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REPAIR CAPABILITIES OF ALLOGENIC STEM CELLS IN DISEASES OF THE ANTERIOR SEGMENT OF THE EYEBALL

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RELEVANCE

Corneal diseases are one of the leading causes of low vision and blindness throughout the world, which serves to increase visual disability among the young and working-age population. The low effectiveness of therapeutic treatment, lack of donor material and frequent rejection reactions after transplantation prompt the search for more effective methods of treating corneal diseases, both inflammatory and dystrophic.

Corneal diseases of various etiologies lead to opacities to varying degrees; a significant proportion of patients subsequently require corneal transplantation (end-to-end or layer-by-layer). Over the course of a year, more than 45,000 corneal donor materials were used for transplantation in the United States. Over the past decade, the need for transplantation has grown dynamically due to the development of cataract surgery and laminar keratoplasty. However, it should be noted that modern methods of keratoplasty have a number of unsolved problems, such as: shortage of donor material, inaccessible pricing policy, graft rejection, increased intraocular pressure and hemophthalmos. A promising area of medicine, without these problems, is cell technology.

The term “stem cell” was first introduced into medical science by Russian scientist Alexander Maksimov in 1908. In 1963, scientists Till and MacCalloch proved that mouse blood cells contain ancestral elements capable of differentiating and restoring all lineages of hematopoiesis. [2]According to Science magazine in 1999, the second most important event after deciphering the double strand of DNA and the Human Genome program was the discovery of human embryonic stem cells. [3]

Stem cells are a reserve of spare undifferentiated cells of the body that have two main tasks of self-reproduction throughout life and differentiation into all tissues of the body. When culturing SCs ex vivo, cells do not obey Hayflick's law, under which a cell must go through several reproduction cycles, after which it stops reproducing. SCs are classified by origin into embryonic, fetal, umbilical cord blood SCs, somatic SCs and induced pluripotent SCs [4].

Embryonic SCs are isolated from the human embryo from the 5th to the 75th day of intrauterine development. They are pluripotent and differentiate into any tissue of the body. Multipotent SCs are cultured from tissue material or from human umbilical cord blood collected at the birth of a child, but the potential of multipotent cells is limited [5] .

The stem cells present in the adult human body are hematopoietic, epidermal, mesenchymal, dermal, liver stem cells, dental pulp, oral mucosa, limbal stem cells, etc. Somatic stem cells differentiate only into a certain type of tissue and are classified as unipatent. However, according to modern literature, mesenchymal stem cells (MSCs) are found in all tissues of the body [6].

New ideas about stem cells were discovered in 2006 by S. Yamanaka, a Nobel laureate who first described induced pluripotent stem cells.[7]
Today there are two directions in the clinical use of stem cells:

1. Cell therapy is the local or systemic administration of a suspension or somatic specialized cells to stimulate growth and reparative processes in tissues.
2. Replacement, transplantation cell-tissue construct based on a biopolymer matrix seeded with SCs for full or partial compensation of damaged tissues and restoration of functions.

Today, the leading countries of the world provide therapy for a wide variety of KS diseases. At the preclinical level, the safety of the use of SC and its immunomodulatory ability have been proven. Treatment protocols

SC has found wide application in neurology, endocrinology, orthopedics, cardiology, dermatology and in the treatment of autoimmune diseases. Organ printing using bioprinters is also based on SCs.[8]

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The wide range in regenerative medicine is due to its features:

- lack of specialization, cells do not perform any function in the body, limiting the role of the "reservoir pool";

-potency- SC is the amazing 240 cell type in the body,

- asymmetric division - division by mitosis, where 2 daughter cells are formed, one of which is a complete copy of the mother cell, the second is determined and has the ability to differentiate,

- "paracrine effect" - the release of a special group of biologically active substances that have anti-inflammatory, reparative and immunomodulatory effects,

- the plasticity effect is characteristic of highly patented SCs. When introduced into the body after cultivation, SCs are able to apply the phenotype of the tissue into which they enter.

- chemotaxis effect - the ability of tissue specificity, when the SC finds the damaged area and attaches to it, thanks to biochemical signals.[9]

Thanks to these abilities, SC therapy is a defining element of medicine. Ophthalmology was one of the first to use SCs in regenerative therapy. In recent years, more and more works devoted to the treatment of a number of diseases have appeared.

Some dystrophic diseases of the cornea are associated with impaired SC formation, i.e. limbal SCs (LSCs). In a healthy human body, limbal SCs ensure homeostasis of the cornea. However, with some injuries (trauma, chemical and thermal burns, after contact lenses, ocular perfimgoid), a deficiency or absence of LSC occurs, which leads to disruption of the regenerative ability of the cornea [11,12,13].

The most promising direction in corneal cell therapy is the use of LSCs, which are unipatent. In 2008, a group of Canadian scientists published the results of their research, where 8 patients underwent LSC transplantation and were observed for 9 years. As a result of treatment, all patients showed improvement in vision and reparative parameters of the cornea. [14,15]

In 2007, Japanese scientists from the University of Tokyo managed to grow a cornea with a diameter of 2 mm from one LSC. The oral mucosa can also serve as a source of SSC for SC therapy. To date, a large number of patients in Japan have been treated with LSCs that were grown from the patient's own mucosa and transplanted into the cornea. In 75% of cases, good optical results were achieved [20,21].

The possibilities of cell technologies are promising and, in the near future, will fundamentally change approaches to treatment in medical practice. However, despite the accumulated world experience, the use of SC therapy in ophthalmology leaves several unresolved issues, such as: poor understanding of the mechanisms of SC therapy, the risk of carcinogenicity, possible changes in the genomic composition of DNA after transplantation, as well as legal and ethical issues in obtaining some SCs. In addition, the most controversial issues in corneal transplantology remain the usefulness of corneal cell lines, the choice of membrane - matrix for seeding, as well as the development of keratoplasty techniques. These questions indicate the need for further research in this direction.

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