUCTION

Switching on new neurons

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Because most of the adult brain cannot make new neurons, neuronal damage is often irreversible. If we could enable new neurons to be grown in the brain and to join with existing circuitry, we might be able to treat conditions such as Parkinson's disease and Alzheimer's disease. A new study brings us a step closer to this ambitious goal.

Researchers have already shown that cells such as fibroblasts and astrocytes can be induced to turn into neurons in culture when they are made to express key genes known as neural conversion factors. This process — called cellular reprogramming — has been applied to the generation of new pancreatic and heart cells *in vivo*, but induced neurons have been generated only *in vitro*. Torper *et al.* now show that either transplanted fibroblasts or endogenous astrocytes can be turned into neurons in rodent brains when the right combination of genes is expressed.

The authors began by using viral vectors to deliver three neural conversion genes — achaete-scute complex homologue 1 (*Ascl1*), brain-2 (*Brn2a*; also known as *Pou3f2*) and myelin transcription factor 1-like (*Myt1l*), collectively known as ABM — into human fibroblasts. Because the genes could only be expressed in

the presence of doxycycline, the fibroblasts were unchanged *in vitro*. However, when the cells were implanted into the brains of rats that were treated with doxycycline, some of the fibroblasts developed typical neuronal morphology and began to express neuronal markers, indicating that they had turned into neurons. By using the same procedure, the authors also generated neurons *in vivo* from implanted human astrocytes.

To test whether endogenous cells could be used to generate new neurons, the authors injected an inducible vector carrying the ABM genes into the striata of mice that

were genetically engineered so that the induced genes would be expressed only in astrocytes. After 6 weeks, some striatal astrocytes had turned into neurons — like the implanted fibroblasts, they looked like neurons and expressed neuronal markers. Although there is a long way to go before these techniques can be tried in humans, the new findings show that cellular reprogramming in the brain is at least possible.

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ORIGINAL RESEARCH PAPER Torper, O. *et al.*
Generation of induced neurons via direct
conversion *in vivo*. *Proc. Natl Acad. Sci. USA* 25 Mar
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