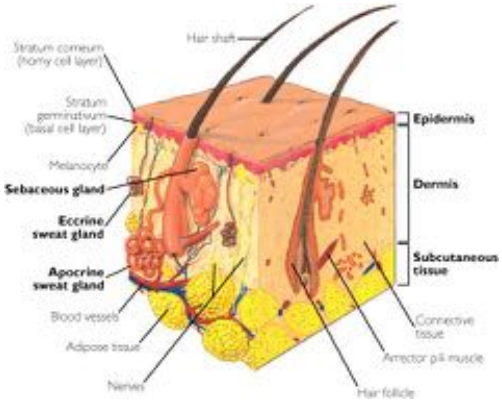
Induced Pluripotent Stem Cell Cultures

Background information

Stem cells are the body's foundation cells; when they receive the correct signals they form every cell type and tissue within the body. Human stem cell research was hampered by stem cell harvest because, originally, pluripotent (meaning they can become any cell/tissue) stem cells were only known to exist in developing embryos. Understandably, harvest of human embryos for scientific experimentation is an ethically fraught area. Over the last few years the human stem cell field has been completely changed by the development of *induced* pluripotent stem cells. Induced pluripotent stem cells, or iPS cells as they are often referred to, are made by taking dermal fibroblasts from a scratch of skin tissue. Ethically this is a highly preferable procedure as the donor consents to the removal of the tissue. It also has the distinct advantage that cells can be taken from donors with known genetic mutations, such as those that cause the prion diseases CJD, GSS or FFI.



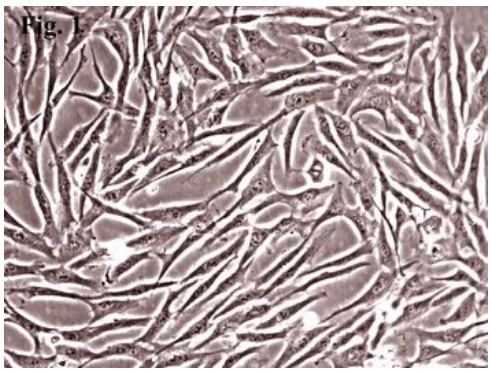
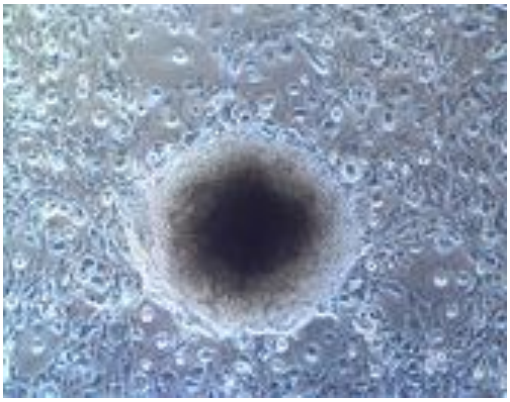


Fig. 1.

The skin fibroblasts are cultured in a liquid environment that mimics the tissue fluid that would normally feed them. Here, they are then exposed to a carefully controlled series of hormones and genetic modification that "reverse engineers" them back to the cells that originally made them, consequently the formation of pluripotent stem cells is induced. Once induced, the iPS cells can be grown in liquid culture indefinitely, provided they are carefully looked after using very precise growth conditions and quality control to ensure no genetic changes can occur, such as those that might cause cancer in a human.



As the iPS cells have the ability to differentiate into any cell type, they can be exposed to a different set of hormones that re-programs them to become neural stem cells. Neural stem cells differ from pluripotent stem cells as they are now committed to only forming new cells of neuronal lineages. By modulating the hormones in the liquid culture the neural stem cells can now be stimulated to form neurones or other brain cells on demand. Using even more refined culture conditions the formation of the new neurones can also be structured, with the new tissue assuming the features of functional human cortex. This technology therefore represents the closest experimental model of a human brain under ethically appropriate circumstances. For prion disease research the benefits are incredible; the processes causing/allowing spread

of the disease agent, the cellular changes that cause the neurones to dysfunction and die, and the efficacy of therapeutic compounds will now be able to be tested in a genuine human model of disease. The process of engineering skin to neuronal cells is shown pictorially below.

Genetic reprogramming and hormone treatment

Fibroblasts iPS cell Neurones