

# Induced pluripotent stem cells

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The discovery in 2006 by Shinya Yamanaka, building on the earlier work of John Gurdon, that certain types of specialised adult cells could be reprogrammed using genetic manipulation to become embryonic-like iPSCs was a major breakthrough. Using retroviral or lentiviral transfection to introduce a combination of transcription factors (OCT3/4, SOX2 and either Kruppel-like factor and C-MYC [together designated the OSKM reprogramming factors] or NANOG and LIN28), it was shown that specialised somatic cells can be reprogrammed to become stem cells. Moreover, iPSCs proliferate in vitro efficiently as ESCs and are pluripotent, thereby circumventing concerns about the use of human embryos. Importantly, the development of iPSCs also means that, at least in principle, an intended recipient of stem cell therapy can themselves provide James Thomson, b. 1938, Professor and Director of Regenerative Biology, Morgridge Institute for Research, University of Wisconsin-Madison, Madison, WI, USA. Shinya Yamanaka, b. 1962, Japanese stem cell researcher, winner of the Nobel Prize in Physiology or Medicine in 2012. Sir John Bertrand Gurdon, b. 1933, British developmental biologist, winner of the Nobel Prize in Physiology or Medicine in 2012 with Shinya Yamanaka. that can then be directed to differentiate into the desired specialised cell type for therapy; because such cells would be autologous they would not provoke an immunological rejection response (Figure 4.4). Alternatively, iPSCs could be obtained from a number of volunteer donors selected on the basis of their HLA type and stored to create a national or international tissue bank of iPSCs. Lines of iPSCs could then be chosen from the bank to provide a fully or partially matched cell transplant for recipients, eliminating or reducing the need for immunosuppression to prevent immunological rejection. One of the problems of reprogramming somatic cells to become iPSCs using retroviruses is that genomic integration of the virus may lead to activation of oncogenic genes, causing tumorigenesis. To reduce this risk, non-retroviral vectors have been used (such as adenovirus and Sendai virus vectors, which do not insert their own genes into the host cell genome) or plasmids, episomal vectors and synthetic RNA. There has also been much recent progress in identifying combinations of small molecules, growth factors and chemicals that mimic the effect of viral transfection with transcription factors and obviate the need for viral vectors altogether. The production process from sourcing cells (e.g. skin fibroblasts or peripheral blood mononuclear cells) to obtaining an adequate number of validated iPSCs may take several weeks.

- Induced pluripotent stem cells

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