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MAGNETIC HYPERTHERMIA OF MICROORGANISMS WITH NATURAL FERRIMAGNETIC PROPERTIES

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Abstract

Aim and Objectives: Biogenic magnetic nanoparticles of microorganisms are not taken into account when neutralized by their magnetic hyperthermia. The aim is to identify microorganisms, which take into account the characteristics of their own biogenic magnetic nanoparticles can lead to a noticeable increase in the effectiveness of magnetic hyperthermia. Methods: Research the study used methods of comparative genomics, in particular, pair alignment using the Genbank database. The alignment of proteomes of magnetotactic bacteria Magnetospirillum gryphiswaldense MSR-1 with the proteomes of pathogenic microorganisms, which were classified according to the site of localization and the type of internal structure of their biogenic magnetic nanoparticles, was carried out. Results: The genomes of 24 strains of pathogenic microorganisms were analyzed belonging to such genus: Staphylococcus, Pseudomonas, Bacillus, Shigella, Clostridioides, Streptococcus, Peptostreptococcus. It was shown that three of them have crystalline intracellular biogenic magnetic nanoparticles, 11 strains have extracellular crystalline, 8 – intracellular amorphous, 3 - extracellular amorphous. The paper also presents calculations of the dipole-dipole strengths of interactions between the amorphous biogenic nanoparticles of Staphylococcus aureus and artificial magnetic nanoparticles. Discussion: We recommend using methods of comparative genomics for the separation of microorganisms with magnetic properties for the selection of a more effective method of neutralization by magnetic hyperthermia. Thus, 3 strains with crystalline intracellular biogenic magnetic nanoparticles can be neutralized by the magnetic hyperthermia, using their own particles as a magnetic material. Other 21 strains with extracellular crystalline, intracellular amorphous and extracellular amorphous magnetic nanoparticles can be neutralized by magnetic hyperthermia using methods of artificial magnetically labeled. It is shown that the forces of dipole-dipole interactions between amorphous magnetic nanoparticles and artificial magnetic nanoparticles are enough to magnetically labeled of Staphylococcus aureus and further neutralize them using magnetic hyperthermia. Conclusions: The use of the natural ferromagnetic properties of microorganisms will increase the effectiveness of the neutralization of magnetic hyperthermia.

Keywords: magnetic hyperthermia; pathogenic microorganisms; neutralization; biogenic magnetic nanoparticles; methods of comparative genomics; magnetic dipole interactions

1. Introduction

Today there is a need to find new ways to destroy pathogenic and conditionally pathogenic microorganisms. This need has arisen due to the fact that pathogenic microorganisms quickly develop resistance to known methods and means of neutralizing them. Thus, the most common human pathogen, *Staphylococcus aureus*, which causes purulent infections, very quickly develops defense mechanisms against known antimicrobial and disinfecting agents [1–2]. Some strains have become immune to all antimicrobials known to date [3–4]. A number of microorganisms are very resistant to drug

therapy: Pseudomonas aeruginosa, Streptococcus pyogenes, Haemophilus influenzae type Streptococcus pneumonia, Enterococcus faecalis, Enterococcus faecium, Clostridium difficile, Escherichia coli, Acinetobacterbaumannii, *Mycobacterium* tuberculosis, Proteus vulgaris, Klebsiellapneumoniae, Neisseria meningitidis, Neisseria gonorrhoeae, Staphylococcus epidermidis, Bacteroides fragilis, etc.

Magnetic hyperthermia may be one of the methods being developed for the neutralization of microorganisms that have developed resistance to antimicrobial agents [5].

Magnetic hyperthermia (MHT) is an alternative method for treating tumors [6], in a temperature range of 42-45 °C [7, 8] is used in a local area of tissue or organ for their destruction. An alternating magnetic field (AMF) acts on magnetic material (magnetic nanoparticles) introduced pathological tissue site [9, 10], as a result of which electromagnetic energy is converted into heat [8, 10, 11].But this method currently is not used by itself for the treatment of tumors, because it due to the fact that it is difficult to maintain the uniformity of tissue heating [12]. It is known that tumor cells are not completely neutralized at a temperature of 43 ° C [13]. When the temperature rises above 43 $^{\circ}$ C, healthy tissues surrounding the tumor undergo significant toxic effects, which is a negative consequence of the use of MHT [13].

However, a number of works [7, 8, 10, 14, 15] indicate that MHT significantly increases the effectiveness of traditional methods for the treatment of tumors (radiation and chemotherapy). Therefore, despite of the imperfection of the method, side effects and its relatively high cost, the research and development of MHT is being continued. Also, the scope of MHT is expanding. Currently, the research is being conducted on the use of MHT for the treatment of inflammatory processes [5] and the neutralization of microorganisms [16]. The main idea of the neutralization of microorganisms MHT is to increase local temperature in suspension with bacteria or in the focus of inflammation with a bacterial infection. this, magnetic To do nanoparticles are pre-introduced into a suspension containing microorganisms, or into the body tissue infected by the bacterial inflammation, and exposed to AMF [5, 16].

The use of biogenic magnetic nanoparticles (BMNs) for the neutralization of microorganisms by MHT was proposed in [5]. Crystalline intracellular

BMNs of magnetotatic bacteria (MTB) were used as magnetic material for MHT [5]. *In vitro* studies were performed by two methods. In the first case, AMF was applied to a mixture of MTB and pathogenic microorganisms *S. aureus*. In the second case, a AMF was applied to AMF and *S. aureus*, which were connected to each other using monoclonal antibodies [5]. The effectiveness of MHT in the first study was 20%, in the second – 50%.

In [16], effective neutralization of MHT of the *Pseudomonas fluorescens* bacteria was observed, which form biofilms and cause spoilage of food and beverages. An aqueous solution of bacteria *P. fluorescens* and magnetic nanoparticles was subjected to a AMF, as a result of which the temperature of the suspension increased. The complete destruction of bacteria was observed at a temperature of 55 ° C, and at 45 ° C inactivation of more than 50% of the total bacteria was observed.

The question of the presence of BMNs in cells and tissues was not considered during exposure to MHT on bacterial suspensions and on inflammatory foci with a bacterial infection [5, 16]. But the effectiveness of exposure to MHT may depend on the presence or absence of BMNs, their properties and localization in bacterial cells [17] and affected tissues [18-19].

2. Methods

The purpose of this work is to identify potential producers of BMNs among pathogenic microorganisms that cause infectious diseases, as well as to classify these microorganisms by their nanostructural localization of BMNs in the cell and the type of internal structure of BMNs.

The experiment used paired alignment methods using the free online program "BLAST" of the National Center of Biotechnological Information (NCBI) [20]. The alignment was carried out using the methods of comparative genomics. The proteomes of pathogenic microorganisms were compared with the proteomes of the magnetotactic bacteria *Magnetospirillum gryphiswaldense* MSR -1, in which the biomineralization mechanism of BMNs was studied in details [21–23].

Spent the alignment of the proteins of the *Mam* group of *M. gryphiswaldense* MSR-1 with proteomes of 24 microorganisms that cause infectious diseases. The genera of microorganisms, which were investigated: g. *Staphylococcus*, g. *Pseudomonas*, g. *Bacillus*, g. *Shigella*, g.

Clostridioides, g. Streptococcus, g. Peptostreptococcus.

Ident and **E-value** were taken into account aligning amino acid sequences of proteins to assess the degree of their similarity.

Ident (I) is the number of identical amino acid residues of the studied proteins with optimal alignment.

E-value is an indicator that reflects the statistical significance of alignment, a decrease in the value of which indicates a lower level of manifestation of the random factor when the amino acid residues of the comparative proteins coincide.

It is also necessary to consider the **length** of the aligned sequences, which should be more than 100 amino acid residues [21, 24].

3. Results and discussion

The results of the alignment of MTB proteins with proteins of microorganism strains are presented in Table. The degree of decoding of the genomes of the microorganisms was also taken into account. The designations that are used in Table: — the genome of the microorganism is completely decoded; — the genome of the microorganism is decoded by 50% — the genome of the microorganism is decoded by 25%.

24 strains of microorganisms were analyzed by the methods of comparative genomics. Table 1 shows microorganisms which are produced by BMNs or can be their producers.

Non-magnetotactic bacteria are divided into 4 groups according to the classification of BMNs by the type of their internal structure (crystalline or amorphous form) and by their localization in the (extracellular or intracellular) Microorganisms that synthesize extracellular amorphous BMNs belong to group 1, and extracellular crystalline BMNs to group 2. Microorganisms that synthesize intracellular amorphous BMNs belong to group 3, and synthesizing intracellular crystalline BMNs to group 4.

Table
Comparison of Mam MTB proteins of M. gryphiswaldense MSR-1 and proteomes of microorganisms
that cause infectious diseases

Name of bacteria, strain	Genome	Group	E-value (I, %)					
			Proteins of M. gryphiswaldense MSR-1					
			mamA	mamB	mamM	mamO	mamE	mamK
S. aureus subsp. aureus 6850	•	2	5e-09 23%	4e-24 25%	5e-30 30%	9e-10 30%	1e-25 41%	0.012 28%
S. aureus subsp. aureus ED133	•	2	2e-09 23%	5e-24 25%	8e-30 30%	9e-10 30%	1e-25 41%	0.012 28%
S. aureus NCTC 8325	•	2	2e-09 23%	6e-24 25%	9e-30 30%	1e-09 30%	1e-25 41%	0.015 28%
S. aureus subsp. aureus ST72	•	2	6e-09 23%	6e-24 25%	1e-29 30%	1e-09 30%	2e-25 41%	0.015 28%
S. aureus subsp. aureus EMRSA16	•	2	3e-09 23%	5e-24 25%	7e-30 30%	1e-09 30%	1e-25 41%	0.014 28%
S. aureus SCOA6009	•	2	3e-09 23%	3e-23 25%	4e-30 30%	1e-09 30%	1e-25 41%	0.013 28%
S. aureus M81493	•	2	5e-09 23%	5e-24 25%	8e-30 30%	1e-09 30%	1e-25 41%	0.013 28%
S. aureus 880	•	2	3e-09 23%	6e-24 25%	9e-30 30%	1e-09 30%	1e-25 41%	0.014 28%
S. aureus subsp. aureus 21269	•	2	4e-09 23%	2e-23 25%	8e-30 30%	9e-10 30%	1e-25 41%	0.86 30%
S. aureus subsp. aureus CO-98	•	2	3e-04 28%	2e-08 25%	6e-35 30%	3e-10 27%	6e-27 36%	0.004 29%
S. aureus A8819	•	2	6e-09 23%	3e-24 25%	5e-30 30%	1e-09 30%	1e-25 41%	0.013 28%
Pseudomonas fluorescensNCIMB 11764	•	3	0.004 33%	2e-10 23%	3e-14 27%	1e-09 27%	2e-32 43%	1e-05 29%

Name of bacteria, strain		Group	E-value (I, %)					
	Genome		Proteins of M. gryphiswaldense MSR-1					
			mamA	mamB	mamM	mamO	mamE	mamK
P. fluorescensABAC62	•	3	0.017 32%	1e-10 26%	1e-16 26%	1e-10 29%	4e-34 45%	6e-04 27%
P. fluorescensBBc6R8	•	4	2e-04 23%	6e-06 27%	2e-15 28%	7e-09 29%	3e-32 43%	1e-06 24%
Bacillus cereus G9241	•	4	2e-07 26%	2e-37 30%	1e-35 30%	1e-04 31%	2e-22 42%	1e-11 25%
Shigelladysenteriae161 7	•	3	0.094 26%	2e-18 28%	2e-14 24%	9e-14 30%	1e-35 47%	4e-08 25%
Shigellaflexneri2a	•	3	2.0 29%	5e-18 27%	6e-14 24%	0.003 30%	3e-22 53%	8e-08 25%
Shigellaflexneri2a str. 2457T	•	3	0.14 25%	2e-10 27%	1e-07 26%	8e-10 26%	8e-36 47%	4e-08 25%
Clostridioidesdifficile CD196	•	3	0.005 31%	2e-40 30%	2e-35 29%	3e-09 29%	2e-35 47%	9e-11 25%
Peptostreptococcussp. MV1	•	3	0.005 21%	8e-20 24%	5e-16 29%	3e-09 28%	1e-31 43%	5e-08 24%
Peptostreptococcus sp. D1	•	3	0.005 27%	8e-22 26%	6e-15 38%	2e-08 25%	3e-28 37%	8e-08 25%
Streptococcus sanguinis SK115	•	1	0.65 28%	3e-29 28%	5e-27 26%	6e-05 26%	7e-26 36%	0.072 23%
Streptococcus pneumoniae 845	•	1	0.006 25%	3e-08 37%	5e-24 24%	7e-05 27%	3e-25 36%	0.01730 %
S. pneumoniae 2070335	•	1	0.016 25%	1e-09 29%	4e-24 25%	7e-04 32%	1e-26 40%	0.01025 %

The alignment results are presented in of Table 1, where 24 strains of microorganisms of 3 strains synthesize extracellular amorphous particles (1st group), 11 strains synthesize extracellular crystalline BMNs (2nd group), 8 strains have intracellular amorphous BMNs (3rd group), 3 strains have intracellular crystalline BMNs (4 group). The genomes of 10 strains of microorganisms are completely decoded, and the genomes of 14 strains have not yet been completely decoded in the NCBI database.

In [5], the researchers did not take into account the fact that *S. aureus* can be producers of BMNs. Table 1 shows that almost all strains of *S.aureus* whose genomes are in the Genbank NCBI database, can be producers of BMNs. In [16], the rate of destruction of *P. fluorescens* is also not theoretically explained, and the magnetic properties of this bacterium are not taken into account. Genetic analysis has shown that some strains of *P. fluorescens* can produce crystalline extracellular BMNs.

We propose several approaches for to the methods of MHT application, taking into account the localization of BMNs in the cell and the type of their internal structure. As a rule, intracellular crystalline BMNs are strong natural nanomagnets that cause the destruction of bacteria when MHT is Microorganisms applied to them [5]. amorphous particles are suggested to neutralize using additional artificial magnetically labeled. Bacteria with crystalline particles can be neutralized using only their own particles, or their action must be enhanced by artificial magnetic nanoparticles. It is necessary to take into account the number of piece magnetic nanoparticles, which will be fixed on the cell surface during the magnetics of bacteria with amorphous BMNs. We also suggest considering whether there are enough dipole-dipole interactions between BMNs and artificial magnetic nanoparticles to fix their on the cell surface of a bacterium.

We recommend to neutralize bacteria which don't synthesize BMNs with magnetically conducting of magnetohydrodynamic mixing[26].

As a result, magnetic nanoparticles will uniformly settle on the cell surface of the microorganism. Thus, magnetic nanoparticles are fixed on the cell surface and as a result bacteria become more sensitive to the action of MHT. So microorganisms should be neutralized by heating magnetic particles on the surface of their cells when exposed to MHT.

Experiments [27] showed that *S. aureus* produce amorphous BMNs. The micrographs presented in [27] show that the magnetic nanoparticles of *S. aureus* are not organized into chains and their sizes can vary from 10 to 150 nm. Artificial magnetic nanoparticles introduced into the suspension during labeling t diameters, from 10 nm and above [16].

A schematic representation of the interaction forces between amorphous BMNs of *S. aureus* and artificial magnetic nanoparticle is shown on Fig. 1.

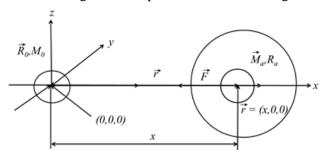


Fig. 1. Schematic representation of the interaction of an amorphous BMNs of *S. aureus* and an artificial nanomagnetite at a magnetically labeled bacteria, where R_0, \vec{M}_0 — the radius and magnetization of an artificial magnetic nanoparticle, respectively, and R_a, \vec{M}_a — the radius and magnetization of an amorphous *S. aureus* nanoparticle, respectively.

The parameters of the physical model for assessing of the strength of the magnetic dipole interaction between amorphous BMNs and artificial magnetic nanoparticles:

 $R_0 = 30$ nm= $3 \cdot 10^{-6}$ cm – radius of the artificial magnetic nanoparticle;

 R_a = 40 nm= $4 \cdot 10^{-6}$ cm - radius of amorphous BMNs [27, 28];

 $M_{0} \approx 500$ EMU- the magnetization of an artificial magnetic nanoparticle;

 $M_a \approx 0.1 \text{EMU}$ – the magnetization of an amorphous biogenic nanoparticle [29].

Thus, we propose the following calculations of the forces of the magnetic dipole interaction between the amorphous BMNs of *S. aureus* and artificial magnetic nanoparticles at magnetism for neutralizing *S. aureus* MHT:

$$\vec{F} = -gradU \tag{1}$$

$$U = -\left[\frac{3(\vec{m}_0 \cdot \vec{r})(\vec{m}_a \cdot \vec{r}) - (\vec{m}_0 \cdot \vec{m}_a)r^2}{r^5}\right]$$
(2)

where: $\vec{n} = \frac{\vec{r}}{r}$, $\vec{m}_0 = \vec{M}_0 \cdot V_0$ – the magnetic moment of an artificial magnetite particle,

 $m_a = \vec{M}_a \cdot V_a$ - the magnetic moment of the amorphous BMNs in *S. aureus*.

As a result of the calculation, a force of $1 \cdot 10^{-14}$ N was obtained, which is significantly less than the specific binding forces of the antigen-antibody, which is equal to $1 \cdot 10^{-9}$ N [30–32]. However, these forces have a close order of magnitude to the forces that are necessary for the functioning of molecular tweezers ($5 \cdot 10^{-14}$ N), which control the movement of DNA inside the cell. Also, these forces are close to the forces that are necessary for the functioning of molecular motors, and range from $5 \cdot 10^{-15}$ N to $6 \cdot 10^{-14}$ N [33, 34]. Such magnetic forces are sufficient to affect vesicular transport and metabolism in tissues and organs [35].

Thus, the forces resulting from the interactions of amorphous BMNs and artificial magnetic nanoparticles are sufficient to magnetize *S. aureus* and further neutralize them with MHT.

Since S. aureus produces BMNs, the experience in [5] could be simplified and made more efficient using magnetic field measurement. At the same we suggest using artificial magnetic nanoparticles as a magnetic material for MHT instead of magnetotactic bacteria. Artificial magnetic nanoparticles will settle on the cell surface and will be fixed there due to the forces of dipole – dipole interactions between artificial particles and the BMNs of S. aureus during magnetic labeling. Thus, the particles will be fixed with the help of magnetic forces.

So, from the studied microorganisms, which are presented in table 1, 3 strains can be neutralized by MHT, using BMNsof *Streptococcus sanguinis* SK115, *Streptococcus pneumoniae* 845, *S. pneumoniae* 2070335. But their genomes are not fully defined. 20 strains can be neutralized with the help of magnetic hyperthermia, using an additional artificial magnetically labeled [25]: *S. aureus subsp. aureus* 6850, *S. aureus subsp. aureus* ED133, *S. aureus* NCTC 8325, *S. aureus subsp. aureus*

ST72, S. aureus subsp. aureus EMRSA16, S. aureus SCOA6009, S. aureus M81493, S. aureus 880, S. aureus subsp. aureus 21269, S. aureus subsp. aureus CO-98, S. aureus A8819, P. fluorescens **NCIMB** 11764, Р. fluorescensABAC62, fluorescens BBc6R8, Bacillus cereus G9241, Shigelladysenteriae 1617, Shigellaflexneri 2a, S. flexneri 2a str. 2457T, Clostridioides difficile CD196, Peptostreptococcus MV1, sp. Peptostreptococcus sp. D1.

3. Conclusions

So, using the methods of comparative genomics, it is possible to determine whether this microorganism produces BMNs and what type of BMNs and to provide a further way for neutralizing these microorganisms using MHT.

Thus, carrying out genetic analysis, the division of microorganisms into groups, the selection of methods of neutralization depending on the magnetic properties of bacteria for each individual group will provide the best result and increase the efficiency of MHT.

References

- [1] Kurono Y., Tomonaga K., Mogi G. (1988) Staphylococcus epidermidis and Staphylococcus aureus in otitis media with effusion. Archives of Otolaryngology-Head & Neck Surgery, vol. 11, no. 114, pp. 1262-1265.
- [2] Payne S.C., Benninger M. S. (2007) *Staphylococcus aureus* is a major pathogen in acute bacterial rhinosinusitis: A Meta-Analysis. *Clinical Infectious Diseases*, vol. 10, no. 45, pp. 121-127.
- [3] Carlin K., Lofmark S., Blad L. (2014) *Swedish work on containment of antibiotic resistance*. Stockholm, Public Health Agency of Sweden, 134 p.
- [4] Tenover F.C. (2006) Mechanisms of antimicrobial resistance in bacteria. *The American Journal of Medicine*, vol. 119, no. 6, pp. 3-10.
- [5] Chen C., Chen L., Yi Y. (2016) Killing of *Staphylococcus aureus* via magnetic hyperthermia mediated by magnetotactic bacteria. *Applied and Environmental Microbiology*, vol. 82, no. 7, pp. 2219-2226.
- [6] John L., Janeta M., Szafert S. (2017) Designing of macroporous magnetic bioscaffold based on functionalized methacrylate network covered by hydroxyapatites and doped with nano-MgFe₂O₄ for potential cancer hyperthermia therapy.

- *Materials Science and Engineering: C*, vol. 78, pp. 901 -911.
- [7] Zee J. (2002) Heating the patient: a promising approach. *Ann Oncol. Aug*, vol. 8, no. 13, pp. 1173-84.
- [8] Heydari M., Javidi M., Attar M. M., Karimi A., Navidbakhsh M., Haghpanahi M., Amanpour S. (2015) Magnetic fluid hyperthermia in a cylindrical gel contains water flow. *Journal of Mechanics in Medicine and Biology*, vol. 15, no. 05, 15500888: 1 16. doi: 10.1142/S0219519415500888
- [9] Hildebrandt, B. (2002). The cellular and molecular basis of hyperthermia. *Critical Reviews in Oncology/Hematology*, vol. 43, no. 1, pp. 33–56.
- [10] Ulashchik V. S. (2014) Lokal'naya gipertermiya v onkologii: ispol'zovaniye magnitnogo polya, lazernogo izlucheniya, ul'trazvuka [Local hyperthermia in oncology: the use of a magnetic field, laser radiation, ultrasound]. *Voprosy* kurortologii, fizioterapii lechebnoy offizicheskoykul'tury [Questions balneology, physiotherapy and medical physical culture], vol. 91, no. 2, pp. 48–57. (In Russian)
- [11] Perigo E. A., Hemery G., Sandre O., Ortega D. (2015) Fundamentals and advances in magnetic hyperthermia. *Applied Physics Reviews*, no. 2, pp. 041302-1 041302-35.
- [12] Freeman C., Halperin E.C., Brady L.W., Wazer D. E. (2008) *Perez and Brady's Principles and Practice of Radiation Oncology*. Philadelphia, Wolters Kluwer Health/Lippincott Williams & Wilkins. pp. 637–644.
- [13] Nikiforov V., Brusentsov N. (2007) Magnitnaya gipertermiya v onkologii [Magnetic hyperthermia in oncology]. *Medical Physics*, no. 2, pp. 51–59.
- [14] Brusentsov N.A., Komissarova L.Kh., Kuznetsov A.A. (2002) Evaluation of ferrifluids containing fotosensitizer for the AC magnetic field action to the tumor cells in vitro. *J. Eur. Cells and Materials*, vol. 3, no. 2, pp. 70–73.
- [15] Ahmed K., Zaidi S.F. (2013) Treating cancer with heat: hyperthermia as promising strategy to enhance apoptosis. *J. Pak. Med. Assoc.*, vol. 63, no.4, pp. 504-8.
- [16] Banobre-Lopez M., Rodrigues D., Espina B. (2013) Control of bacterial cells growths by magnetic hyperthermia. *IEEE transactions on magnetics*, vol. 49, no. 7, pp. 3508–3511.
- [17] Horobets S.V., Horobets O.Yu., Butenko K.O., Chyzh Yu. M. (2014)

- Biomineralizatsiya mahnitnykh nanochastynok bakterialnymy symbiontamy lyudyny [Biomineralization of magnet nanoparticles with bacterial symbionts of man]. *Medical perspectives*, vol. 19, no. 2, pp. 4-12. (In Ukrainian)
- [18] Chekhun V., Horobets S., Horobets O., Demyanenko I. (2011) Mahnitochutlyvi nanostruktury endohennoho pokhodzhennya v klitynakh kartsynomy Erlikha [Magneto-sensitive nanostructures of endogenous origin in Ehrlich carcinoma cells]. *Material science of nanostructures*, no. 2, pp. 102-109. (In Ukrainian)
- [19] Chekhun V., Horobets S., Horobets O., Demyanenko I. (2011) Mahnitni nanostruktury v pukhlynnykh klitynakh [Magnetic nanostructures in neoplasm cells]. *Visnyk of the National Academy of Sciences of Ukraine*, no. 11, pp. 13-20. (In Ukrainian)
- [20] BLAST: Basic Local Alignment Search Tool [Internet]. Blast.ncbi.nlm.nih.gov. 2019 [cited 02.07.2019]. Available from: http://blast.ncbi.nlm.nih.gov.
- [21] Li W., Pio F., Pawlowski K., Godzik A. (2000) Saturated BLAST: an automated multiple intermediate sequence search used to detect distant homology. *Bioinformatics*, vol. 16, no. 12, pp. 1105-1110.
- [22] Schubbe S., Wurdemann C., Peplies J., Heyen U, Wawer C., Glockner F. (2006). Transcriptional Organization and Regulation of Magnetosome Operons in Magnetospirillumgryphiswaldense. *Applied and Environmental Microbiology*, vol. 72, no. 9, pp. 5757-5765. doi: 10.1128/AEM.00201-06.
- [23] Ullrich S., Kube M., Schubbe S., Reinhardt R., Schuler D. (2005) A Hypervariable 130-Kilobase Genomic Region of *Magnetospirillum gryphiswaldense* Comprises a Magnetosome Island Which Undergoes Frequent Rearrangements during Stationary Growth. *Journal of Bacteriology*, vol. 187, no. 21, pp. 7176-7184. doi: 10.1128/JB.187.21.7176-7184.2005.
- [24] The Statistics of Sequence Similarity Scores/ National Center for Biotechnology Information. Available at:
- https://www.ncbi.nlm.nih.gov/BLAST/tutorial/Altsc hul-1.html.
- [25] Gorobets O. Yu., Gorobets S.V., Sorokina L.V. (2014) Biomineralization and

- synthesis of biogenic magnetic nanoparticles and magnetosensitive in clusions in microorganisms and fungi. *Functional Materials*, vol. 21, no. 4, pp. 427-436.
- [26] Gorobets S., Gorobets O., Kovalyov O., Hetmanenko K., Kovalyova S. (2016) Examining the properties of dry magnetically controlled biosorbent, obtained by the method of mechanical and magneto-hydrodynamic agitation. *Eastern-European Journal of Enterprise Technologies*, vol. 84, no. 6/10, pp. 57–63.
- [27] Vainshtein. M., Suzina N., Kudryashova E., Ariskina E. (2002) New magnet-sensitive structures in bacterial and archaeal cells. *Biology of the Cell*, vol. 94, pp. 29–35.
- [28] Lins U., Farina M., (2001) Amorphous mineral phases in magnetotactic multicellular aggregates. *Arch. Microbiol.*, vol. 176, pp. 323–328.
- [29] Machala L., Zboril R., Gedanken A. (2007) Amorphous Iron (III) Oxides A Review. *J. Phys. Chem. B*, vol. 111, no. 16, pp. 4003–4018. doi: 10.1021/jp064992s.
- [30] Kirschvink J. L., Kobayashi-Kirschvink A., Woodford B.J. (1992) Magnetite biomineralization in the human brain. *Proc. Nat. Acad. Sci. USA*, vol. 89, pp. 7683–7687.
- [31] Drummond D.C., Meyer O., Hong K. (1999) Optimizing Liposomes for delivery of chemotherapeutic agents to solid tumors. *Pharmacological reviews*, vol. 51, no. 4, pp. 691–743.
- [32] Dobson J.P., Grassi P. (1996) Magnetic Properties of Human Hippocampal Tissue Evaluation of Artefact and Contamination Sources. *Brain Res. Bull.*, vol. 39, pp. 255–259.
- [33] Bely V., Schlager M.A., Foster H., Reimer A.E., Carter A.P., Yildiz A. (2016) The mammalian dynein-dynactin complex is a strong opponent to kinesin in a tug-of-war competition. *Nat. Cell. Biol.*, vol. 9, no. 18, pp. 1018–1024.
- [34] Hill D.B., Plaza M.J., Bonin K., Holzwarth G. (2004) Fast vesicle transport in PC12 neurites: velocities and forces. *Eur. Biophys. J.*, vol. 33, no. 7, pp. 623-32. doi: 10.1007/s00249-004-0403-6.
- [35] Mikeshyna H.I., Darmenko Y.A., Gorobets O. Yu., Gorobets S.V., Sharay I.V., Lazarenko O.M. (2018) Influence of biogenic magnetic nanoparticles on the vesicular transport. *Acta Physica Polonica*, vol. 133, no. 3, pp. 731–733.

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Магнітна гіпертермія мікроорганізмів з природними феримагнітними властивостями

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Мета: Зазвичай у практиці знешкодження мікроорганізмів магнітною гіпертермією не враховують наявність у останніх власних біогенних магнітних наночастинок. Мета дослідження виявити мікроорганізми, для яких врахування характеристик їх власних біогенних магнітних наночастинок може привести до помітного зростання ефективності магнітної гіпертермії. Методи: У дослідженні використано методи порівняльної геноміки, зокрема, попарне вирівнювання з використанням бази Проведено вирівнювання протеомівмагнітотаксисної Magnetospirillumgryphiswaldense MSR-1 з протеомами патогенних мікроорганізмів, які були класифіковані за місцем локалізації і типом внутрішньої будови їх біогенних магнітних наночастинок. Результати: Проаналізовано геноми 24 штамів патогенних мікроорганізмів, які належать до таких родів: Staphylococcus, Pseudomonas, Bacillus, Shigella, Clostridioides, Streptococcus, Peptostreptococcus. Показано, що 2 із них мають кристалічні внутрішньоклітинні біогенні магнітні наночастинки, зовнішньоклітинні кристалічні – 11 штамів, внутрішньоклітинні аморфні – 8 штамів, зовнішньоклітинні аморфні – 3 штами. Також в роботі представлені розрахунки сил дипольдипольних взаємодій між аморфними біогенними наночастинками Staphylococcusaureus та штучними магнітними наночастинками. Обговорення: Ми рекомендуємо використовувати методи порівняльної геноміки для поділу мікроорганізмів за магнітними властивостями для підбору більш ефективного способу знешкодження магнітною гіпертермією. Так 3 штами, що продукують кристалічні внутрішньоклітинні біогенні магнітні наночастинки, можна знешкодити методом магнітної гіпертермії, використовуючи у якості магнітного матеріалу їх власні наночастинки. 21 штам із зовнішньоклітинними кристалічними, внутрішньоклітинними аморфними та зовнішньоклітинними аморфними біогенними магнітними наночастинками, можна знешкодити магнітною гіпертермією, використовуючи методи штучного магнітомічення. Показано, що сил диполь-дипольних взаємодій між аморфними магнітними наночастинками та штучними магнітними наночастинками достатньо для того, щоб магнітомітити S. aureus і в подальшому знешкоджувати їх за допомогою магнітної гіпертермії. Висновки: Отже, врахування природних феримагнітних властивостей мікроорганізмів підвищить ефективність знешкодження магнітною гіпертермією.

Ключові слова: магнітна гіпертермія; патогенні бактерії; знешкодження; біогенні магнітні наночастинки; методи порівняльної геноміки; магнітодипольні взаємодії

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Цель: Обычно в практике обезвреживания микроорганизмов магнитной гипертермией не учитывают наличие в последних собственных биогенных магнитных наночастиц. Цель исследования выявить микроорганизмы, для которых учет характеристик их собственных биогенных магнитных наночастиц может привести к заметному росту эффективности магнитной гипертермии. **Методы:** В исследовании использованы методы сравнительной геномики, в частности, попарное выравнивание с использованием базы данных Genbank. Проведено выравнивание протеомовмагнитотаксисной бактерии *Magnetospirillum gryphiswaldense* MSR-1 с протеомами патогенных микроорганизмов, которые были классифицированы по месту локализации и типу внутреннего строения их биогенных магнитных наночастии. **Результаты:** Проанализированы геномы24 штаммов патогенных

микроорганизмов, принадлежащих к таким родам: Staphylococcus, Pseudomonas, Bacillus, Shigella, Clostridioides, Streptococcus, Peptostreptococcus. Показано, что 3 из них имеют кристаллические внутриклеточные биогенные магнитные наночастицы, внеклеточные кристаллические – 11 штаммов, внутриклеточные аморфные - 8 штаммов, внеклеточные аморфные - 3 штамма. Также в работе представлены расчеты сил диполь-дипольных взаимодействий между аморфными биогенными наночастицами Staphylococcus aureus и искусственными магнитными наночастицами. Обсуждение: Мы рекомендуем использовать методы сравнительной геномики для разделения микроорганизмов с магнитными свойствами для подбора более эфективного способа обезвреживания магнитной гипертермией. Так, 3 штамма с кристаллическими внутриклеточными биогенными магнитными наночастицами можно обезвредить методом магнитной гипертермии, используя в качестве магнитного материала их собственные частицы. 21 штамм с внеклеточными кристаллическими, внутриклеточными аморфными и внеклеточными аморфными магнитными наночастицами, можно обезвредить магнитной гипертермией, используя методы искусственного магнитомичения. Показано, что сил диполь-дипольных взаимодействий между аморфными магнитными наночастицами и искусственными магнитными наночастицами достаточно для того, чтобы магнитометить S. aureus и в дальнейшем обезвреживать их с помощью магнитной гипертермии. Выводы: Использование природных ферромагнитных свойств микроорганизмов повысит эффективность обезвреживания магнитной гипертермии.

Ключевые слова: магнитная гипертерми; патогенные бактерии; обезвреживание; биогенные магнитные наночастицы; методы сравнительной гномики; магнитодипольные взаимодействия

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