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In silico study of the interaction features of microRNAs obtained from the diet

To investigate the effect of diet on the expression of genes is a new direction that has every chance to influence the development of diseases. Due to this, exogenous diet derived miRNA can make a positive contribution to genes of mRNA, opening up new opportunities for the use of food mi-RNAs to maintain health and fight diseases. There is considerable interest in the use of circulating miRNAs derived from the diet as biomarkers, and the potential for the use of dietary-derived mammalian miRNAs may represent a powerful new therapeutic strategy for the treatment of diseases. According to this assessment, miRNAs play a beneficial role in the genesis of socially significant diseases such as obesity, diabetes, endocrine diseases. This article attempts to collect possible information to strengthen the theory of dietary miRNAs and its action. More precisely, the mechanisms of miRNAs and mRNA target genes that are associated with genes accountable for the appearance of endocrine diseases, the binding sites of miRNA and mRNA target genes have been revealed. A special mechanism in the progress in the diseases is played by a violation of the regulation of the expression of target genes, which makes it possible to detect the disease at early stage. The bioinformatics computational approach of binding genes and miRNA was performed using the *NewGeneralScanning* program. As a result of the databases of genes and miRNAs involved in diseases of the endocrine systems were composed. Genes and miRNA binding sites have been identified, the expression of which is disrupted in significant diseases of endocrinology.

Keywords: miRNA, mRNA, genes, dietary miRNA, endocrinology diseases, binding sites, markers, genetic expression.

Introduction

The meaning of uptake of food-derived active small RNAs (sRNAs) in recipient organisms may have significant mechanisms and play important role for our understanding of oral therapy and nutrition. Exosomal miRNA widely are presented in the animal and plant products, e.g., in biological liquids (synovial fluid, blood, saliva, urine) and the supernatant of cell cultures [1]. Changesor dys-regulation in miRNAs composition may influence anomalous expression of genes and proteins [2]. It has been acknowledged that miRNAs are furthermore contained in plants (vegetables, fruits) and animal products, also deficiency of same dietary origin of miRNAs cannot be remunerated for by internal synthesis [3]. miRNAs are engaged in the gastrointestinal tract and absorbed into the blood, transported to cells. The exogenous exosomes are released and pass into the circulation, which is so obsessed by altered organs [4]. It was being tested that dietary miRNAs engaged and penetrated by mammalians to the shape of exosomal to participate in life direction and engage in reactions to pathological causing in the organism, especially to cells to contribute the tumor-suppressive consequence of exosomal miRNAs derived from milk [5, 6]. Dietary bioactive pieces through miRNAs may influence and affect intensity of numerous genes.

Food miRNAs are RNA molecules with a length of less than 200 nucleotides, which are usually participated in the regulation of other cellular processes. In particular, miRNAs are involved in the post-transcriptional regulation of gene expression. This process is known as RNA interference [7]. After processing, miRNAs bind specific complementary sequences in messenger RNA transcripts and regulate gene expression by repressing translation and/or degradation of the target mRNA. The absorption of dietary miRNAs obtained from the diet considered that through an effect to the expression of genes. A gene expression processes the absorbing organism, was first found in *Caenorhabditis elegans* [8]. It was found that these RNAs suppress many genes after serving as a matrix for the formation of miRNAs, when dsRNAs were added to the diet or expressed in the bacteria that make up the diet of this organism. There is considerable interest in the use of circulating miRNAs derived from the diet as biomarkers [9], and the potential for the use of dietary-derived mammalian miRNAs may represent a powerful new therapeutic strategy for the treatment of diseases [10]. According to this assessment, miRNAs play a beneficial role in the genesis of socially signifi-

cant diseases such as obesity, diabetes, endocrine diseases. This article attempts to collect possible information to strengthen the theory of dietary miRNAs and its action in different kingdoms.

Diseases of the endocrine system are recognized one of the common diseases in our society. Endocrine diseases occur in the process of disruption of the normal hormonal background, which leads to the development of hyperfunction, hypofunction, and dysfunction of the endocrine organs. Current problems of modern endocrinology are the diagnosis and treatment of diseases such as diffuse toxic goiter, thyroiditis, autoimmune thyroiditis, and diabetes mellitus, diabetic nephropathy, acromegaly, prolactinoma, insulinoma, Itsenko-Cushing and Larone syndrome, hyperparathyroidism and obesity [11]. Hormonal disorders can be associated not only with the consequence of external influences, but also with hereditary factors of genes. Genes in the endocrine system are linked to the activation of function by encoding protein hormones, transport proteins, receptors, transcription factors and other molecules. For example, information about the mutation of the *RET* gene allows you to prevent the risk of developing cancer and start therapy using preventive methods [12]. And also the detection of a *PROP1* gene mutation eliminates the need for surgical treatment, and to continue treatment with STH drugs [13]. Recently, there has been a surge of interest in the role of small non-coding RNAs, and several reports focus on the effect of miRNAs on their target genes, which are related to nephropathy. Predictive in silico analysis of specific target genes showed that these mRNAs associated with the realization of metastatic potential are involved in several signaling pathways and regulate as yet unexplored genes that can be studied in the future. The appearance of diseases of the associated endocrine system is associated with a change in gene expression, which occurs in two directions, with increased expression, miRNAs can be used as oncogenes, and with reduced expression they can be a suppressor [14]. A decrease in the expression of some mRNAs results for the decrease in gene expression. Offering the information about gene anomalous makes it important to set up the case of mutation and diagnose diseases at an early stage, before heavily level of diseases [15]. As a result of the databases of genes and miRNAs involved in diseases of the endocrine systems were created. The connections of genes and miRNA, the expression of which is disrupted in significant diseases of endocrinology, have been revealed.

This observation confirms the important overview to research for needed biomarkers that in the future will characterize of the endocrinology diseases. The search for biomarkers is complicated by the biological specialty of each personal body, individual lifestyle, as well as taking various drugs and biological active nutritional supplement.

Experimental

Using bioinformatical methods, it was possible to classify a database of genes and microRNAs associated with the disease. In the *NCBI database (http://www.ncbi.nlm.nih.gov/)* and *DisGeNET (https://www.disgenet.org/)* a search for target genes was performed. Thanks to the publications that were published on the website *(http://www.ncbi.nlm.nih.gov/pubmed/)* the connection of the gene with the disease was found out. At the same time, it is necessary to identify a group of corresponding genes participated in the occurrence of pathology for the main types of endocrine diseases. The miRNA nucleotide sequences were downloaded from *miRBase (http://www.mirbase.org/).* In the process, it was found out that some genes and miRNAs are associated with several endocrine diseases. Bio informatic calculation of the binding characteristics of disease genes and miRNAs was performed using the New General Scanning program. The New General Scanning program determines the following miRNA-miRNA binding characteristics: (a) initiation of miRNA-mRNA binding from the first nucleotide of miRNA; (b) localization of miRNA CC in the 5'-untranslated region (5'UTR), coding domain sequence (CDS) and 3'-untranslated region (3'UTR) of mRNA; (c) nucleotide interaction patterns of miRNA and mRNA; (d) free energy of interaction between miRNA and mRNA (ΔG, kJ/mol); (e) ratio ΔG/ΔGm (%) (ΔGm equals free energy of binding of miRNA to its fully complementary nucleotide sequence). New General Scanning finds hydrogen bonds between adenine (A) and uracil (U), guanine (G) and cytosine (C). The free interaction energy (ΔG) of the G and C pair is 6.37 kJ/mol, the A and U pair is 4.25 kJ/mol, and the G and U, A and C pair is 2.12 kJ/mol [16, 17]. The number of hydrogen bonds in the interactions is G-C — 3; A-U — 2; G-U and A-C one each, respectively. The work revealed that certain genes and miRNAs from the diet showed an association with the above diseases.

Results and Discussion

We have created databases of genes and miRNAs participated to the occurrence of endocrine diseases. A total of 2009 genes and 6596 miRNAs responsible for the development of diseases of the endocrine sys-

tems were identified. A bioinformatic analysis of their interactions was carried out using the New General Scanning program, as a result of which 846 genes and 4689 miRNAs were selected. 142 genes have been identified, the expression of which is disrupted during the development of diseases of the endocrine system. These genes include: *ABCC8, ACE, ACSL1, ACVR1B, ADD1, ADGRL2, ADRB1, AHSG, AKT2, ANGPTL8, APC, APOA1, APOA5, AQP4, ARMC5, ATM, ATP1A1, ATP2A2, ATP2A3, ATRNL1, ATXN2L, BAX, BDNF, BMP2, BMP4, BSCL2, C3, CACNA1D, CARTPT, CCN2, CCND1, CD2AP, CD81, CDH23, CDK5R1, CDON, CISD2*, etc. (Table 1). And for the purpose to do research, there are used miRNAs which are obtained from *Arachis hypogaea, Bos taurus, Brassica oleracea, Capra hircus, Citrus sinensis, Citrus reticulata, Cucumus melo, Cucumus sativus, Equus caballus, Festuca arundinacea, Gallus, Helianthus annus, Helianthus argophyllus, Malus domestica, Oryza sativa, Ovis aries, Phaseolus vulgaris, Prunus persica, Solanum lycopersicum, Solanum tuberosum, Theobroma cacao, Triticulum aestivum, Vitis vinifera* and *Zea mays*.

Table 1

Genes responsible for development of endocrinology diseases

Diseases	Genes (PMID)	Diseases	Genes (PMID)
Acromegaly	ACE (28712073), BAX (16343104), CYP11B2 (17003099), E2F1 (31828584), EHMT1 (30948746), FTO (28913579), GIPR (28179449), IGF1R (25871641), INS (17652220), KL (30818110), MTHFR (26154858), NPPB (18037753), TNFRSF11B (29895074), TRH (24111551)	Goiter	ACVR1B (11069203), ATRNL1 (31347686), BAX (11351299), PIK3CA (31347686), CDH23 (15375577), CCND1 (11288983), DIO2 (17940114), FOXE1 (26267147), GLIS3 (29083325), GRPEL1 (23535966), IDH2 (11713206), KLLN (23724128), PTCH1 (31127647), PTGDS (16684826), SDHB (28780189), SPAG9 (19820019), SPP1 (29355489), TEK (11397875), TRH (3097618), WDR62 (30884127)
Alloxan diabetes	ACE (22191573), ACSL1 (9452481), ATP2A2 (16123366), ATP2A3 (16123366), BAX (23090186), HMOX1 (18375438), MAP3K5 (18342293), PDX1 (16123366), PPARA (14563825), PRKCA (12198386), SERPINE1 (21757225), SIRT1 (23792339), STS (24497646), TGFB1 (23090186), YWHAH (18342293)	Hyperaldosteronism	ADD1 (12107246), APC (18247045), ATP1A1 (23416519), ARMC5 (24905064), KCNJ5 (25322277), CACNA1D (26606680), CRH (24302625), KCNK9 (19878209), CYP11B2 (28388725), DRD2 (11864730), NR3C1 (29167167), OCRL (29567944), PPARA (29222092), SCNN1A (15475529), SERPINE1 (19625761), SFRP2 (24087794), TGFB1 (19625761)
Autoimmune thyroiditis	ADGRL2 (26301688), ATXN2L (26301688), C3 (31579073), CD81 (27860532), CXCL11 (31813786), GAS6 (31129420), INS (15928253), LPP (22922229), NKD1 (26301688), PTCH1 (16405407), PTPN22 (28948825), SMAD3 (25429627), SMN1 (27476469), SMN2 (27476469), TNFRSF25 (9064334)	Hyperinsulinism	ABCC8 (29493090), ACE (25154650), AKT2 (29484683), BSCL2 (30552349), CARTPT (30649980), DBH (27778639), EHMT1 (30938760), FANCC (22482891), FASN (31164724), HMOX1 (19171794), HNF1A (29493090), INS (30131390), NR3C1 (31199473), RPS6KB1 (15692808), SH3BP4 (30637573), SERPINE1 (10595645), SIRT1 (30506571), PDX1(31207434), PIK3CA(31467576), PIK3CD (31467576), PPARA (31547433),
Cushing Syndrome	ACE (16924268), ARMC5 (29370219), BDNF (28982330), CACNA1D (26743443), CDH23 (28413019), CRH (31041631), CTNNB1 (28911199), CYP11B2 (30769265), DRD2 (11864730), E2F1 (27935805), FASN (18782871), GIPR (28931750), IGF1R (11888846), IGF2 (11888846), KCNJ5 (17525485), LGR6 (12587537), NR3C1 (31613324)	Hyperparathyroidism	ACE (17142213), APC (26163537), CCND1 (21541686), FECH (30094461), HNF1A (23979948), KL (31135568), MAFK (15009006), MTHFR (23534584), SDHB (16688763), TNFRSF11B (20808842), USP6 (24742829), ZNRD2 (15009006)
Diabetes Mellitus	ABCC8 (17259403), ACE (22064603), ACSL1 (22308341), ACVR1B (11334431), ADD1 (15187197), ADRB1 (18378355), AHSG (20124547), AKT2 (15166380), ANGPTL8 (30191588), APC (15240665), APOA1 (14988232), APOA5 (19765959),	Hypothyroidism	ACE (31396276), ANGPTL8 (31380419), APC (27457726), APOA1 (27457726), APOA5 (15941710), AQP4 (30593981), ATM (29847168), ATP2A2 (26064889), ATXN2L (29666563), BDNF (30119135), PIK3CA (31495205), PIK3CD (31495205),

	AQP4 (19748503), ARMC5 (15988104), ATM (21315178), ATP2A2 (25270119), BAX (9576088), BDNF (27981512), BMP2 (29857981), BMP4 (26769046), BSCL2 (16435205), C3 (29029276), CARTPT (30649980), CCN2 (12446618), CCND1 (30462152), CD2AP (15149332), CDH23 (28245897), CISD2 (29237418), CRH (30280757), CTNNB1 (29135090), CXCL11 (28753646), CYP11B2 (27992114) DBH (29225702), DIO2 (29641285), E2F1 (29526568), EHMT1 (31725337), EIF2S3 (28055140), ELN (31096818), ENPEP (29156994), ERBB3 (30927244), FASN (31202106), FGFR1 (31082455), FN1 (29960272), FOS (26599598), FTO (30933732), FZD5 (31726413), GAS6 (30508521), GATA3 (28765956), GIPR (30910378), GLIS3 (31340201), HAMP (31296086), HFE (30657865), HHIP (31794697), HMOX1 (31332605), HNF1A (31215021), ICA1 (11029035), IGF1R (31847392), IGF2 (30536889), IGF2BP2 (25661373), IGFBP5 (30684263), INS (29890547), KCNJ5 (11544614), KL (31185930), KRAS (30443000), LDLR (30831097), LGR6 (30030074), MAFA (23975026), MAP3K5 (29627323), MTHFR (30675189), NEFL (31138085), NOG (29943307), NPPB (31567942), PIK3CA (31539141), PIK3CD (31317389) PON1 (31597668), PPARA (31029826), PRKCA (31743046), PTCH1 (31726413), PTF1A (26184423), PTGDS (20136655), PTPN22 (31732921), RCAN1 (30583978), RPS6KB1 (29496905), SERPINE1 (28321652), SIRT1 (30599900), SLC25A4 (28223503), SMAD3 (31071302), SPP1 (30268840), STAT3 (31848914), STS (28040286), TEK (31102457), TGFB1 (31461798), THBS2 (31391172), TNFRSF11B (30855435), ZFHX3 (27790247)		PPARA (29720336), CDK5R1 (22987596), PTPN22 (27182965), CRH (30508752), CTNNB1 (28191619), DIO2 (30508752), SIRT1 (30736780), EHMT1 (28870812), ELN (30595370), ENPP1 (15811553), FASN (30272292), STAT3 (30027933), FGFR1 (30595370), TGFB1 (18190611), FOXE1 (28727628), TRH (30590076), HAMP (31700042), ZIC2 (28870812)
		Insulinoma	ABCC8 (15613469), CACNA1D (8529524), CCND1 (29225069), CORO1A (26756113), CRHR1 (21106875), CTNNB1 (19427668), EHMT1 (31731177), HAMP (28179377), IGF2 (27667266), INS (31249641), KL (28993191), PDX1 (22114719), SMAD3 (22275377), STAT3 (11024034)
		Parathyroid Adenoma	CCND1 (23660642), E2F1 (31535356), ENPEP (31751311), FZD5 (22576020), IDH2 (27038812), GLIS3 (30403657), KL (18682507), MAFK (15009006), SFRP1 (27071708), SH3BP4 (30347604), SMAD3 (12161532), TBC1D9 (17299072), ZNRD2 (27038812)
Diabetic Nephropathy	ABCC8 (24357461), ACE (28177196), ADD1 (15187197), APOA1 (28478047), ATP2A2 (28761152), BDNF (20557422), BMP4 (30158674), C3 (31798904), CCN2 (30720184), CTNNB1 (29572435), E2F1 (23902294), EHMT1 (31373167), FN1 (29568954), GAS6 (28513288), HHIP (31794697), HNF1A (28502589), IGF1R (27082896), IGF2 (31182468), INS (31737684), MAP3K5 (31154867), MTHFR (23822721), PIK3CA (30899370), PIK3CD (22056625), PPARA (31585912), PTGDS (29253627), SMAD3 (31734275), STAT3 (29291386)	Prediabetes syndrome	AHSG (30515292), ANGPTL8 (26910534), BDNF (27062899), BMP4 (29943307), CRHR1 (29948652), EHMT1 (29082261), FTO (26334876), HNF1A (26240958), HAMP (28841871), HHIP (31590446), IGF2 (29939900), IGF2BP2 (25755232), INS (28473613), INTS3 (30307821), NOG (29943307), SERPINE1 (31690939), SPP1 (29151224), TNFRSF11B (29151224)
Endemic Cretinism	DIO2 (15911145), FOXE1 (23079472), TRH (782770)	Prolactinoma	BMP4 (22366961), CCND1 (24373949), CDH23 (28413019), DRD2 (22127489), E2F1 (16766265), ERBB3 (19401448), FGFR1 (22801565), FOS (3398845), LIFR (12574225), PIK3CA (29726995), PIK3CD (29726995), PPARA (30021235), SDHB (26259135), SMAD3 (30946881), TGFB1 (30946881), TNFRSF11B (29895074), ZNRD2 (29230669)

miR-23b has recently been established to be associated with diseases, such as diabetes mellitus, prediabetes syndrome, gestational diabetes, hypothyroidism, that reduced the inhibition of gene expression [18]. miR-23b was derived from animal products *Equus caballus, Ovis aries.* Inflammatory regulation factor-associated miRNAs in animal models and milk-derived miR-12030, miR-9007, miR-1582, miR-1648-5p, miR-1637, miR-2127, miR-11976, miR-7475-5p, miR-2885 have been shown a higher score occurrence of diseases.

Interaction analysis showed that miR-1281 has binding sites with 9 genes: *ATM, BMP4, CTNNB1, IGF2BP2, KCNK9, KLLN, SIRT1, SMAD3, ZFHX3*. In this case, binding occurs in all cases in 5'UTR. The binding energy values vary in the range from -85 to -93kJ/mole. Changes in the expression of these genes, in turn, are associated with the occurrence in the following diseases of the endocrine system: diabetes mellitus, hypothyroidism, prolactinoma, diabetic nephropathy, Cushing's syndrome, insulinoma, prediabetic syndrome, hyperaldosteronism, alloxan diabetes, hyperinsulinism, autoimmune thyroiditis, parathyroid adenoma, etc [19]. In the gene of mRNA, *CTNNB1* gene has a connection with diabetes mellitus, in addition, there is a connection with diseases such as Cushing's syndrome, diabetic nephropathy, hypothyroidism, insulinoma. miR1281 has been found to promote differentiation of *Bos taurus* animal products.

In turn, miR-7475-5p has binding sites with 7 genes: *ACVR1B, KCNK9, MAFK, NKD1, PPARA, YWHAH, ZFHX3.* In this case, binding occurs in all cases in 5'UTR. The binding energy values vary in the range from -110 to — 115 kJ/mole. In our result, it was shown that miR-7475-5p derived from *Gallus* has a high score. Changes in the expression of these genes, in turn, are associated with the causing of the following diseases of the endocrine system: diabetes mellitus, hyperaldosteronism, parathyroid adenoma, hyperparathyroidism, autoimmune thyroiditis, alloxan diabetes, diabetic nephropathy, diabetes mellitus during pregnancy, prolactinoma, hyperinsulinism, hypothyroidism, etc. It was noted that miR-9007 which is presented in *Equus caballus*, in turn, binds only to three genes: *ADRB1, CXCL11*, and *INS*. The binding sites are located in the 5'UTR sections, respectively. The interaction energy had values of -83kJ/mole for the *ADRB1* genes, — 84 kJ/mole for the *CXCL11* gene, and -82 kJ/mole for the *INS* gene. The genes *ADRB1*, *CXCL11* are associated with diabetes mellitus. The *INS* gene is associated with acromegaly, autoimmune thyroiditis, diabetes mellitus, prediabetes syndrome, diabeticnephropathy, gestational diabetes, hyperinsulinism, insulinoma. miR-2885 (derived from *Bos taurus*) binds to five genes: *AKT2, BMP2, CDK5R1, HMOX1, NOG* [20]. In addition to the *CDK5R1* gene, binding sites are located in the 5'UTR regions [21, 22]. And the interaction energy ranges from -106 to -129kJ/mole.

Also with three genes: *NR3C1, DRD2* and *ZIC2* forms miR-3141 interactions. Binding sites are located in the 5'UTR sites. The energy indices of their interaction are in the range of -93 (-99) kJ/mole. The *NR3C1* gene is associated with diabetes mellitus, hyperaldosteronism, hyperinsulinism, Cushing's syndrome. The *DRD2* gene encodes the dopamine receptor, a protein located on the surface of neurons, coupled with G proteins and inhibiting adenylate cyclase under the influence of dopamine [23]. The *ANKK1* gene is located in the regulatory zone of the *DRD2* gene and regulates its expression.

Only with two genes *ACL1* and *CCND1* forms miR-1552-3p interactions. The binding sites are located in the 5'UTR regions, and the interaction energy varies in the following values: -99-(-101) kJ/mole. The *CCND1* gene has a connection with diabetes mellitus, parathyroid adenoma, prolactinoma, hyperparathyroidism, insulinoma. The binding characteristics of miRNA and mRNA their target genes responsible for the development of oncological and borderline gastrointestinal diseases are presented in Table 1 and Figures 1, 2. And more detailed information about miRNAs is presented in Table 2.

Figure 1. Interaction mechanism of miRNAs and mRNAs of the genes participated in development of endocrinology system diseases

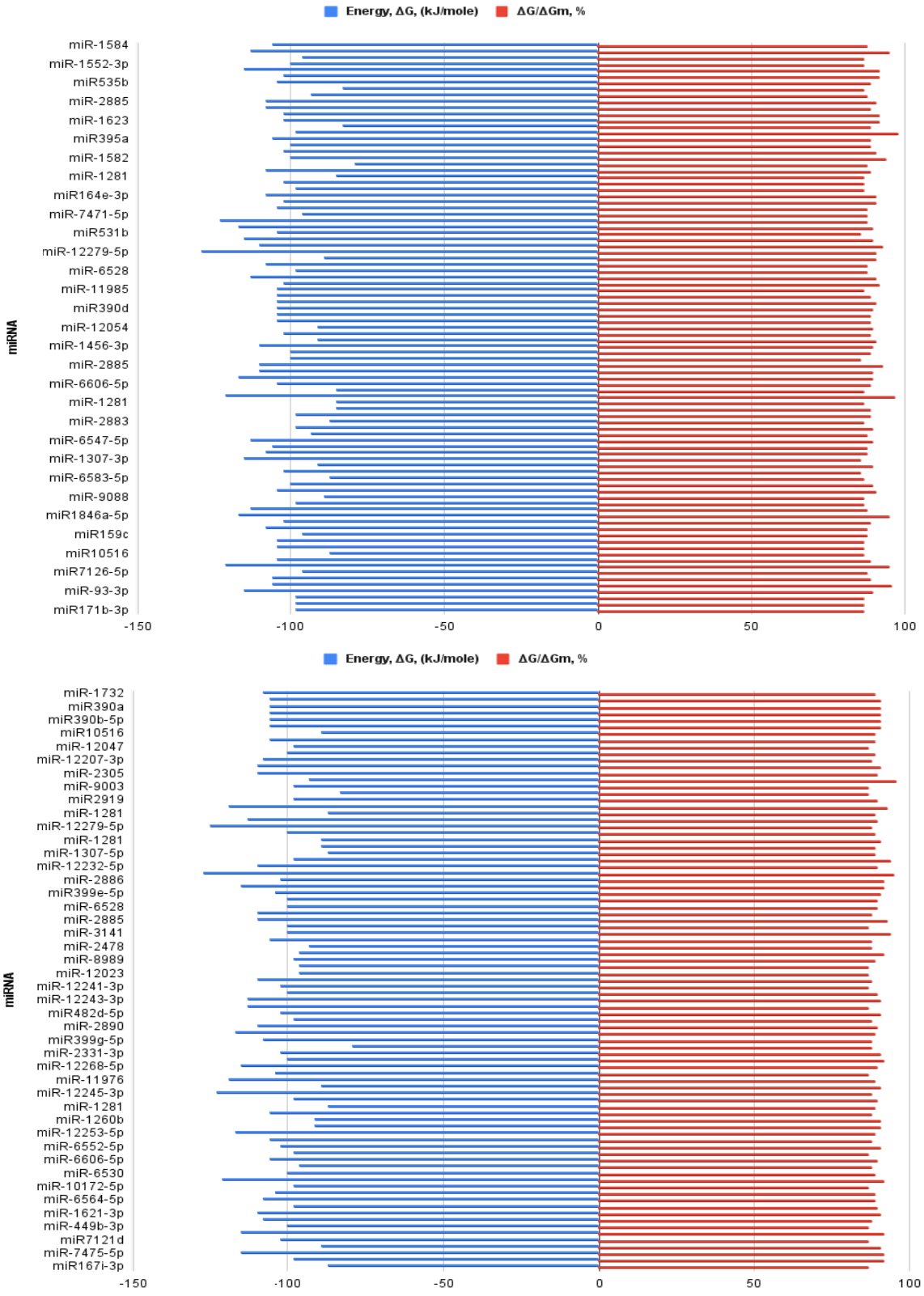

Figure 2. Parameters of binding sites for miRNAs and mRNAs of the genes participated in development of endocrinology diseases

Table 2

Types of miRNAs are derived from animal products and fruits or vegetables

The *ADD1, ENPP1*, and *PPARA* genes have binding sites of one miRNA — miR-12023, expression changes of which are indicated for diseases such as gestational diabetes, hypothyroidism, alloxan diabetes, diabetes mellitus, diabetic nephropathy, gestational diabetes, prolactinoma, hyperaldosteronism, hyperinsulinism, hypothyroidism. miRNA binding sites are located in 5'UTR and 3'UTR. The free binding energy is high and varies within -98-(-110) kJ/mole (Fig. 2).

Similarly, to the above genes, the *ACL1, PIK3CD* genes bind to miR-8989 that derived from *Equus caballus* [24]. The *ALDH2* gene also has a binding site for miR-1552-3p. miRNA binding sites are located only in 5'UTR. The free binding energy varies within -97-(-99) kJ/mole. For these two genes, changes in expression are indicated for diseases of the endocrine system such as diabetes mellitus, diabetic nephropathy, gestational diabetes, prolactinoma, hyperinsulinism, hypothyroidism.

In the analysis of endocrine diseases, the highest energy values (ΔG =-127kJ/mole) are shown for binding sites of miR-11976 to *LPP* genes. The lowest energy values (ΔG =-78kJ/mole,) were for miR-138-5p binding sites to the *SDHB* genes. Most of the binding sites are localized in 5'UTR [25].

miR-2131-3p, miR-1584, miR-12030, miR-7475-5p, miR-2899, miR169c-3p, miR395a, miR-1814, miR-6568-5p have been identified that are participated in the occurrence of diabetes mellitus disease. And also miR-7475-5p, miR-12214-5p, miR-1281, miR-6552-5p, miR-1770, miR-3141 are presented in *Bos taurus, Gallus,* which are useful in the development of hypothyroidism [26-28]. miR390, miR390a-5p have binding sites in the mRNA of the *HFE* gene responsible for the development of diabetes mellitus, the presence of interactions has been established with the following miRNAs [29] (Fig. 2). The binding sites are in 5'UTR, and the free energy is determined within -106 kJ/mole. The *SERPINE1* gene interacts with miR-

2331-3p. Changes in its expression are associated with the development of alloxan diabetes, diabetes mellitus, prediabetes syndrome, diabetic nephropathy, gestational diabetes, hyperaldosteronism, hyperinsulinism [30]. The binding sites are located in the 5'UTR section. And the binding energy values are -102 kJ/mole. The *PTSN1* gene has binding sites for two miRNAs (miR-6528, miR-12243-3p), which are associated with the development of diseases such as autoimmune thyroiditis, diabetes mellitus, gestational diabetes [30]. Binding sites are localized in 5'UTR. The binding energy has high values that range from -110(-113) kJ/mole. The *CARTPT* gene is a target for five miRNAs (miR-390b, miR-390b-5p, miR-390d, miR-390-5p, miR-390). And all these miRNAs are obtained of plants, especially *Citrus sinensis, Malus domestica, Oryza sativa, Solanum lycopersicum, Solanum tuberosum, Theobroma cacao, Triticum aestivum, Vitis vinifera, Zea mays, Cucumis melo.* There are different views to the models of plant miRNAs as an affected source to correct the expression of their target genes [31, 32]. Several types plant miRNAs have been detected to be present in human tissues to target genes regulating the processes in disease control. In addition, a big kingdom of exogenous miRNA delivery suggests to use in herbal and nutria medical way on human health [33]. Its expression is associated with the development of diabetes mellitus and hyperinsulinism. The binding sites are in 5'UTR. The interaction energy varies in the values of -104 kJ/mole. The gene *CRHR1* that responsible for the diseases, such as insulinoma and prediabetes syndrome, established by binding higher score of 97 with miR-1648-5p. And the miR-169c-3p of *Citrus sinensis, Solanum tuberosum, Zea mays* showed a high score of 98, within the gene *APC* responsible for the diabetes mellitus, hyperaldosteronism, hyperparathyroidism, hypothyroidism.

An analysis of the interactions of miRNA with the corresponding target genes responsible for the development of endocrine diseases showed that among the 9 common gene sequences obtained, the maximum energy is -115 kJ/mole, for the binding site of *ZFHX3* with miR-7475-5p at a score of 92. All binding sites are localized at the 5'UTR region of the genes. Analysis of interactions of miRNA and mRNA genes revealed miRNAs: miR-23b, miR-12030, miR-9007, miR-1582, miR-1648-5p, miR-1637, miR-2127, miR-11976, miR-7475-5p, miR-2885, miR-1281, miR-3141, miR-1552-3p, miR-12023, miR-8989, miR-2131-3p, miR-1584, miR-2899, miR169c-3p, miR395a, miR-1814, miR-6568-5p, miR-12214-5p, miR-1281, miR-6552-5p, miR-1770, miR-2331-3p, miR-6528, miR-12243-3p, miR-390b, miR-390b-5p, miR-390d, miR-390-5p, miR-390 that are involved in the manifestation of endocrine diseases. Thus, the results included in this study can provide insight into the mechanism of communication of endocrine diseases and help develop new diagnostic biological markers and therapeutic influences for patients.

Conclusion

As a result of this work, miRNAs and mRNA binding sites of target genes participated in the development of endocrine diseases were created. The interactions of miRNAs with associated genes have been proved, as well as the142 genes responsible for the development of diseases and the expression of which is disrupted in significant diseases of endocrinology. These genes include: *ABCC8, ACE, ACSL1, ACVR1B, ADD1, ADGRL2, ADRB1, AHSG, AKT2, ANGPTL8, APC, APOA1, APOA5, AQP4, ARMC5, ATM, ATP1A1, ATP2A2, ATP2A3, ATRNL1, ATXN2L, BAX, BDNF, BMP2, BMP4, BSCL2, C3, CACNA1D, CARTPT, CCN2, CCND1, CD2AP, CD81, CDH23, CDK5R1, CDON, CISD2*, etc. miR-1281 binding sites have been established with 9 genes: *ATM, BMP4, CTNNB1, IGF2BP2, KCNK9, KLLN, SIRT1, SMAD3, ZFHX3,* associated with the development of endocrine diseases, respectively. According to the results obtained, the main high data indicators were miRNAs of *Bos taurus, Gallus, Equus caballus*. And the miR-169c-3p of*Citrus sinensis, Solanum tuberosum, Zea mays* showed a high score of 98, within the gene *APC* responsible for the diabetes mellitus, hyperaldosteronism, hyperparathyroidism, hypothyroidism. All binding sites are localized at the 5'UTR region of the genes. Analysis of interactions of miRNA and mRNA genes revealed miRNAs: miR-23b, miR-12030, miR-9007, miR-1582, miR-1648-5p, miR-1637, miR-2127, miR-11976, miR-7475-5p, miR-2885, miR-1281, miR-3141, miR-1552-3p, miR-12023, miR-8989, miR-2131-3p, miR-1584, miR-2899, miR169c-3p, miR395a, miR-1814, miR-6568-5p, miR-12214-5p, miR-1281, miR-6552-5p, miR-1770, miR-2331-3p, miR-6528, miR-12243-3p, miR-390b, miR-390b-5p, miR-390d, miR-390-5p, miR-390 that are involved in the manifestation of endocrine diseases.

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Рационнан алынған миРНҚ өзара әрекеттесу ерекшеліктерін in silico зерттеу

Диетаның ген экспрессиясына әсерін зерттеу — бұл аурудың дамуына әсер етудің барлық мүмкіндігі бар жаңа бағыт. Осының арқасында экзогендік тағамнан алынған миРНҚ денсаулықты сақтау және аурулармен күресу үшін тағамдық мРНҚ-ны пайдаланудың жаңа мүмкіндіктерін аша алады. Рационнан алынған айналымдағы миРНҚ-ларды биомаркер ретінде пайдалануға үлкен қызығушылық бар және рационнан алынған сүтқоректілердің миРНҚ-сын қолдану мүмкіндігі ауруларды емдеудің жаңа, күшті терапевтік стратегиясын ұсынуы мүмкін. Осы бағалауға сәйкес, миРНҚ семіздік, қант диабеті, эндокриндік аурулар сияқты әлеуметтік маңызы бар аурулардың генезисінде бейбіт түрде қолайлы рөл атқарады. Мақалада азық-түлік миРНҚ теориясын және оның әрекетін нығайту үшін мүмкін болатын ақпаратты жинауға әрекет жасалды. Дәлірек айтқанда, эндокриндік аурулардың дамуымен байланысты мақсатты гендердің мРНҚ және мРНҚ өзара әрекеттесуі анықталды, мақсатты гендердің миРНҚ және мРНҚ байланыстыру орындары анықталды. Аурудың дамуында мақсатты гендердің экспрессиясын реттеудің бұзылуы ерекше рөл атқарады, бұл ауруды ерте анықтауға мүмкіндік береді. Гендік-миРНҚ-ны байланысын зерттеуге арналған биоинформатикалық есептеу әдісі NewGeneralScanning бағдарламасының көмегімен жүзеге асырылды. Алынған мәліметтер нәтижесінде эндокриндік жүйенің ауруларына қатысатын гендер мен миРНҚ мәліметтер базасы құрылды. Маңызды эндокринологиялық ауруларда экспрессиясы бұзылған гендер мен мРНҚ байланыстыру орындары анықталды.

Кілт сөздер: миРНҚ, мРНҚ, гендер, диеталық миРНҚ, эндокринологиялық аурулар, байланысу аймақтары, маркерлер, ген экспрессиясы.

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In silico изучение особенностей взаимодействия микроРНК, полученных из рациона

Исследование влияния диеты на экспрессию генов — это новое направление, которое имеет все шансы повлиять на развитие заболеваний. Благодаря этому миРНК, полученная из экзогенной пищи, может открывать новые возможности для использования пищевых миРНК для поддержания здоровья и борьбы с болезнями. Существует значительный интерес к использованию циркулирующих миРНК, полученных из рациона, в качестве биомаркеров, и потенциал использования миРНК млекопитающих, полученных из рациона, может представлять собой новую мощную терапевтическую стратегию для лечения заболеваний. Согласно этой оценке, миРНК играют благоприятную роль в генезе социально значимых заболеваний, таких как ожирение, диабет, эндокринные заболевания. В настоящей статье предпринята попытка собрать возможную информацию для укрепления теории пищевых миРНК и ее действия. Точнее, определено взаимодействие миРНК и мРНК генов-мишеней, которые связаны с развитием эндокринных заболеваний, определены сайты связывания миРНК и мРНК генов-мишеней. Особую роль в развитии заболевания играет нарушение регуляции экспрессии генов-мишеней, что дает возможность обнаружить заболевание на ранней стадии. Биоинформатический вычислительный подход к изучению связывания генов и миРНК был выполнен с использованием программы NewGeneralScanning. В результате полученных данных были созданы базы данных генов и миРНК, участвующих в заболеваниях эндокринных систем. Выявлены сайты связывания генов и миРНК, экспрессия которых нарушается при значимых эндокринологических заболеваниях.

Ключевые слова: миРНК, мРНК, гены, диетическая миРНК, эндокринологические заболевания, сайты связывания, маркеры, экспрессия гена.