

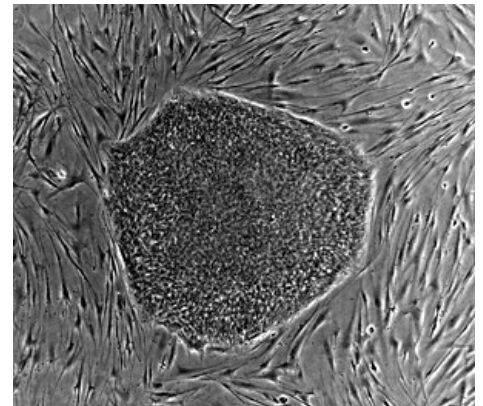
Stem cells

Stem cells (SC) are cells capable of repairing damaged or worn parts and maintaining homeostasis . Cells with an indefinite ability to self-renew, whose mitotic division produces one cell identical to the parent (to maintain a pool of stem cells) and a cell that can give rise to at least one highly differentiated cell type.

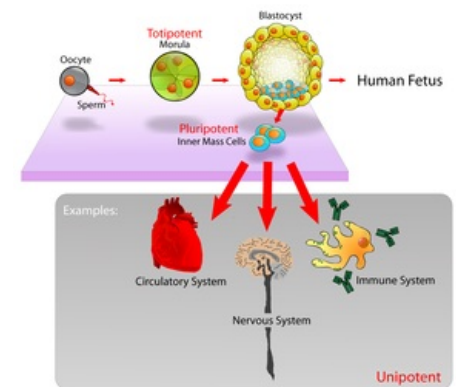
1. undergoes multiple mitotic divisions to regenerate;
2. daughter cells differentiate into more than one cell type (including some ASCs);
3. during transplantation , they are capable of functional resettlement of the tissue of their origin;
4. in vivo contribute to the formation of differentiated cell populations (even without damage).

Basic types of SC

1. **Embryonic carcinoma cells ECC** - from testicular tumors (heteroploid);
2. **embryonic stem cells ESC** - from the inner cell mass of preimplantation embryos (euploid);
3. **EGC embryonic germ cells** - from germ cells of postimplantation embryos (euploid);
4. **umbilical cord blood stem cells** - umbilical cord blood contains several types of stem cells (hematopoietic, mesenchymal)
5. **amniotic fluid stem cells AFC** - from amniotic fluid (euploid);
6. **adult (organ) ASC stem cells** - from adult tissues (euploid) (eg HSC, NSC);
7. **induced iPSC stem cells** - with gene manipulations (insertion of 3-4 genes - Oct-3 and 4, SOX genes; Klf and Myc genes, Nanog, LIN28) of modified somatic cells (fibroblasts), similar to ESC.



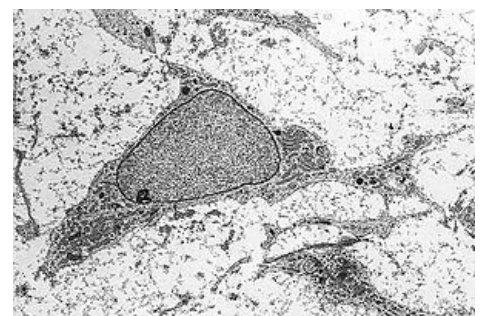
Shluk lidských embryonálních kmenových buněk



Diferenciace buněk

Distribution according to the fate of SC

1. **Totipotent SC** or omnipotent SC can create a whole new individual (embryoblast and trophoblast) - eg zygote 2-cell mouse blastomere, 4-8-cell human blastomere.
2. **Pluripotent SCs** can be specified in any cell of the human body. They are not able to create a new individual (ie they cannot form a trophoblast) - first described in teratocarcinomas (= gonadal tumors containing cells of all 3 primary germ leaves arising from ECC). Stem cells can be classified according to when and where they formed during the development of the organism and how useful they are. Pluripotent stem cells can be the source of all cell types . Embryonic stem cells are best *characterized*= ES) mouse and human. These are pluripotent cell lines derived from undifferentiated embryonic cells, which are characterized by almost unlimited self-renewal in undifferentiated form and a very broad differentiating ability (pluripotency). Thus, they have similar properties to undifferentiated embryonic germ cells (EGC). Candidates of both lines (ES and EG) from human embryo blastocysts or embryonic gonads can differentiate into a number of different somatic cell types. Human pluripotent stem cells are a potential source of regenerationdifferentiated cells in the replacement of damaged or diseased tissues by cell transplantation. Embryonic stem cells, which are located on the inner part of the blastocyst, are fully pluripotent and can proliferate indefinitely in an undifferentiated state, or differentiate into all cell variants in vivo and many in vitro.
3. **Multipotent SCs** give rise to more than 1 cell type (HSC, NSC). Stem cells from adult tissues (or embryos from later stages of development) are more limited in their ability to grow and differentiate . E.g. Hematopoietic stem cells can produce all types of blood elements "in vivo", but they grow little in cell culture and are not suitable for producing cells from other tissues. Stem cells of later stages of development occur in most organs - hematopoietic , gastrointestinal, epidermal, liver, mesenchymal or nerve stem cells. Until recently, it was thought that these multipotent progenitor cells(MAPC) can only differentiate into cells of the same cell line (tissue specific). However, it has been shown that after transplantation of bone marrow or enriched hematopoietic stem cells, skeletal muscle or myocardial, endothelial myoblasts, as well as epithelium of the lungs, intestine, biliary tract and liver, skin or neuroectoderm , could be detected . Other experiments have shown that nerve or muscle stem cells can differentiate into hematopoietic cells. In the experiment, it was shown that MAPCs require the environment of embryonic stem cells (ie the environment of blastocysts) to apply their plasticity (ie multipotency in differentiation and multiplication).) with the expression of their genetic markers: Oct-4, Rex-1, SSEA-1. This seems promising for the treatment of degenerative and congenital diseases.



Mesenchymální kmenová buňka

4. **Oligopotent SCs** can differentiate into multiple cell types. (Lymphoid stem cells - T and B lymphocytes, NK)
5. **Unipotent (progenitor cells - not stem)** give rise to one cell type (spermatogonia). Use for therapeutic purposes (infertility treatment).

Acquisition of therapeutic SC

ESCs are prepared from early human embryos after in vitro fertilization

- Eggs are routinely fertilized in laboratory conditions - some are placed in the mother's uterus, others are frozen and stored in liquid nitrogen, most of which are then destroyed;
- a potential resource for research or therapy in major diseases;
- criticism - the destruction of future human life.

ESC cultured from human embryonic primordial cells

- Undifferentiated cells that would develop into oocytes or sperm in the gonads;
- the source is fetuses after abortion.

ESC as a product of therapeutic cloning

- Redifferentiation of readily available patient cells into those needed for healing;
- creating an embryo from a somatic cell of the human body;
- the patient is a specialized somatic cell (from the oral mucosa, skin), its nucleus is inserted into the enucleated oocyte and the resulting embryo is used to produce ESCs and cells for cell therapy;
- advantage - the genetic identity of the patient and the ESC, the immune system accepts the transplanted cell.

iPSCs caused by gene mutations

- Clinical testing, no ethical issues.

Bone marrow ASC (1 of 10 10)

- Plasticity = the ability of tissue-specific SCs to acquire tissue cell types of different origins;
- possibility of use as so-called autologous grafts.

Alternative pathways for cell therapy

1. Creation of universally acceptable SCs;
2. creating an extensive set of human ESCs among which to find an SC for any patient.

Links

related articles

- Germ cells

Reference

1. KLABUSAY, Martin. Stem cells in cardiology: past, present and future of cellular therapy of damaged myocardium. *Internal medicine for practice* [online] . 2009, vol. 11, vol. 10, p. 453, also available from < <http://www.solen.cz/pdfs/int/2009/10/05.pdf> >. ISSN 1803-5256.

References

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- MASOPUST, Jaroslav, et al. *Cell pathobiochemistry*. 1st edition. Prague: Charles University, 2nd Faculty of Medicine, 2003. 344 pp. 79. ISBN 80-239-1011-6 .