ECRONICON OPEN ACCESS

EC DENTAL SCIENCE
Thematic Article

Stem Cells, The Current State of Researches on this Problem and the Main Directions of their Development. From Theory to Clinical Practice

Andrey Orlov[1]*, A S Grigiryan[2], I N Saburina[3], and A F Fidarov[4]

[1]*Educational Institute of Additional Professional Education MH RF, Russia*

[2]*Central Research Institute of Dentistry and Maxillofacial Surgery MH RF, Russia*

[3]*Research Institute of Pathophysiology and General Pathology RAMS, Russia*

[4]*Russian Medical Academy of Postgraduate Education, Russian MH, Moscow, Russia*

***Corresponding Author:** Andrey Orlov, Educational Institute of Additional Professional Education MH RF, Russia.

Received: March 06, 2017; **Published:** March 21, 2017

A famous Russian scientist, histologist and embryologist Maksimov A.A. first used the term stem cells in 1908 in his speech at an international hematologist's congress in Berlin. In his studies, he put forward an idea of derivation of hemapoetic cell from lymphocyte like cells.

Since than the doctrine of SC, their origin, functions and their place in vital processes of humans and animals has gained widespread currency and has been augmented by a great number of discoveries.

One of the most important milestones in SC doctrine evolution were the studies of Freedenstein and his school.

One cannot overestimate the importance of SC studies for medicine. Not incidentally, SC discovery was acknowledged the third event in order of importance in biology after duplex DNA decoding and the program «Human genome».

It is known that biological systems on levels including organismic, tissular and cellular are based on the principle of multiple guarding and compromises between economy and sufficient effectiveness of the function they perform which enables their optimal integral effectiveness.

Another example of mechanism of restriction and degrees of freedom in embryogenesis might be antagonistic relations of a range of genes on the stages of embryogenesis mentioned in the article by Saburina I.N. and Repin B.S.: In the course of gastrulation and formation of mesoderm, endoderm and ectoderm there happens an irreversible of loss of expression of canonic genes, takes place which control pluripotency of genome ESC: Oct 4, Nanog, FoxD3, Rex-1.

One of the adaptations of kinetics of SC division is asymmetrical distribution of cell lines in progeny cells that retain multipotency in cells, which undergo differentiation and therefor fall out of SC pool.

The phenomena of asymmetrical SC Division

Asymmetrical division of SC is an essential condition for healthy growth of organism of animals and humans. It is one of the most ancient adaptations with the help of which multicellular organisms are formed from zygote.

The same mechanism is present not only in higher organisms, but in more primitive genus such as Drosophila as well.

The formation of organs of multicellular organism is carried out by consecutive cycles of division of cell, some part of which retain multipotent potential, that is part of cells stay in SC pool, while the rest of cells start differentiating and thus loses multipotency.

Fatty tissue is a source of self-renewal of SC which retain this ability throughout their lifetime and not only maintain overall quantitative constancy and balance of a reserve of SC, but replenishing of populations of differentiated cells as well, which is of no less importance for maintaining homeostatic status of the organism.

Violation of this balance can lead to dire consequences. Thus, reduced release of stem cells from the process of asymmetric cell division can lead to tissular destruction and atrophic processes while hyperproduction of stem cell may cause cancer growth.

Stem cells of Drosophila were used as a classic model for the study of mechanisms of ADSC.

These studies conducted on the drosophila proved the existence of two mechanisms of asymmetric division of stem cells: genetically determined and characterized by localization within niches, in which the influence of the microenvironment is realized.

Mechanisms of asymmetric division was a studied-on Drosophila neuroblasts.

The first version of asymmetric division is implemented in two daughter cells that divide asymmetrically along the apical-basal axis, along with this, in the basal complex of neuroblast gene expression takes place: Numb, Miranda, Prospero which are responsible for asymmetric division. One of the daughter cells divides once again, and then transforms into a ganglia differentiated cell.

As for the second option of asymmetric division, the Drosophila male and female stem cells of germinal line serve as an example of ADSC, the former are controlled by external determinants, they are in a microenvironment that determines the characteristics of stem cells. This complex of microenvironment factors that determine the characteristics and behavior of stem cells is called a niche. Within the niche, there is a system of signals, which plays a crucial role in controlling SC behavior and in restriction of physiological expansion.

At the same time, it is indicated that the mechanisms of ADSC of vertebrates, might be more complex, therefore have certain peculiarities in comparison with more primitive organisms.

SC plasticity, its significant for the organism and mechanism of limits of expansion

First note, multipotent SC is some multiplication of types of cells, resulting from cell division and ultimately their differentiation. Therefore, the mesenchymal stem cells generate three types of tissue: adipose, bone and cartilage tissues. Until recently, it was about the limits of multipotency of SC adult organism, so the limits of multipotency is the main difference between SC multipotency of adult organism and SC pluripotency of embryo.

It was believed that unlike embryo pluripotency SC which are capable of giving rise to all types of tissues, SC of adult mammalian under normal conditions can differentiate only within their tissue belonging.

However, data received in recent decades shows the opposite, namely the plasticity of adult SC goes far beyond the tissue to which it belongs.

The development of new experimental strategy based on breeding SC form system of genetically determined dynamic relationships, inherent in ontogenesis of multicellular organisms including humans and animals, helped to reveal opportunities for reversion of phenotypic characteristics of the SC with their return lost plasticity.

Thus, the evidence was obtained of plasticity bone marrow SC, namely, the ability of hematopoietic bone marrow SC and mesenchymal bone marrow SC to trans differentiate.

In 1997 M. Eglitis and E. Mezey published data according to which the hematopoietic bone marrow SC of an adult mouse transplanted into the brain gave rise to glial cells.

In another study, the ability of cells derived from bone marrow stroma cells has been demonstrated to give a line of SC which differentiate into cells with neural phenotype manifested in the expression of mRNA, nestin, Enolase 2 and associated with the microtubule system of the cytoplasm protein 1b (MAP1b). Over time neurogenic activation of transcription factors, such as Engrailed-1 and Nurr 1 was observed in some cases.

Data confirming similar ability of skeletogenic human cells was also published by S. Shultz and P. Lucas.

Thus, results of studies in recent years have allowed to turn to the best practices in the development of protocols of regeneration of nerve cells including using cells derived from muscle tissue. Moreover, it was established that even heterologous cellular material could be effective. The introduction of human precursors in mice causes development of axonal regeneration in animals, with the participation of donor cells.

Special attention should be given to the data published in a number of articles on the epithelium-mesenchymal plasticity of multipotent mesenchymal stromal cells in normal and pathological conditions.

It was pointed out that the pursuit of phenotypic unifying cuts heterotopy scale and thereby plasticity phenomenon of adult SC genetically inherent in their ability to diversification, trans differentiation of SC associated with their histogenetic plasticity that can be played under certain conditions is hidden from researchers.

It is a very important point in terms of strategy, because it is the possibility to identify the phenotypic heterogeneity, which gives an idea of the phenomenon of SC plasticity, it allows to monitor and investigate the mesenchymal-epithelial conversion of adult SC.

From theory to practice

Introduction of new concepts was hampered by the emergence of data on complications, which involve systemic application of a cellular material obtained from adults and propagated *in vitro*, which will be discussed below.

Nonetheless in some areas very encouraging reports appeared, that indicate the effectiveness of use of adult SC as a method of realization of regenerative medicine strategies. So, it became known of the experience of the use of adult SC derived by the authors on the level of totipotency in the complex treatment of Parkinson's disease.

It was reported that SC injection was successfully used in the affected area in osteoarthritis.

In addition, there is data on the use of autologous SC of the bone marrow transplants that increased remitting effect of breast cancer treatment in cases where other therapies proved ineffective.

However, the use of adult SC, especially farmed on the level of pluripotency involves serious risks. The authors indicate that SC, which have acquired high levels of plasticity, are similar to tumor cells, in terms behaviour as well as pluripotency.

There are certain indications that the use of adult cells could pave the way for tumor genesis.

Bronchiolitis obliterans is a heavy and fairly common complication of systemic implantation of allogeneic hematopoietic SC.

Development and implementation of the concept of SC plasticity in dentistry and maxillofacial surgery

Perhaps, dentistry and Maxillofacial Surgery can be regarded one of the well-developed areas of practical application of cellular technologies.

Firstly, the tooth pulp tissue proved to be the best source of SC, which is characterized primarily by ease of preparation of the cell material, its viability and plasticity.

A number of studies indicate the prospects of this source of cells. Animal experiments have confirmed the researchers' expectations.

The use of cells derived from the pulp of baby tooth, wisdom tooth and periodontal ligament is extremely promising.

A number of studies has demonstrated the ability to induce high pluripotency and plasticity of SC from immature pulp of the tooth (wisdom tooth).

Two things attracted attention: cells derived from dental pulp tended to form bone structures with organized vascular system, that is virtually reproduced the formation of mature bone tissue (but not dentine!).

Recently, data on a new and more effective approach to solving the problem of cell therapy have been published focused on regeneration of the pulp and the dental tissue with the use of SC. The strategy proposed by the authors was to use Granulocyte-colony stimulating factor (G-CSF) in order to saturate the SC population with cells of dentine poetic line.

This epigenetic impact caused activation of breeding subpopulations of SC endowed with phenotypic characteristics of the pulp cells, including the ability to carry out dentin genesis, and apoptosis-resistant and with no tendency to genetic aberrations.

Conclusion

Historically, the development of the doctrine of the SC and their role in vital processes in animal and human bodyes is characterized by the accumulation of basic data in the forms and manifestations of their functional activity at different stages of development of the organism and the control mechanisms for their implementation at the various stages of ante and post-natal ontogenesis.

The following items should be considered the most important events and at the same time, steps towards the development of the doctrine of the SC:

- 1908 - Formulation of the idea of the existence of SC - immature progenitor cell lines by A.A. Maximov.
- 60s of the 20th century - the development of the general theory of stem cells by A.Y. Friedenstein and his school on material obtained from the bone marrow.
- the end of the 20th century - studying ACD as a homeostatic mechanism
- Develop strategies based on the epithelial mesenchymal conversion and other forms of adult cell plasticity. The development of ideas about the pluripotency of stem cells, including the various stages of ontogenesis and study of the properties of adult stem cell plasticity, developing methods of reprogramming stem cells.

The doctrine of the SC entered the 21st century with a powerful information lead and thoroughly developed strategies based on well-reasoned theoretical concepts, which in many areas have been translated into clinical practice.

This review has been given due care required in the practical application of cellular technologies, especially when it comes to interventions on genetically determined levels of stem cell function.

This review focuses on the state of research on problems with the SC and the prospects of their development. At the same time, it shows the urgency of this problem for the Dentistry and Maxillofacial Surgery.

Volume 8 Issue 6 March 2017