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БАЯНДАМАЛАРЫ

ДОКЛАДЫ

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РЕСПУБЛИКИ КАЗАХСТАН

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CHARACTERISTICS OF miRNA INTERACTION WITH mRNA OF ISCHEMIC HEART DISEASE CANDIDATE GENES

Abstract. Ischemic heart disease (IHD) is the most serious cardiovascular disease and one of the leading causes of death worldwide. An important role in the pathophysiology of IHD play such processes as the processes of inflammation and immune response, metabolism of homocysteine and folate, development processes of endothelial dysfunction and oxidative stress and homeostasis system. Accordingly, the identified genes that are directly involved in these processes. In addition, miRNA (mRNA-inhibiting RNA) may affect the expression of these candidate genes. Using bioinformatics methods, the most efficient associations of miRNA and target genes were established. This research presents the characteristics of miRNA interactions with mRNA of candidate IHD genes. Candidate genes were identified that had a free energy of interaction with miRNA equal to -120 kJ / mole and higher in the following interactions: in 5'UTR - *ALDH2* and ID02142.3p-miR; *CELSR2* and ID00457.3p-miR; *DDAH2* and ID01272.3p-miR; *DNMT1* and ID02052.5p-miR; *DOCK7* and ID00061.3p-miR; *EGFR* and ID02457.3p-miR; *FOLH1* and ID01428.3p-miR; *IL6R* and miR-6089; *NOS3* and ID02363.5p-miR; *NPC1* and ID00551.3p-miR; *PPP1R17* and ID01693.5p-miR; *PRKCH* and ID00520.5p-miR; *SERPINE1* and ID01098.3p-miR; in CDS - *ABCG8* and ID03064.3p-miR; *ADORA2A* and ID02697.3p-miR*; APOA1* and ID00457.3p-miR*; CDKN2B* and ID02899.3p-miR; *IL6R* and ID01806.3p-miR; *TIMP2* and ID00098.5p-miR; *TNF* and ID02050.3p-miR*; TRIB1* and ID03208.5p-miR; *VWF* and ID01238.5p-miR. Associations were also revealed in the 3'UTR region with an interaction free energy of -115 kJ/mole and higher: *AGTR2* and ID01213.5p-miR; *APLNR* and ID00616.5p-miR; *CXCL12* and ID00483.3p-miR; *FADS2* and miR-1224-3p; *FCGR2A* and miR-1273g-3p; *GCKR* and ID02928.3p-miR; *IL6R* and ID00913.5p-miR; *KCNJ11* and ID03288.5p-miR; *PPP1R3B* and ID00913.5p-miR; *TFPI* and miR-1273g-3p; *TIMP2* and ID01941.5p-miR. The results obtained could be used as molecular genetic markers of IHD for the diagnosis of this disease.

Key words: ischemic heart disease, associations, miRNA, mRNA, candidate genes.

Introduction. Ischemic heart disease (IHD) is one of the leading causes of disability and premature death worldwide. IHD is a consequence of atherosclerosis of the coronary arteries, which feed the myocardium and supply it with oxygen. According to the World Health Organization, the main forms of IHD include angina pectoris, myocardial infarction, cardiosclerosis, cardiac arrhythmias, and conduction disorders, heart failure, and sudden coronary death. IHD is often accompanied by hypertension, type 2 diabetes, hypercholesterolemia since these diseases have common risk factors and pathogenetic mechanisms [1]. IHD, like other cardiovascular diseases (CVD), is a multifactorial disease. In addition to environmental and epidemiological factors, there are also genetic risk factors for this disease. [2,3]. Genome Wide Association Studies (GWAS) are currently identifying genetic factors that contribute to the risk of cardiovascular disease. [4]. Within the framework of such studies, the effect of miRNA on the risk of occurrence and course of coronary heart disease is also being studied.

Recent studies have shown that miRNAs play an important role in biological processes such as cell proliferation or differentiation and apoptosis. miRNAs are associated with important diseases, including

cancer and CVD [5-8]. The miRNAs themselves are small non-coding ribonucleic acids that negatively regulate gene expression at the post-transcriptional level, inhibiting mRNA translation, or promoting mRNA degradation [9]. It has been determined that about a third of genes are regulated by miRNA. Each miRNA can target multiple mRNAs, and each mRNA can target different miRNAs [10,11].

Studies investigating the effect of various miRNAs on CVD risk. For example, miRNAs have been identified that are involved in the formation of atherosclerotic plaques, which leads, respectively, to the development of IHD. For example, miR-21 is involved in the modifications of endothelial cells, which leads to disruption of the functionality of these cells. [12]. MiR-155, miR-124, and miR-146 are involved in the activation of monocytes and maturation of macrophages [13-15]; miR-122, miR-33 in increasing the level of low-density lipoproteins [16,17]; miR-126, miR-92a, and miR-27 in the formation of the fibrous operculum [18-20].

It has been shown that changes in the expression or functioning of some of miRNAs are associated with the development of many human diseases, including CVD, oncological, infectious, neurodegenerative, and autoimmune diseases [21–25]. Therefore, studies of miRNAs and their interactions with mRNAs could help to identify highly sensitive genetic markers of IHD and be used in the diagnosis of the disease.

Materials and methods. In this research, the nucleotide sequences of the candidate IHD genes were obtained from GenBank (http://www.ncbi.nlm.nih.gov). Nucleotide sequences of 2565 miRNAs were downloaded from the miRBase (http://mirbase.org, Release 22.1) and 3707 miRNAs were obtained from the article by Londin E. et al. [26]. The search for miRNA target genes was performed using the MirTarget program [27]. This program defines the following binding characteristics: the beginning of the miRNA binding site (BS) in the mRNA; miRNA BS positions (3'UTR, 5'UTR, CDS); free energy of interaction (ΔG, kJ / mol); and schemes of nucleotide interactions between miRNA and mRNA. The ratio ΔG / ΔGm (%) was determined for each interaction where ΔGm equals the binding of miRNA free energy to its complete complementary nucleotide sequence.

Results and discussion. The search for miRNA binding sites was carried out in the 5'UTR, CDS, and 3'UTR regions of the mRNA of candidate IHD genes to reveal the features of miRNA interaction in these mRNA regions. To select the most effective associations of miRNA and candidate genes, the following criteria and characteristics of the interaction of miRNA with mRNA 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 probability of participation of a candidate gene in the study of diseases based on its functions.

Table 1 shows the binding characteristics of miRNA and mRNA of candidate IHD genes in the 5'UTR region. Considering the above criteria, miRNAs interacting with mRNAs with a free energy (ΔG) equal to -120 kJ/mole and higher can be recommended as associations: *ALDH2* and ID02142.3p-miR; *CELSR2* and ID00457.3p-miR; *DDAH2* and ID01272.3p-miR; *DNMT1* and ID02052.5p-miR; *DOCK7* and ID00061.3p-miR; *EGFR* and ID02457.3p-miR; *FOLH1* and ID01428.3p-miR; *IL6R* and miR-6089; *NOS3* and ID02363.5p-miR*; NPC1* and ID00551.3p-miR; *PPP1R17* and ID01693.5p-miR; *PRKCH* and ID00520.5p-miR; *SERPINE1* and ID01098.3p-miR. Relatively, in comparison with the rest of the mRNA, CDS, and 3´UTR regions, in this region, a greater number of interactions with the maximum indices of free energy (ΔG) were revealed.

Interactions characterized by the value of ΔG / ΔGm equal to 95% and higher were established, as this indicates an almost complete complementarity of the interaction between miRNA and mRNA. Among them: *EGFR* and ID02457.3p-miR; *HMOX1* and ID01152.3p-miR.

Table 1 – Characteristics of miRNA interactions in the 5'UTR of the mRNAs of IHD candidate genes

Gene	miRNA	Start of site, nt	ΔG, kJ/mole	ΔG/ΔGm, %	Length, nt
ABCA1	miR-4435	331	-110	91	22
ABCG8	ID00122.5p-miR	55	-110	90	22
ADORA2A	ID00254.3p-miR	188	-110	90	22
AGT	miR-3126-5p	326	-108	91	22
ALDH2	ID02142.3p-miR	8	-123	92	21
ANKS1A	ID00128.3p-miR	136	-113	91	22
BRCA2	ID01563.5p-miR	25	-115	93	21
CDK18	miR-6124	63	-102	92	20
CELSR2	ID00457.3p-miR	15	-123	91	22
CNR1	miR-4743-3p	374	-100	92	21
CX3CR1	ID01330.3p-miR	164	-119	89	23
CYP2C8	miR-4709-5p	49	-104	91	22
DDAH2	ID01272.3p-miR	185	-121	88	24
DNMT1	ID02052.5p-miR	137	-134	90	24
DOCK7	ID00061.3p-miR	3	-127	92	22
EDNRA	miR-4496	384	-108	91	22
EGFR	ID02457.3p-miR	89	-132	95	22
EPHX2	ID03324.3p-miR	72	-115	90	22
ESR2	ID01280.3p-miR	41	-117	92	22
F5	ID00323.3p-miR	7	-110	90	22
FOLH1	ID01428.3p-miR	292	-132	91	24
HMOX1	ID01152.3p-miR	75	-113	95	20
HTR2A	ID00038.3p-miR	600	-104	91	21
HTR2C	ID02500.3p-miR	424	-119	90	22
ICAM1	ID00195.3p-miR	106	-117	89	23
IL6R	miR-6089	345	-138	93	24
IL15	ID01713.5p-miR	63	-115	92	20
KCNK5	ID01038.5p-miR	161	-108	94	20
NOS1	ID02207.5p-miR	594	-113	91	21
NOS3	ID02363.5p-miR	200	-123	88	24
NPC1	ID00551.3p-miR	34	-121	88	24
PLA2G7	miR-4722-5p	40	-119	90	23
PON2	ID02200.3p-miR	8	-119	90	22
PPP1R17	ID01693.5p-miR	187	-121	89	23
PRKCH	ID00520.5p-miR	279	-121	90	22
SELP	ID03109.5p-miR	49	-106	94	21
SERPINE1	ID01098.3p-miR	30	-123	88	24
TCF21	miR-7110-5p	252	-108	91	21
TRIB1	miR-4669	359	-113	91	22

Most of the single interactions were observed in the CDS region of the mRNAs of IHD target genes, which are presented in table 2. The following interactions with free energy (ΔG) equal to -120 kJ / mole and higher were noted: *ABCG8* and ID03064.3p-miR; *ADORA2A* and ID02697.3p-miR; *APOA1* and ID00457.3p-miR; *CDKN2B* and ID02899.3p-miR; *IL6R* and ID01806.3p-miR; *TIMP2* and ID00098.5p-miR; *TNF* and ID02050.3p-miR; *TRIB1* and ID03208.5p-miR; *VWF* and ID01238.5p-miR. In this region of mRNA of IHD candidate genes, the maximum complementarity between miRNA ID00524.3p-miR and mRNA of *F2* gene is observed, equal to 100%. In addition, mRNA and miRNA associations with a lower ΔG/ΔGm value equal to 95% were noted: *IL1RL1* and miR-4275; *KIF6* and miR-6852-3p; *MADD* and ID02815.3p-miR.

Table 2 – Characteristics of miRNA interactions in the CDS of the mRNAs of IHD candidate genes

Gene	miRNA	Start of site, nt	ΔG, kJ/mole	ΔG/ΔGm, %	Length, nt
ABCB1	miR-6751-3p	2063	-106	93	21
ABCC6	miR-6851-3p	705	-108	93	21
ABCG8	ID03064.3p-miR	1727	-136	89	24
ADORA2A	ID02697.3p-miR	1360	-121	90	23
AGTR1	ID02795.5p-miR	102	-117	92	22
ALDH2	miR-4687-3p	170	-110	91	21
APOA1	ID00457.3p-miR	841	-123	91	22
APOC2	miR-623	173	-115	90	23
CCDC92	miR-129-5p	974	-106	93	21
CDKN2B	ID02899.3p-miR	412	-132	89	24
CSMD1	miR-6858-5p	8979	-117	92	22
CXCR4	miR-3119	736	-93	92	20
CYBA	ID01251.3p-miR	578	-119	92	22
CYP3A5	miR-6886-3p	582	-106	91	21
DAB2IP	miR-3960	2748	-115	92	20
ENPP1	ID03416.5p-miR	32	-119	93	20
F2	ID00524.3p-miR	532	-119	100	21
F7	ID00290.5p-miR	215	-119	89	23
FADS2	ID01205.5p-miR	1447	-110	90	22
FBXW7	ID02514.3p-miR	1243	-108	93	22
FOLH1	miR-6809-3p	2529	-102	91	21
GCKR	ID00306.5p-miR	820	-119	92	22
GP1BA	miR-4632-3p	1812	-113	90	22
GSTM1	ID01955.3p-miR	462	-108	89	23
HMGCR	miR-3920	914	-98	90	22
HP	ID00253.5p-miR	1178	-98	92	20
IL1RL1	miR-4275	936	-81	95	17
IL6R	ID01806.3p-miR	483	-125	89	23
ITGB3	ID02639.5p-miR	52	-115	89	23
ITIH4	ID00354.3p-miR	1682	-100	92	20
KCNJ11	miR-3676-3p	1430	-102	92	20
KIF6	miR-6852-3p	1230	-87	95	17
LTA	miR-6831-5p	581	-117	90	24
MADD	ID02815.3p-miR	516	-115	95	21
MEF2A	ID02266.5p-miR	1831	-104	94	20
MEFV	miR-6813-5p	1132	-115	90	23
MMP2	miR-1285-5p	1375	-104	92	21
MMP3	ID00314.3p-miR	132	-119	93	23
MTRR	ID00723.5p-miR	1751	-108	89	23
NLRP3	ID00662.3p-miR	3638	-102	92	20
NOS1	miR-512-3p	930	-106	91	22
NOS3	miR-6501-3p	982	-115	90	23
NPC1	miR-4459	1031	-119	93	22
PCSK9	ID01810.3p-miR	1052	-115	89	23
PON1	miR-5003-3p	330	-100	92	21
PPP1R3B	miR-4740-5p	903	-110	90	22
SELE	ID03022.3p-miR	829	-100	90	22
TFR2	miR-5571-3p	1181	-100	94	19
TGFB1	miR-6742-5p	2046	-110	90	22
THRA	ID01676.3p-miR	1931	-108	91	22
TIMP2	ID00098.5p-miR	901	-127	90	23
TNF	ID02050.3p-miR	230	-121	92	23
TRIB1	ID03208.5p-miR	756	-127	90	24

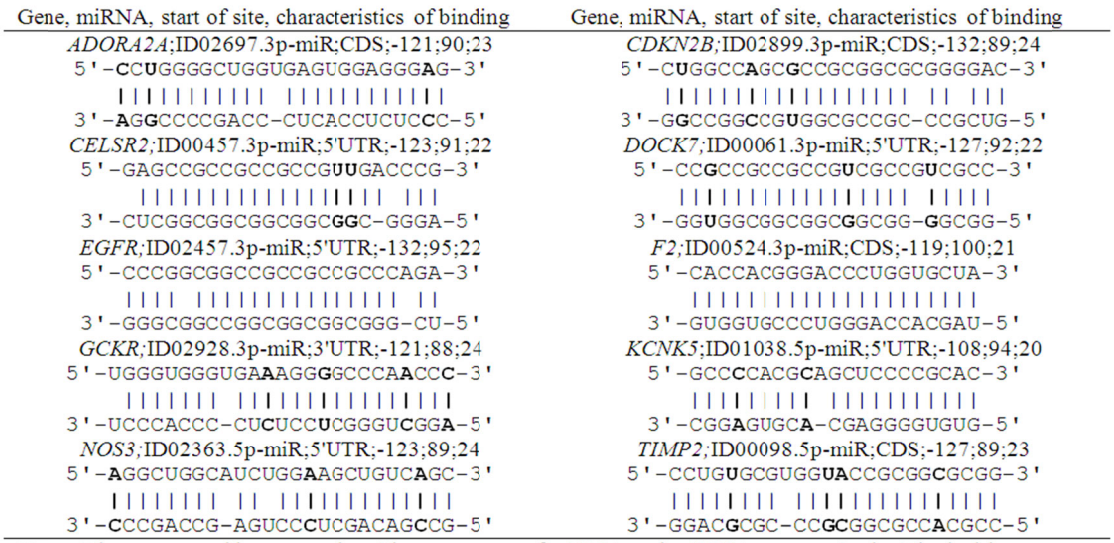
Table 3 shows the interactions of various miRNA and mRNA genes of candidate IHD genes in the 3'UTR region. Single binding sites in the 3'UTR region, where the free energy of interaction ΔG, kJ / mole from -115 and more: *AGTR2* and ID01213.5p-miR; *APLNR* and ID00616.5p-miR; *CXCL12* and ID00483.3p-miR; *FADS2* and miR-1224-3p; *FCGR2A* and miR-1273g-3p; *GCKR* and ID02928.3p-miR;

IL6R and ID00913.5p-miR; *KCNJ11* and ID03288.5p-miR; *PPP1R3B* and ID00913.5p-miR; *TFPI* and miR-1273g-3p; *TIMP2* and ID01941.5p-miR. The results show that the mean free energy of hybridization of binding sites located in the 5'UTR and CDS regions is higher compared to the miRNA binding sites in the 3'UTR. The high value of ΔG of binding sites in CDS and 5'UTR of mRNA may be associated with the high content of guanine and cytosine in the binding sites. Also, interactions of miRNA and mRNA with the value of ΔG / ΔGm from 95% and higher were noted: *FADS2* and miR-1224-3p; *FCGR2A* and miR-1273g-3p; *HFE* and miR-5095; *THSD7A* and miR-574-5p.

Table 3 – Characteristics of miRNA interactions in the 3'UTR of the mRNAs of IHD candidate genes

Gene	miRNA	Start of site, nt	ΔG, kJ/mole	ΔG/ΔGm, %	Length, nt
ACE	miR-4516	4114	-96	96	17
ADIPOQ	ID01360.3p-miR	1651	-104	91	21
AGTR2	ID01213.5p-miR	2307	-121	90	23
APLNR	ID00616.5p-miR	1981	-119	89	24
CDK18	miR-4487	2501	-100	94	19
CHI3L1	ID01707.5p-miR	1497	-110	93	22
CTCF	ID02282.5p-miR	3865	-108	91	22
CXCL12	ID00483.3p-miR	932	-119	90	23
EBF1	miR-10a-3p	4920	-100	90	22
EDN1	miR-548az-5p	1222	-100	90	22
F7	miR-1909-5p	2993	-110	91	21
FADS2	miR-1224-3p	2762	-115	96	21
FADS3	ID00022.3p-miR	1515	-108	91	21
FCGR2A	miR-1273g-3p	1509	-115	98	21
FGF2	miR-1285-5p	3097	-102	91	21
FTO	miR-1273g-3p	3671	-106	91	21
GCKR	ID02928.3p-miR	1956	-121	88	24
GHR	ID02880.3p-miR	4139	-108	91	22
HFE	miR-5095	2195	-110	95	21
HMOX1	miR-3155a	1227	-106	91	21
HTR2C	miR-3942-3p	2281	-91	91	21
IGFBP3	ID01696.3p-miR	1753	-108	91	21
IL10	ID01332.3p-miR	1200	-110	90	22
IL6R	ID00913.5p-miR	3063	-115	90	23
KCNJ11	ID03288.5p-miR	2844	-115	89	23
KIF6	ID00666.3p-miR	3234	-113	91	22
LTA	ID01127.3p-miR	1258	-98	92	21
LRP1	miR-3926	14288	-102	91	21
MEF2A	miR-1277-5p	2196	-98	90	24
PCSK9	miR-6877-3p	2468	-110	91	21
PPP1R3B	ID00913.5p-miR	2150	-117	92	23
NPC1L1	ID01202.5p-miR	4192	-106	91	22
NQO1	ID01404.5p-miR	1719	-110	90	23
SELPLG	ID02248.5p-miR	1818	-106	94	20
TFPI	miR-1273g-3p	2703	-115	98	21
TIMP2	ID01941.5p-miR	1427	-117	89	24
THSD7A	miR-574-5p	7941	-115	95	23
VKORC1	miR-3679-5p	830	-115	92	23

Figure 1 shows examples of significant associations of some miRNAs with mRNA target genes, which illustrate hydrogen bonds between interacting nucleotides. With complete complementarity and high free energy of interaction, the likelihood of miRNA interaction with mRNA molecules increases.



Note: The upper and lower nucleotide sequences of mRNA and miRNA, respectively. The bold type indicates the nucleotide of non-canonical pairs U-G, A-C.

Figure 1 – Schemes of significant miRNAs interactions with mRNAs of IHD candidate genes

The genes studied by us involved in the development of IHD are combined into groups in accordance with the processes in which the proteins encoded by them are involved. For example, the genes whose products are involved in the cascade of reactions of inflammation and immune response are genes for interleukins *IL-1A*, *IL-1B*, *IL-10*, *IL-6*, *IL-15* of their receptors - *IL4R*, *IL6R* [28]. The genes of the hemostasis system *F7, F2, FGB* are also risk factors for venous thrombosis and the risk of coronary artery disease [29,30]. Genes for the enzymes of homocysteine and folate metabolism — *MTHFR*, *MTRR*, and *MTR* genes significantly affect the risk of IHD [31]. Genes whose dysfunctions can contribute to the development of endothelial dysfunction and oxidative stress — *NOS3* gene leads to endogenous NO deficiency and is one of the key links in the pathogenesis of IHD [32].

Conclusion. The association of a large number of genes with ischemic heart disease reflects the great complexity of this disease. An important point is the establishment of a causal relationship between one or another genetic marker and the development of coronary artery disease. If the miRNA biomarker plays a role in the development of IHD, knowledge of the features of the interactions of candidate genes with various miRNAs that can affect the level of expression and functioning of a particular gene will make it possible to establish promising diagnostic and therapeutic genetic markers of IHD.

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ИШЕМИЯ ЖҮРЕК АУРУЫ КАНДИДАТТЫҚ ГЕНДЕРІНІҢ mRNA-МЕН miRNA ӨЗАРА ӘРЕКЕТТЕСУ СИПАТТАМАЛАРЫ

Аннотация. Ишемия жүрек ауруы (ИЖА) жүрек қан тамырлары ауруының қауіптісі әрі әлем бойынша өлімнің негізгі себебі болып саналады. ИЖА-ның патофизиологиясында қабыну және иммундық жауап, гомоцистеин мен фолий метаболизмі, эндотелий дисфункциясы мен тотығу стресінің дамуы және гомеостаз жүйесі сияқты үдерістер маңызды рөл атқарады. Тиісінше, аталған үдерістерге тікелей қатысатын гендер анықталды. Сонымен қатар, кандидат-гендер экспрессиясына барлық негізгі биологиялық үдерістерде, соның

ішінде жүрек-қантамыр жүйесінің түрлі патологиясында маңызды рөл атқаратын miRNA (mRNA-inhibiting RNA) деп аталатын тиімді реттеуші әсер етуі мүмкін. Биоинформатика әдістерін қолдану арқылы miRNA мен нысана гендердің ең тиімді ассоциациясы құрылды. Жұмыста кандидат ИЖА гендерінің mRNA-мен miRNA өзара әрекеттесуінің сипаттамалары келтірілді. Зерттеуде таңдалған критерийлерге сүйене отырып, келесі өзара әрекеттесу жағдайында miRNA-мен -120 кДж / мольге тең және одан жоғары өзара әрекеттесудің бос энергиясы бар келесідей кандидат гендер анықталды: 5'UTR - *ALDH2* және ID02142.3p-miR; *CELSR2* және ID00457.3p-miR; *DDAH2* және ID01272.3p-miR; *DNMT1* және ID02052.5p-miR; *DOCK7* және ID00061.3p-miR; *EGFR* және ID02457.3p-miR; *FOLH1* және ID01428.3p-miR; *IL6R* және miR-6089; *NOS3* және ID02363.5p-miR; *NPC1* және ID00551.3p-miR; *PPP1R17* және ID01693.5p-miR; *PRKCH* және ID00520.5p-miR; *SERPINE1* және ID01098.3p-miR; CDS - *ABCG8* және ID03064.3p-miR; *ADORA2A* және ID02697.3p-miR*; APOA1* және ID00457.3p-miR*; CDKN2B* және ID02899.3p-miR; *IL6R* және ID01806.3p-miR; *TIMP2* және ID00098.5p-miR; *TNF* және ID02050.3p-miR*; TRIB1* және ID03208.5p-miR; *VWF* және ID01238.5p-miR. Алынған нәтижелер ИЖА ауруын диагностикалау үшін молекулалық-генетикалық маркерлер ретінде қолданыла алады.

Түйін сөздер: ишемиялық жүректің аурулары, ассоциациялар, miRNA, mRNA, кандидат гендер.

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ХАРАКТЕРИСТИКИ ВЗАИМОДЕЙСТВИЙ miRNA С mRNA КАНДИДАТНЫХ ГЕНОВ ИШЕМИЧЕСКОЙ БОЛЕЗНИ СЕРДЦА

Аннотация. Ишемическая болезнь сердца (ИБС) является наиболее серьезным сердечно-сосудистым заболеванием и одной из ведущих причин смерти во всем мире. Важную роль в патофизиологии ИБС играют такие процессы, как процессы воспаления и иммунного ответа, метаболизма гомоцистеина и фолатов, процессы развития эндотелиальной дисфункции и оксидатного стресса и система гомеостаза. Соответственно, выявлены гены, которые непосредственно участвуют в данных процессах. Помимо этого, на экспрессию данных генов-кандидатов могут влиять эффективные регуляторы, так называемые miRNA (mRNA-inhibiting RNA), которые играют большую роль во всех ключевых биологических процессах, в том числе и при различных патологиях сердечно-сосудистой системы. С помощью биоинформатических методов были установлены наиболее эффективные ассоциации miRNA и генов-мишеней. В данной работе представлены характеристики взаимодействий miRNA с mRNA кандидантных генов ИБС. Основываясь на критериях, выбранных в нашем исследовании, были определены кандидатные гены, имеющие свободную энергию взаимодействия с miRNA равной -120 kJ/mole и выше в следующих взаимодействиях: 5'UTR - *ALDH2* и ID02142.3p-miR; *CELSR2* и ID00457.3p-miR; *DDAH2* и ID01272.3p-miR; *DNMT1* и ID02052.5p-miR; *DOCK7* и ID00061.3p-miR; *EGFR* и ID02457.3p-miR; *FOLH1* и ID01428.3p-miR; *IL6R* и miR-6089; *NOS3* и ID02363.5p-miR; *NPC1* и ID00551.3p-miR; *PPP1R17* и ID01693.5p-miR; *PRKCH* и ID00520.5p-miR; *SERPINE1* и ID01098.3p-miR; в CDS - *ABCG8* и ID03064.3p-miR; *ADORA2A* и ID02697.3p-miR*; APOA1* и ID00457.3p-miR*; CDKN2B* и ID02899.3p-miR; *IL6R* и ID01806.3p-miR; *TIMP2* и ID00098.5p-miR; *TNF* и ID02050.3p-miR*; TRIB1* и ID03208.5p-miR; *VWF* и ID01238.5p-miR. Были выявлены ассоциации в области 3'UTR с показателем свободной энергии взаимодействия равной -115 kJ/mole и выше: *AGTR2* и ID01213.5p-miR; *APLNR* и ID00616.5p-miR; *CXCL12* и ID00483.3p-miR; *FADS2* и miR-1224-3p; *FCGR2A* и miR-1273g-3p; *GCKR* и ID02928.3p-miR; *IL6R* и ID00913.5p-miR; *KCNJ11* и ID03288.5p-miR; *PPP1R3B* и ID00913.5p-miR; *TFPI* и miR-1273g-3p; *TIMP2* и ID01941.5p-miR. Полученные результаты могут быть использованы в качестве молекулярно-генетических маркеров ИБС для диагностики данного заболевания.

Ключевые слова: ишемическая болезнь сердца, ассоциации, miRNA, mRNA, кандидатные гены.

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