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БАЯНДАМАЛАРЫ

ДОКЛАДЫ

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FEATURES OF miRNA ASSOCIATIONS WITH mRNA OF MYOCARDIAL INFARCTION CANDIDATE GENES

Abstract. Cardiovascular diseases, in particular myocardial infarction, are one of the most common causes of death in the world. To date, the risk assessment strategy infarction and post-infarction complications represent a significant problem sensitivity and predictive value of modern methods and markers, so the identification of new genetic markers is an actual problem. In this research, functionally significant candidate genes were studied, which are involved in the processes associated with the pathogenesis of myocardial infarction, in lipid metabolism, thrombus formation, endothelial dysfunction, and inflammatory reactions. However, in addition to genes, it has been determined that miRNA is also involved in the development of myocardial infarction by regulating the expression of target genes. This paper presents characteristics of miRNA interactions with mRNAs of candidate myocardial infarction genes. We have identified 34, 51 and 36 target genes that have miRNA binding sites in the 5'UTR, CDS, and 3'UTR regions, respectively. Based on the criteria chosen in our study, candidate genes were identified that have a free energy of interaction with miRNA equal to -120 kJ/mole and higher in the following associations: in 5'UTR - ID02142.3p-miR and *ALDH2*; ID00909.3p-miR and *ALOX5*; ID00216.3p-miR and *CD40*; ID01272.3p-miR and *DDAH2*; ID01774.5p-miR and *IL6R*; miR-6752-5p and *KLF4*; ID03332.3p-miR and *LAMA3*; ID02363.5p-miR and *NOS3*; ID02800.3p-miR and *OPA1*; ID01310.3p-miR and *PDE4D*; ID03397.3p-miR and *PTGS2*; ID01098.3p-miR and *SERPINE1*; ID01018.3p-miR and *SGPP1*; ID02430.3p-miR and *SHH*; ID01652.3p-miR and *THBS1*; ID01770.3p-miR and *ZNF202*; in CDS - ID00457.3p-miR and *APOA1*; ID00425.5p-miR and *BTN2A1*; ID01632.5p-miR and *CCL5*; ID02899.3p-miR and *CDKN2B*; miR-6894-5p and *CYP1A2*; ID01806.3p-miR and *IL6R*; ID01403.5p-miR and *PLAUR*; ID02950.3p-miR and *SEMA3F*; ID03332.3p-miR and *SGPP1*; ID02062.3p-miR and *SIRT6*; ID02050.3p-miR and *TNF*; ID01804.3p-miR and *XBP1*; ID00182.5p-miR and *ZNF202*; in 3'UTR - ID01293.5p-miR and *SMTN*; ID01882.5p-miR and *TNNI3*. The identified associations can be used as genetic markers in the diagnosis of myocardial infarction.

Key words: myocardial infarction, target genes, binding site, miRNA, mRNA.

For a long time, cardiovascular diseases (CVD) have been the leading cause of death in developed countries of the world and, according to forecasts, will keep it in the coming decades [1, 2]. Currently, one in three deaths in Europe is due to CVD [3]. In the structure of mortality from CVD, the first place is taken by myocardial infarction (MI) [4]. The MI based on atherosclerotic arterial damage, against which the developing circulatory disorders infarction with subsequent development of a necrotic process [5]. Myocardial necrosis after a heart attack is accompanied by heart failure, myocardial rupture, arrhythmia, and can also lead to sudden cardiac death. Today, in the strategy for assessing the risk of heart attack and post infarction complications, a significant problem is the sensitivity and prognostic value of modern methods and markers, therefore, the identification of new markers with high specificity and sensitivity is an urgent task [6-9].

There is an increasing number of scientific papers investigating miRNAs (mRNA-inhibiting RNA). They have been shown to be associated with various diseases, including heart failure [10-12], malignant neoplasms [13, 14] and multiple sclerosis [15, 16], as well as a decisive role in the mechanisms of MI

development, such as rupture of atherosclerotic plaques, thrombosis and heart cells necrosis after blockage of a coronary artery [17]. The miRNA are small (about 22 nucleotide pairs) non-coding RNAs that are able to influence gene networks through transcriptional and translational regulation [18]. They are able to bind to the 5'-untranslated region (5'UTR), 3′-untranslated region (3′UTR) or protein coding region (CDS) of mRNA of the target gene and inhibit its translation or initiate degradation [19]. In vitro studies have shown that when entering the cells of the recipient, miRNAs are functionally active and capable of acting as chemical messengers to regulate intercellular interactions [18]. Thus, the profiling of miRNAs may reflect the state of selected groups of cells and the detection of specific alterations in expression. Sensitivity to pathological changes in cells makes miRNA promising diagnostic markers of pathological processes both at their beginning and during the control of ongoing therapy [20].

Materials and methods. The miRNA base consisted of 2565 miRNAs that were downloaded from miRBase (http://mirbase.org) and 3707 miRNAs taken from the publication Londin E. et al. [21]. Nucleotide sequences of mRNA of candidate myocardial infarction genes were obtained from the NCBI database (http://www.ncbi.nlm.nih.gov). In the study of miRNA target genes additionally was found information about the mRNA expression levels in cardiac tissues prone to pathological changes in cardiovascular diseases – RPKM (reads per kilobase per million of mapped reads). The RPKM values for the mRNA genes were taken from Human Protein Atlas (https: //www.prooteinatlas.org).

The miRNA binding sites in the 5'UTR, CDS and 3'UTR of mRNA of genes predicted by the program MirTarget [22, 23]. This program determines the following binding characteristics: initiation of binding site of miRNA and mRNA; localization of miRNA binding sites in 5'UTR, CDS and 3'UTR regions of mRNA; free energy of interaction (ΔG, kJ/mole), estimated for the entire nucleotide sequence of miRNA; schemes of interaction between miRNA and mRNA nucleotides. The ratio ΔG/ΔGm (%) was determined for each site, where ΔGm is the free energy of miRNA binding with a completely complementary nucleotide sequence. The program determines the position of binding sites in mRNA, starting from the first nucleotide of the 5'UTR of mRNA. The MirTarget program takes into account hydrogen bonds between adenine (A) and uracil (U), guanine (G) and cytosine (C), G and U, A and C. [24, 25].

Results and discussion.

The search for miRNA binding sites was carried out in the 5'UTR, CDS, and 3'UTR mRNA of candidate MI genes in order to reveal the features of miRNA interaction in these regions. To select the most effective associations of miRNA and candidate genes, the following criteria and characteristics of the interaction of miRNA with mRNA of target genes were selected: the free energy of the interaction of miRNA with mRNA of the candidate target gene; the degree of complementarity of miRNA nucleotides and mRNA binding sites of the candidate gene; the possibility of a candidate gene participating in the disease under study based on its function.

Table 1 shows the characteristics of miRNA binding with mRNA of 34 candidate MI genes. Based on the above criteria, miRNAs interacting with mRNA with free energy (ΔG) equal to -120 kJ/mole and more could be recommended as associations: ID02142.3p-miR and *ALDH2*; ID00909.3p-miR and *ALOX5*; ID00216.3p-miR and *CD40*; ID01272.3p-miR and *DDAH2*; ID01774.5p-miR and *IL6R*; miR-6752-5p and *KLF4*; ID03332.3p-miR and *LAMA3*; ID02363.5p-miR and *NOS3*; ID02800.3p-miR and *OPA1*; ID01310.3p-miR and *PDE4D*; ID03397.3p-miR and *PTGS2*; ID01098.3p-miR and *SERPINE1*; ID01018.3p-miR and *SGPP1*; ID02430.3p-miR and *SHH*; ID01652.3p-miR and *THBS1*; ID01770.3p-miR and *ZNF202*. Also, one association of ID01152.3p-miR and mRNA of the target gene *HMOX1* was revealed, which was characterized by a ΔG/ΔGm value of 95%, which indicates an almost complete complementarity of the interaction between miRNA nucleotides and nucleotides of the binding site.

Most of the single interactions were observed in the CDS of mRNA target genes for MI, which are presented in Table 2. A total of 51 candidate genes with binding sites for different miRNAs were identified. The following interactions with free energy (ΔG) equal to -120 kJ/mole and higher are noted: ID00457.3p-miR and *APOA1*; ID00425.5p-miR and *BTN2A1*; ID01632.5p-miR and *CCL5*; ID02899.3p-miR and *CDKN2B*; miR-6894-5p and *CYP1A2*; ID01806.3p-miR and *IL6R*; ID01403.5p-miR and *PLAUR*; ID02950.3p-miR and *SEMA3F*; ID03332.3p-miR and *SGPP1*; ID02062.3p-miR and *SIRT6*; ID02050.3p-miR and *TNF*; ID01804.3p-miR and *XBP1*; ID00182.5p-miR and *ZNF202*.

In addition, mRNA and miRNA associations with a high ΔG/ΔGm value equal to 95% or more were noted: ID01734.5p-miR and *CLEC16A*; miR-6165 and *HNRNPUL1*; ID00182.5p-miR and *ZNF202*.

Table 1 - Characteristics of miRNA interactions in the 5'UTR of the mRNAs of MI candidate genes

Gene; RPKM	miRNA	Start of site, nt	ΔG, kJ/mole	ΔG/ΔGm, %	Length, nt
ABCA1; 1.8	miR-4435	331	-110	91	22
ADRB1; 8.8	miR-1587	31	-106	93	20
AGT; 60.3	miR-3126-5p	326	-108	91	22
ALDH2; 106.1	ID02142.3p-miR	8	-123	92	21
ALOX5; 2.1	ID00909.3p-miR	68	-121	90	23
CD40; 4.7	ID00216.3p-miR	10	-123	91	23
CYP2C8; 0.1	miR-4709-5p	49	-104	91	22
DDAH2; 18.1	ID01272.3p-miR	185	-121	88	24
DPP4; 0.8	ID02385.3p-miR	369	-108	93	20
HMGA1; 11.3	ID02247.3p-miR	350	-117	92	21
HMOX1; 5.7	ID01152.3p-miR	75	-113	95	20
HSPA12B; 6.4	ID01651.5p-miR	36	-119	92	22
ICAM1; 9.9	ID00195.3p-miR	106	-117	89	23
IL6R; 2.8	ID01774.5p-miR	329	-129	90	23
KCNMA1; 0.1	ID03120.3p-miR	36	-117	92	21
KDR; 6.7	ID02534.5p-miR	143	-119	92	22
KLF4; 18.2	miR-6752-5p	101	-121	92	22
LAMA3; 0.8	ID03332.3p-miR	13	-138	93	24
LPL; 112.3	miR-4430	287	-96	94	18
NOS3; 5.1	ID02363.5p-miR	200	-123	88	24
OPA1; 9.6	ID02800.3p-miR	161	-121	90	22
PDE4D; 2.8	ID01310.3p-miR	66	-121	92	22
PROCR; 11.4	miR-6779-5p	70	-110	91	21
PTGS2; 2.8	ID03397.3p-miR	108	-123	92	21
PTX3; 15.0	miR-6866-5p	36	-106	91	23
SELP; 2.4	ID03109.5p-miR	49	-106	94	21
SERPINE1; 50.6	ID01098.3p-miR	30	-123	88	24
SGPP1; 2.1	ID01018.3p-miR	48	-123	88	24
SHH; 0.1	ID02430.3p-miR	12	-121	89	23
SLC5A3; 0.6	ID00754.3p-miR	165	-102	91	21
STAT3; 31.8	ID00570.3p-miR	28	-115	92	22
SOD1; 83.9	miR-634	47	-108	91	22
THBS1; 36.2	ID01652.3p-miR	113	-129	92	23
ZNF202; 1.5	ID01770.3p-miR	70	-123	94	22

Table 2 - Characteristics of miRNA interactions in the CDS of the mRNAs of MI candidate genes

Gene; RPKM	miRNA	Start of site, nt	ΔG, kJ/mole	ΔG/ΔGm, %	Length, nt
ABCA1; 1.8	ID00653.3p-miR	6416	-110	90	23
AGTR1; 2.2	ID02795.5p-miR	102	-117	92	22
AHSG; 0.1	miR-6794-5p	955	-108	93	20
ALOX12; 0.1	miR-4506	1046	-98	92	20
APOA1; 7.6	ID00457.3p-miR	841	-123	91	22
ARG1; 0.2	miR-6878-3p	760	-104	92	21
BTN2A1; 6.1	ID00425.5p-miR	280	-121	88	24
CASR; 0.1	ID01787.3p-miR	2421	-115	89	23
CCL5; 2.9	ID01632.5p-miR	181	-121	89	23
CDKN2B; 0.4	ID02899.3p-miR	412	-132	89	24
CLEC16A; 3.5	ID01734.5p-miR	3005	-119	95	22
CXCR4; 4.5	miR-3119	736	-93	92	20
CYP1A2; 0.1	miR-6894-5p	514	-123	92	24
ENPP1; 0.6	ID03416.5p-miR	32	-119	93	20
GCLC; 2.7	miR-545-5p	1129	-93	90	22
GHRL; 0.1	miR-4686	140	-110	91	23
GNB3; 3.0	miR-6736-3p	1167	-104	91	21
GSTM1; 5.5	ID01955.3p-miR	462	-108	89	23
HNRNPUL1; 16.1	miR-6165	867	-104	96	19
IL6R; 2.8	ID01806.3p-miR	483	-125	89	23
IL12B; 0.1	miR-6893-3p	788	-113	90	22

IL19; 0.1	miR-24-1-5p	980	-104	91	22
ITGB3; 1.9	ID02639.5p-miR	52	-115	89	23
ITIH4; 2.0	ID00354.3p-miR	1682	-100	92	20
KCNJ11; 4.3	miR-3676-3p	1430	-102	92	20
LTA; 0.0	miR-6831-5p	581	-117	90	24
MED23; 2.2	miR-4513	4238	-110	90	22
MEF2A; 14.9	ID02266.5p-miR	1831	-104	94	20
MMP3; 0.0	ID00314.3p-miR	132	-119	93	23
PCSK9; 0.0	ID01810.3p-miR	1052	-115	89	23
PON1; 0.0	miR-5003-3p	330	-100	92	21
PLAUR; 3.0	ID01403.5p-miR	233	-123	91	23
PROCR; 11.4	miR-4783-5p	407	-117	92	21
S100A1; 15.6	ID00654.3p-miR	221	-110	93	21
SCN5A; 21.4	miR-3677-5p	1873	-115	92	22
SELE; 2.7	ID03022.3p-miR	829	-100	90	22
SEMA3F; 4.6	ID02950.3p-miR	2519	-125	89	23
SGPP1; 2.1	ID03332.3p-miR	325	-132	89	24
SHBG; 0.1	miR-6746-5p	821	-115	90	22
SIRT6; 4.1	ID02062.3p-miR	919	-123	92	22
SORBS2; 33.1	miR-761	1477	-108	91	22
STAT3; 31.8	ID00857.5p-miR	1116	-119	90	23
TGFB1; 11.8	miR-6742-5p	2046	-110	90	22
TIMP1; 130.2	ID03340.5p-miR	207	-115	89	23
TNF; 0.4	ID02050.3p-miR	230	-121	92	23
TNNI3; 2151.5	ID01282.3p-miR	322	-119	90	23
UCP3; 0.5	ID01606.3p-miR	406	-115	89	23
UGT1A1; 0.0	ID00091.5p-miR	465	-117	89	23
XBP1; 29.4	ID01804.3p-miR	110	-134	91	23
UCP2; 3.3	miR-6878-3p	509	-102	91	21
ZNF202; 1.5	ID00182.5p-miR	935	-125	97	23

Table 3 also shows examples of various miRNAs and mRNAs of 36 candidate genes in the 3'UTR region. Single binding sites in the 3'UTR, where the free energy ΔG, kJ/mole from -120 and more were found only in two binding sites: ID01293.5p-miR and *SMTN*; ID01882.5p-miR and *TNNI3*. Associations of miRNA and mRNA with the value of ΔG/ΔGm from 95% and higher were also noted: miR-4307 and *ATP10D*; ID01837.3p-miR and *GATA2*; miR-5095 and *HFE*.

Table 3 - Characteristics of miRNA interactions in the 3'UTR of the mRNAs of MI candidate genes

Gene; RPKM	miRNA	Start of site, nt	ΔG, kJ/mole	ΔG/ΔGm, %	Length, nt
ABCC9; 4.5	ID02637.3p-miR	6665	-104	89	23
ALPK1; 1.1	ID03324.3p-miR	5268	-115	90	22
AP3D1; 21.2	ID01954.3p-miR	4735	-110	91	22
ATP10D; 2.0	miR-4307	4877	-89	95	19
CASR; 0.0	ID01309.3p-miR	4776	-113	90	23
COL5A2; 7.4	ID02790.5p-miR	5721	-96	92	20
CXCL12; 17.8	ID00483.3p-miR	932	-119	90	23
CYP4F3; 0.0	ID01838.5p-miR	2964	-113	90	24
DKK1; 0.2	ID00436.3p-miR	1580	-106	91	23
EDN1; 2.9	miR-548az-5p	1222	-100	90	22
FADS3; 28.3	ID00022.3p-miR	1515	-108	91	21
GAA; 11.7	ID02018.3p-miR	3637	-113	91	21
GATA2; 4.2	ID01837.3p-miR	2340	-119	97	22
GCLC; 2.7	ID02601.5p-miR	3162	-117	92	21
GJA4; 20.6	miR-642a-3p	1279	-106	91	22
HFE; 0.9	miR-5095	2195	-110	95	21
HMOX1; 5.7	miR-3155a	1227	-106	91	21
HSPA12B; 6.4	miR-4701-5p	2709	-110	91	22
IL19; 0.0	ID01545.3p-miR	1547	-113	93	21
IL6R; 2.8	ID00913.5p-miR	3063	-115	90	23
LRP1; 23.2	miR-3926	14288	-102	91	21
LTA; 0.0	ID01127.3p-miR	1258	-98	92	21
MEF2A; 14.9	miR-1277-5p	2196	-98	90	24

PCSK2; 0.7	miR-3907	3744	-110	90	22
PCSK9; 0.0	miR-6877-3p	2468	-110	91	21
PDE4D; 2.8	ID02141.5p-miR	7731	-100	90	22
PLAUR; 3.0	ID01251.3p-miR	1417	-119	92	22
PSMA6; 36.6	ID02529.5p-miR	954	-106	93	20
SEMA3F; 4.6	ID01386.5p-miR	3293	-119	92	22
SF3A2; 14.8	ID03095.3p-miR	1518	-108	93	22
SH2B1; 7.9	ID01213.5p-miR	4530	-119	89	23
SMTN; 33.4	ID01293.5p-miR	3166	-125	92	22
SPTLC3; 0.8	miR-574-5p	2182	-113	93	23
TGFBR1; 2.9	miR-938	1900	-106	91	22
TNNI3; 2151.5	ID01882.5p-miR	792	-123	88	24
USP25; 6.7	miR-1277-5p	4247	-98	90	24

When studying the RPKM index, it was noted that some of the candidate genes, the expression index of which was 10 or less, had more single binding sites with different miRNAs than candidate genes with high RPKM values. Among the candidate genes of MI with high rates of expression (RPKM) are: *AGT* (60,3), *ALDH2* (106,1), *AP3D1* (21,2), *CXCL12* (17,8), *DDAH2* (18,1), *FADS3* (28,3), *GAA* (11,7), *GJA4* (20,6), *HMGA1* (11,3), *HNRNPUL1* (16,1), *KLF4* (18,2), *LPL* (112,3), *LRP1* (23,2), *MEF2A* (14,9), *PROCR* (11,4), *PSMA6* (36,6), *PTX* (15,0), *S100A1* (15,6), *SCN5A* (21,4), *SF3A2* (14,8), *SERPINE1* (50,6), *SMTN* (33,4), *SOD1* (83,9), *SORBS2* (33,1), *STAT3* (31,8), *TGFB1* (11,8), *TIMP1* (130,2), *THBS1* (36,2), *XBP1* (29,4). The genes of the troponin complex *TNNC1* and *TNNI3*, which are involved in the risk of various types of cardiomyopathies [26, 27], among all the genes studied had the highest RPKM values, 1572 and 2152, respectively.

Inflammation plays a key role in MI development and other cardiovascular diseases due to interactions between genetic and environmental factors. One of the largest studies on this topic is the work of B. Brown et al. [30], in which the influence of polymorphisms of 35 genes of the inflammation system was analyzed, among which were also studied candidate genes of MI - *IL6*, *SELP*, *SELE*, *ADRB2*, *LTA*, *TNF*, *NOS3*, *TGFB1*, *ICAM1* [28-30].

TGFB1 gene encoding transforming growth factor-β (TGF-β) is considered as a candidate gene that can also affect the development of CVD. Among the atheroprotective properties of the cytokine TGF-β, researchers include the ability to stabilize fibrous plaque, inhibition of proliferation of vascular smooth muscle cells, and hindering the migration of endothelial cells; however, dysregulation of TGF-β functioning can disrupt these processes. [31, 32].

Proteins of the ABC superfamily have the ability to modulate and transport various substrates such as sugars, amino acids, proteins, toxins, ions, and alter the pharmacokinetics of drugs. The phylogenetically highly conserved transport protein ABCB1 (ATP binding cassette transporter 1) is involved in the systemic response to inflammation and plays an important role in the development and progression of cardiovascular diseases. Respectively, gene *ABCB1* is involved in tissue damage in acute MI [33].

Conclusion. The association of a large number of genes with myocardial infarction reflects the complexity of the disease. Therefore, it is important to establish the associations of these genes with miRNA. The data obtained in this work expand the understanding of the dependence of the expression of candidate myocardial infarction genes on miRNA. These data allow us to consider the miRNA target genes in a promising diagnostic and therapeutic molecular markers investigated diseases.

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МИОКАРД ИНФАРКТІСІНІҢ КАНДИДАТТЫҚ ГЕНДЕРІНІҢ miRNA-МЕН mRNA ҚАУЫМДАСТЫҚТАРЫНЫҢ ЕРЕКШЕЛІКТЕРІ

Аннотация. Жүрек қан тамыр аурулары, атап айтқанда миокард инфарктісі, әлемдегі өлімнің ең көп таралған себептерінің бірі. Бүгінгі таңда инфаркт пен инфарктан кейінгі асқынулардың қаупін бағалау

стратегиясында қазіргі әдістер мен маркерлердің сезімталдығы мен болжамды құндылығы маңызды мәселе болып табылады, сондықтан жоғары ерекшелігі мен сезімталдығы бар жаңа маркерлерді анықтау өзекті мәселе болып тұр. Бұл зерттеу миокард инфарктісінің патогенезімен, липидтер алмасуымен, тромбозбен, эндотелий дисфункциясымен және қабыну реакцияларымен байланысты процестерге қатысатын функционалды маңызды кандидат-гендерді зерттеді. Алайда, әртүрлі биологиялық процестерге қатысатын гендерден басқа, miRNA сонымен қатар осы аурудың кандидат гендер экспрессиясын реттеу арқылы миокард инфарктісінің дамуына қатысады. Бұл ғылыми жұмыста miRNA-ның миокард инфарктісінің кандидат-гендерінің mRNA-мен өзара әрекеттесуінің сипаттамалары келтірілген. Сәйкесінше 5'UTR, CDS және 3' UTR -де miRNA байланыстыратын сайттары бар 34, 51 және 36 кандидат гендер анықталды. Біздің зерттеуімізде таңдалған критерийлерге сүйене отырып, miRNA-мен өзара әрекеттесудің еркін энергиясы -120 кДж/моль және одан жоғары келесі қауымдастықтарда анықталған: 5'UTR-ID02142.3p-miR және *ALDH2*; ID00909.3p-miR және *ALOX5*; ID00216.3p-miR және *CD40*; ID01272.3p-miR және *DDAH2*; ID01774.5p-miR және *IL6R*; miR-6752-5p және *KLF4*; ID03332.3p-miR және *LAMA3*; ID02363.5p-miR және *NOS3*; ID02800.3p-miR және *OPA1*; ID01310.3p-miR және *PDE4D*; ID03397.3p-miR және *PTGS2*; ID01098.3p-miR және *SERPINE1*; ID01018.3p-miR және *SGPP1*; ID02430.3p-miR және *SHH*; ID01652.3P-mir және *THBS1*; ID01770.3P-mir және *ZNF202*; CDS - ID00457.3p-miR және *APOA1*; ID00425.5p-miR және *BTN2A1*; ID01632.5p-miR және *CCL5*; ID02899.3p-miR және *CDKN2B*; miR-6894-5p және *CYP1A2*; ID01806.3p-miR және *IL6R*; ID01403.5p-miR және *PLAUR*; ID02950.3p-miR және *SEMA3F*; ID03332.3P-miR және *SGPP1*; ID02062.3P-miR және *SIRT6*; ID02050.3p-miR және *TNF*; ; ID01804.3p-miR және *XBP1*; ID00182.5P-miR және *ZNF202*; 3'UTR - ID01293.5p-miR және *SMTN*; ID01882.5p-miR және *TNNI3*. Анықталған ассоциацияларды миокард инфарктісін диагностикалауда генетикалық маркер ретінде қолдануға болады.

Түйін сөздер: миокард инфарктісі, кандидат гендер, байланыстырушы сайт, miRNA, mRNA.

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ОСОБЕННОСТИ АССОЦИАЦИЙ miRNA С mRNA КАНДИДАТНЫХ ГЕНОВ ИНФАРКТА МИОКАРДА

Аннотация. Сердечно-сосудистые заболевания, в частности инфаркт миокарда, являются одной из самых распространенных причин смертности в мире. На сегодняшний день в стратегии оценки риска инфаркта и постинфарктных осложнений существенную проблему представляют чувствительность и прогностическая ценность современных методов и маркеров, поэтому выявление новых маркеров, обладающих высокой специфичностью и чувствительностью, является актуальной задачей. В данном исследовании были изучены функционально значимые гены-кандидаты, которые принимают участие в процессах, связанных с патогенезом инфаркта миокарда, в обмене липидов, тромбообразовании, эндотелиальной дисфункции и в воспалительных реакциях. Однако помимо генов, вовлеченных в различные биологические процессы, было определено, что miRNA также участвуют в развитии инфаркта миокарда посредством регуляции экспрессии генов-мишеней данного заболевания. В данной научной работе представлены характеристики взаимодействий miRNA с mRNA кандидантных генов инфаркта миокарда. Выявлены 34, 51 и 36 генов-мишеней, имеющие сайты связывания miRNA в 5’UTR, CDS и 3’UTR, соответственно. Основываясь на критериях, выбранных в нашем исследовании, были определены кандидатные гены, имеющие свободную энергию взаимодействия с miRNA равной - 120 кДж/моль и выше в следующих ассоциациях: в 5’UTR - ID02142.3p-miR и *ALDH2*; ID00909.3p-miR и *ALOX5*; ID00216.3p-miR и *CD40*; ID01272.3p-miR и *DDAH2*; ID01774.5p-miR и *IL6R*; miR-6752-5p и *KLF4*; ID03332.3p-miR и *LAMA3*; ID02363.5p-miR и *NOS3*; ID02800.3p-miR и *OPA1*; ID01310.3p-miR и *PDE4D*; ID03397.3p-miR и *PTGS2*; ID01098.3p-miR и *SERPINE1*; ID01018.3p-miR и *SGPP1*; ID02430.3p-miR и *SHH*; ID01652.3p-miR и *THBS1*; ID01770.3p-miR и *ZNF202*; в CDS - ID00457.3p-miR и *APOA1*; ID00425.5p-miR и *BTN2A1*; ID01632.5p-miR и *CCL5*; ID02899.3p-miR и *CDKN2B*; miR-6894-5p и *CYP1A2*; ID01806.3p-miR и *IL6R*; ID01403.5p-miR и *PLAUR*; ID02950.3p-miR и *SEMA3F*; ID03332.3p-miR и *SGPP1*; ID02062.3p-miR и *SIRT6*; ID02050.3p-miR и *TNF*; ID01804.3p-miR и *XBP1*; ID00182.5p-miR и *ZNF202;* в 3'UTR - ID01293.5p-miR и *SMTN*; ID01882.5p-miR и *TNNI3.* Выявленные ассоциации можно использовать в качестве генетических маркеров при диагностике инфаркта миокарда.

Ключевые слова: инфаркт миокарда, гены-мишени, сайт связывания, miRNA, mRNA.

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