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# Functions of biogenic magnetic nanoparticles in organisms

***S.V.Gorobets, O.Yu.Gorobets***

National Technical University of Ukraine "KPI", 37 Prospect Peremogy, 03056 Kyiv, Ukraine

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The functions of the biogenic magnetic nanoparticles both in bacteria and multicellular organisms are studied in this paper using methods of bioinformatics and the modeling experiments in the field of magnetochemistry. Thus it was revealed that biogenic magnetic nanoparticles are necessary not only for the navigation in a magnetic field of the Earth but for accumulation of paramagnetic species such as Fe ions and oxygen and for regulation of transport processes in a cell by changing concentration gradients of different species according to their magnetic susceptibility. The similarity between the genes of magnetosome island of magnetotactic bacteria and human genes have been studied by means of bioinformatics methods for prediction of functions and physiological origin of biogenic magnetic nanoparticles in multicellular organisms. As a result, it was revealed that human proteins (which are the homologues with the proteins of magnetosome island) have been implicated in pathogenesis of a number of diseases, characterized by the elevated level of biogenic magnetic nanoparticles.

В работе с помощью методов биоинформатики и модельных экспериментов в области магнитохимии изучены функции биогенных магнитных наночастиц как в бактериях, так и в многоклеточных организмах. Показано, что биогенные магнитные наночастицы служат не только для навигации в геомагнитном поле, но и для накопления парамагнитных компонент, таких как ионы железа и кислород, а также для регуляции транспортных процессов в клетке путем изменения градиентов концентрации различных компонент в зависимости от их магнитной восприимчивости. Методами биоинформатики изучено сходство между генами магнитосомного островка магнитотаксисных бактерий и генами человека для предсказания функций и физиологического происхождения биогенных магнитных наночастиц в многоклеточных организмах. Обнаружено, что белки человека (которые являются гомологами белков магнитосомного островка) вовлечены в патогенез ряда заболеваний, характеризующихся повышенным количеством биогенных магнитных наночастиц.

## *1.Introduction*

The purpose of this work is to predict functions of biogenic magnetic nanoparticles both in bacteria and multicellular organisms including human. The following problems are solved for reaching the purpose of this work. The homologues of the proteins of magnetosome island of magnetotactic bacteria have been revealed in human by means of bioinformatics methods for prediction of functions and physiological origin of biogenic magnetic nanoparticles in multicellular organisms. The diseases are studied in pathogenesis of which the human proteins (which are the homologues with the proteins of magnetosome island) are implicated. The force acting on paramagnetic ions in aqueous solution of electrolyte in the vicinity of ferromagnetic particles in modeling experiments is compared with the force acting on paramagnetic ions in the vicinity of the biogenic ferrite nanoparticles in a cell.

## 2. Results and discussion

### 2.1. Biogenic magnetic nanoparticles in bacteria

It is known that living organisms, including microorganisms (bacteria, yeast, fungi and etc.), contain compounds that belong to different classes of magnetic materials: dia-, para-, ferro-, antiferro- and ferrimagnets (ferrites). Moreover, ferro-, antiferro- and ferrimagnets are magnetically ordered substances. Percentage of substances and elements with different magnetic properties determines the degree of response of biological objects on the external magnetic field. Therefore, paramagnetic and diamagnetic types of microorganisms are distinguished [1, 2]. Magnetic properties of microorganisms also depend on the rate and direction of a number of metabolic reactions [3]. Thus, dead cells are more diamagnetic than the living [4], and magnetic susceptibility of microorganisms depends on their age and external factors [5, 6]. Also, biosystems have the greatest magnetic susceptibility when accumulate in the structure magnetically ordered compounds, including magnetite ($Fe_3O_4$) [7–14].

Thus, in 1975 intracellular magnetite crystals (called magnetosomes) were found in a number of procaryotes [7, 8]. Magnetosomes are self-assembled a chain of dozens of individual ferrite nanoparticles. Each magnetic nanoparticle is coated with a membraine (so called magnetosome vesicle). Number of magnetic nanoparticles in the chain and their sizes vary in the range of from 10 to 40 nm [7–14], according to other data — from 35 to 120 nm [9], corresponding to certain types of bacteria. Also it was discovered that these magnetic nanoparticles are located along the long axis of the bacteria, usually on the side of the flagellum or bundle of flagellum, i.e. near the movement organ of cells. According to existing hypothesis these bacteria are able to navigate in the Earth's geomagnetic field due to existence of magnetosomes, in other words — bacteria have magnetic tropism which is called magnetotaxis or magnetotropism, also the term "magnetic" bacteria is used. Discovery of magnetite in bacteria has set the question about physiological function of this ferromagnetic material [8]. Is magnetotaxis the only function of magnetosomes? This question is still open. As for the biomineralization of magnetic nanoparticles inside of magnetosome vesicles, it is regulated at genetic level as it was recently proved [15]. Specific genes (*mam* — *magnetosome membrane* and *mms* — *magnetic particle membrane specific* genes) and proteins (so called *magnetosome membrane proteins*) are responsible for synthesis of magnetosomes [15]). These specific genes are involved in magnetite biomineralization in magnetotactic bacteria and they belong to genomic magnetosome island. In particular, the proteins MamB, MamE, MamO, MamM, MamN belong to the genomic magnetosome island [15].

The expression of the *mam* and *mms* genes is down-regulated in nonmagnetic cells under iron limitation and, to a lesser extent, during aerobic growth compared to that in magnetite-forming cells grown microaerobically under iron-sufficient conditions [15]. The quantity of magnetic nanoparticles decrease significantly or their production stops at all under down-regulated condition for the *mam* and *mms* genes [15].

### 2.2. Biogenic magnetic nanoparticles in tissues of multicellular organisms and human

Later research showed that many multicellular organisms biochemically synthesize biogenic magnetite and other ferrite compounds like maghemite ($\gamma$–$Fe_3O_4$) [14–21] and greigite ($Fe_3S_4$), which has a magnetic moment three times less than magnetite [22, 23]. Biomineralized magnetite was found in the fossil remains of organisms that are dated from the era Prekambiyskoy [24], molluscs [19], arthropods [20], fishes [22], animals [19–22, 24], in brain tissues [27–30] and other human organs [29]. In particular, biogenic magnetite has been found in tissues and organs of sharks, skates, dolphins, many migratory birds, snails, hornets, bees, and so on [8, 24, 30]. Thus, in [25] it was shown using ultra-sensitive magnetometer of superconductivity that ferrite nanoparticles affiliate to numerous tissues of human brain (cortex, cerebellum, and meninges — membranes surrounding the brain) in amount from 5 to 100 million nanoscale crystals per gram of pia and dura. The distribution of these particles size has two maxima: in the vicinity of small particles with an average size of 33.4±15.2 nm, and in the vicinity of large size in the range from 90 nm to 200 nm. The transition from the superparamagnetic to single domain state occurs for magnetite

nanoparticles size from 25 nm to 30 nm [31], so there are both superparamagnetic and single domain component in the human brain. These magnetite nanoparticles are organized into linear, membrane-bound chains a few micrometers in length, with up to 80 crystals per chain [32]. Despite intensive study of the properties of biogenic ferrite nanoparticles, their origin and physiological function in multicellular organisms remains open question for today.

### *2.3. Human diseases accompanied by increase of amount of biogenic magnetic nanoparticles*

In works [33–35], the diseases are revealed which are accompanied by the change of quantity of biogenic ferrite nanoparticles. The role of the strongly ferrimagnetic biogenic magnetite in neurological and neurodegenerative diseases such as Alzheimer's, Parkinson's, Huntington's diseases and epilepsy was studied in the papers [36–39]. One of the characteristics of many neurodegenerative diseases is the disruption of normal iron homeostasis in the brain [33]. Elevated iron levels are associated with many types of neurodegenerative disease, such as Alzheimer's, Parkinson's and Huntington's diseases. However, it is not obligatory that these elevated iron levels correlate with elevated levels of the iron storage in transport proteins, ferritin and transferrin. As such, a little is known about the form of this excess iron. It has been recently proposed that some of the excess iron in neurodegenerative tissue may be in the form of the magnetic iron oxide magnetite. For the first time it was demonstrated that the concentrations of magnetite are found to be significantly higher in three samples of Alzheimer's disease tissue than in three age- and sex-matched controls [39]. Recent experimental works indicate also that nanoscale magnetic biominerals (primarily magnetite and maghemite) may be associated with senile plaques and tau filaments found in brain tissue affected by these diseases. Body iron stores that increase with age could be pivotal to Alzheimer's disease pathogenesis and progression [34]. The concentration of superparamagnetic biogenic magnetite and/or maghemite is significant and appears to be proportional to the concentration of ferritin, which varies with progression of the disease — neuroferritinopathy [35].

The first detection of biogenic magnetic nanoparticles in various human tumor tissues (melanoma, breast, ovary, testicle, sarcoma, meningioma, glioblastoma, astrocytoma, glioma, metastasis) using SQUID magnetometry was carried out in the paper [40]. However, a special covariance between ferritin expression and quantity of biogenic magnetite nanoparticles was unable to be demonstrated in the study [40]. The magnetic methods described in the work [40] showed that human meningiomal brain tumor tissues contained an order of magnitude higher concentration of ferrimagnetic particles than non-tumor hippocampus [41]. The rate of formation of biogenic nanoparticles of magnetite (and/or maghemite) was higher in tumor tissue, since the size of nanoparticles in the healthy hippocampal tissue is less than in the tumor tissue, where conditions are more favorable for the growth of larger particles [41]. In addition, the authors of [41] observed that the amount of blood in the tumor tissue is on the average higher than in the healthy hippocampal tissue. But the correlation between the supply of blood to tissue and formation of magnetite and/or maghemite was not found. There is no evidence also about changes of quantity of biogenic magnetic nanoparticles with aging that does not correlate with the data on the expression of ferritin with aging [41, 42].

### *2.4. Iron-containing proteins as precursors of synthesis of ferrite nanoparticles?*

It is known that ferritin is one of the intracellular iron proteins contained in each cell, and is one of the key proteins in iron metabolism [43]. It consists of a spherical protein shell with a diameter of 12 nm, and the nucleus of the antiferromagnetic ferrihydrite ($5Fe_3O_4{\cdot}9H_2O$) with a diameter 8 nm [44, 45]. Despite numerous studies the exact structure and morphology of the nucleus it is still contradictory [46]. According to the most current research [46] it is considered that the core of ferritin consists of a maximum of eight subunits that are compatible with eight channels in a membrane protein that provide iron in the central cavity. Small subunits of ferrihydrite (about 2 nm) inside the nucleus are connected in such a way that remains the central region with low density and large surface area to ensure rapid turnover of iron in biological systems [46]. Also analysis of individual nuclei using transmission elec-

tron microscopy and electron nanodiffraction has shown that some nuclei are composed of one of the several possible inorganic phases: antiferromagnetic ferrihydrite — in most nuclei or magnetite [47–49]. As magnetite includes both types of iron ions $Fe^{3+}$ and $Fe^{2+}$, under certain conditions, oxidation-reduction cycle can occur even within ferritin [46]. However, these statements are not completely reliable because it is suggested that in case of ferrihydrite exposure to electron beam in the process of measurement may provoke its conversion to magnetite [46].

In our opinion, magnetic force microscopy could be an alternative method to verify the results of works [47–49] because it allows to distinguish antiferromagnetic phase of ferrihydrite from magnetite, without changing the physical and chemical properties of samples. In [48, 49] the assumption was made that the physiological and pathological ferritin in the human brain may be a precursor for magnetite (maghemite) nanoparticles with sizes large enough to have a residual magnetization at room temperature. Furthermore, in [41] the hypothesis was formulated in the continuation of this idea that biogenic growth of ferrite nanoparticles starts with nanometer-size and different stages of growth detected in all tissue samples that is confirmed by the detection of broad distribution in size ferrite nanoparticles in human brain tissue.

Correlation between an expression of ferritin and concentration of biogenic magnetic nanoparticles was also investigated in [39]. In [42, 50] it was shown that ferritin expression increases with aging. However, no correlation of magnetite and/or maghemite content with age was found in either type of tissue [41]. Also abnormalities in the expression of ferritin observed for many types of cancers that was analyzed in detail in [51]. But according to the results of [40] distribution of ferritin is not correlated with the distribution of magnetite in the human brain; this implies that magnetite does not form spontaneously from ferritin [40]. Therefore in contrast to bacteria the physiological origin of biogenic magnetic nanoparticles in multicellular organisms is still open. And the following questions arise consequently: What are the functions of biogenic magnetic nanoparticles in multicellular organisms? Are there common functions of biogenic magnetic nanoparticles in bacteria and in multicellular organisms? What is the physiological origin of biogenic magnetic nanoparticles in multicellular organisms? Is there regulation of biomineralization of biogenic magnetic nanoparticles in both bacteria and multicellular organisms at genetic level? In the case if the biomineralization of biogenic magnetic nanoparticles in multicellular organisms is genetically regulated it is important to reveal if this is the result of homology (common ancestry) or convergent evolution (common selective pressure)?

Methods of bioinformatics are invented for comparison of nucleotide and protein sequences of organism with the purpose of obtaining new knowledge. Such comparison can be carried out, for example, by means of the free software, supplied by the National Center for Biotechnology Information (USA) http://www.ncbi.nlm.nih.gov/. As well as the genes (and expressed proteins) of magnetotactic bacteria are known which are responsible for the biomineralization of magnetite but the human genes (and proteins), involved in process of formation of the biogenic magnetite are not known for today. That is why the purpose of application of bioinformatics methods in this work is revealing human proteins which are similar to the proteins of magnetosome island of magnetotactic bacteria. Estimation of the statistical significance of the revealed similarity between the protein sequences allows confirm conservation of the function of biomineralization of magnetite for the human homologues of the proteins of magnetosome island.

### *2.5. Similarity between the genes of magnetosome island and human genes*

The similarity between the genes of magnetosome island and human genes have been studied in this paper by means of bioinformatics methods for clarifying the questions, mentioned above. The matches between the genes of magnetosome island of bacterium *Magnetospirillum gryphiswaldense* and human genes have been analyzed. The significant matches have been found by means of the free software, designed for comparative analysis of protein sequences, — BLAST (http://blast.ncbi.nlm.nih.gov/Blast.cgi) between:

MamE and "serine protease" region of human genes HTRA1, HTRA2, HTRA3, HTRA4 that encode the members of the trypsin family of serine proteases (HtrA family proteins).

• HTRA1 has also been suggested to be a regulator of cell growth. Variations in the promoter region of this gene are the cause of susceptibility to age-related macular degeneration (AMD) type 7 [52]. Recent studies on the molecular pathology of AMD suggest important roles for oxidative stress, induction of hypoxia, generation of reactive oxygen species (ROS) [53]. The high oxygen tension in the retina coupled with light provides a permissive environment for the generation of oxidative post-translational modifications. Oxidative protein modifications accumulate in the eye with age and possibly contribute to AMD pathogenesis. Why ocular tissues in AMD patients are more susceptible to oxidative damage than normal eye tissue remains to be determined [54]. The expectation value is equal to $10^{-24}$.

• HTRA2 encodes the protein which is also localized in mitochondria with release to cytosol following apoptotic stimulus. The protein is considered to induce apoptosis by binding the apoptosis inhibitory protein baculoviral IAP repeat-containing 4. Nuclear localization of this protein has also been observed [52]. The serine-protease HTRA2 required for several cellular processes including mitochondrial function, autophagy, chaperone activity, and apoptosis, has been implicated in the pathogenesis of both Alzheimer's disease (AD) and Parkinson's disease (PD). Loss of HtrA2 function leaded to nerve cell loss in mouse models and has been linked to neurodegeneration in PD and Huntington's disease (HD). Under physiological conditions HtrA2 is thought to be involved in protection against cellular stress, but the cytological and molecular mechanisms of the processes are not clear. HtrA2 deficiency caused an accumulation of reactive oxygen species and reduced mitochondrial membrane potential [55]. The expectation value is equal to $5{\cdot}10^{-22}$;

• HTRA3 is regulated by oxygen tension: low oxygen enhanced, while the transition from low to high oxygen decreased HtrA3 protein production in syncytiotrophoblast [56]. The HtrA family proteins are serine proteases that are involved in important physiological processes, including maintenance of mitochondrial homeostasis, apoptosis and cell signaling. They are involved in the development and progression of several pathological processes such as cancer, neurodegenerative disorders and arthritic diseases [52]. The expectation value is equal to $4{\cdot}10^{-24}$. HTRA4 encodes protein which contains a putative signal peptide, an insulin growth factor binding domain, a Kazal protease inhibitor domain, a conserved trypsin domain and a PDZ domain. Based on studies on other related family members, this enzyme may function as a secreted oligomeric chaperone protease to degrade misfolded secretory proteins. Other human HtrA proteins have been implicated in arthritis, tumor suppression, unfolded stress response, apoptosis, and aging [52]. The expectation value is equal to $5{\cdot}10^{-24}$.

MamO and "serine protease" region of human genes HTRA1 (the expectation value is equal to $10^{-7}$), HTRA2 (the expectation value is equal to $10^{-5}$) that encode the members of the trypsin family of serine proteases (HtrA family proteins).

MamB and "Cation_efflux" region of human genes SLC30A9, SLC30A4 that encode zinc transporter 9 and zinc transporter 4 (Cation efflux family).

• SLC30A9 encodes the protein which is expressed in human embryonic lung; ZNT-9 is human embryonic lung protein; it belongs to solute carrier family 30 member 9 [52]. Interruption of blood flow after cardiac arrest limits the delivery of oxygen and glucose to neurons causing ATP reduction which has numerous consequences including neurotoxicity, DNA damage, and production of free radicals [57]. In model [57] only 28 significantly differentially expressed transcripts in total after global ischemia were found. Among the moderately up-regulated genes, it is noteworthy that 7 transcripts affected by ischemia belonged to ion transport and included 2 zinc transporters: SLC30A9 (ZNT9) and SLC30A10 (ZNT10). The SLC30 proteins are CDF (cation diffusion facilitator) proteins and plasma membrane efflux transporters [58]. The mechanism of transport for many CDF proteins appears to be via zinc/H + or K + antiports. Therefore, despite their name, CDF proteins do not serve as diffusion facilitators but rather as secondary active transporters, using the gradient of other ions to drive the transport of zinc [59]. The expectation value is equal to $2{\cdot}10^{-15}$.

• SLC30A4, or ZNT4, belongs to the ZNT family of zinc transporters. ZNTs are involved in transporting zinc out of the cytoplasm and have similar structures, consisting of 6 transmembrane domains and a histidine-rich cytoplasmic loop [60]. Alterations in Zn transport proteins ZNT-1, ZNT-4 and ZNT-6 may contribute to the pathology observed in preclinical AD subjects before

onset of clinical symptoms [61]. The expectation value is equal to $4 \cdot 10^{-8}$.

MamM and "MMT1" region of human gene SLC30A9 (the expectation value is equal to $10^{-6}$) and "Cation_efflux" region of human gene SLC30A4 (the expectation value is equal to $2 \cdot 10^{-5}$) that encode zinc transporter 9 and zinc transporter 4 (Cation efflux family).

MamN and "P_permease" region of human gene OCA2. This gene encodes the human homologue of the mouse p (pink-eyed dilution) gene. The encoded protein is believed to be an integral membrane protein involved in small molecule transport, specifically tyrosine — a precursor of melanin. Mutations in this gene result in type 2 oculocutaneous albinism. Although the precise function of the P protein is unknown [52]. The expectation value is equal to $6 \cdot 10^{-18}$.

### *2.6. Mechanisms of influence of a constant magnetic field on biosystems*

A lot of experimental material is accumulated in the direction of studying the influence of magnetic fields on biosystems. Almost there is no biosystems, in which magnetic fields have no influence, although all aspects of the mechanisms of this influence have not yet been elucidated. Research of processes and mechanisms of action of magnetic field on the structure and function of living organisms at different levels of complexity plays the most important role for studying this problem. This is one of the most important problems of modern biophysics, especially as the emergence of magnetobiological effects in biological systems should be considered as constantly present an environmental factor that has the same meaning in the life of living organisms, like temperature, humidity, pressure and other natural factors. Since no doubt that Earth's natural magnetic field is essential for normal functioning of biosystems. Influence of magnetic fields on biosystems promoted the emergence and development of such sciences as magnetobiology, magnetochemistry, biophysics etc. Thus, the value of the magnetic fields in laboratory experiments, commonly used, are weak and should not lead to noticeable effects from a theoretical point of view. The situation is complicated by the fact that most of the experiments are carried out processing the organism as a whole (including bacteria). It is important to study the quantitative effects of magnetic fields [62–66] for some structure and biological functions of organisms or microorganisms for identification of the mechanism of influence of magnetic fields for biosystems. At this time, about a dozen of models of magnetic field influence on biosystems are designed which are systematized in [67]. Most of them are concerned of weak alternating magnetic fields. As for constant magnetic fields, the mechanisms of their influence on mechanical particles in granular, liquid and gaseous environments were studied deeply enough. The theory that explains the movement, separation and "capture" dia-, para-, ferri-, antiferro- and ferromagnetic particles under the influence of spatially inhomogeneous (i.e. gradient) and constant in time magnetic field was established and experimentally verified [68–70]. In this connection it should be noted that the influence of magnetic fields on para- and diamagnetic substances is 3–6 orders of magnitude less than on the magnetically ordered substances such as ferromagnets and ferrites. However, the problem of safety of strong magnetic fields (more than 3 T) became actual after the detection of biogenic ferrite particles in the human body and in connection with a spread of wide use in medicine NMR method [71]. But the authors of [71] estimated that the magnetic fields of 9.4 T is unlikely even to disrupt the normal functioning of cells through stimulation biogenic magnetite nanoparticles. The feature of the approach of these works [71–76] is account of the possibility of the mechanical damage of cells due to the movement of magnetite nanoparticles in uniform constant external magnetic field. But according to the authors of the work [71] an existence of high gradient magnetic field, created by the biogenic ferrite nanoparticles, is not taken into account.

The existence of own magnetic field of magnetic nanoparticles leads to change of the type of mass transfer from diffusion to convection in their vicinity, to the change of the rate of electrochemical reactions, to self-organized formation of phases with different magnetic susceptibilities, to the emergence of electric potential difference between surface regions of magnetic particles during the electrochemical reactions under certain conditions [77–87]. Indeed, it is easy to compare the force acting on paramagnetic ions in aqueous solution of electrolyte in the vicinity of ferromagnetic particles in [82–87] with the force acting on paramagnetic ions in the vicinity of ferrite

nanoparticles in the cell in an external magnetic field:

$$F = \frac{1}{2}\chi\nabla\mathbf{H}^2,$$

where $\chi$ is magnetic susceptibility of paramagnetic species (for example, of ions), **H** — superposition of an external magnetic field and magnetic field, created by magnetized particle.

The operator *grad* can be replaced for estimations by $1/a$, where $a$ is the typical size of particles, which create a gradient magnetic field. $H = 1000$ E, $a \approx 10 \div 1000$ μm in experimental research [82–87]. Then it is possible to estimate: $H^2/a \approx (1000)^2/a$ vary in the interval from $10^9$ to $10^7$ Oe$^2$/cm.

Cell contains magnetite nanoparticles which can create its own magnetic field of about 1000 Oe because these biogenic magnetic nanoparticles are magnetized in the magnetic field of the Earth if their sizes exceed the threshold size of transition to the superparamagnetic state. The size of these magnetic nanoparticles in the cell, as mentioned above, are within the range from 10 to 200 nm (from $10^{-6} \div 10^{-5}$ cm) [7–14].

So, $H^2/a \approx 10^{12} \div 10^{11}$ Oe$^2$/cm around the magnetic nanoparticles in the cell, which is several orders of magnitude bigger than gradients that are achieved in experimental studies, conducted in [82–87]. Thus, the gradient magnetic field of biogenic magnetic nanoparticles and related magnetochemical effects can be additional non-mechanical factor influencing on transport processes, diffusion and electrical potentials in the cell.

By the way the possible mechanisms of influence of magnetized particle on transport processes and chemical reactions in cells can be summarized as follows. The magnetized particle creates gradient magnetic field and the gradient magnetic force gives rise to the following effects: separation of reactants and reaction product (ions and other species) with different magnetic susceptibility; anisotropy of chemical reaction rate; formation of heterogeneous state of initially homogenous medium; change of chemical reaction rate; change of diffusion mass transport mechanism into magnetohydrodynamic convection; creation of electric cell voltage due to concentration nonuniformity at the surface of the magnetized particle [82–87].

## 3. Conclusions

Significant matches exist between the genes of magnetosome island (MAM genes) and certain regions of human genes in the "twilight zone" with expectation value range $10^{-10} < E < 10^{-5}$ and more similar alignment pairs with $E < 10^{-10}$. In particular, the human genes with MAM matching regions encode the members of the trypsin family of serine proteases (human HtrA proteins) and cation efflux family (zinc transporters — ZnT).

MAM genes are involved in magnetosome formation containing biogenic magnetic nanoparticles as well as products of MAM matching human genes have been implicated in pathogenesis of a number of diseases, characterized by the elevated level of biogenic magnetic nanoparticles.

MAM genes are oxygen regulated as well as there are data about correlation of the expression of MAM matching human genes and oxidative stress and their oxygen regulation.

There is no significant matches between the genes of magnetosome island (MAM genes) and the iron storage or transport proteins, ferritin and transferrin confirming the absence of correlation in distribution of ferritin and the distribution of biogenic magnetite in the human brain.

Magnetic force microscopy is an effective method for detection of spatial distribution of the biogenic magnetic nanoparticles. It was shown by means of MFM that duration of cultivation of Ehrlich carcinoma cells in the external magnetic field 160 mT influences on the quantity of the biogenic magnetic nanoparticles and their self-organization in a complex superstructures [88].

As well as the function and physiological origin of biogenic magnetic nanoparticles are still open in multicellular organisms. It is possible to formulate a hypothesis that the biogenic magnetic nanoparticles both in bacteria and multicellular organisms are necessary not only for the navigation in a magnetic field of the Earth but for: accumulation of paramagnetic species such as Fe ions and oxygen; regulation of transport processes in a cell by changing concentration gradients of different species according to their magnetic susceptibility, for example, the biogenic magnetic nanoparticles can render an influence on transport protein using the gradient of other ions to drive the transport of certain ion.

The hypothesis was proposed for the first time in [89]. The hypothesis is confirmed by

the modeling experiments from works [82—87] and estimation comparing the gradient magnetic force in the vicinity of an biogenic magnetic particle in a cell and in the modeling magnetochemical experiments [82—87]. The methods of bioinformatics are described, for example, in the [90].

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# Функції біогенних магнітних наночастинок в організмах

***С.В.Горобець, О.Ю.Горобець***

З застосуванням методів біоінформатики і модельних експериментів в області магнітохімії вивчено функції біогенних магнітних наночастинок як в бактеріях, так і в багатоклітинних організмах . Виявлено, що біогенні магнітні наночастинки служать не тільки для навігації у геомагнітному полі, але й для накопичення парамагнітних компонент, таких як іони заліза і кисень, а також для регуляції транспортних процесів у клітині шляхом зміни градієнтів концентрації різноманітних компонент в залежності від їх магнітної сприйнятливості. Подібність між генами магнітосомного островця магнітотаксисних бактерій і генами людини вивчено методами біоінформатики для передбачення функцій та фізіологічного походження біогенних магнітних наночастинок у багатоклітинних організмах. В результаті виявлено, що білки людини (які є гомологами білків магнітосомного островця) задіяні у патогенезі низки захворювань, що характеризуються підвищеною кількістю біогенних магнітних наночастинок.