MODERN TRANDS ON BIOECONOMY DEVELOPMENT IN THE WORLD: THE INTRODUCTION OF NBIC-TECHNOLOGIES IN BIOMEDICINE

***Igor Matyushenko**, PhD in Technical Sciences, Professor*
Department of Foreign Economic Relations and Touristic Business,
V.N. Karazin Kharkiv National University, Kharkiv, Ukraine
igormatyushenko@mail.ru
***Victoria Khaustova**, PhD in Economy, Associative Professor*
Scientific research center for industrial development problems
of National academy of sciences of Ukraine, Kharkiv, Ukraine
x_river@mail.ru

Abstract:

The article reviews modern trends in bio-economy development on the basis of biotechnologies application in medicine and pharmaceutics. It provides the main directions for modern medical nanotechnologies development and utilization of nanomaterials in medicine. It has proved that the practical implementation of NBIC bio-technologies would manifest itself in the development of personified medicine, including also gene-diagnostics; proteomics; pharmacogenomics; bio-analytical technologies; nanotechnologies application for medicinal drugs; bio-informatics. The forecast for NBIC convergence manifestation in medicine is provided till 2030: recombinant DNA, biochips, biological spare parts, civil and military exoskeletons, bio-gerontology, stem cells and their usage, self-assembly and production on DNA basis, and convergent "smart" materials.

Keywords: *bio-economy, biomedicine, NBIC-technologies, convergence, molecular and cell biotechnologies*

INTRODUCTION

Many well-known and recognized scientists and specialists consider that in the XXI century bio-economy together with nano-economy as well as info-cognitive economy would play a more decisive role in developing and implementing high technologies in the national and global scales. At the beginning of the XXI century, second decade, the convergent NBIC-technologies are increasingly becoming a real tool, with the help of which the mankind hopes to reach its goals and solve the availble global problems. Global scientific community regard bio-technologies as "*global technologies"* similarly to nanotechnologies and information & cognitive technologies, because bio-technologies include a wide spectrum of scientific disciplines and economic sectors, and are spread over great territories of the globe [1 – 8].

By different estimations bio-medicine as one of NBIC-technologies components will lead to the most radical break-through in the innovation endeavors. As it is expected, in the XXI century nano- and bio-technologies' achievements would create new therapy methods as well as potential pre-conditions to enhance human physical capabilities.

MATERIALS AND METHODS

Content analysis has been used as the main method of research, which allowed to make a meaningful analysis of classic papers and researches of modern economists-practitioners devoted to the peculiarities of the modern prospects of bioeconomy, biomedicine and using of NBIC-technologies.

RESULTS

1. Outlook on bio-nano-technologies' implementation in medicine and pharmaceutics.

Bio-technical revolution has actually started since the XX century last decade and created a powerful wave of innovative products and services in medicine, agriculture, power engineering, i.e., practically in the majority sectors of the global economy. At the beginning of the XXI century EU has developed "Strategy For Europe On Life Sciences And Biotechnology", which has become a basis for EU countries to develop their national policies in the sphere of biotechnologies [9]. That document recognizes that after the information revolution and Information-Communication Technologies (ICT) development biotechnologies and life sciences have become the second innovation wave.

As of today, Organization for economic cooperation and development (OECD) has provided two definitions of biotechnologies: a simple one and a more comprehensive one, which is based on the list notation of the biotechnological equipment. In a simple variant *biotechnology* is a set of fundamental and applied researches as well as engineering solutions directed to use biological objects, systems or processes in industrial scale. In a broader sense OECD experts have proposed the following *list of the modern convergent biotechnologies,* which are used in medicine, pharmaceutics and biotechnological industry, bioenergy and agriculture, etc. [10; 11]:

- *DNA/RNA:* genomics, pharmacogenomics; gene sensors or gene detectors; DNA/RNA-sequencing/synthesis and amplification (determining macro-molecules' primary structure; strengthening the process of DNA/RNA copying; genetically based profiling, etc.);
- *Proteins and other molecules:* sequencing/synthesis and construction of proteins and peptides, including big hormone molecules; improved system of medical drug delivery to specific human body points on the bases of big molecules; proteomics; proteins isolation and purification, alarming and identifying cell receptors;
- *Cell and tissue cultures and their engineering:* fermentation that uses bioreactors; bioprocesses; bio-treatment; wood softening with the help of wood destroying fungi; bio-desulfation; biological treatment of the soil contaminated with organic waste with the help of fungi; bio-filtration, etc.;
- *Genes and RNA-vectors*: gene therapy, virus vectors;
- *Bioinformatics*: genomes databases' engineering; protein sequencing; modelling complex biological processes, including systems biology;

- *Nano-biotechnologies*: tools and processes that use nano- and micro-technologies to engineer equipment for studying bio-systems and to be also applied in the systems of medical drugs delivery in human body, diagnostics, etc.

On the basis of the "comprehensive" definition of biotechnologies, OESD has developed a conceptual model for biotechnological and statistical indicators, which incorporates a wide spectrum of scientific-technological and innovative performances, and could be used for determining "contents of the bio-society", formulating the national and global innovative bio-policy and developing bio-strategy. At the same time, *the difference between pharmaceutical industry and modern industrial biotechnology* is noted in the practical domain: pharmaceutics develops comparatively low-molecular drugs, while biotechnologies – big bio-molecules, as, for example, functional proteins and anti-bodies. As of today, erythropoietin protein (it stimulates creation of erythrocytes) may serve as an example, as well as recombinant human insulin, human interferon, human and animal growth hormone, therapeutic antibodies, etc.

Outlook on innovations in biotechnology and living systems was discussed in OECD in 2007-2008 within the framework of International Futures Program (IFP) [12]. At the same time OEDD implemented the project "The Bio-economy to 2030" as the most important element of NBIC-revolution [13].

As to OECD experts, bio-economy by 2030 would rest on the following aspects:

- Full knowledge of the gene structure and cell processes in human body;
- Production of "renewable biomass" for agriculture and bioenergetics;
- Comprehensive and integrated application of biotechnologies in different economy sectors, including agriculture and power engineering, which would considerably influence global environment and climate.

As of today, *medicine* is experiencing revolution as regards etiology, pathogenesis, and human illness treatment, which is attributed to the developments in molecular biology and genetics, molecular medicine and pharmaceutics domains. *The main trends in practical implementation of fundamental research results* in those spheres include: [14, P.11–12]:

- Development of the *personified medicine*, which is connected with the development of unique high-technological types of diagnostics and treatment. Exactly this type of medicine is becoming the foundation for preventing and treating the most spread human infectious and chronical diseases, including cardiovascular diseases, oncological diseases, neurodegenerative diseases and metabolism malfunctions. The advantage of *gene diagnostics* lays in the fact that it helps identify a potential threat of any disease development before its clinical signs, which prevents the disease development and alleviates its progression with taking into account the individual features of the patient's body;
- Research conducted within the framework of *proteomics* is paid a special attention today. Post-genome events, connected with the synthesis of multiple proteins, reflect the functioning of each specific patient's genome;
- Creation of original pharmaceutical drugs on the basis of up-to-date scientific research results in the field of molecular biology and medicine, the action of which considers the individual sensitivity to drugs, and which is studied by *pharmacogenomics.* Many pharmacogenetic phenomena, observed during drugs application, occur in pharmacokinetic processes;
- Design and creation of innovative medical drugs stipulate development of pharmaceutical research on the basis of new *bio-analytical technologies* which help considerably increase the efficiency of medicinal substances delivery to the place of its action and also increase patients' safety during drugs application;
- Creation of new medicinal forms with the help of *nanotechnologies*;
- Setting up algorithms and analytical methods, creation of databases that provide for understanding biological texts' functioning mechanisms and develop targeted pharmaceutical impacts, which are studied by *bio-informatics*.

The modern research techniques are impossible without inter-disciplinary approach, which provides for unification of different science technologies, like, for example, biotechnology, biochemistry, biomedicine, biophysics, bio-statistics, and bio-informatics [15]. Creation of the modern medical nanotechnologies, the main development directions of which are presented in Table 1, belongs to such inter-disciplinary investigation capability [16, P.102–103].

Table 1

Guidelines for modern medical nanotechnologies development

№	Medical&biological effects	Nanoparticles and their agents	Spheres of application
1	2	3	4
1.	Catalysis of active oxygen synthesis	Silicon nanoparticles suspensions; Fullerenes with grafted photosensitizers	Oncology (alternative to surgery & radiotherapy); Infections, including also virus diseases; Some metabolism malfunctions (atherosclerosis, diabetes, etc.); Wounds, traumas
2.	Matrix for the system with medicinal substances, hormones, immune-active substances	Nanotubes, dendrimers, nano-crystals, fullerenes, etc.	Wide scope of diseases; Efficiency and selectivity enhance; enzymopathy, hormonal diseases
3.	Intracellular accumulation and transportation through cellular membrane	Nanoparticles of quantum dots, fullerenes, nano-spheres, nanoparticles with biomaterials	Oncology (decrease of the general toxic chemotherapy); “cell therapy” – capability of rectifying genetic defects; ageing delay
4.	Change of tissue’s properties and structure	Many types of nanoparticles and nano-products	Plastic surgery (adipopexia, amyotrophy, etc.)
5.	Creation of blood vessels (neoangiogenesis)	Aggregated nanoparticles with nano-active materials	Ischemic conditions, heart attacks, strokes, etc.
6.	Creating implants	Composite materials on the basis of nanoparticles	Organs prostheses (eyesight, hearing, sections of pancreas, liver, electric stimulators)
7.	Information transfer channels, creation of micro-computer devices	Platinum, gold nanoparticles; micro-circuits on the basis of nanoparticles	Prostheses of neurotic fibers and centers
8.	Intravascular gas and nutrients transportation	Nano-emulsions and nano-foam	Blood deficit, anemia, limitations of enteral feeding, etc.
9.	Navigation (guided) self-moving devices	Composite materials; Power plants on carbon nano-tubes; nano-tubes as panels	“Sanitary performers” (“wipers” to clean internal parts of vessels, remove tophus, etc.)
10.	Strengthening body parts, protection from mechanical injuries	Carbon nano-tubes, nano-composites	“Bodyguard”, internal armor vest
11.	Effect of self-cleaning, decontamination, health improvement	Nanoparticles of metal oxides (titan, barium, calcium)	Wide assortment of devices for sanitary, hygiene, food manufacturing, etc.

Prepared according to [16, P.102–103].

Hence, the main spheres of nano-biomaterial utilization in medicine are as follows: medical appliances, therapy and diagnosis of diseases, implantations, tissue engineering, and microelectronics (nano-components of micro-electromechanical systems (MEMS)); toxins adsorption and their clearance; biological utensils, diagnostics (nano-sensors, nanoparticles detection in bio-objects) [17, P.78].

Table 2 presents three main market segments in accordance with the area of application [18, P.55].

Table 2

Main market segments of nanotechnologies in the sphere “Medicine and biotechnologies” in accordance with the area of application

Medicine and biotechnologies		
Medical research, clinical diagnostics, medical appliances	Pharmaceutical drugs and medicinal compounds	End-use products
- Nano-HPLC systems (high performance liquid chromatography); - bio-magnetic separation; - transfection reagents; - nano-membranes; - nano-manipulators; - bones replacements; - anti-microbe bandage materials; - spintronic sensors; - scalpels’ blades; - surgical needles; - medical clothing; - medical tubing; - anti-infectious coating for medical appliances; - contrasting agents for magnetic-resonance tomography; - scanning measuring tips of microscopes; - fluorescent agents for optical imaging	- Medicinal agents delivery; - medicinal compounds with enhanced solvability; - cancer treatment drugs inserted into nano-liposomes; - hormone therapy on the basis of nano-phospholipids; - AMD therapy based on aptamers	- sunscreen means and cosmetics to protect from UV radiation; - antioxidants; - food supplements; - food products and beverages

Prepared according to [18, P.55].

Market segment of nano-products “Nano-medicine and biotechnology” also includes medicinal drugs, medical research methods and clinical diagnostics appliances, end-use products (cosmetics and food supplements), as well as food products and beverages, at the creation of which nano-materials and/or nanotechnologies are applied.

It’s quite obvious that nano-materials are created and utilized by the end-products’ manufacturers in all industrial economic sectors. Table 3 gives examples of using nano-materials which are commercially produced right now and are available in the open market [18, P.68–71].

Table 3

Examples of nano-materials utilization on the global market of nano-materials in “Medicine and biotechnologies” sector

Sector	Nano-materials types	
	Nano-size films and nano-level coatings	Hard nanoparticles
Medicine and biotechnology	- Nano-porous membranes (polymers) for water treatment appliances; - Nano-porous polymers to coat glasses and lenses; - Thin silver films for anti-bacterial dressing materials	- Titan oxide, zinc oxide for sun screening creams and personal hygiene means; - Calcium phosphate, hydroxyapatite for synthetic bone tissue and tooth implants; - Aptamers – medicinal drugs to treat skin neovascular age degeneration; - Dendrimers in markers when measuring cardiac function; - Gold nanoparticles for immunological tests and optical electronic microscopy - Quantum dots (Si, Ge) to carry analysis with the help of marked molecules; - Rare-earth luminophors to analyze bio-structures marked with molecules; - Dendrimers (facilitate DNA penetration into cells) in reagents for transfection in gene engineering; - Colloidal silver when producing biologically active supplements; - Iron oxide (super-parametric nanoparticles) for magnetic separation during biological, biochemical, immune and genetic analysis; - Iron oxide, contrasting substances for imaging during magnetic resonance; - Nanoparticles of silicon oxide (antioxidants) when producing biologically active food supplements with antioxidant action; - Oil nano-spheres (deliver bio-particles through cell walls) for disinfectants

Prepared according to [18, P.68–71].

Table 4 gives the forecast of reaching the stage of nano-materials’ commercial usage, which are still at the design stage, for the nano-industry sectors in the period 2009–2015 [18, P.73–81]. Table 5 shows the present and future stages in nanoparticles application [19, P.54–56].

Table 4

Forecast for under-design nano-materials to reach a commercial stage on the global market of nano-materials in “Medicine and biotechnologies” sector

№	Nano-material type	Nano-material name	Years					
			2009	2010	2011	2012	2013	2014
1.	Thin films and nano-level coating	Coating that protects from magnetic fields impact during MRT (magnetic-resonance tomography) (HAP-coating) – nano-materials from iron and ceramics to coat medical equipment (vessels’ walls and other organs)	➢	•	✓			
		Nano-structured calcium phosphate films and hydroxyapatite, bio-compatible coating for medical devices and implants	•	✓				
2.	Hard nanoparticles	Aptamers for molecular bio-drugs when imaging in positron-emission tomography devices	➢		•	✓		
		Lipids, polymers, dendrids (dendrids’ polymer particles) for dot delivery of medicinal drugs to the action spot	+	➢		•	✓	

3.	Hollow nanoparticles	Carbon nano-tubes, fullerenes, nano-capsules for medicinal drugs' dot delivery devices	+	➢		•	✓	
4.	Monolithic materials with nano-structure	Nano-structured titan to create implants with increased bio-compatibility	•		✓			
5.	Nano-composites	Collagen fiber/potassium phosphate (hydro-collagen fiber /potassium phosphate (hydroxyapatite) to replace bone and binding tissue	+	➢			•	✓

+ Fundamental research and developments;
➢ Applied research and technology development;
• Exploratory prototypes and their usage;
✓ Beginning of commercial production and market entry

Prepared according to [18, P.73–81].

Table 5

Present-day and future status of nanoparticles use

Sphere of application	Under development	In the market	Well-studied
Medicine, health protection	- Nano-crystal medicines for easy disintegration; - Insulin to be inhaled; - Nano-spheres for drugs to be inhaled; - Bone growth stimulants; - Usage of quantum dots to detect viruses; - Anti-cancer treatment; - Coating for implants (e.g., hydroxyapatite)	- Sun-tan protection creams and lotions that use Zn and Ti_2; - Molecular marking: quantum dots, CdSe; - Means of delivering water low solvency medicines	- Fungicide based on Zn; Au for bio-marking and identification; - Agents of contrast imaging for magnetic resonance, that use super-paramagnetic iron oxide

Prepared according to [19, P.54–56].

2. Prospects of the development of main manifestations of NBIC-technologies in medicine.

Main manifestations of NBIC-technologies in medicine and prospects of their development till 2020 and 2030 include [15, P.79–94]:

1) Medical biotechnology manifested the most prominent success in the field of ***recombinant DNA (pDNA)***, the technology of which helps "build-in" genes responsible for human proteins coding, into a cell genome of yeast and mammals. In the result, there appears a possibility to induce the cells-recipients to produce the required protein [18, P.214]. The term *"synthetic biology"* was firstly introduced in the USA in 1980, when bacteria gene engineering was carried out with utilization of pDNA technology. Synthetic biology was further developed in such an event as bioengineering that include also assembly of natural biological systems and particles in artificial systems. Exactly this complex of processes is an integral part of synthetic biology.

Therefore, *synthetic biology* – is an interdisciplinary high level research branch, which includes synthesis of complex biological and biologically inspired systems that have functions absent in nature to include also human beings. Synthetic biology main idea – to design, construct and engineer biological systems and equipment that are capable to process information, create materials and corresponding structures, generate energy, sustain or improve human health, etc. In future, using nano-technologies potential, engineering of synthetic biological systems would be implemented at different levels beginning from cell and tissue, and finishing with synthetic organisms. Synthetic biology is directed to redesign the existent natural biological systems and organs to be used in human organism [15, P.81].

In synthetic biology NBIC-technologies convergence manifests itself most prominently, because research in this field has been carried out jointly by engineers, industrial technologists, scientists from the industrial branches of molecular biology, organic chemistry, informatics, nano-biotechnologies, etc. For example, biological elements are transformed into micro-machines thus creating artificial bio-systems imitating living systems characteristics (such technologies have become known as *biomimetics*). One more direction in synthetic biology research is creation of such gene engineering branch that could have provided for *shifting from cell level to creating big artificial systems* using the same methods as at building bridges, computers and buildings [19].

Table 6 contains examples of therapeutic pDNA products, which are available now for clinical use [20, P.215–216]. Table 7 summarizes the variants of human proteins synthesis using pDNA, including also the already available and under design variants [20, P.216–217].

Table 6

Drugs based on pDNA-technology application

Product	Action
Alfa-interferon	Chronic hepatitis C, hairy cells leukemia, chronic granulomatosis, multiple sclerosis
Beta-interferon	Chronic hepatitis C, hairy cells leukemia, chronic granulomatosis, multiple sclerosis
Proteins of bone tissue morphogenesis	Induce bone regeneration
Calcitonin	Provides for calcium arresting in bones
Blood clotting factor IX	Hemophilia B
Colony stimulating factor	Provides for lymphocytes-B growth
DNAase (pulmozyme)	Suppresses mucus secretion (bone fibrosis)
Epidermal growth factor (EGF)	Provides for injured skin treatment
Erythropoietin	Stimulates production of red blood cells
Blood clotting factor VII, VIII	Provides for blood clotting
Gamma-interferon	Chronic hepatitis C, hairy cells leukemia, chronic granulomatosis, multiple sclerosis
Glucocerebrosidase	Gaucherie disease
Granulocytic Colony stimulating factor (G-CSF)	Neuropenia (agranulocytosis), bone marrow transplantation
Granulocytic-monocytic Colony stimulating factor	Bone marrow transplantation
Vaccine against hepatitis B	Antigens that induce immune response at hepatitis B
Human growth hormone (HGH)	Induce bones’ growth
Insulin	Diabetes treatment
Insulin-like growth factor (IGF-1)	Induce growth
Interleukin-2	Stimulates immune system
Interleukin -10	Thrombocytopenia prophylactics
Monoclonal anti-bodies	Influence specific protein structures that are used in cancer diagnostics and treatment as well as at autoimmune disease
Plasminogen activators	Thrombus disintegration
Prourokinase	Anti-coagulant
Relaxin	Causes muscle relaxation during labor
Superoxide dismutase	Minimize injuries at hypoxia; antioxidant
Plasmogene tissue activator (activase)	Thrombus disintegration
Tumor necrosis factor (TNF)	Attacks cancer cells; applied when treating rheumatoid arthritis

Prepared according to [20, P.215–216].

Table 7

Capabilities to produce human proteins using recombinant DNA technology

Production method	Current status	Advantages	Disadvantages
1	2	3	4
In bacteria	Methods of primary production	It's easy to sustain bacteria in a culture; as a rule they secrete protein	Many proteins are impossible to get in the end-form
In yeast cells	Widely used	Proteins are synthesized in the most approximated to human form	Cells must be lysed to get protein; yeast is harder to sustain in culture than bacteria
In mammals' cells	Used in several cases, especially by hybrids	Proteins are synthesized in the most approximated to human form	Cells are very hard to sustain in culture; pollution with viruses or prions could occur
In human cells	Under development	Proteins are synthesized in the required for humans form	The risk of polluting with viruses or prions is the highest; cells are very fragile; gene-engineering modifica-tion is required to cultivate cells
In insects' cells	Under development	High production speed	Insects' cells are very different from mammals' cells; cultivation methods are under development
In transgene animals	So far not used in treatment, but some products are very close to it	Relatively inexpensive if comparing with methods that use cells' culture	Require long time for maturing; drugs may be detrimental for animals; pollution with viruses or prions may occur
In transgene hens' eggs	At the early development stage	Quick maturing; easy to get the product; animals are protected from drugs action	Hard to get transgene eggs
In transgene plants	Some products are used for treatment, others are under development	Relatively inexpensive if comparing with methods that use cells' culture; cheaper than using transgene animals; drugs are not toxic for plants	Migration of transgenes into wild populations (outcrossing); unsafe for environment, especially seeds that are the most lucrative place for protein concentration

Prepared according to [20, P.216–217].

Developed countries' interest to synthetic biology, as, for example, NBIC-technologies conversion option, keeps growing. For example, Synthetic biology engineering research center (SYNBERC) was set up in the USA with the financial support from National Science Foundation (NSF). It brings together a number of leading scientific research universities. For example, in the Massachusetts Technology Institute the research is under way to study biologic oscillators and meters, bacterial switches, photo-sensitive bacterial bio-films and other materials as well as equipment that implement the synthetic biology principles [21; 22]. Moreover, research in the sphere of synthetic biology is supported in the EU within the framework of NEST program (New and Emerging Sciences and Technologies) and by the project SYNBIOSAFE, which was started in 2007 [15, P.82].

Since 2002 the US National Intelligence Council, under the auspices of the National Defense Research Institute (NDRI), has been financing the Rand Corp. company's research in the sphere of high technologies' synergy, and primarily the nano- bio- information-communication technologies. In the result of that work a number of adding to each other reports has been prepared to discuss prospective global trends in that sphere for the period up to 2010, 2015, 2020, 2025 and up to 2030 [23–27].

According to Rand. Corp. specialists NBIC-technologies convergence will help considerably increase synthetic biology capabilities in such domains as:

- *Genetic profiling and DNA analysis*. Newly developed equipment and system chips would help increase human disease diagnostics depending on the character and genetics of ethnical groups, capabilities to develop medicinal drugs for a specific patient and also would provide for bio-sensors creation. Such equipment will find its place in the development of security systems, appliances for police, but it's necessary to consider the current legislation as regards its supplementing with the normative principles of specific persons' DNA identification, which would also be helpful for the available biochemical technologies (e.g., person identification by retina or fingerprints). Genetic identification and bio-sensors, which have been developed on the basis of genetic engineering, would become one of the most important tools for law-enforcement bodies as well as for medical people when creating a system to monitor population disease rate and health status. At the same time individual DNA profiling creates serious problems attributed to the need of preserving confidentiality of private life and the need of enhancing the scope of DNA monitoring. Whereas, it will require the developed countries governments to elaborate a long-term policy in this sphere as well as drafts of national and international norms and regulations that would account such global threats;
- *Development of technologies for genome decoding and proteomics, that research proteins and genes functions.* Thanks to bio-informatics achievements it would be possible to develop break-through technologies when combining genetic coding and sequencing on the basis of the corresponding computer programs and other information-communication technologies (ICT). At the same time that research sphere faces considerable technical problems as, for example, insufficient knowledge of gene coding mechanisms, genetic transduction (transfer of the genetic feature from one micro-organism to the other), isomeric modulations and other mechanisms;
- *Eugenics and cloning*. It includes research and utilization of genetic engineering opportunities to "improve" a human being with the help of cloning. At the same time, such research certainly creates considerable contradictions and protests having civilization, cultural, moral-ethical and religious nature. Human cloning would become possible by 2015–2020 and would be accomplished only in the countries, where prohibitive legislation is absent.
- *Genetically modified organisms.* Production of genetically identical organisms on the basis of cloning would mainly be used in genetic engineering to produce grain, in cattle breading and for animals that are used for scientific purposes. The available and applied now traditional methods of genetic manipulation – spraying, selection and irradiation – would be intensified at the expense of introducing, removing and modifying genes in genetically modified organisms (GMO). Research in the sphere of GMO would proceed in the direction of food taste improvement, creation of ultra-lean meat products with the decreased content of "bad" fats, salts and chemicals that negatively impact human health and cause today a wide spread of allergic diseases. Genetic modifications would also concern trees and plants for further production of bio-fuel and raw materials of paper industry. At the same time, as plants and organisms genetic modification is becoming more and more an international practice, it has become more difficult to differentiate genetically modified components in food products. Together with food biological safety, biologic modification mechanisms may be used by humans for military purposes like development of the up-to-date bio-weapons as well as the corresponding protection from such weapons. Therefore, there is a risk that non-controlled creation of eugenics or engineering programs may lead to creating biological organisms dangerous for people and animals;

2) Biochips. At present semiconductors industry experience gradual transition from silicon chips production to biochips. But biochips series production faces two main problems: firstly, biological components in electronics have not yet reached the level of standardization for scale production; secondly, there still exists a different "ideology" in the biology of biochips design and production. The US Massachusetts Technology Institute has already developed a specific range of standard bio-elements that contain more than 1 thousand bio-components (they have been called "bio-bricks"). In reality that range includes the corresponding bio-elements that are classified by the principle of their implementation in electronics (e.g., bio-invertors or bio-converters, bio-switches, bio-meters, bio-amplifiers, displays' bio-components, etc.). Moreover, there are functioning companies that are involved into bio-production on the basis of synthetic biology principles [15, P.82].

3) Biological spare parts and military exoskeletons; bio-gerontology. Scientific research in the field of creating "biological spare parts" to perform "repairs" of a human body has the aim of both replacing different human organs and/or parts and strengthening human's physical capabilities and functions. Among the approaches that have been practically applied are the following:

- *Human tissue engineering and regenerative medicine* are directed first of all at creating organic and artificial tissues, organs and materials to replace the lost ones, treat the ill ones or improve the available human body organs as well as at the development of nano-coating for implants and surgical instruments. Rand Corp. experts consider that "tissue engineering" is a new medical branch [23–28]. At present such technologies as skin growth are used for treating wounds and burns; cartilaginous tissue growth - for "repairing" and replacing injured human cartilaginous joints . In the USA these technologies are on the stage of clinical research. Growing functional tissues for myocardium is becoming also a reality.

  The development of the mentioned medical trends would depend on creation of bio-compatible scaffolds, elaboration of the corresponding transplants, multi-cell tissues and new multifunctional materials with using bio-technologies for growing human artificial tissues and organs. For example, such ceramics as bioactive calcium-phosphate-silicon glass, hydroxyapatites and calcium phosphates could serve as chemical materials to grow bones and their regeneration. Bioactive polymers (e.g., polypeptides (artificial proteins)) could be used as surgical nets and tampons or as hydro-gels that stimulate tissue growth. Artificial blood substitutes could change the conditions of blood storage, increase the level of safety to prevent accidental penetration of infection with blood, etc. Practically since 2015 the production of biomedical structures oriented on a patient's specific needs will start. For example, the practice of individually oriented production of ceramic artificial bones to replace the broken or injured arms, legs and scull bones will become more spread. Computer tomography and the facilities for quick prototypes production (using nano-printers) will be required for that purpose. Neuro-prosthetics and sensorium's prosthetics, like implants to replace retina and remove cochlear injuries, bypasses for spinal marrow and other nerve endings, artificial communication and stimulating devices that decrease human blindness and deafness, will also be of wider use;

- *Creation of different exoskeletons*, for example, will help a human being to lift up, transfer to substantial distances heavy loads as well as to move in case of losing locomotion organs or in case of their disease [27]. In the US National Intelligence Council report on global post-crisis trends in the period till 2025 it has been marked: "The technology of augmenting human strength includes mechanical and electronic systems that enhance and ensure human capabilities [26]. They include the attachable exoskeletons with mechanical drives that are enacted by the devices in thighs, elbows and other joints. Exoskeletons may remind a robot-humanoid that is put on a human body and is using sensors, interfaces for different devices, power systems and driven activation appliances, that track and react to the actions of arms and legs, enabling the carrier with additional capacities in physical force and in means to control it" [28]. At present in Japan and USA some of the exoskeleton technologies have been transferred to industrial companies that plan to commercialize them and start their scale production. The present day leasing of such a robot costs USD 1,700 per month [29];

- *Bio-gerontology* – deals with studying "cell and molecular grounds of diseases and organism's ageing process" and could be applied to identify and treat diseases, compensate loss of capabilities connected with ageing [26]. Supporting technologies include improvement of biosensors that in real time perform monitoring of human health, receive information on health state, consider different impacts on DNA structure and specific reactions to DNA-drugs, and provide different mechanisms that ensure totally targeted medicines' action" [28]. The research of telomeres (end portions of chromosomes), which during mitosis prevent genome's injury and also impact ageing mechanism, is world known. American scientists in 2009 received a Nobel Prize in medicine for determining telomere's structure and separating the protein that restores their structure (and therefore, a cell becomes immortal). Those discoveries help increase human life longevity and decrease the period of losing working ability. Thanks to discovery of telomerase it has become possible to regenerate tissue and bring it to healthier condition.

4) Stem cells and their use.

Stem cells' usage for human "bio-repairing" relates to their unique property – capacity of unlimited self-renewal and restoration of other different types cells. Ordinary cell division occurs not more than 50-80 times, after that the process of apoptosis self-ignites. While stem cells can divide 600 and more times. The grounds for stem cells "immortality" lays in the capacity to generate protein telomerase that renews chromosomes' ends. The capacities of different stem cells to generate different cells' types vary. For example, impregnated ovum has the capacity to generate practically all 350 types of grown human organism cell tissues' types. There are progenitor cells, multi-potent cells (they can differentiate in various directions within the limits of tissue derivatives of a single germ layer), pluripotent cells (they characterize non-differential embryonic tissue, capable to implement a number of variants in the process of differentiation) [30; 31].

The first step in developing stem cells technology was to obtain bio-material from human and animal embryonic stem cells, but in the US, as early as 2001, such operation was initially recognized as non-ethical, because it concerned human life destruction. USA and Japan are the leaders in stem cells research. Scientists from Spain, Germany and Great Britain also reached a great success in that field, but those countries also introduced a number of legislative restrictions on such type developments. According to Rand Corp. forecast, research and therapy using stem cells to increase or transform brain or other functions as well as to treat different human body organs (like heart, kidneys, liver and pancreas) will grow by 2020–2030 [25–27].

There is an alternative to using embryonic stem cells. These are stem cells separated from adult human being tissue ("adult" stem cells – ASC), which can also be used for growing tissues and organs. As early as 2006, a group of scientists from Wake Forest University, North Carolina (USA), announced that they were able to grow bladders for 7 patients out of those cells. During 2006–2009 a group of researchers from Northwestern university from Chicago (USA) obtained stem cells from bone marrow of a number of "complicated" patients, after that they destroyed all working immune cells in the body with the help of special chemicals and transferred the stem cells back. Gradually, stem cells produced a new generation of immune cells that did not attack the brain. At the beginning of 2009 the first in the world therapy was announced to improve health of a patient with multiple sclerosis (from the group of 23 people the condition of 17 people improved three years later after the therapy, and none of them experienced any health deterioration) [15, P.86].

Moreover, *xenotransplantology* – transplantation of foreign tissue – has been actively developing. It may remove moral-ethical barriers in using stem cells. For example, baboons or pigs could be genetically modified or cloned to produce the corresponding transplants for humans. Rand Corp. specialists think that such technologies would spread only after 2015, because when using such a technology there could be a "jump of retro-viruses" from animals to humans after the transplantation. Additionally, the moral-ethical issue should be adjusted together with the problem of patenting such transplantations [25–27].

5) Self-assembly and production on DNA basis; convergent "smart" materials.

Self-assembly with using DNA molecules could be implemented on the basis of biomimetic production systems that mainly copy natural schemes and are used on the basis of "functionalization of small non-organic units having DNA molecules with further assembly of those units into more complicated structures" [32]. Self-assembly with using DNA in future will provide for creating biosensors or nano-lithographical equipment for the purpose of forming up the corresponding bio-molecules.

Besides, a revolution in the field of creating "smart" materials and equipment to be used in industrial production is expected to occur. New materials, created on the basis of NBIC-technologies convergence, will be used for producing end-products, components and systems, which are smaller in size, "smarter", more functional and environmentally friendly than all the existent natural and artificial materials. For example, "smart" nano-materials would be such materials that combine sensors with driving devices and computers; or it could be micro- or nano-robots, created on the basis of biomimetics of insects or birds, which would be used to identify harmful materials in the environment, in aerospace explorations, in drones, etc. Also the corresponding construction materials for buildings, bridges, roads would be developed to react to weather change and to perform automatic repairs of cracks in the structures, coatings, etc. In general, the concept of molecular nano-production, which implements the principle "from-down-to-top" (from nano- to macro-level), can bring the change of the economy technological build-up, but not earlier than 2030 [27].

Therefore, in medicine and health care bio-technologies are used in the field of therapy, diagnostics, pharmacogenetics (branch of the genetics, the subject of which is genetically determined organism's reactions to medicines), functional food products and nutraceuticals (food products with pharmacological properties), as well in the medical equipment. Some bio-technologies, like, for example, bio-pharmaceutics and «in vitro» diagnostics, have already been commercialized and have access to the world market.

For example, experimental bio-therapy with using bio-technologies, includes *cell engineering, therapeutic vaccination, research in the field of stem cells, lytic viruses, genes, etc.* OECD determines the indicated directions as "experimental", because they have not been widely market-wise approved by government authorities of OECD countries, which are responsible for designing and approving the corresponding legal decisions in the field of medicine. At the same time exactly those spheres determine the most advanced trends in medical bio-technologies area, which are increasingly used by bio-technologic companies during development, testing and production of pharmaceutic products. For example, research and clinical testing of new molecular drugs bio-NME (New Molecular Entities) demonstrate the bio-pharmaceutics development level in OECD countries. For example, as of today, globally developed bio-NME averagely has undergone 56% of testing. Denmark has the lowest level of bio-therapy per capita, the second place belongs to Switzerland, the USA ranks the third [12; 13].

By 2030, and especially by 2050, health care costs in OECD countries and other world countries would increase. If in 2005 OECD countries budget outlays for health care were on overage 5.7% GDP, by 2050 they could reach 12.8% GDP. But if we also consider private sector, the outlays would be even higher. This could be attributed mostly to the application of new technologies in health care sphere, including also bio-technologies and converged NBIC-technologies. Main application of nano-technologies in health care sphere, for example, would be connected with the production of nano-size equipment and appliances that would be able to interact with bio-molecules both on cell surface and inside it [11, P.40].

Therefore, biomedicine as one of the directions to use NBIC-technologies convergence, would, by different estimates, cause the most radical break-through in this innovations sphere. As expected, in the XXI century nano-technologies achievements will lead to creating new methods in therapy as well as potential preconditions for increasing human physical capacities.

CONCLUSIONS

On the basis of the above mentioned facts we may *conclude*:

1. Biotechnologies similarly to nano-technologies, information-communication and cognitive technologies, in the global scientific community are regarded as "*global technologies"* because they include a wide spectrum of scientific disciplines, economy sectors and are spread over huge territories of the planet. According to the leading world experts, the list of the modern convergent biotechnologies that are used in medicine, pharmaceutical and biotechnological industries, in bioenergetics and agriculture, should include: *DNA/RNA; proteins and other molecules; cell and tissue cultures and their design; genes and RNA-vectors; bioinformatics; nano-biotechnologies.*

2. Biomedicine, as one of the directions that use convergence of NBIC-technologies, by different evaluations would cause the most radical break-through in this branch of innovations. As expected, in the XXI century nano-technologies achievements would provide for creating new methods in therapy as well as potential preconditions to increase human physical capacity. *Practical implementation of the fundamental developments* in the mentioned branches would manifest itself in the development of *personified medicine*, to include also *gene-diagnostics; proteomics; pharmacogenomics; bio-analytical technologies;* implementation of *nano-technologies for medicinal drugs; bio-informatics.*

3. The main directions of nano-biomaterials application in medicine are as follows: medical tooling, diseases therapy and diagnostics, implantations, tissue engineering, micro-electronics (nano-components of micro-electronic-mechanical systems – MEMS); toxins adsorption and their removal from body; bio-tooling, diagnostics (nano-sensors, nanoparticles detection in bio-objects).

4. The main manifestations of *NBIC-technologies convergence in medicine* and future trends of their development till 2020 and 2030 are as follows: *recombinant DNA (pDNA), biochips, biological spare parts, civil and military exoskeletons, bio-gerontology, stem cells and their usage, self-assembly and production on DNA basis, convergent "smart" materials.* NBIC-technologies convergence would help considerably increase the synthetic biology capabilities in the following directions: *genetic profiling and DNA analysis; development of genome decoding technologies and proteomics that investigate proteins and genes functions; eugenics and cloning; genetically modified organisms.* By 2030 the developed countries would considerably increase their budget for health care which would be attributed to the growing utilization of biotechnologies and converged NBIC-technologies in health care system.

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