Genetically reprogrammed skin cells bypassing the need for embryonic stem cells – A ray of hope for ethical science!!

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Not yet assigned a definite role in the human body, stem cells are known to be mere 'blank slates' proposed to treat various diseases that require an enormous repair system like diabetes, Parkinson's, Alzheimer's and several neuro-motor disorders. Before James Thompson brought stem cells to the scientific world in 1998, the embryonic stem cells (ESCs) were just a researcher's dream and now they are a political hot potato. Due to the fact that these cells could only be taken from human embryos, the funding for research in this area has been restricted and banned in several parts of the world, including the United States. An alternative approach with adult stem cell research has been therefore suggested to circumvent the morally and legally vexing issues in ESC research.

Recently, in the last quarter of 2007, a new approach towards stem cells therapy that skirts some of the major ethical and practical problems, has been realized and announced by two scientific groups, one led by the 'pioneer of stem cells'. James Thomson at the University of Wisconsin (USA), and the other led by Shinya Yamanaka at the University of Kyoto (Japan). This method neither involves cloning nor destruction of human embryos which is regarded as immoral and unethical, a major hindrance for the proposed therapeutic cloning. The groundbreaking research[1,2] instead claims to have achieved success in tinkering the skin cells into the 'master cells' that are as versatile as the stem cells derived from the human embryo.

Once the method is perfected and practised, skin cells from various patients with conditions like diabetes, spinal cord paralysis, etc. can be most effectively turned into stem cells. These could then be grown into 'spare-part machinery' tissue and transplanted without fear of any rejection by the body's immune system, because the cells are genetically identical.

With his initial experiments done on mice in 2006, Yamanaka had achieved reprogramming of skin cells. This was done by replacing four genes/transcription factors: *Oct3/4* (also called *Pou5f1*), *Sox2*, *Klf4* and *c-Myc* in skin cells (dermal fibroblasts), followed by subsequent selection for *Fbx15* (also called *Fbxo15*) expression using a viral vector for induction of these somatic cells to stem cells[3].

In 2007, Yamanaka's team used the same technique to reprogramme skin cells by utilizing adult human fibroblasts from the facial skin of a woman aged 36 years and connective tissue of a man aged 69 years. Ten novel lines from 50,000 skin cells were generated as a result of this exercise[1].

Thompson, on the other hand, utilized foreskin of a newborn and foetal skin cells to generate the lines at a lower success rate, i.e. one line out of 10,000 skin cells, using a separate set of genes (*Oct3/4*, *Sox2*, *Nanog* and *Lin28*) for induction of skin cells to stem cells[2].

The fear of delay in the progress of stem cell therapy sparked from the fraudulent custom-made, patient-specific lines[4–6] from 'bench to bedside', has been somewhat lessened by this research. Both the groups are confident of establishing promising *iPS* (induced pluripotent stem cells) and disease-specific *iPS* and effectively reprogramming them into cardiac, liver or neural cells, which could be specifically useful for understanding the disease mechanism, and screening of safe drugs and, finally, for successful transplantation. This is solely because of the fact that the induced cells can do what the ESCs do. That is, the induced pluripotent human stem cells have normal karyotypes, express telomerase activity, express cell-surface markers and also the genes that characterize human ESCs, and maintain the developmental potential to differentiate into advanced derivatives of all three primary germ layers (*in vitro* and *in vivo*; teratoma formation). However, both the research groups agree that ESC research should continue in parallel, to ensure that the induced cells indeed behave in the same way as their embryonic counterparts. In addition, caution will be required to combat the side effects of utilizing retroviruses, which have been used as a carrier vehicle for genes in these experiments. The new type of stem cells were generated by manipulating genes with retroviruses, which might themselves induce mutations that could cause cancer, and one of the altered genes is known to be implicated in some tumours. This only means that more research will be needed before the induced cells can be actually used for clinical applications and therapy, but they could have immediate utility for investigating genetic diseases. Having said that, most of the stem-cell specialists now believe that this novel approach is going to pave a promising way to research into the genetic causes of disorders and in the search for therapies not only for such diseases, but also for repairing tissues damaged in numerous other ways. With this leap forward in stem cell research, we can now at least be sure of what it takes to 'tip the balance' between somatic cells and the so called 'blank slates', stem cells. It is just a set of few 'defined genetic factors'. A 'masterpiece of science' indeed!

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