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BRIEFLY ON STEM CELLS AND REGENERATIVE MEDICINE FOR PRACTICE

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Stem cells can be used in cellular therapy. This happened in order to replace damaged cells or having aim to regenerate organs. The definition of stem cells can be extended. From this point of view, we can mention taking in consideration the idea in which it is known that these cells form the base of the building body. More than, we can mention, that stem cells are characterized by two knowing properties – namely differentiation and self-renewal. Based on the observation that differentiation of adult stem cells into specific derivatives can be controlled by laboratory techniques, it is anticipated that adult stem cells may become the basis of therapies for many, and various types of medical conditions. Taking on stem cells, regenerative medicine (RM) it is known as being one of the hottest topics in biotechnology nowadays.

From this purpose, stem cells can be used in regenerative medicine (RM). The principles of regeneration are found in different types of cultures, from long time ago, centuries etc.

Key words: diagnostic, stem cells, human body, transplantations, regenerative medicine.

It is known a few about global anticipation for stem cell-based therapies that are safe and effective.

So, various pre-clinical studies present encouraging results on the therapeutic potential of specific cell types including they tissue which who derived stem cells.[1]

1.a Stem cells. As a definition, stem cells are a population of undifferentiated cells characterized by the ability to extensively proliferate namely self-renewal., Usually starting from a single cell namely *clona* and differentiate into other different types of cells and tissue namely, *potent* cells. There are a lot of sources of stem cells with varying potencies. Pluripotent cells are embryonic stem cells. This cells derived from the inner cell mass of the embryo and induced pluripotent cells. Also there are formed the following reprogramming of somatic cells. Pluripotent cells can differentiate into tissue from all endoderm, mesoderm, and ectoderm [2].

Multipotent stem cells may differentiate into tissue derived from mesenchymal stem cells. Mesenchymal stem cells form cartilage, bone, adipose tissue.

Beside using stem cells in cellular therapy, as we mention previously, In addition, stem cells have expanded our understanding of development as well as the pathogenesis of specific disease. In this context, cell lines from specific pathology, can also be propagated and used in drug development [3, 4].

Stem cells are unspecialized cells that can give rise to specialized cells, through the differentiation process. Also, stem cells are characterized by two properties namely differentiation and selfrenewal [5].

The definition of stem cells can be extended, in the idea in which it is known that these cells form the base of the building body. From this point of view, stem cells are those that create tissues and organs, blood and immune system. Stem cells are divided into two categories, namely embryonic and adult [6].

Embryonic stem cells are only present in the early embryo and eventually give rise to all cells that they give constitute a whole organism. The advantage of embryonic stem cells for regenerative medicine is that they can be used for any type of tissue. It also should be noted that embryonic stem cells are harvested from embryos in early stages of development. However embryonic stem cells as such are used in a limited way, since they are tumorigenic in vivo [7].

Adult stem cells are present in the body after birth. Although it has been hypothesized that adult stem cells can only turn into tissue cells, some studies suggest that they can also generate cells from other tissues, in which case we are talking about property called plasticity or transdifferentiation of these cells. Adult stem cells are harvested from adult tissues, particularly cord blood, peripheral blood, and bone marrow, as wells form such tissues as fat, skin, and skeletal striate muscle [8].

If most cells in the human body can give rise, only cells of the same type and in contrast, the stem cells are unique in being able to give rise to many types of cells.

According to current hypotheses a single adult stem cell should be capable of giving rise to a clone of cells that are genetically identical. It is envisaged that further studies will show the possibility that a stem cell can produce a clone of cells in cell culture and also to prove that a population of stem cells purified able to repopulate a certain type of tissue after transplantation [9].

In this context, it has been shown that adult stem cells can be used for transplantations. In particular hematopoietic stem cells from bone marrow are frequently used for treatment of blood diseases. In order to identify adult stem cells several methods can be used. One is aimed at labeling the cells in a living tissue with molecular markers and subsequently determines the specialized cells that they generate. The second method relates on the extraction of cells from a living animal body, followed by labeling the cell culture and, finally, carrying out a transplantation of these cells in an animal experiment, in order to determine the cells to repopulate the tissue of origin [10, 11].

Following the isolation of stem cells, they can be cultured in vitro and treated with growth factors or transfected with new genes, to determine the types of cells that may become differentiated. Given the importance of involving adult stem cells in producing new cell types and their involvement in transplants, and the resulting use of adult stem cells for therapeutic purposes, the main potential of adult stem cells is in the field of regenerative medicine. Based on the observation that differentiation of adult stem cells into specific derivatives can be controlled by laboratory techniques, it is anticipated that adult stem cells may become the basis of therapies for many, and various types of medical conditions [12, 13].

Compared to adult stem cells, embryonic stem cells have the potential that they can give rise to all the hundreds of cell types in the human body. In this context, it can be exemplified by saying that while a blood stem cell can only give rise to blood, embryonic stem cell can make blood, bones, skin, brain, and others. Additionally, embryonic stem cells are programmed by nature in order to build tissues and organs, while adult stem cells are not programmed by nature, as described above. From this point of view it is estimated that embryonic stem cells have a greater natural ability in repairing diseased organs [14, 15].

2a. Stem cell classification and practicum data.

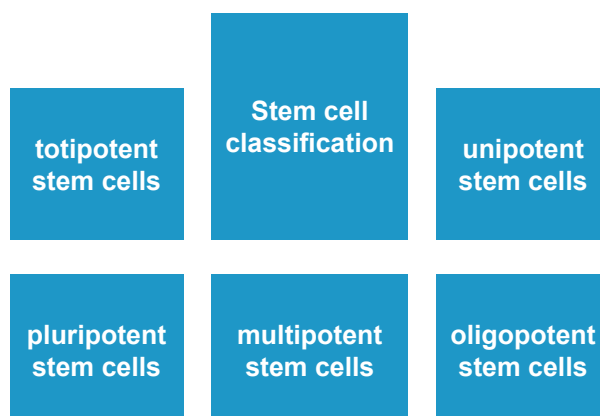


Figure 1 – Stem cell classification

Embryonic stem cells are obtained from left-over embryos from fertility treatments and are active only a few days. These cells are obtained usually in a vessel in specialized laboratories, which otherwise would have been discarded. Concerned by news on stem cells, researchers were attracted by stem cells called «iPS» cells. Results of studies have shown that this type of cell had similar properties as, but are not derived from an embryo. From this point of view, there are ethical issues related using of iPS stem cells. Additionally, it has to be noted, that iPS cells can be made from the patient's own cells. Therefore, it seems that iPS cells could be given back to a patient without risk of an immune rejection, so in this case transplantation would not give rise to graft rejection. This is relevant given the various reported cases of deaths occurring due to stem cell therapies. This obliges open collaboration between patient and medical staff involved in transplantation, whereby decisions are made only by consent and by respecting the principles of medical ethics [16, 17].

The idea of using stem cells for treatment of various pathological conditions, is exemplified by the transplantation of stem cells from a patient who suffered from a heart attack. In this case, the stem cell therapy would be applied to repair the part of the heart that has undergone structural and functional changes due to a myocardial infarction. Birth provides an opportunity to help families storing umbilical cord blood of the newborn. From this point of view it should be noted that patients who undergo a transplantation, recovered better when they receive stem cells from a related donor than from unrelated one. In this context, most ongoing studies are oriented towards regenerative medicine, with the aim to repair the body of the patient with their own stem cells. Particularly, children who can be treated with their own stem cells from stored umbilical cord

blood will have easy access to this type of therapies, also late in life [18].

Good to know a few about history of this study purpose, about stem cells and regenerative medicine. So from centuries, it is known the idea of regeneration that first started in myths and legends.

Regenerative medicine is acknowledged that their research performance has been somewhat disappointing. Scientists and researchers, look at how the historical development of the regenerative medicine scientific field has changed the translational strategy. This is then linked to a discussion of the preclinical and postclinical challenges, which offer insights for the future progression of regenerative medicine field. [19]

3a. Historical data. In history, in 1954, Dr. Joseph Murray performed the first transplant in a human body. He practice the transferred a kidney from one identical twin to another. This surgical procedure, had a great impact on medical history. This medical surgical point, was the culmination of > 50 years of transplantation and grafting research. Chronic pathologies, were on the rise and also the associated process of tissue degeneration was becoming evident. More than, the available clinical interventions were capable of treating symptoms, for curing the disease. Next point, once a loss of tissue function occurred, it was nearly impossible to regain.

In the 1960s and 1970s created urgency for disruptive technologies and led to the creation of tissue engineering (TE) [20].

4a. Briefly on regenerative medicine and tissue engineering. So, tissue engineering (TE) uses a combination of technological approaches that moves it in traditional transplantation and replacement therapies.

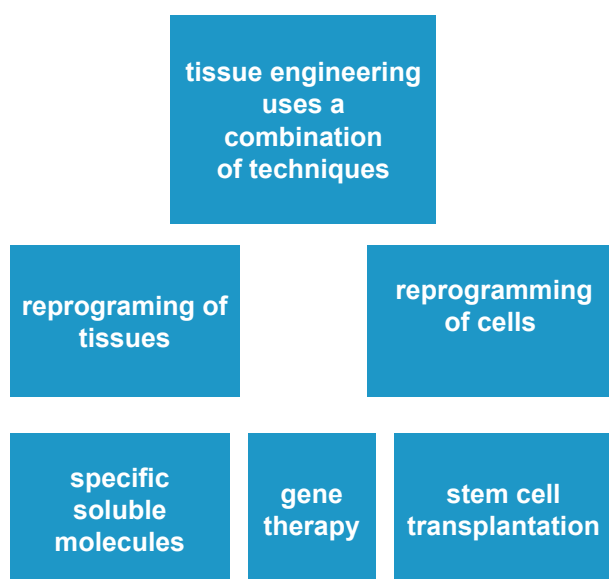


Figure 2 – Tissue engineering methods

Referring to regenerative medicine and tissue engineering, including stem cells use and also combining factors mentioned above, but also because researchers had been successfully keeping tissue alive *in vitro* and understanding the biological processes involved in regeneration and degeneration, possible therapeutic outcomes came into fruition [21].

The comparability of stem cell lines from different individuals is needed for iPSC lines. The impact is to be used in therapeutics – critical quality procedures. Viral testing is an important point. In this context, when assessing the quality of stem cells, all tests for harmful human adventitious agents must be performed. Bacterial or fungal sterility tests can be divided into specific lines, as culture- or broth-based tests [22]. Single nucleotide polymorphism array is a procedure using for typeing of DNA microarray. This procedure detects population polymorphisms by enabling the detection of subchromosomal changes. Also is a procedure for detection of the copy-neutral loss of heterozygosity. Finally, we can mention about DNA microarray technique, that is knowing as well as an indication of cellular transformation [23].

Flow cytometry is a modern technique. This method that use light, in practicum is perform to count and to detect, profile cells in a heterogeneous fluid mixture.

Phenotypic pluripotency assay recognizing nondifferentiated cells with a great success in stem cell therapy [24].

Quality control can be achieved by using epigenetic analysis as histone modification or DNA methylation.

Karyotype establish. In this scientific direction, a long-term culture of hESCs can accumulate culture-driven mutations. Because of that, it is nice, to give attention to genomic integrity [25].

CONCLUSION

In conclusion, the scientific study of stem cells and their applications in the treatment of various human diseases will remain the subject of intense study, today and in the future. Corroborating this, regenerative medicine is such an active field that will have considerable implications for human pathologies.

Because the regenerative medicine field of research, with applicability in medical practice, is essentially comprised of ideas on cell renewal and tissue healing. Nowadays, scientists look attention at the influence of regenerative medicine, using stem cells, in routine medical practice for treat and for cure.

REFERENCES

1 Li M., Ma J., Gao Y., Yang L. Cell sheet technology: a promising strategy in regenerative medicine. *Cytotherapy*. 2019; 21(1): 3-16.

- 2 Weinberg R. S. Transfusion medicine and hemostasis. Elsevier; 2019. Overview of cellular therapy; pp. 505-512.
- 3 Mahla R. S. Stem cells applications in regenerative medicine and disease therapeutics. *Int J Cell Biol.* 2016; 2016: 6940283.
- 4 Barker C. F. & Markmann, J.F. Historical overview of transplantation. *Cold Spring Harb. Perspect. Med.* 3, 1-18 (2013).
- 5 Sampogna G., Guraya S.Y. & Forgiione, A. Regenerative medicine: historical roots and potential strategies in modern medicine. *J. Microsc. Ultrastruct.* 3, 101-107 (2015).
- 6 Slingerland A.S., Smits, A.I.P.M. & Bouten, C.V.C. Then and now: hypes and hopes of regenerative medicine. *Trends Biotechnol.* 31, 121–123 (2013).
- 7 Park IH, Zhao R, West JA, et al. Reprogramming of human somatic cells to pluripotency with defined factors. *Nature.* 2008;451(7175):141–6.
- 8 Terzic A., Pfenning, M.A., Gores, G.J. & Harper, C.M. Jr. Regenerative medicine build-out. *Stem Cells Transl. Med.* 4, 1373–1379 (2015).
- 9 Kaul, H. & Ventikos, Y. On the genealogy of tissue engineering and regenerative medicine. *Tissue Eng. Part B Rev.* 21, 203–217 (2015).
- 10 Broughton K.M. & Sussman M.A. Enhancement strategies for cardiac regenerative cell therapy. *Circ. Res.* 123, 177–187 (2018).
- 11 Allickson J. G. Emerging translation of regenerative therapies. *Clin. Pharmacol. Ther.* 101, 28–30 (2017).
- 12 Heathman T. R., Nienow, A.W., McCall M.J., Coopman K., Kara, B. & Hewitt, C. J. The translation of cell-based therapies: clinical landscape and manufacturing challenges. *Regen. Med.* 10, 49–64 (2015).
- 13 Aoi T, Yae K, Nakagawa M, et al. Generation of pluripotent stem cells from adult mouse liver and stomach cells. *Science.* 2008 Epub ahead of print.
- 14 Mount N. M., Ward, S.J., Kefalas, P. & Hyllner, J. Cell-based therapy technology classifications and translational challenges. *Philos. Trans. R. Soc. B Biol. Sci.* 370, 20150017 (2015).
- 15 Yang L, Soonpaa MH, Adler ED, et al. Human cardiovascular progenitor cells develop from a KDR⁺ embryonic-stem-cell-derived population. *Nature.* 2008; 453(7194): 524
- 16 Nakagawa M, Koyanagi M, Tanabe K, et al. Generation of induced pluripotent stem cells without Myc from mouse and human fibroblasts. *Nature Biotech.* 2008; 26(1):101–106.
- 17 Smit F. E. & Dohmen, P. M. Cardiovascular tissue engineering: where we come from and where are we now? *Med. Sci. Monit. Basic Res.* 20, 1–3 (2014)
- 18 Wernig M, Zhao JP, Pruszak J, et al. Neurons derived from reprogrammed fibroblasts functionally integrate into the fetal brain and improve symptoms of rats with parkinson's disease. *Proc Natl Acad Sci USA.* 2008; 105(15):5856 – 61.
- 19 Greenfield JP, Ayuso-Sacido A, Schwartz TH, et al. Use of human neural tissue for the generation of progenitors. *Neurosurgery.* 2008; 62(1): 21–37.
- 20 Yamanaka S, Jinliang Li, Kania G, et al. Pluripotency of embryonic stem cells. *Cell Tissue Res.* 2008; 331: 5–22.
- 21 Ptaszek L.M., Mansour M., Ruskin J.N., Chien K.R. Towards regenerative therapy for cardiac disease. *Lancet.* 2012; 379 (9819): 933–942.
- 22 Li M., Ma J., Gao Y., Yang L. Cell sheet technology: a promising strategy in regenerative medicine. *Cytotherapy.* 2019; 21(1):3–16.
- 23 Weinberg R. S. Transfusion medicine and hemostasis. Elsevier; 2019. Overview of cellular therapy; pp. 505–512.
- 24 Mahla R.S. Stem cells applications in regenerative medicine and disease therapeutics. *Int J Cell Biol.* 2016; 2016: 6940283.
- 25 Kolios G., Moodley Y. Introduction to stem cells and regenerative medicine. *Respiration.* 2013; 85(1):3–10.

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КРАТКО О СТВОЛОВЫХ КЛЕТКАХ И РЕГЕНЕРАТИВНОЙ МЕДИЦИНЕ ДЛЯ ПРАКТИКИ

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Стволовые клетки можно использовать в клеточной терапии. Это необходимо для замены поврежденных клеток или с целью регенерации органов. Определение стволовых клеток можно расширить. С этой точки зрения мы можем упомянуть принятие во внимание идеи, согласно которой известно, что эти клетки образуют основу строительного материала. Более того, мы можем упомянуть, что стволовые клетки характеризуются двумя известными свойствами, а именно дифференцировкой и самообновлением. Основываясь на наблюдении, что дифференцировку взрослых стволовых клеток в специфические производные можно контролировать с помощью лабораторных методов, ожидается, что взрослые стволовые клетки могут стать основой для лечения многих и различных типов заболеваний.

Теоретическая и экспериментальная медицина

Регенеративная медицина базируется на использование стволовых, в настоящее время широко известна как одна из самых обсуждаемых тем в биотехнологии. В то же время ученые обращают внимание на влияние регенеративной медицины с использованием стволовых клеток в рутинной медицинской практике для лечения. С этой целью стволовые клетки можно использовать в регенеративной медицине. Принципы регенерации разных типов культур известны с давних времен. В конце 20 века возникла необходимость в высокоэффективных клеточных технологиях, что привело к созданию тканевой инженерии.

Ключевые слова: диагностика, стволовые клетки, организм человека, трансплантация, регенеративная медицина.

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ТӘЖІРІБЕ ҮШІН ДІҢ ЖАСУШАЛАРЫ ЖӘНЕ РЕГЕНЕРАТИВТІ МЕДИЦИНА ТУРАЛЫ ҚЫСҚАША ТАЛДАУ

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Дің жасушаларын жасушалық терапияда қолдануға болады Бұл зақымдалған жасушаларды ауыстыру немесе органдарды қалпына келтіру үшін қажет. Дің жасушаларының анықтамасын кеңейтуге болады. Осы тұрғыдан алғанда, дің жасушалары құрылыс материалының негізін құрайтыны белгілі деген идеяны ескере отырып айта аламыз. Сонымен қатар, дің жасушалары екі белгілі қасиетпен сипатталады, атап айтқанда дифференциация және өзін-өзі жаңарту. Ересектердің дің жасушаларының ерекше туындыларға дифференциациясын зертханалық әдістерді қолдану арқылы бақылауға болатынын байқауға сүйене отырып, ересек дің жасушалары көптеген және әртүрлі ауруларды емдеуге негіз болуы мүмкін деп болжанады. Дің жасушаларын қолдануға негізделген регенеративті медицина қазір биотехнологиядағы ең көп талқыланатын тақырыптардың бірі ретінде кеңінен танымал. Сонымен қатар, ғалымдар емдеу үшін әдеттегі медициналық тәжірибеде дің жасушаларын қолданатын регенеративті медицинаның әсеріне назар аударады. Осы мақсатта дің жасушаларын регенеративті медицинада қолдануға болады. Дақылдардың әртүрлі түрлерін қалпына келтіру принциптері ерте заманнан белгілі. 20 ғасырдың аяғында жоғары тиімді жасушалық технологияларға қажеттілік туындады, бұл тіндік инженерияны құруға әкелді.

Кілт сөздер: диагностика, дің жасушалары, адам ағзасы, трансплантация, регенеративті медицина.