

# INTERVIEW WITH DIRECTOR OF CRYOBANK OF INSTITUTE OF CELL THERAPY, LAUREATE OF THE STATE PRIZE OF UKRAINE, DR. G. S. LOBYNTSEVA

Having analyzed the most sensational scientific discoveries of the last decades, as well as the most cited scientific articles and international projects, which were supported with the largest grants, we came to the conclusion that most of them are devoted to the study of stem cells properties and their possible clinical application in regenerative medicine. Therefore, it is not surprising that banking of cells and tissues has become the most thriving industry in different countries. Just only from 2005 to 2013 there was a more 20-fold increase in the number of biotech companies in the world. At present, the preservation of own biological material in a biobank equates to biological insurance. More often researches of Ukrainian scientists appear in programs of international forums on stem cells and regenerative medicine.

With the request to tell about the current state of biotechnology in Ukraine, the popularity of cryostorage services of cord blood stem cells and other cells and tissues among Ukrainians, as well as prospects for the development of regenerative medicine in our country, we asked the leader of the national cryobiology, laureate of the State Prize of Ukraine, Director of Cryobank of the Institute of Cell Therapy, Ph.D. Galina Lobyntseva.



**Ed:** *Dr. Lobyntseva! Over the years, stem cells have not left the front pages of scientific and popular publications. Discoveries, devoted to stem cells, were repeatedly awarded with the Nobel Prizes. Sensational news about the healing of AIDS cases and victory over cancer are connected with the use of stem cells. While at the same time in different parts of the world there are enough scandalous reports on illegal use of stem cells, side effects of cell therapy, revoked licenses from biotech companies and clinics. What is the real situation in the world of cellular technologies today? Is it science? Business? What are the real achievements and challenges of the branch at the moment?*

## Dr. Lobyntseva G.:

Today, there is a limit of opportunities of surgical techniques and drug therapy: new chemical agents that appear repeatedly on the pharmaceutical market have greater selective effect, greater bioavailability, less side effects compared to their predecessors, but in most cases they can not completely restore the lost function; and synthetic implants do not provide an effect of a living organ. Therefore, doctors and biologists have been hardly and successfully attempting to reproduce the method of the Creator – to receive an organ or its part from a stem cell that has already happened once in our body at the very beginning of our life. An interest in stem cells is absolutely justified: science does not know any better and promising biomaterial for reconstruction of functional tissue. This explains the huge investment and attention of both scientists and public, aimed at the development of this particular field of science.

Every day cell therapy enters the everyday medical practice more confidently. The well-known bone marrow transplantation, or rather hematopoietic stem cells, which for decades has been used successfully

in the treatment of hemoblastoses, congenital immune deficiencies and metabolic diseases, is also a kind of cell therapy.

Many patients prior to transplantation of bone marrow cells need to undergo myeloablative treatment to reduce a number of malignant cells in the patient's body and immune system suppression to reduce the likelihood of graft rejection. This stage of treatment depends on the particular disease and may include radiation therapy, intensive drug therapy or a combination of both methods.

However, considering the complexity of finding a compatible bone marrow donor, invasiveness and high cost of the procedure, alternative sources of hematopoietic stem cells, such as umbilical cord and peripheral blood, are growing in popularity in the last decade. The staff of Cryobank of the Institute of Cell Therapy made significant progress in investigation of the possibility of obtaining hematopoietic stem cells from the placenta.

Although it is still an experimental method of cell therapy, the use of stem cells in the treatment of myocardial infarction, diabetes, cirrhosis, cerebral palsy, post-stroke conditions and many other diseases is quite successful.

To answer your question, I want to say that biotechnology is not only a trend in science and clinical medicine, but a new industry. Every innovative scientific elaboration, especially if it is a medicine, is only possible to convey to the patient by its commercialization. If the company does not establish commercial production of a new medicine, the patient will not buy it at the pharmacy, and the discovery, which can help people, will not leave a scientific laboratory. It is very well that industrial enterprises are increasingly interested in development of biotechnology, and large pharmaceutical plants introduce cellular and immunobiological preparations in their products.

Of course, often reports on substandard medicines, doctors-charlatans, illegal medical practice do not bypass and regenerative therapy. But we do not refuse taking prescribed medicine; we have just become more careful about the choice of distributors and pharmacies.

Currently, the government is strengthening the control not only over the production and import of medicines, but also over the quality of medical services in the country. If we have heard that there was closed a clinic which carried out cell therapy without a license it does not mean that all such clinics operate unfair. Therefore, patients should be more responsible in choosing a medical institution or Biobank, where they are going to save the cord blood, and check the license for such type of activity. Association of cryobanks, created in Ukraine, is doing a lot to eliminate biobanks that do not meet licensing requirements and international standards.



**Ed:** *And how successful are methods of cell therapy in Ukraine? Are they popular with Ukrainian doctors and patients?*

## Dr. Lobyntseva G.:

Ukrainian cryobiology, the level of which is directly linked with the development of cell-based therapies, has a very long history. And in this

regard we should note outstanding achievements of the Kharkov Institute for Problems of Cryobiology and Cryomedicine, NASU. It is in Ukraine in 1984, MD Tsutsaeva A. A. froze first samples of umbilical cord blood in Europe, and the first message about infusion of umbilical cord blood in patients dates back to 1939. Unfortunately, a lot of achievements of Ukrainian scientists are not familiar to the international community because of the certain secrecy of domestic science in the Soviet era. Our scientists rarely took part in foreign conferences, and published mainly in the domestic Russian-language journals, so their articles are still unavailable to foreign colleagues. Therefore, even in our days we often read about some innovative discovery of foreign scientists, knowing that this was done in Ukraine many years ago. Also, for many years it was impossible to apply new therapies in clinical practice due to the lack of opportunities to put on stream costly medical services or to establish commercial production of innovative cell preparations.

The situation has changed significantly in the last 12 years, when in 2003 there was established the Institute of Cell Therapy, which has become the engine of biotechnological progress in the country. In 2004 Cryobank of Institute of Cell Therapy offered Ukrainian citizens an exclusive service - preservation of cord blood stem cells, production of individual placental products for the health and beauty, and a little later - preservation of reproductive cells and tissues. This service is focused first of all on cancer patients of reproductive age, whose cancer treatment is accompanied by the risk of fertility loss.

In 2008, the Institute of Cell Therapy became the first medical institution in the country, which the Ministry of Health granted a permit to participate in clinical trials using stem cells cryopreserved in the cryobank of Institute. And in 2012 for the first time in Eastern Europe, there were completed 5-year clinical trials of treatment of acute pancreatitis and critical limb ischemia, conducted by the Institute of Cell Therapy jointly with leading clinics of the country. Reports were received and formally approved by the Ministry of Health of Ukraine.

At present Institute of Cell Therapy under the auspices of the Coordinating Centre for Transplantation of Organs, Cells and Tissues of the Ministry of Health of Ukraine continues clinical trials of using cryopreserved cord blood stem cells in treatment of diabetes, viral hepatitis, liver cirrhosis, cardiomyopathy.

In 2014, the Institute of Cell Therapy received a prestigious international quality certificate ISO 9001:2008. Cryobank of Institute of Cell Therapy is the only Ukrainian bank of cord blood, which has successfully passed international certification ISO 9001:2008.

 **Ed:** *Institute of Cell Therapy offers an extremely popular in the western countries service of umbilical cord blood preservation at birth, which can not be considered as cheap. Is preservation of umbilical cord blood popular with Ukrainian parents, especially now, when we are witnessing a significant economic decline in Ukraine?*

#### **Dr. Lobyntseva G.:**

In 2006, European Association for Bone Marrow Transplantation has announced cord blood as an alternative source of hematopoietic stem cells along with the bone marrow. Thus, in about every 5th case cord blood stem cells are applied instead of bone marrow in the treatment of hematological malignancies and other disorders requiring the replacement of a pathological hematopoietic organ with a donor one.

The number of stem cell transplantations of umbilical cord blood in patients under the age of 18 years, is even greater than the number of bone marrow transplants. And more than 30,000 such operations have been performed all over the world. This explains the great interest of the world community to the cord blood and reasonable desire of conscious parents to keep a stock of stem cells collected at birth, as a biological insurance for their family.

In developed countries, along with family-operated autologous banks of cord blood, there exist public banks with government funding. Thus,

according to world statistics, public cord blood banks keep more than 500,000 samples, and over 1 000 000 cord blood samples are stored in autologous banks by caring parents. In Ukraine, unfortunately, private storage of umbilical cord blood is only available at the expense of the family, and this service is quite popular with Ukrainian parents. The cost of processing and storage of cord blood stem in Cryobank of Institute of Cell Therapy is the lowest in Ukraine. Moreover, compared with a similar service available on the market, we offer a premium package for the price of a base one.

The Institute of Cell Therapy is the only Cryobank in Ukraine offering placenta storage. Patients, who preserved placenta, get the entire set of placental preparations and cosmetics made free of charge. Due to economic and political circumstances, Ukraine is not experiencing now the best of times in the history of the independent state, but we are proud of the consciousness of Ukrainian parents who, despite the decline in the standard of living in the country, have not lost interest in this service. For its part, to make the preservation of umbilical cord blood more affordable to most Ukrainian families, we have developed a flexible system of discounts, and guarantee that the cost of package of our services is economically justified by the cost of expendable materials of the highest quality.

 **Ed:** *Is it necessary to store cord blood in the Biobank for the lifetime, if stem cells can be successfully obtained from bone marrow, peripheral blood, adipose tissue, dental pulp? And we also know that Institute of Cell Therapy has successfully cultured cells from these sources?*

#### **Dr. Lobyntseva G.:**

Firstly, adipose tissue and dental pulp allow isolating mesenchymal stem cells, which are perspective for the regeneration of bone and cartilage tissue, treatment of cardiovascular diseases, bioengineering purposes. Cord blood, bone marrow and peripheral blood contain hematopoietic stem and progenitor cells of the blood; they are used in treatment of malignant diseases of blood. Obtaining of bone marrow is quite traumatic procedure, requiring general anesthesia, and may be contraindicated. Obtaining of necessary amount of hematopoietic stem cells from peripheral blood to restore hemopoiesis is possible only after pre-stimulation of hematopoiesis, which involves the use of rather expensive growth factors. Therefore, cord blood is the most available and cheap source of stem cells, both hematopoietic and mesenchymal.

Umbilical cord blood harvesting is carried out without any contact with a newborn and is not be associated with any risk or discomfort for a mother. In addition, science has proved that young stem cells have a significantly higher ability to repair damaged tissue. At allogeneic application they are less likely to cause immunological complications.

 **Ed:** *Cryobank of Institute of Cell Therapy is the first in Ukraine. How many samples of umbilical cord blood are stored in the Cryobank to date, and how many families have used stored cells? Were the stored stem cells applied in Ukraine? In what diseases? And how effectively?*

#### **Dr. Lobyntseva G.:**

Currently, Cryobank of Institute of Cell Therapy has stored cord blood cells from more than 8,000 families. Every year more and more of our clients come to us with a request to give their cell deposit, as there is a need of cell therapy in families. Only in the last 2 years there were 16 such requests, some clients used the stored material repeatedly. After all, a way to preserve umbilical cord blood in Cryobank of Institute of Cell Therapy in separate cryovials allows its fractional application. Cord blood stem cells stored at the Institute of Cell Therapy were used in the families of our clients for the treatment of multiple sclerosis, hepatitis C, Alzheimer's disease, a number of autoimmune diseases such as ankylosing spondylitis, immunodeficiency and cerebral palsy. Their treatment was

carried out on the basis of the leading hospitals and research institutes of Ukraine which have experience of working with stem cells. One sample was used during cardiac surgery in the newborn.

In many cases, physicians have noted positive dynamics after the cell therapy: from slight decrease in pathological symptoms to improvement of overall condition and quality of patient's life. In some cases doctors have not made any final conclusions about the effectiveness of the treatment due to very short period of observation. But there was not any single case of deterioration of the patient's state or side effects of preparations of cord blood stem cells produced in Institute of Cell Therapy.

**Ed:** *Is it possible to treat patients abroad with the use of biological material, processed and stored in Ukraine? Do foreign colleagues accept Ukrainian techniques?*

**Dr. Lobyntseva G.:**

Yes, of course! And first of all I want to say that there is no Ukrainian or American method of preservation of umbilical cord blood. Most cryobanks in the world carry out the processing of umbilical cord blood, using so-called Rubinstein's protocol which foresees saving of leucocyte-platelet layer of umbilical cord blood. However, as I have said, preparation are of great importance, particularly anticoagulants and preservatives, as well as consumables, which are used for this purpose, mode of cryopreservation and the accuracy of the results of laboratory researches. We are working on our own patented technology which allows you to save 80-90% of hematopoietic cells, assessed by culturing.

Cryobank of Institute of Cell Therapy complies with international standards of GMP and ISO. Also, all production processes are adapted to the requirements of international directives FACT and AABB.

Institute of Cell Therapy is a full member of the International Society for Stem Cell Research (ISSCR), the International Placenta Stem Cell Society (IPLASS). Quite often we are consulted on production process and clinical problems of our patients by Western experts. We also more often provide advisory support. While you should understand that patients are often treated with cell therapy in the most severe cases and in serious condition, when the preferred treatment is in the medical center, located as close as possible to the place of residence of the patient, and fortunately, the level of medicine in Ukraine today contributes to this.

**Ed:** *Dr. Lobyntseva, share with us your professional dreams and plans? What new developments of Institute of Cell Therapy will please the scientific community in the nearest future, and what new technologies, capable to help Ukrainian patients, do you plan to implement a national health care?*

**Dr. Lobyntseva G.:**

Firstly, we would love to create or support the establishment of a public cord blood bank in Ukraine so that hematopoietic stem cell transplants become more affordable to Ukrainian patients. We have enough experience, appropriate laboratory facilities and a large supply of donor cord blood stem cells, harvested with the informed consent from women in childbirth. We use this material for clinical trials.

Equally important is the further integration of Ukrainian bank with foreign registries of hematopoietic stem cells. In recent years, many of our fellow citizens have emigrated abroad, and, considering the specificity of their immunophenotype, it can be difficult to choose a compatible bone marrow transplant in foreign registries in the case of blood disease. However, to implement this idea we need a support of government programs and charitable foundations. Also at the final stage of clinical trials there are treatments for diabetes, cardiomyopathy, viral hepatitis and liver cirrhosis. We would love to implement them in practical health care in the nearest future, as well as the technology of treatment of intervertebral hernia, developed by A. P. Romodanov Institute of Neurosurgery in collaboration with the Institute of Cell Therapy.

We talked about the biotechnology: placental mesenchymal and hematopoietic stem cells that have passed pre-clinical animal studies can be a valuable material for clinical use in various pathological conditions. Therefore, the creation of an industrial complex for production (culture laboratories), cryopreservation and storage in Cryobank of certified preparations of these cells also requires special attention and financing.

There are a lot of questions about the mechanism of action of stem cells, so it would be good to have a large vivarium for research in animal models of pure lines.

We hope that the signed agreement with the European Commission on Ukraine joining as an associate member of the European Union without the contribution to the program "Horizon 2020", will contribute to the development of scientific research in this area.



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