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Focus
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The promise of Induced Pluripotent Stem Cells (Ips Cells)

Role of stem cells (SC)

- **Organism growth:** a single cell, the zygote, constructs an adult made up of 100,000 billion cells broken down into over 200 specialised tissues.
- **Replacement of used cells:** every year, an adult loses and replaces the equivalent of his/her body weight.

Stem cell division

By means of asymmetric mitosis, one stem cell produces:
- One identical cell ensuring self-renewal and
- One cell involved in a differentiation process.

SC differentiation level

There are four types of stem cells
- **Totipotent SC:** ranging from zygotes to 8-cell embryos; each of these totipotent cells is capable of *generating an organism.*
- **Pluripotent SC:** the 100 to 200 embryo cells at the blastocyst stage are capable of producing *all the tissues* in an organism.
- **Multipotent SC:** produce all the cell lines for a *specific tissue.* (For example, a haematopoietic stem cell will produce red blood cells, platelets, leukocytes, etc.)
- **Unipotent SC:** produce all the cells from *a specific line* (for example: an erythroblastic stem cell will only produce red blood cells and not platelets or leukocytes).

Embryonic stem cells (ESC)

These *pluripotent* cells are cultured from a 5-6 day old embryo (*blastocyst*).

Embryo obtained by IVF

Not used by the couple, or deemed to be of insufficient quality to be implanted, or created solely for research purposes.

Embryo obtained by cloning

Insertion of a differentiated cell nucleus into an enucleated egg cell of the same species: performed since 1997 (Dolly the sheep) in some animal species; very difficult for the human species (two lines in the United States in 2008).

Embryo obtained using other techniques

Parthenogenesis (doubling of the haploid genome of an egg cell. Insertion of a human nucleus into an enucleated rabbit or cow egg cell (cybrid)).

Embryonic cell production and use

- This poses **technical problems:** allograft histocompatibility; specific "therapeutic" human cloning difficulties
- And **ethical problems:** legislation on the matter differs greatly from country to country; research using ES cells is authorised in Great Britain, Belgium and Sweden, prohibited in Austria and Poland, and strictly monitored in France.

"Adult" stem cells

These cells are present in all the tissues of an organism, throughout the life of the organism and are multi- or unipotent

Haematopoietic SC

These were the first stem cells used with bone marrow transplants; cytokines make it possible to simulate a specific line: erythropoietin for red blood cells, G-CSF for granulocytes, etc. They are used in gene therapy to treat some genetic diseases.

Skin and mucosal SC

Used in autologous skin grafts and trachea transplants (bronchial epithelium).

Nervous system SC

Limited neuron renewal takes place throughout the life of an organism.

Liver SC

These cells make it possible to graft a liver lobe removed from a live donor. The donor's liver is renewed and the graft regenerates a whole liver in the patient.

Cord blood SC

These cells are used in allografts from samples stored in banks. There are only 6 public banks in France, which is insufficient to meet demand. As a result, it is necessary to purchase cord blood cells from private or public/private international banks.

Induced pluripotent stem cells (iPS cells)

In August 2006, S. Yamanaka and K. Takahashi (U. of Kyoto) published their technique for transforming differentiated cells into induced pluripotent stem cells. They introduced four genes (Oct4, Sox2, Klf4 and c-Myc), selected from 24 genes involved in embryonic cell pluripotency, into mouse fibroblasts.

In 2007, the same Japanese team and James Thomson's team in the U.S. transformed human fibroblasts into pluripotent cells.

Many researchers around the world devote themselves to studying induced pluripotent stem cells:

To improve the efficiency of their production

And the quality of the iPS cells produced, particularly to eliminate the risk of the development of cancer.

To explore their use in human disease

- Study models of numerous diseases (iPS cell lines supplied to researchers by Harvard University, etc.).
- Pharmacological toxicity and therapeutic effect trials.
- Ex vivo repair of a mutated gene (human trials in progress).

Conclusion

iPS cells versus ES cells: iPS do not pose the ethical problems of human embryonic cells, they are autologous and the adult cells processed are easy to obtain (pulling out one hair may be enough!). The enthusiasm they arouse is understandable but the follow-up available is insufficient to assess their lifetime and their functional quality. All research methods on stem cells, whether they are embryonic, adult or induced, should remain operational.