The announcement on 8 October 2012 that the Nobel Prize for Physiology or Medicine had been awarded jointly to Professor Sir John Gurdon and Professor Shinya Yamanaka for their work on changing differentiated adult cells into pluripotent stem cells\(^1\), \(^2\) reminded me of some treasured memories from the distant past, and encouraged some great hopes for the future.

**Oxford and Geneva**

On graduating at Oxford in 1960, I was invited to stay in the Department of Zoology and Comparative Anatomy and join Michael Fischberg’s experimental embryology research group. One of the established members of the team was John Gurdon, who had developed a method for cloning *Xenopus laevis*, the South African clawed frog, by transferring nuclei from early embryonic cells into enucleated eggs.

As they differentiate, the somatic (body) cells of some invertebrates (such as copepod crustaceans and roundworm nematodes) lose genetic material in ways which can be seen at the microscopic level, by a process known as chromosome diminution\(^3\) or chromosome elimination\(^4\), whereas the full genetic complement is retained in the germ line (the cells that give rise to eggs or sperm for sexual reproduction). Another of Fischberg’s students, Cuillin Bantock, worked on chromosome elimination in a dipteran insect, the gall midge (*Mayetiola destructor*). In some elegant experiments, he showed that, as the fertilised eggs of the gall midge divide to form an early embryo, the nuclei which will form the germ line migrate into a special cytoplasm at one end of the egg, which protects them from the chromosome diminution which befalls the nuclei which will form the somatic cells. If this “germ plasm” is damaged by exposure to ultraviolet light, the resulting gall midges are sterile, as chromosome diminution has occurred in all their cells.\(^5\)

Amphibian eggs also have a similar germ plasm with a similar chemical composition, and ultraviolet irradiation of the part of the egg cytoplasm in which it is located, results in total or partial sterility of the animals which develop from eggs treated in this way. Hence, like the Americans, Robert Briggs and Thomas King, who had pioneered the original nuclear transplantation technique in the Northern leopard frog, *Rana pipiens*, Fischberg wondered whether a diminution or elimination process, analogous to that which occurs in invertebrates, also occurred in higher animals, albeit at a sub-microscopic level, and whether the transplantation of nuclei from adult cells would reveal deficiencies which reflected the loss of genetic material as they differentiated to become uniquely specialised types of somatic cells.

Fischberg’s ideas were spelled out in an article in *Scientific American*, co-authored with another member of the group, Antonie Blackler, where they concluded that “the nuclear changes due to natural differentiation” are “stable, heritable and apparently irreversible”.\(^5\) However, Gurdon threw a spanner into the works of that hypothesis, by showing that nuclei transferred from functioning intestinal epithelium cells from *Xenopus* larvae into enucleated eggs, developed into adult frogs.\(^6\), \(^7\)

At about that time, Gurdon went to be a postdoctoral fellow in California, and Fischberg left Oxford to become Professor of Zoology in the University of Geneva, accompanied by Blackler, two graduate students (Kate Hammer and me), and several hundred frogs. We took with us the *Xenopus* produced from the larval intestinal cell nuclei by Gurdon, and one of our Swiss associates, Vreni Uehlinger, showed that the frogs were fertile and could produce normal offspring.\(^8\)

The aim of my own DPhil project was to transplant nuclei from malignant cancer cells into enucleated eggs, to see what might be revealed about them. The problem with this was that no cancers had previously been found in *Xenopus*, and, even if we succeeded in finding some, no markers were known that could be used to distinguish cancer cells from the normal cells that would also be found in the tumours. I did find a