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The prediction of biogenic magnetic nanoparticles biomineralization in human tissues and organs

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Abstract. In this study, human homologs of magnetosome island proteins basing on pairwise and multiple alignment of amino acid sequences were found. The expression levels of genes, which encode magnetosome island proteins of *M. gryphiswaldense* MSR-1, that were cultured under oxygen deficiency conditions and also under microaerobic conditions were compared to the expression levels of genes that encode the relevant homologs in human organism. The possibility of BMN biomineralization in human tissues and organs, in which BMN were not experimentally found before, was predicted.

1. Introduction

Biogenic magnetic nanoparticles (BMN) are ferrite nanocrystals (magnetite, maghemite, greigite) formed during the genetically controlled biosynthesis. This mechanism is called biomineralization. BMN biomineralization is the most studied in magnetotactic bacteria (MTB). Magnetic nanoparticles are situated inside special membrane structures - magnetosome islands (MI). Magnetite biomineralization is induced under microaerobic conditions. There is a distinct correlation between the extracellular levels of oxygen and magnetite quantity in *Magnetospirillum gryphiswaldense*. Magnetite biomineralization occurs at the oxygen levels below the threshold of 2 kPa (2%) and the largest number of BMN was found inside MI at 25 Pa (0.025%). Higher level of oxygen completely inhibit BMN formation [1].

BMN presence is experimentally confirmed in different human tissues [2, 3]: liver, heart, spleen [4] adrenal glands, slatted bone and brain [5]. Moreover, several studies have shown increased BMN concentrations during neurodegenerative diseases [6, 7, 8] and cancer [9, 2] in the affected area.

The main objective of this study is the prediction and detection of human organs and tissues in which BMN biomineralization occurs by using bioinformatics methods.

Since the mechanism of biomineralization BMN is the same for all three kingdoms of organisms, the prediction of biomineralization could be based on finding MI MTB homologous proteins in human and relevant gene analysis [10].

2. Experimental procedure

Mechanism of BMN biomineralization is based on a set of MI MTB proteins. They are mamA, mamB, mamM, mamE, mamO, mamN. In this paper, only the first three proteins, acting as protein-protein interaction and transport of cations Co^{2+} , Zn^{2+} , Cd^{2+} , were analyzed respectively.



Homologs were found by means of pairwise and multiple alignment of amino acid sequences methods using BLAST program of National Center for Biotechnology Information (NCBI). Proteome of *M. gryphiswaldense* MSR-1 was used as a microorganism for the original sequences of mam proteins obtaining, as the most researched. MamA, mamB and mamM proteins were chosen because their expression levels were experimentally obtained for *M. gryphiswaldense* MSR-1 cultured under oxygen deficiency conditions as well as under microaerobic conditions [1].

Evaluation on the similarity was performed basing on the I and E-value indices with the thresholds $> 18\%$ and < 0.05 , respectively. I (%) - number of identical amino acid residues in comparing proteins. E-value is an indicator that reflects the statistical significance of the alignment, reducing the value that indicates a lower level of coincidence chance [11].

The comparison of the gene expression levels was conducted by using an average of FPKM (Fragment per Kilobase of Exon per Million Fragments Mapped). The data were obtained using The Human Protein Atlas.

3. Results and discussion

In this research human homologs of MI MTB proteins were found. They are: pex-5 protein as a mamA homolog, SLC30A9, SLC39A4, SLC39A3 as mamB homologs and SLC30A9, SLC39A4 as mamM homologs. In addition, the expression levels of genes that encode MI MTB proteins and the expression levels of genes that encode the relevant homologs in human organism were compared. The results of the genes expression levels comparison are represented in the table 1.

Table 1. The results of the comparison of the expression levels of genes, encoding MI MTB proteins and the expression levels of genes, encoding the relevant homologs in human organs and tissues. “+” - the expression level of genes, encoding homologs in human organism is higher than the relevant expression level of genes in MTB, “-” is respectively lower.

	mamA		mamB		mamM	
	Pex-5	SLC30A9	SLC39A4	SLC39A3	SLC30A9	SLC39A4
Endometrium	+	+	-	-	+	+
Cerebral cortex	+	+	-	+	+	-
Lung	+	+	-	-	+	+
Ovary	+	+	-	-	+	+
Prostate	+	+	-	-	+	+
Stomach	+	+	+	-	+	+
Thyroid gland	+	+	-	+	+	+
Testis	+	+	-	+	+	+
Kidney	+	+	+	-	+	+
Smooth muscle	+	+	-	+	+	-
Duodenum	+	+	+	-	+	+
Gall bladder	+	+	-	-	+	+
Bone marrow	+	-	-	+	+	+
Tonsil	+	+	-	-	+	+
Urinary bladder	+	+	-	+	+	-
Adrenal glands	+	+	-	+	+	+
Esophagus	+	+	-	-	+	+
Small intestine	+	+	+	-	+	+
Colon	+	+	+	-	+	+
Fallopian tube	+	+	-	+	+	+
Rectum	+	+	-	-	+	+
Salivary gland	+	+	-	-	+	+

BMN biomineralization can be predicted in human tissues and organs, in which the expression levels of three mam homologs is higher than the expression levels of mam proteins in *M. gryphiswaldense* MSR-1, cultured under microaerobic conditions, as it is represented in the table 1.

4. Conclusions

In this paper, the possibility of BMN biomineralization in human tissues and organs, in which BMN were not experimentally found earlier was predicted. This tissues and organs are endometrium, cerebral cortex, lung, ovary, prostate, stomach, thyroid gland, testis, kidney, smooth muscle, duodenum, gall bladder, bone marrow, tonsil, urinary bladder, esophagus, small intestine, colon, fallopian tube, rectum, salivary gland.

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