John B. Gurdon

(Sir) John Gurdon is a researcher of great distinction. A classical scholar turned scientist, he was working in the Department of Zoology at Oxford during the 1960s, trying to answer an old question: does the differentiation of cells in a growing animal – the formation of liver, spleen and kidney, muscle, intestine and heart – from undifferentiated (uncommitted) precursor cells involve the loss of particular genes, or is it merely a question of certain genes being turned off? It is unlikely to involve the gain of specific genes, since a full complement is present in the germ cells; in any case where would other genes come from? Gurdon used the technique of nuclear transplantation, developed in 1952 by Robert Briggs and Thomas King. They had shown that if the nucleus of a tadpole embryo at the blastula stage (by which point cells have already begun to differentiate) is injected into an enucleated frog egg, a free-swimming tadpole is formed (at least 40% of the time). However nuclei isolated from cells at a later (gastrula) stage did not do so well. Also it was not quite clear that the ‘host’ frog egg had been completely enucleated. The results were therefore somewhat equivocal.

Gurdon decided on a bold strategy. He would test nuclei taken from adult frog intestinal cells. Such cells are clearly well differentiated in their actions: the absorption of foodstuffs and salt through specific enzymes and their release into the circulation, for example. Moreover by taking nuclei from frogs that had been genetically marked, he would be able to tell the difference between a tadpole that was derived from the ‘differentiated’ nucleus, and one that was derived from residual genetic material in the host egg. Many attempts, and many failures, followed. But Gurdon persevered. After all, he needed only one success to settle the issue, since he could be sure that if an emerging tadpole bore the genetic marker, its genes came solely from a differentiated cell. Finally he succeeded in producing a healthy, free – swimming tadpole by the nuclear transplantation technique. He had cloned an amphibian. In fact he produced several tadpoles, each of course derived from a different nucleus. Gurdon did not wait for the tadpoles to metamorphose. The answer was clear: differentiated cells – at least those from the small intestine – have totipotency. His coup was quickly recognised, and he was offered a senior position at Cambridge (in an institute that has subsequently been named after him). His translation from Oxford to Cambridge caused Francis Crick to quip (to Rodney Porter, the chairman of biochemistry) ‘so the intellectual climate of Oxford is no longer sufficiently stimulating for some’.

Gurdon has not, as yet, been awarded a Nobel Prize. Yet I – and I have no doubt many others - am firmly of the opinion that his demonstration of
totipotency in differentiated cells, represents a scientific advance that is well worthy of this distinction; Briggs and King, sadly, could not be included, since neither is still alive. Not only did these experiments reveal completely new possibilities in embryology, not only did they open the way to make the cloning of mammals like Dolly the sheep and Cumulina the mouse possible, but the achievements of Gurdon (and Briggs and King) now form the basis for the future potential use of human stem cells to cure a host of debilitating diseases: from Alzheimer's to Zollinger-Ellison syndrome.