Nanotechnology, Nanobiology, Nanomedicine and Their Perspectives

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Abstract:- The role of nanotechnology in the solution of biological and medical problems using nanocomputer methods in diagnostics and treatment is considered in this paper. The problem of creation of new technology by means of programmed probes, where the following main elements are presented: the creation of micro transmitters, processors, "sensors", "manipulators which perform the process" and "effectors" is analysed in details. Microsurgical "robot tentacles" have the ability to self-setting. Significant achievements have been gained with the aim of creating nanomaterials, nanodiagnostics, transportation of therapeutic drugs. Those achievements are considered, which have been obtained in the direction of cancer diagnostics and treatment, as well as for treatment of damaged tissues with nanotechnologically prepared tissues. Nanotechnology already has some high sensitive methods to detect malignant tumor at the level of blood molecules and even the predisposition of a patient to malignant tumor. The device, developed on the principles of sensors allowing the identifying the viruses, which are spread in the environment should be noted. The capsules for the regulation of insulin concentration in the blood of patients suffering from diabetes I type are undergoing a clinical examination. Oxygen transporter or a respirocyte is created; its structure and function are considered in details. The fact of crotocytes creation, where a fibrous mass, releasing in the damaged area of the tissue, presented in the depth of the formation of these crotocytes should be considered as a remarkable achievement. The formation of fibrous net is observed and under its impact the bleeding is stopped for some seconds. It turns out that using nanotechnological methods, there are great prospects for solving biological and medical problems.

Keywords:- Nanobiology, Nanomedicine, Diagnostics and Nanotechnological Treatment, Transporters, Sensors.

I. INTRODUCTION

According to the lecture delivered by Nobel Prize Laureate Richard Feinman in 1959 - "There is plenty of rooms at the bottom" [1], a perspective for creation of such nanorobots has been set, which according to the special programs will operate in the human organism. They will have the ability to penetrate into any tissue, organ or organelle and, according to the recorded program the ability to repair damaged areas. This process may be performed by means of microtransmitters (sensors), micro engines, accelerators, micropumps and micro valves. Today the information on a great future of nanotechnology has become a reality. It's true that in the opinion of many scientists Richard Feinman's prediction was not serious, but soon from theoretical reality this idea has gained a great practical value. All this gives the opportunity to implement the programmed reactions at the level of nanometric dimensions of biological structures using the newest technologies. As some of the most important technologies likely are to emerge in the first half of the 21st century, nanotechnologies appear to be an incredibly important topic in biology and medicine and as a result, the experts gathered by the NSF predict that the market for nanotech products and services by 2018 only in the USA will exceed 2 trillion [2, 3].

Today, programmed probes are already being created, in which the following main elements will be presented: micro transmitter, processor, "sensor", the process performing manipulator and effector with micro surgical "robot tentacles". The nanorobots will have the ability to self-setting. Thus, one of the stages of nanotechnology will be the creation of self-renewing probes, which in the opinion of many scientists will be the century apocalypse. Fortunately, there are a lot of examples of self-setting in the living organisms, for instance: the decay and self-setting of embryonic tissue and hemoglobin, the denaturationrenaturation of proteins and nucleic acids, etc. [4, 5].

According to the theoretical calculations, the processor's volume by 10.000 logic system should not exceed 100 nm³. This is quite enough to make an ultramicro computer, which is significantly smaller, as compared to subcellular organelles. For example, a diameter of blood red cells is 8 μ in average, which exceeds an artificial processor about 80 times. All this gives the microcomputer the opportunity to penetrate into the cell for performing the operations.

Three main directions in nanobiology and nanomedicine were identified: 1. The creation of nanomaterials. 2. Nanodiagnostics. 3. The creation of transporters of medicinal drugs.

Among the nanotech materials, a special interest has been caused by the fact that by means of nanosubstances the targeted synthesis of separate tissues and the replacement of "own" tissues of the organism become possible, so as to exclude an immunological conflict. Today the imitative material, having three dimensional 8 nanometer diameter of bone tissue has already created. By its mineralization a hydroxyapatite has been obtained. Hydroxyapatite is the main mineral of bone tissue and hard tooth tissues. Ceramics based on it does not cause a rejection reaction and is able to actively bind with healthy bone tissue. Due to these properties, hydroxyapatite can be successfully used in the restoration of damaged bones, as well as in the composition of the bioactive layer for the better implant growth. In future it gives great hopes for the treatment of damaged tissue with nanotechnologically prepared tissues.

According to their structure, nanoparticles are divided into three groups:

A. Liposomes

Essentially, liposomes are composed of phospholipids bilayer that occurs like vesicles. These tiny structures have a hydrophilic head, which means that they are dissolved in water. However, they also have a hydrophobic tail, which is made up of the lipid layers. These structures are particularly useful in medicine and the delivery of drugs.



B. Dendrimers

Dendrimers are a type of nanoparticle that has the tendency to be highly branched. This type of nanoparticles is also divided into the globular structured nanoparticles having a central core and globular structured ones that lack a central core. Dendrimers are also widely used in various industries, as well as in medicine [6].



Fig 2:- The scheme of dendrimer synthesis, double projection, N - the number of terminal groups.

C. Carbon Nanotubes

Carbon nanotubes are the structures of nanoparticles that appear as cylindrical structures. These carbon allotropes have unique properties that make them important for various applications, including electronics and optics among many others [7].



Fig 3:- The structures of eight allotropes of carbon:

The microcapsules coated with the membranes having nanopores, prepared by special chemical technology are successfully used in the transport of medicinal drugs and for the treatment and rehabilitation of damaged organs or tissues through the time delay release [8-10].

The prospects and achieved successes in the creation of devices for nanotech diagnostics are of particular interest. It's already a long time as in the United States of America, in the center of nanotechnology, under the leadership of Baker are working to create such microtransmitters (sensors), which will be used for detecting and ablation of malignant tumor cells in the organism. Such nanotech dendrimers (in Greek - dendron tree) are made from superbranched polymers. The size of dendrimer or nanosensor does not exceed 5 nm. According to the project, these smallest sensors will be located in the lymphocyte. While contacting the cell of damaged area, the nanosensor begins a fluorescent light. The registration of this luminescence will be recorded by means of specially made scanning device. The scanning will take place in 15 seconds [11-13].

Using the advantages of the drug delivery system, the immunostimulatory cytokine interleukin -2 (IL-2) was first adsorbed in nano-vesicles (NV-DOX_{IL-2}) loaded with doxorubicin (DOX), with high efficiency of encapsulation using a facile solvent-free method. After intravenous injection to mice with melanoma, NV-DOX_{IL-2} accumulates in the tumor and significantly suppresses tumor growth with negligible systemic toxicity. Bear in mind the

application of this strategy, interferon- \Box [IFN- \Box] was additionally introduced to the combinatorial system to develop cytokine cocktails adsorbed HVs. This type of NVs can significantly inhibit the primary tumor growth and lung metastasis in triple negative breast cancer. With the use of underlying mechanism, the cytokine cocktails adsorbed NVs can facilitate the maturation of dendritic cells, promote the infiltration and activation of CD8+Tlymphocytes and natural killer cells, and increase the recruitment of CD₄₅-immune cells and Ly6G-neutrophils [14].

An analytical device Intel Raman Bioanalyzer System has been created in the corporation "Intel". This device will enable us to identify diseases at the level of blood serum molecules using laser beams. The above nanotechnology is based on the principle of detecting microscopic defects in semiconductor crystals. Unfortunately, today in biology there is no such method for detecting diseases at the molecular level. Therefore, it should be considered as the beginning of a new epoch in biomedical diagnostics. A great part of scientists thinks that such a device will give us the opportunity to reveal a malignant tumor at blood molecular level and even the predisposition of patients to malignant tumor [15].

Based on the above-said, at present the nanotech methods are widely used for the identification and elimination of AIDS and malignant tumor cells. Today a device has been actually introduced, which gives the opportunity to reveal AIDS without the intervention of professional physicians. This device is Point Care, by means of which for labeling erythrocytes the gold nanoparticles are used instead of fluorescent substances [16].

The creation of autonomous nanodevices also intensively takes place for medical diagnostics. For example, in medical practice a few millimeters length video camera with installed lighting system is used to reveal gastrointestinal damage. It is a thousand times larger than nanotech equipment, which easily penetrates into the organism and its operation is controlled from the outside. Nanotech equipments are equipped with specific sensors and manipulators, by means of which it is possible to carry out nanosurgical operations. Such can also be introduced through the esophagus and registered by the computer.equipment.

Scanning probe microscopes are macro analogues of nano surgical micromanipulators, by means of which even the displacement of atoms is possible it will be done using "nano forceps" size with 50 nanometers. The operation is regulated **exogenously**. The nanoobjects can also be displaced by means of laser beams, which practically are accomplished on DNA example by means of "optical forceps, connected to DNA terminal nucleotide. 96-yearold Eshkin was awarded a prize for the development of optical forceps technology [17]. This will be done with nano forcets of size 50 nanometers. Nanotech sensors and analyzers are widely used for diagnostics as "laboratory chips", Nanotech nanosensor apparatus is already created, by means of which the identification of swine flu has become possible in public places. The patients who have contracted the flu are the source of a number of volatile products from the alveolar and respiratory epithelium. These products include a range of volatile organic compounds and nitric oxide. They can be used as biomarkers to identify the disease. A portative device has been created on the basis of microsystem with three sensors that detect the biomarkers of swine flu infection [18]. Particularly, by their usage the great achievements were gained in the creation of medicinal drug transporters and the treatment of diseases.

In 2001 Sheinberg has shown the elimination of mouse tumor cells by nano test (a miniature machine), particularly, by means of temperature shock of tumor cells with ultra-violet rays. For this reason, using nano catheter actinium 225 was administered in mouse. As a result of its impact, the structure of tumor cells was destroyed following by their total elimination. The life expectancy of mice subjected to actinium impact has increased about 9 times. It is noteworthy that after an autopsy even a trace of tumor cells were detected by means of a special sensor [14].

The tumor-inhibitory effect of the drugs was tested on the Lewis lung carcinoma model using the male mice of C57Bl/6J line. It was found that C60 + Dox complex in a low therapeutic dose enhances the inhibition of tumor growth to much higher extent than that for the sequential administration of pristine C60 fullerene and Dox, or their administration as single agents, namely the maximum therapeutic effect reached 61.5% for the tumor growth inhibition. The proposed tumor treatment by C60 + Dox complex is considered to be promising in cancer therapy [19].

In order to fight tumors, using nanometric particles, iron oxide coated with organic aminosilane was locally injected in the tissue of tumor. Then it was subjected to the action of magnetic field, which induced vibration, as a result the temperature increases, temperature shock damages and decays tumor cells. Naturally raises the question why the accumulation of nanoparticles occurs predominantly in tumor cells. As it turned out, tumor cells have no effective lymphatic drainage system.

In terms of nanotechnology, the experts in this field had gone much further, as they used nanocapsules (lipid coacervate), labeled with guide lectin, isolated from target cell as a similar transporter. Based on the principles of antigen-antibody interaction, lectin is specifically connected namely to the target cell.

Nanocapsules are mainly used for the transport of medicinal preparations; however, they have many functions. Their size is about 1 mkm; the size of pores is varied within the ranges of 0.1-1.0 nanometer. Such capsules are already in the process of clinical testing for the

regulation of insulin concentration in the blood of patients with diabetes I type. The first successes have already been obtained. It is not excluded that in the nearest future insulin synthesizing cells will be placed in the nanocapsule. They will be protected from their discharge from the organism by the immune system [8, 10, 20].

The oxygen transporter or respirocyte has already been created, which will be used for oxygen provision at ischemic heart diseases. Respirocyte has an oval shape, into which oxygen is pressed. The diameter of sphere is 1 mkm. It is resistant even to 1000 atmospheres. Unlike the respirocyte, oxygen pressure in hemoglobin does not exceed 0.5 atmosphere, out of which only 0.13 atmospheres may be released into the tissue. It is noteworthy that if one liter of microcapsule respirocyte consists of about 530 L oxygen, the volume of oxygen in 1 L of blood is 0.2 L. This volume is quite sufficient for the provision of aerobic processes with oxygen taking place in the organism during 36 hours. So, at acute ischemia for the provision of the organism with oxygen the injection of 0.5 ml respirocyte into the blood is quite enough.



Fig 4:- Respirocytes - Artificial Mechanical Red Blood Cells

In our opinion, especially perspective is the creation of respirocyte having the ability for the exchange of oxygen and carbon dioxide, the action of which will be dependent on the concentration of oxygen and carbon dioxide, existing in the organism. In particular, the release of carbon dioxide and the absorption of oxygen in the lungs will take place. On the contrary, the release of oxygen and the absorption of carbon dioxide will take place in the tissues.

Many scientists are successfully working on creating artificial mitochondria in hypoxic conditions for the maximal provision the cells with ATP.

So-called crotocytes or the bioorganic formations participating in the blood coagulation are of great interest. In appearance they resemble respirocytes with the difference that a fibrous mass is presented in the depth of their formation, which is released in blood damaged area; a fibrous net is created, where the red blood cells will be placed and the bleeding from the organism will be stopped. From the above-said, it becomes clear what a great role will be given to the introduction of this technology during the wound to save the lives of people with hemophilia. By the use of nanotech methods the employees of Massachusetts Institute and University of Hong Kong have created such a liquid, one drop of which can stop the bleeding from any wound in 15 seconds. The drugs for blood coagulation have the greatest value not only for saving the lives of patients with hemophilia, but also during surgical operations, as the time spent for the stopping bleeding is greater, than the time for the operation itself. It is calculated that at the wound with 1 cm length and 3 cm depth the blood loss is about 6 mm³, which is very dangerous for human life.

By using nanotech means the mutations of DNA and the primary structure of proteins, the pathogens of infectious diseases and toxic substances can be established, the discharge of which from the organism by nanometric membranes appears to be not very difficult. The variations of DNA genes have been revealed by nanosensors, which appear to be the precondition that the recognition of mutated nucleotide out of 200.000 pairs in DNA is permitted. The method of electronic nanomethod has been used for the DNA sequencing.

By means of nanocapsules it is possible not only delivery of drug in damaged areas, but also the regulation of medicinal drugs concentration. It should be noted that each person shows an individual sensitivity to this event.

So called "wet" nanotechnology is of great interest, which provides for the micro transformation of the mechanisms acting directly in the living organism.

"Wet" nanotechnolog

This approach is based on the use of ready-made mechanisms, existing in the nature. This idea was first formulated by an American biochemist White in 1967. He suggested the use of mechanisms consisting of nucleic acid molecules and enzymes. A year later White proposed to use genetically modified viruses, as the mechanisms for cell repair.

➢ Biotechnology

The use of existing organisms as a basis for the creation of bio-robots promises a number of benefits. The initial organism provides ready-made systems of energy supply, reproduction, displacement, self-repair, etc. There are the proven methods for receiving genetic modifications, the experience in the use of micro organisms with various purposes.

➢ Virus as a robot

At present, viruses are already actively used for the introduction of new genetic material into the cells. In perspective, one can imagine the use of a variety of robotviruses capable of recognizing a specific cell type in a specific physiological state. Depending on the specific situation, such a robot-virus will be able to kill this cell (for example, disease pathogen) or to introduce the necessary DNA or RNA molecules into the cell, up to the complete replacement of damaged genetic material.

➤ The cell-robot

The cells in the human organism are able to move purposefully, sometimes for long distances, to destroy other cells or vice versa, be embeded in damaged tissue in place of dead cells. It is not too hard to imagine the cells that are artificially modified so that they destroy atherosclerotic plaques, regenerate damaged organs, limbs, etc. The cells can carry labels, allowing them to watch their replacement throughout the organism, to release the substances into the environment, bearing the diagnostic information.

These are: proteins, nucleic acids, enzymes and genetically *ex vivo* modified and transplanted viruses, by means of which the rehabilitation of destroyed mechanisms in the cells will take place. Naturally that artificially constructed enzymes will have a leading role in these processes. Currently, functionally active enzymes are already constructed, the use of which seems very promising in industry. Taking into account that all enzymes have a protein nature and consist of 20 amino acids, and then it is possible to synthesize about 10^{100} artificial enzymes that is not yet implemented in the nature. The viability of biosphere is realized only by the action of 10^{14} enzyme.

Molecular nanotechnology and nanorobots do not seem to be too distant future for nanotechnologies. After their realization the treatment rules will be changed fundamentally. One of the areas of molecular nanotechnology is of special interest – the creation of isolated genes with structural and functional parts based on the computer. This will be such a design, which will work in the cell. There are connecting polymerase of DNA, start and stop codons and splicing-connecting areas in the cell. The number and position of axons and introns will be subjected to the formation of purposeful design in the genes created by the computer.

II. CONCLUSION

As it seems, nanomedicine identifies great prospects for the recognition of mutated genes and degenerated cells, the reparation of organs, tissues and organelles, the renewal, overcoming old age and life prolongation. Nanomedicine is not a fantasy, it is a reality and in the opinion of many scientists, we should expect great results in the next 10 years.

REFERENCES

- [1]. There's Plenty of Room at the Bottom (http://www.zyvex.com/nanotech/feynman.html).
- [2]. C. Lee Ventola (2017), Progress in Nanomedicine: Approved and Investigational Nanodrugs. 42(12):742–755.
- [3]. Robert A. Freitas Jr. Zyvex. Progress in Nanomedicine and Medical Nanorobotics Corporation, Richardson, Texas, USA.
- [4]. Aleksidze N. Basics of general biochemistry. The Publishing-House "Innovation", 2016. (in Georgian).
- [5]. Self replication and nanotechnology http://www.zyvex.com/nanotech/selfRep.html)

- [6]. Semchikov Yu. D. (1998). Dendrimers a new class of polymers // Soros Educational Journal..12: 45–51.
- [7]. Masami Aizawa Milo, S. P. Shaffer. (2003). Silylation of multi-walled carbon nanotubes. Chemical Physics Letters. 3689(1–2):121-124.
- [8]. Maya Menaker Raskin, Inbar Schlachet, Alejandro Sosnik. (2016). Mucoadhesive nanogels by ionotropic crosslinking of chitosan-g-oligo(NiPAam) polymeric micelles as novel drug nanocarriers. 11(3):205-215.
- [9]. Rao N, Gahane L, Ranganayakulu S. (2014) Synthesis, applications and challenges of nanofluids. IOSR Journal of Applied Physics: 8:21-28.
- [10]. Bolocan A, Mihaiescu DE, Andronescu E, Voicu G, Grumezescu AM, et al. (2015). Biocompatible hydrodispersible magnetite nanoparticles used antibiotic drug carriers. Rom J Morphol Embryol. 56:365-370.
- [11]. Massadeh S, Al-Aamery M, Bawazeer S, AlAhmad O, AlSubai R et al. (2016). Nano-materials for Gene Therapy: An Eficient Way in Overcoming Challenges of Gene Delivery. Biosens Bioelectron 7:1-2. 2015.
- [12]. Jinjun Shi, Philip W. Kantoff, Richard Wooster, Omid C. Farokhzad. (2017). Cancer nanomedicine: progress, challenges and opportunities. Nature Reviews Cancer.17:20–37
- [13]. Shi J, Kantoff PW, Wooster R, Farokhzad (2017). OC1,4Cancer nanomedicine: progress, challenges and opportunities. Nat Rev Cancer. 17(1):20-37.
- [14]. Xianya DanZhang, Zhiping Zhang. (2019).
 Immunostimulatory cytokine and doxorubicin coloaded nanovesicles for cancer immunochemotherapy. Nanomedicine: Nanotechnology, Biology and Medicine. 18:66-77.
- [15]. S. V. Prylutska, V. F. Korolovych, Yu. I. Prylutskyy, M. P. Evstigneev, U. Ritter, (2015). Tumor Inhibitory Effect of C60 Fullerene Complex with Doxorubicin Scharff. Nanomed. Nanobiol. 2:49- 53.
- [16]. PointCare. https://www.pointcare.com/.
- [17]. Optical pinset. https://www.bbc.com/ukrainian/features-russian-45726540.
- [18]. Nanotechnology Sensors Detecting Swine Flu in Public Places. Nanotechnology sensors | Bioengineer Talks.
- [19]. Ramirez A, Corro G, Zehe A, Thomas A (2018). Nanotechnological Approach to the Treatment of Diabetes. Am J Med Sci 6:19-26.
- [20]. R. A. Freitas, Jr., Artif. (1998). Cells, Blood Subst. Immobil. Biotech. 26: 411-425.