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The features of cord blood banking bioeconomy in Ukraine and abroad



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ABSTRACT

The paper highlights the features of cord blood stem cells banking worldwide, modern trends of development of this biomedical industry, problems and prospects. The role of the sector of public and family cord blood banks in shaping of the market of storage of human cells and tissue is considered. The data of sociological surveys in Ukraine and abroad, to evaluate the level of awareness of future parents and medical community about the value and possibilities of storage of cord blood is presented. The study revealed favorable preconditions and emphasized the social importance of creating a public cord blood bank in Ukraine in the perspective of its integration with international registries of hematopoietic stem cells.

KEYWORDS: umbilical cord blood; stem cells; cord blood bank; bioeconomy

In recent years the umbilical cord blood as the source of various populations of stem cells and a unique biological material for the production of certain immunobiological drugs (artificial tears, platelet gel, enriched with growth factors plasma) attracts increasing attention of the scientists, physicians, businessmen [1-4]. The umbilical cord blood stem cells are actually used in the treatment of about 80 diseases [5] and officially were announced as bone marrow alternative by the European Group for Blood and Marrow Transplantation (EBMT) [3].

From the moment of the first cord blood application in 1988 more than 35,000 transplants of cord blood derived stem cells were performed worldwide for the treatment of cancer and regenerative therapy of other diseases in children and adults [2]. In USA the Office of Cellular, Tissue and Gene Therapies (OCTGT), Food and Drug Administration (FDA) approved several cord blood stem cells based drugs, such as Allocord, Hemacord, Ducord [6, 7]. In 2012, in Canada the first cellular drug Prochymal for the treatment of graft-versus-host disease was approved and the efficacy of this medication is also being studied for the therapy of diabetes mellitus type 1 [7]. In Belarus 17 cellular technologies based on the use of autologous transplant of mesenchymal and hematopoietic stem cells were registered, in particular for the treatment of pharmacotherapy-resistant multiple sclerosis, also for the plastics of large defects of the front abdominal wall, treatment of graft-versus-host disease, diabetes mellitus, hypoparathyreosis and others [8]. Ukrainian scientists also have significant achievements in the field of manufacturing of immunobiological drugs, containing cord blood stem cells [3, 14]. Thus, in 2012 the Ministry of Health of Ukraine officially approved the methods of treatment of critical lower limbs ischemia and pancreatectomy using cord blood stem cells, developed by the Institute of Cell Therapy (Kyiv) [3, 9]. Hence, wide application of the umbilical cord blood drugs in clinical practice and significant financing of studies on their therapeutic potential in the developed world mediates the importance of cord blood banking and facilitates the development of the entire biotechnological industry [2, 3, 7].

The world's first cord blood bank was created in 1991 at the New York Blood Centre in USA [10]. Actually cord blood banks are actively functioning both in the countries with high social standards and developing countries [11]. The world market of cord blood banking in 2012 was evaluated for \$12.4 billion and due to specialists' prognoses will make \$15.23 billion till 2019, having reached from 2013 to 2019 annual index of growth on the level of 5.6 % [11].

The umbilical cord blood banking may be public and private (family, autologous) [1, 3, 10, 12]. Public banks of cord blood predominantly are created at the transplant centers and are operated using state financing or funds of the charity organizations [3]. Public banking of cord blood is based on the free of charge donation of cord blood sample by the women after childbirth [1, 10]. Information on cord blood samples, stored in public banks, is introduced in the international registries of the donors of hematopoietic stem cells and upon request the transplant of the certain phenotype is transferred to the relevant transplantation center inside the country or abroad [7]. Private cord blood banks offer willing parents the opportunity to preserve the umbilical cord blood collected at childbirth for the own needs of the family in the case of a disease due to the agreement signed with the bank [3]. Autologous cord blood banking is considered as a kind of biological insurance and cord blood storage is the most popular service in the field of banking of human cells and tissues [3, 7].

Controversial is the issue on the exact number of cord blood banks, functioning actually in the world, since the practice when a certain biobank offers its services through numerous daughter companies in different countries is very common [13]. Thus, due to the data of Parent's Guide to Cord Blood Foundation at least 434 cord blood banks of a family type (together with daughter companies) offer their services to expectant parents but only 214 from them are true banks (with laboratories) [13].

In 2003, the Parent's Guide to Cord Blood Foundation counted that the number of cord blood samples, stored in the banks of a family type in USA

overexceeded 3-fold the reserve of public banks [13]. A similar proportion between the amount of stored material in autologous and public cord blood banks was confirmed by the analogous study conducted 10 years later [13]. Due to another data, as of today 3 billion samples were stored in the cord blood banks worldwide, from which 650,000 – in public banks and 2.5 mln – in family cord blood banks [17]. Such difference in the number of cord blood samples stored in the public and private cord blood biobanks is explained by the higher marketing activity of the family cord blood banks and often by insufficient funding of expenses for processing and cryostorage of the biological material in public banks [13]. It should also be noted that despite the fact that the number of private cord blood banks is significantly higher compared to that of the public ones, these are the latter that play the leading role in the formation of industry [11].

The benefits of the family cord blood banking are supported by the fact that the evidence to find a donor stem cell transplant in the public bank is low, whereas autologous storage of biological material guarantees the immediate availability of the matching transplant [15]. The index of release of the cord blood samples for clinical use in the world's biggest cord blood banks of the family type makes between 10 and 100 for 100,000 stored samples [13]. At the same time rapid development of cord blood transplants for the treatment of thalassemia in siblings is noted in Asia and this is the situation, when family cord blood banks provide the needs of the state health care service in hematopoietic stem cells transplants, that are not properly met by the state banks of cord blood [13].

Northern America is the dominating regional market of cord blood banking; Europe keeps the second place [11]. The development of cord blood banking in these countries is largely due the government policy that supports this industry. Thus, the leading positions of the North America on the arena of cord blood banking are mediated by the support of their activity by the governmental organizations and wide use of the methods of cell therapy in clinical practice in USA and Canada [7, 11]. The high awareness of the US and Canada population on the value of cord blood and covering of the expenses for its storage by the insuring companies also favoured the boost of this industry in the Northern America [11].

In 2005, the Institute of Medicine (IOM) in the USA issued so called broaden report on the banking of the umbilical cord blood, containing accurate recommendations for the medical personnel on the provision of all expecting parents the objective information on the possibilities of cord blood preservation before childbirth [7, 16]. The Department of Health and Human Resources in its turn founded the National Cord Blood Inventory (NCBI) Program, supporting cord blood banking for the treatment of patients as well as scientific investigations [17]. Stored cord blood stem cells are available for physicians and patients for unrelated stem cells transplants within the C. W. Bill Young Cell Transplantation Program [7, 16]. Actually in USA 28 states legalized the educational programs on cord blood, that cover 78 % of all childbirths [16]. The majority of states in the USA follow the IOM recommendations and several states are on different stages of the development of legislative procedures on the necessity to inform expectant parents on the possibilities of cord blood storage [7, 16].

In recent years the quick development of cord blood banking was marked in China and India [1, 2, 11]. Densely populated countries of the Pacific region, due to experts' prognoses, will mediate a significant increase of the market of cord blood banks in the period between 2015 and 2022 [11]. This will be enhanced by significant investments in the industry by the main market players, support of the government as well as rise of the level of health care in these countries [2, 11]. The economics of the developing countries is also characterized by the huge potential for the expansion of cord blood banking industry [11]. In recent years, cord blood banking is actively developing both in the countries of the Arabic world [17]. Family cord blood banks occupied the largest part on the industry market in 2014 [2, 11]. Although due to prognoses, the support of public banks by the government as well as free storage of cord blood will favor the increase of their number on the world market in the period of 2015-2022 [11].

According to experts' prognoses, the increase of awareness of expectant parents on the importance of cell therapy definitely will favor

the development of cord blood banking in several coming years. Indeed, due to the data of sociological surveys as of today the expectant parents in different world countries are not well informed about the relevance of cord blood preservation for the benefit of their families [3, 11, 12, 18]. Thus, the study, published in 2006 in the Journal of Reproductive Medicine showed that one third of expectant parents does not know about the possibility of cord blood preservation and the rest respondents called themselves minimally informed [11]. This study also showed that 84 % parents expected that obstetrician-gynecologists, who took care of them during pregnancy, will provide them information on cord blood storage but only 14 % respondents received expected answers from the physicians or nurses [11]. And sociological survey, conducted in the January 2014 by the agency BioInformant Worldwide LLC (600+ answers from expectant parents or individuals, who became parents recently) showed that actually the index of awareness of expectant parents on the value of cord blood and possibilities of its storage did not change significantly, despite the efforts on the popularization of cord blood banking, that are made in different countries of the world [11].

In Ukraine the results of sociological studies conducted in 2015 and in 2010 showed that about 90 % respondents aged 19-65 knew the terms «stem cells» and «cell therapy», what is 20 % higher than the indices of the same survey of 2006 [18]. Also due to the results of the sociological survey of 2015 the number of persons with positive attitude to cell therapy increased for 13.5 % compared to the relevant index of 2010 [3, 12]. Maybe this is due to the active highlighting of the advances of regenerative medicine in mass media during recent several years in Ukraine, in particular the announcements on the official approval of cell therapy treatments, developed by the Ukrainian scientists by the Ministry of Health in Ukraine in 2012 and the Nobel Prize of 2012, awarded for the discovery of the induced pluripotent stem cells [3]. Half of the respondents both in 2010 and in 2015 in Ukraine answered that they knew that the umbilical cord blood was the source of stem cells what is 10 % higher than the relevant index of 2006 [3, 19]. However, if in 2010 every second respondent confirmed their readiness to preserve the umbilical cord blood after childbirth as a biological insurance, as of 2015 this option of answer was chosen only by 30 % surveyed residents of the different regions of Ukraine [3, 12]. Also the number of respondents, whose decision on cord blood storage will depend on the cost of this service in 2015 increased almost for 30 % compared to the data of sociological survey conducted in Ukraine in 2010 [3, 12]. These indices may be explained by the significant economic crisis in Ukraine, that is noted in 2014-2017.

The results of survey of pregnant women in Ukraine showed that 97 % of them heard about stem cells and more than 80 % knew that the umbilical cord blood is the rich source of them [3]. About 50 % of surveyed pregnant women had positive attitude to cell therapy but only 1.3 % respondents were going to sign a treaty on cord blood storage with one of the biobanks after childbirth [3]. According to the results of survey, the cost of services of cord blood cryostorage is too high for 87.1 % of surveyed pregnant women, other 5.7 % respondents noted that they did not trust cord blood banks [3]. Obtained data as of 2015 are equivalent with the relevant study, conducted in 2010 [3, 12]. As the results of the sociological survey of 2015 showed, only 8.4 % obstetrician-gynecologists recommend cord blood storage to their patients, however as due to the data of survey of 2010 and 2015, nobody of the surveyed physicians discourages pregnant women from such a decision [3, 12].

The results of the mentioned studies show high awareness of the population of modern Ukraine of the different sociological categories on the up-to-date stem cell based technologies as well as the positive attitude both from the side of the expectant parents and medical community to the cord blood preservation, what is the consequence of the active educational and marketing activity of the national family cord blood banks in Ukraine. Taking into account the high number of deliveries in Ukraine, compared with the other countries of Europe, peculiarities of the HLA-phenotype and high migration activity of the population

of Ukraine, the international integration of the national bank of cord blood would be important also for the world registry of hematopoietic stem cells [3].

Due to the experts' opinion, the development of cord blood banking in the world today is inhibited by the high cost of this service as well as the necessity to get numerous accreditations for the biobanks [11]. The search request «cord blood» was determined to be one of the most expensive key words in the Google Search engine, making more than \$20 for the click of the world searching traffic and about \$40 for the click of the search traffic of the USA [19].

The following threats were distinguished for the future development of biobanking of cord blood worldwide:

- new accreditation demands, increasing the expenses of the bank;
- decrease of the number of cord blood transplants in USA and some other regions;
- low turnover index of preserved samples;
- high cost of transplant of the preserved cord blood samples;
- complications in the increase of the awareness of the obstetrician-gynecologists on the value of the umbilical cord blood;
- low highlighting of this topic by mass media, including main news portals [1, 2, 11].

The other uncontrolled factors, that threaten the development of industry include new legislation, changes in reimbursements for transplants, necessity of patenting the technologies, changes in acceptance of the family and public cord blood banking by the society, recommendations of the important medical organizations, changes in the support by the government [7, 11].

At the same time the opportunities for the development of cord blood banking are the following:

- market broadening perspectives by means of increase of the awareness of the population on the value of the umbilical cord blood stem cells;
- new clinical data, supporting the application of hematopoietic and mesenchymal stem cells from the umbilical cord tissue;
- improved tolerance of the cell therapy by the society;
- the opportunity of cross-linked cooperation through the creation of associations of cord blood industry;
- tendency to diversification inside industry, when cord blood banks are transformed into stem cell banks, storing not only cord blood but also the umbilical cord tissue, placental tissue, amniotic fluid etc. [11]

The Parents Guide to Cord Blood Foundation developed a new index, named Parent's Guide Price Index – PGPI™, characterizing the cost of storage of stem cells in the family type cord blood bank compared to the economy of the country, where the bank is functioning [13]. The analysis of this index showed that despite the fact that cord blood storage service is the most expensive in the Northern America and Western Europe, the latter are the countries where the largest part of the population can afford banking of biological material [13]. In Ukraine, because of the low level of life and undeveloped insurance culture of the population, the umbilical cord blood is preserved only in 0.1-0.2 % deliveries, mostly in the capital and largest cities [3].

The important aspect of the provision of high quality services of storage of biological material by biobanks is the accreditation of the

bank by the respective accreditation committees. According to studies, conducted by the Parents' Guide to Cord Blood Foundation more than 1/3 of umbilical cord blood banks worldwide do not have any accreditation, about 30 % of banks are accredited by ISO and 28 % – by AABB and/or FACT (with or without ISO) [13]. It should be noted that the cost of services of accredited cord blood banks of the family type predominantly is not higher for the clients compared to the banks without accreditation [13]. Thus, the cord blood banks that achieved the highest compliance do not burden their clients by the expenses for the adaptation of manufacturing procedures according to demands of the accreditation committees [7, 13]. Hence, according to the recommendations of the authoritative American organization «Parents Guide to Cord Blood Foundation» the parents should be encouraged to choose the accredited cord blood banks since the highest level of services of these laboratories does not cost more compared to unaccredited biobanks [13]. In Ukraine, the only cord blood bank which in 2014 obtained the international accreditation ISO 9001:2008 is the cryobank of the Institute of Cell Therapy [7].

In recent years the family biobanks in addition to preservation of the umbilical cord blood stem cells are increasingly introducing a new service of umbilical cord storage [7]. This service is positioned as the opportunity to obtain the reserve of the population of mesenchymal stem cells in addition to hematopoietic stem cells [7]. Interestingly, in European countries the cost of storage of the umbilical cord tissue is two-fold lower compared to the cost of the service of the umbilical cord blood cryopreservation in the countries in Asia and Oceania [12]. About 13 % biobanks of the world offer this service as the only one [13]. The majority of biobanks, offering simultaneously the storage both of umbilical cord blood and umbilical cord are localized in the countries of Europe, the number of such enterprises in USA, Canada, Eastern Europe, Asia and Oceania is little lower [14]. The preservation of the umbilical cord actually enjoys the lowest popularity in the countries of Africa as well as Southern and Central America [13].

The storage of the umbilical cord implicates two technological approaches: isolation and cryopreservation of mesenchymal stem cells as a ready off-the-shelf GMP-product and/or preservation of tissue fragment with the perspective of isolation of the cell population in case of necessity of its clinical application in future. The latter is supported by the arguments on the rapid development of science and probability of the discovery of the new, unknown yet populations of stem cells, which it will be possible to isolate from the cryopreserved tissue [7].

The experts prognose the significant expansion of the service on preservation of the umbilical cord in different world countries as well as its automatization, directed at the manufacturing of the more standardized products [7, 13]. The American Association of Blood Banks even elaborated new accreditation demands to the banks of somatic cells, which address also the isolation of cells from the umbilical cord tissue [13].

Thus, during recent 25 years the umbilical cord blood banking shaped as the separate biomedical industry with extremely high expansion on all continents and taking into account the rapid development of science the perspectives of application of cell preparations in clinical practice, emergence of the new services on the market, support of biotechnologies by the leading experts of the field we dare to predict the further development of the banks of human cells and tissues worldwide.

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