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Editorial
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New Technologies for Solving Actual Problems of Biomedicine

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Editorial

This year marks the 10th anniversary of the publication of works on the production of induced human pluripotent stem cells (hiPSC) [1,2]. It was a decade that truly revealed the potential of using hiPSC in fundamental and applied, biomedical research, and also highlighted the problems that have yet to be solved. At the moment, there are two main directions for using hiPSC:

1. The use of hiPSC as a source of material for replacement cellular and tissue therapy.
2. Use of hiPSC to model pathological conditions *in vitro*.

Unfortunately, the number of clinical trials using hiPSC and their differentiated derivatives is not yet great. In fact, there is now one registered study using retinal pigment epithelial cells derived from autologous hiPSCs [3]. The development of this direction is hampered by a number of objective reasons. One of the reasons lies in the oncogenic potential of hiPSC, in that they are capable of forming teratomas [4]. This problem can be solved thanks to the development of cell sorting technologies using reliable markers, which make it possible to separate completely differentiated cells from undifferentiated or partially differentiated cells. Another, and perhaps most serious, problem is the accumulation of gene and chromosomal mutations in the process of cell cultivation [5]. Now, this problem can be solved only by selecting the most intact cell clones using full genomic sequencing or analysis using high-resolution chips. In addition to the above, in general, the progressive development of hiPSC clinical application technologies is the high cost and complexity of the infrastructure, which allows us to obtain hiPSC lines under GMP conditions. Solving these problems requires coordinated, joint action of the scientific community. These actions should not only come from researchers working in basic science, but also from clinicians, doctors and regulatory organizations at the national and global levels. In addition to the use of hiPSC in regenerative medicine, the direction of research related to the creation of cellular disease models is progressively developing [6]. Unlike regenerative medicine, the cells used for modeling diseases are not subject to such stringent requirements. They can be obtained in conventional laboratories that do not meet GMP standards. This greatly enhances progress in this area. At the present time, many cell lines of patients suffering from various diseases, diseases of all organs and systems have been obtained. The development of protocols for the directional differentiation of hiPSC in the relevant cell types also does not stand still. Now there are methods for obtaining cardiomyocytes, neurons of various types, cells like hepatocytes, etc. Of course, these protocols should be improved in terms of obtaining more mature cells that reproduce the pathological phenotype as much as possible. In addition, a huge problem in the field of *in vitro* disease modeling is that in most cases, numerous interactions between different types of cells that exist in the living body are not considered. Partially this problem is solved by the use of technology of organoids [7,8]. Organoids are three-dimensional structures consisting of more than one type of cells. They are more advanced model systems, both for basic research in the field of tissue physiology and developmental biology, and for the search for medicines. Another great tool for creating and researching cellular models based on hiPSC are genome editing systems, such as CRISPR-Cas9. Due to its efficiency and ease of use, this system has already found the widest application, including for the study of models of hereditary diseases [9,10]. Using it, you can create isogenic cellular models and study in detail the roles of genes and regulatory elements of the genome in pathological processes. In its totality, the technology of

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induced pluripotency, directed differentiation of pluripotent cells, technology of creation of 3D organoids and editing of genomes are a unique tool for studying the functioning of genomes and cells in normal and pathological conditions. Accelerating progress in these areas gives grounds for cautious optimism, gives some confidence that the next decade will give us real opportunities for drug and cell therapy of diseases.

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