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MIR-1322 BINDING SITES IN MRNAS OF GENES INVOLVED IN THE DEVELOPMENT OF NEURODEGENERATIVE AND ONCOLOGICAL DISEASES

Existence of miRNA binding sites in 3′-UTR, 5′-UTR and CDS regions of the mRNA of animal genes is confirmed. The efficiency of miRNA-induced repression increases with the number of sites. The binding of miRNA can be significant if the gene contains repeats of the site sequences in the coding region. It is shown that miR-1322 has polysites in CDS region of mRNAs of dozens of human genes. Experimental verification of functionality of the large number of sites is time-consuming and labor intensive. One of the ways to predict miRNA binding sites is to check the existence of these sites in mRNA of orthologous genes and to analyze their divergence during evolution. The analysis of conservation of miR-1322 polysites in CDS of mRNAs of ATN1, BCL6B, HTT, MAGI1, MLLT3, MN1, THAP11, TBP human genes and their orthologues was carried out. The studied genes are involved in development of neurodegenerative and oncological diseases. The obtained results show that polysites for binding miR-1322 are found in mRNAs of orthologous genes of many animal species. In the process of evolution, the number of binding sites changes, that indicates species dependence of efficiency of regulation of these genes expression by miR-1322. In addition to general contribution to the study of pathogenesis mechanisms caused by participation of ATN1, BCL6B, HTT, MAGI1, MLLT3, MN1, THAP11 and TBP genes our analysis allows to propose an adequate experimental animal model for further study of regulation of described genes expression by miR-1322.

Key words: miR-1322, mRNA, orthologous genes, socially significant diseases.

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Нейродегенеративті және онкологиялық аурулардың дамуына қатысатын гендерінің mRNA-мен miR-1322 байланысу сайттары

Жануарлар гендерінің mRNA-ғы 3′-UTR-де ғана емес, сонымен қатар 5′-UTR және CDS аймақтарында miRNA байланысу сайттары болуы анықталды. miRNA-ның әсерінен болған репрессиясының тиімділігі байланысу сайттардың санымен көбеюде. Геннің кодтау аймағындағы қайталайтын тізбектері бар болса, miRNA-ның байланысуы жоғары болу мүмкін. Ондаған адам гендердің mRNA-ғы CDS аймақтарында miR-1322-ның полисайттары бар болуы көрсетілген. Көптеген сайттардың функционалдығын эксперименттік тексерісі көп еңбекті болып табылады. miRNA үшін сенімді сайттарын анықтаудың бір жолы – ортологиялық гендердің mRNA-сында

бұл сайттардың бар екендігін дәлелдеу және эволюция барысында олардың алшақтықтарын талдау. ATN1, BCL6B, HTT, MAGI1, MLLT3, MN1, THAP11, TBP адам гендердің және олардың ортологтардың mRNA-ғы CDS аймақтарында miR-1322 полисайттардың консервативтілігінің талдауы жүргізілді. Зерттелген гендер нейродегенеративті және онкологиялық аурулардың дамуына қатысады. Зерттеу нәтижелері көптеген жануарлар түрлерінің ортологиялық гендердің mRNA-да miR-1322 байланысу сайттары бар екендігін көрсетті. Эволюция барысында, байланысу сайттардың саны өзгереді, бұл өзгерістер осы гендердің miR-1322-мен жүргізілетін экспрессиялық реттеу тиімділігі түрге тәуелді екенін көрсетеді. Алынған нәтижелер ATN1, BCL6B, HTT, MAGI1, MLLT3, MN1, THAP11 және TBP гендердің қатысуымен пайда болған патогенез механизмдерін зерттеуіне жалпы үлес береді, сонымен қатар, біздің талдау сипатталған гендердің экспрессиясын миР-1322 арқылы реттеуді одан әрі зерттеу үшін тәжірибелік жануарлардың моделін ұсынуға мүмкіндік береді.

Түйін сөздер: miR-1322, mRNA, ортологиялық гендер, әлеуметтік маңызды аурулар.

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Сайты связывания miR-1322 в mRNA генов, участвующих в развитии нейродегенеративных и онкологических заболеваний

Установлено существование сайтов связывания miRNA не только в 3′-UTR, но и в 5′-UTR и CDS областях mRNA генов животных. Эффективность miRNA-индуцированной репрессии возрастает с увеличением числа сайтов связывания. Предполагается, что связывание miRNA может быть значительным, если ген содержит повторы последовательностей сайтов в кодирующей области. Было показано, что miR-1322 имеет полисайты в CDS областях mRNA десятков человеческих генов. Экспериментальная верификация функциональности большого числа сайтов является трудоемкой. Одним из способов определения достоверности сайтов для miRNA является доказательство существования данных сайтов в mRNA ортологичных генов и анализ их дивергенции в течение эволюции. Проведен анализ консервативности полисайтов miR-1322 в CDS mRNA ATN1, BCL6B, HTT, MAGI1, MLLT3, MN1, THAP11, TBP генов человека и их ортологов. Рассмотренные гены вовлечены в развитие нейродегенеративных и онкологических заболеваний. Результаты исследования показали, что полисайты для связывания miR-1322 обнаруживаются в mRNA ортологичных генов многих видов животных. В процессе эволюции число сайтов связывания изменяется, что указывает на видовую зависимость эффективности регуляции экспрессии данных генов, осуществляемой miR-1322. Помимо общего вклада в изучение механизмов патогенеза, вызванного участием ATN1, BCL6B, HTT, MAGI1, MLLT3, MN1, THAP11, TBP генов, проведенный нами анализ позволяет предложить адекватную экспериментальную модель животного для дальнейшего изучения регуляции экспрессии описанных генов посредством miR-1322.

Ключевые слова: miR-1322, mRNA, ортологичные гены, социально значимые заболевания.

Introduction

miRNAs are short non-coding RNAs (with 18-25 nucleotides in length) capable of binding to mRNA and repressing protein synthesis (Bartel, 2004: 281-297). It is assumed that in animals, interaction of miRNA with the 3'-UTR region of mRNA genes is predominant. To date, most scientific papers are devoted to miRNA interaction with 3'-UTR region of mRNAs. However, in recent years, the existence of sites for miRNA in 5'-UTR and CDS regions of animal mRNAs has been established (Tay, 2008: 1124-1128; Lytle, 2007: 9667-9672; Berillo, 2013: 1016-1024). It is seemed that sites localized in CDS effectively inhibit translation, while sites located in 3'-UTR are more effective in initiating mRNA degradation (Hausser, 2013: 604-615). In a number of studies using Ago-RNA immunoprecipitation and reporter assays, miRNAs have been found to bind to the 5'UTR, CDS and inhibit translation (Tay, 2008: 1124-1128; Lytle, 2007: 9667- 9672; Schnall-Levin, 2010: 15751-6; Hafner, 2010: 129-141). The efficacy of miRNA-mediated repression increases with the number of sites (Schnall-Levin, 2011: 1395-1403).

It is assumed that miRNA binding to mRNA can be significant if the gene contains repeats of site

sequences in coding region. It was shown that miR-1322 has multiple sites in CDS region of mRNAs of dozens of human genes. The presence of multiple binding sites in close proximity significantly increases the probability of interactions between miRNAs and mRNAs, even if mutations occur (Niyazova, 2015: 962637). Moreover, miR-1322 miRNAs has binding sites in 5′ UTRs, CDSs, and 3′ UTRs most of them are located in CDSs. One way to determine the reliability of sites for miRNAs is to prove the existence of these sites in mRNAs of orthologous genes and to analyze their divergence during evolution (Hafner, 2010: 129-141; Gaidatzis, 2007: 69; Atambayeva, 2017: 428). A*TN1, BCL6B, HTT, MAGI1, MLLT3, MN1, THAP11, TBP* genes are involved in the development of neurodegenerative and oncological diseases (Matilla-Dueñas, 2012: 172-188; Wang, 2014: 192-200; Wang: 2015: 20252-20265; Thion, 2016: 1310-1315; Harjes, 2003: 425-433; Zhang, 2011: 381-385; Bergerson, 2012: 4512-4523; Dejosez, 2008: 1162-1174). To determine possibility of regulation of A*TN1, BCL6B, HTT, MAGI1, MLLT3, MN1, THAP11* and *TBP* genes expression by miR-1322 we studied the arrangement and evolution of miR-1322 binding sites in mRNAs of these genes. Detection of effective miRNA binding sites is a promising direction for diagnosis and therapy of many diseases.

Materials and Methods

The nucleotide sequences of mRNAs of *ATN1, BCL6B, HTT, MAGI1, MLLT3, MN1, THAP11, TBP* human genes (*Homo sapience – Hsa*) and their orthologous genes (*Ailuropoda melanoleuca – Ame, Balaenoptera acutorostrata scammoni – Bac, Bos mutus – Bmu, Bos taurus – Bta, Callithrix jacchus – Cja, Camelus ferus – Cfe, Canis familiaris – Cfa, Capra hircus – Chi, Chlorocebus sabaeus – Csa, Cricetulus griseus – Cgr, Equus caballus – Eca, Felis catus – Fca, Gorilla gorilla – Ggo*, *Heterocephalus glaber – Hgl, Loxodontaa fricana – Laf, Lipotes vexillifer – Lve, Macaca fascicularis – Mfa, Macaca mulatta – Mml*, *Monodelphis domestica – Mdo, Mus musculus – Mmu, Nannospalax galili – Nga, Nomascus leucogenys – Nle, Oryctolagus cuniculus – Ocu, Ovis aries – Oar, Pan paniscus – Ppa, Pan troglodytes – Ptr, Panthera tigrisaltaica – Pti, Pteropus alecto – Pal, Pongo abelii – Pab*, *Pantholops hodgsonii – Pho, Rhinopithecus roxellana – Rro, Rattus norvegicus – Rno, Saimiri boliviensis boliviensis – Sbo, Sus scrofa – Ssc, Tupaia chinensis – Tch, Ursus maritimus – Uma*) were downloaded from NCBI GenBank (http://www.ncbi.nlm.nih.gov). Nucleotide sequences of human mature miR-1322 (GAUGAUGCUGCUGAUGCUG) were downloaded from the miRBase database (http://mirbase.org).

The miR-1322 binding sites in CDS region of mRNAs of *ATN1, BCL6B, HTT, MAGI1, MLLT3, MN1, THAP11, TBP* genes were predicted using the MirTarget program. This program defines the features of binding: a) the localization of miRNA binding sites in 5'UTR, CDS and 3'UTR of mRNAs; b) the free energy of hybridization (ΔG, kJ/mole); c) schemes of nucleotide interactions between miRNAs and mRNA. The ratio ΔG/ΔGm (%) was determined for each site (ΔGm equals the free energy of miRNA binding with its perfect complementary nucleotide sequence). The miRNA binding sites located on the mRNA with a ratio of ΔG/ΔGm of 80% or more were considered. Described binding sites are polysites arranged in series. The program determines position of binding sites beginning from the first nucleotide of 5'UTR mRNA. The MirTarget program also takes into account the hydrogen bonds between adenine (A) and uracil (U), guanine (G) and cytosine (C), G and U; A and C (Ivashchenko, 2014: e620530)

Results and Discussion

Using MirTarget program, miR-1322 binding polysites in CDS region of mRNAs of *ATN1, BCL6B, HTT, MAGI1, MLLT3, MN1, THAP11, TBP* genes were detected. mRNAs and miR-1322 interaction characteristics are shown in the table 1. Free energy of hybridization (ΔG) of miR-1322 with mRNAs of *ATN1, BCL6B, HTT, MAGI1, MLLT3, MN1, THAP11, TBP* genes is within -83 ÷ -93 kJ/mole. With the increase in length of polysites, probability of their interaction with miRNAs also increases. ΔG/ΔGm of miR-1322 binding polysites ranged from 84 to 93%.

The function of Atrophin-1 protein, encoded by *ATN1* gene, is not yet fully understood (http://www.ncbi.nlm.nih.gov). *ATN1* gene contains CAG repeats that encode polyglutamine sequence in the protein. In a healthy person, the number of CAG repeats varies from 6 to 35. The presence of more trinucleotide repeats of CAG is the cause of a rare neurodegenerative disorder – Dentato-rubro-pallido-Lewis atrophy (DRPLA). DRPLA is characterized by cerebral ataxia, myoclonic epilepsy, choreoathetosis and dementia (Matilla-Dueñas, 2012: 172-188). Inhibition of expression of mutant ATN1 protein is considered as a promising strategy for the treatment of DRPLA. In CDS region of mRNA of *ATN1* gene 15 sites for

miR-1322 binding at the position from 1687 to 1751 nucleotides were found. The region of *ATN1* gene, which contains miR-1322 binding sites in CDS of mRNA, encodes a polyglutamine sequence that is flanked by conserved oligopeptides in a number of orthologs (Table 2). ΔG/ΔGm value of miR-1322 interaction with the mRNA binding sites of *ATN1* gene is in the range of 83 to 92%. Most orthologs in mRNA of *ATN1* gene have a decrease in the number of miR-1322 binding sites. However, increase in the number of binding sites was found in *Ursus maritimus, Equus caballus* and *Felis catus* and is equal to 28, 23 and 17, respectively. Based on the analysis of miR-1322 binding sites number and their physicochemical characteristics, *Felis catus* (17 miR-1322 binding sites) can be proposed as a model object for studying the regulation of *ATN1* gene expression.

Table 1 – Characteristics of miR-1322 polysites in mRNAs of ATN1, BCL6B, HTT, MAGI1, MLLT3, MN1, THAP11, TBP genes

Gene (number of binding sites)	The position of the beginning of binding site, nt	The free energy of interaction, ΔG, kJ/mole	ΔG/ΔGm, %
Hsa-ATN1 (15)	1687 ÷ 1732	-84 ÷ -93	83 ÷ 92
Hsa-BCL6B (6)	764 ÷ 779	-87 ÷ -89	85 ÷ 88
Hsa-HTT (18)	197 ÷ 248	-89 ÷ -91	88 ÷ 90
Hsa-MAGI1 (15)	1730 ÷ 1772	-85 ÷ -89	83 ÷ 88
Hsa-MLLT3 (34)	731 ÷ 836	-83 ÷ -89	81 ÷ 88
Hsa-MN1 (23)	2519 ÷ 2591	-85 ÷ -89	83 ÷ 88
Hsa-THAP11 (27)	548 ÷ 630	-85 ÷ -93	83 ÷ 92
Hsa-TBP (29)	451 ÷ 547	-85 ÷ -89	83 ÷ 87
Note: In parentheses the number of miR-1322 binding sites			

Table 2 – Oligopeptides of orthologous ATN1 proteins encoded by miR-1322 binding sites

Region of ATN protein containing the oligopeptide encoded by miR-1322 binding sites	Object
STGHPPAPT.HHHH**QQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQHH**GSSGPPPPGA	*Uma*
STAHPPAPTHHHHH**QQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQHH**.....GSSGPPPPGA	*Eca*
STGHPPAPTHHHHH**QQQQQQQQQQQQQQQQQQQQQQQQQQQQHH**.....GSSGPPPPGA	*Fca*
STAHPPVSTHHHHH**QQQQQQQQQQQQQQQQQQQQQQQQQQQQHH**.....GNSGPPPPGA	*Hsa*
STGHPPAPTHHHHH**QQQQQQQQQQQQQQQQQQQQQQQQQQQQH**.....GSSGPPPPGA	*Ame*
STAHPPAPAHHHHH**QQQQQQQQQQQQQQQQQQQQQQQQQQQQHH**.....GSSGPPPPGA	*Cfe, Pal*
STAHPPVSTHHHHH**QQQQQQQQQQQQQQQQQQQQQQQQQQQQHH**.....GNSGPPPPGA	*Ptr*
STAHPSAPTHHHHH**QQQQQQQQQQQQQQQQQQQQQQQQQQQQHH**.....GSSGPPAPGA	*Laf*
STAHPPVSTHHHHH**QQQQQQQQQQQQQQQQQQQQQQQQQQQQHH**.....GNSGPPPPGA	*Ppa*
SAAHPPASTHHHHH**QQQQQQQQQQQQQQQQQQQQQQQQQQQQHH**.....GSSGPPPPGA	*Pab*
STAHPPAPAHHHHH**QQQQQQQQQQQQQQQQQQQQQQQQQQQQHH**.....GSSGPPPPGA	*Ssc*
STAHPPAPAHHHHH**QQQQQQQQQQQQQQQQQQQQQQQQQQQQHHH**.....GSSGPPPPGA	*Ocu*
STAHPPASTHHHHH**QQQQQQQQQQQQQQQQQQQQQQQQQQQQHH**.....GSSGPP.PGA	*Csa,Rro*
STAHPPASTHHHHH**QQQQQQQQQQQQQQQQQQQQQQQQQQQQHH**.....GSSGPPP.GA	*Mml, Mfa*
STAHPPASTHHHHH**QQQQQQQQQQQQQQQQQQQQQQQQQQQQHH**.....GNSAPPPPGA	*Sbo*
Note: oligopeptides encoded by miR-1322 binding polysites are indicated in bold type	

BCL6B gene is a homologue of the proto-oncogene of 6 B-cell lymphoma (BCL6). BCL6B inhibits hepatocellular carcinoma metastases in vitro and in mice (Wang, 2014: 192-200). It is suggested that BCL6B suppresses the growth of colon cancer cells, activating the signal system involving P53 (Hu, 2015: 651-662). In CDS mRNA of BCL6B gene, 6 miR-1322 binding sites were identified in the region from 764 to 779 nucleotides of mRNA with an interaction value of 85-88% of the maximum value of ΔG/ΔGm ratio. The region of mRNA of *BCL6B* gene, which contains miR-1322 binding sites in CDS, encodes polyserine. For the group of 23 mammalian species, polyserine in BCL6B protein is flanked by conservative octapeptides (Table 3).

Table 3 – Oligopeptides of orthologous BCL6B proteins encoded by miR-1322 binding sites

Region of BCL6B protein containing the oligopeptide encoded by miR-1322 binding sites	Object
RLPSGDEA**SSSSSSSSSSSSSSSSSSSSS**EEGPIPGP	*Ptr*
RLPSGDEA**SSSSSSSSSSSSSSSSSSSS**.EEGPIPGP	*Ppa*
QLPSADEA**SSSSSSSSSSSSSSGS**......EEGPIPGP	*Ssc*
RLPSGDEA**SSSSSSSSSSS**.........EEGPIPGP	*Hsa, Ggo*
GLPSGDEA**SSSSSSSSGS**..........EEGPIPGP	*Pal*
RLPSGDEA**SSSSSSSSS**...........EEGPIPGP	*Nle*
RLPSGDEA**SSSSSSSS**............EEGPIPGP	*Pab*
QLPSGDEA**SSSSSSSS**............EEGPISSP	*Chi*
RLPSGDEAC**SSSSSSS**............EEGATPGL	*Rno*
RLPSGDEA**SSSSSSS**............EEGPILGP	*Cja*
RLPSGDEA**SSSSSSS**............EEGPISGP	*Bac*
QLPSGDEA**SSSSSSS**............EEGPISSP	*Oar, Pho*
RLPSGDEA**SSSSSS**.............EEGPIPGP	*Csa, Laf*
RLPSGDEA**SSSSSS**.............EEGPISGP	*Lve*
GLPSGDEA**SSSSSS**.............EEGPIPGP	*Eca*
RLPSGDEAC**SSSSS**.............EEGTTPGL	*Mmu*
RLPSGDEA**SSSSS**.............EEGPIPGP	*Rro, Mml, Mfa, Tch*
Note: oligopeptides encoded by miR-1322 binding polysites are indicated in bold type	

Most species of *BCL6B* gene orthologs in mRNA contains decrease in the number of miR-1322 binding sites. However, *BCL6B* mRNAs of *Pan troglodytes, Pan paniscus* and *Sus scrofa* contain 17, 16 and 9 miR-1322 binding sites, respectively. In mRNA of *Rattus norvegicus*, there are 4 binding sites for miR-1322 with an interaction energy ΔG of -85 kJ/m and -89 kJ/m. mRNA of *BCL6B* gene of *Mus musculus* contains only 1 miR-1322 binding site with an interaction value of 81% of the maximum value of ΔG/ΔGm ratio. When studying the possibility of regulation of *BCL6B* gene expression by miR-1322 molecule in mammals, difference in the number of miR-1322 polysites in mRNA of *BCL6B* gene orthologs should be taken into account, as well as the value of miR-1322 – mRNA interaction.

mRNA of *HTT* gene also contains miR-1322 binding polysites and encodes a hantingtin HTT protein containing a polyglutamine tract. Wild types of *HTT* gene of different people have different amounts of CAG repeats (9-35). Huntington's syndrome develops when the number of trinucleotide repeats increases to 36-40 or more (http://www.ncbi.nlm.nih.gov). HTT is expressed in all mammalian cells (the highest concentration is in brain and testes). HTT, interacting with proteins involved in processes of endocytosis, apoptosis, morphogenesis and transcription, can also be involved in the regulation of all these processes (Harjes, 2003: 425-433). It is found that mRNA region of *HTT* gene with CAG repeats (197-248 nucleotides) contains 18 miR-1322 binding sites with ΔG/ΔGm ratio of 85 to 90%. miR-1322

binding sites are found in 15 mammalian species mRNAs of HTT gene orthologous (Table 4). mRNA of human *HTT* gene contains the greatest number of miR-1322 binding sites. A decrease in the number of miR-1322 binding sites in mRNAs of *HTT* gene orthologs is observed. So, there are 13 miR-1322 binding sites in mRNA of *Sus scrofa*, 10 miR-1322 binding sites in mRNA of *Bos taurus*, 8 miR-1322 binding sites in mRNA of *Cricetulus griseus*, 6 miR-1322 binding sites in mRNA of *Pan troglodytes* and *Pan paniscus*, 5 miR-1322 binding sites in mRNA of *Chlorocebus sabaeus, Macaca mulatta, Nomascus leucogenys, Canis familiaris* and *Ovis aries*. Decapeptide flanking polyglutamine from the N-terminal in HTT protein is highly conserved. The polyproline amino acid sequence flanking the binding sites from C-terminus of HTT is variable in orthologous proteins. When studying the regulation of *HTT* gene expression by miR-1322 molecule in mammals, the difference in the number of miR-1322 binding polysites in mRNA of *HTT* gene in orthologs should be considered.

Table 4 – Oligopeptides of orthologous HTT proteins encoded by miR-1322 binding sites

Region of HTT protein containing the oligopeptide encoded by miR-1322 binding sites	Object
MKAFESLKSF**QQQQQQQQQQQQQQQQQQQQQQQ**PPPPPPPPPP	*Hsa*
MKAFESLKSF**QQQQQQQQQQQQQQQQQQ**.....LPPPPPQPPQ	*Ssc*
MKAFESLKSF**QQQQQQQQQQQQQQQQ**.....PPPPPQPPQP	*Bta*
MKAFESLKSF**QQQQQQQQQQQQQQ**.....SPPPPSPPPC	*Cgr*
MKAFESLKSF**QQQQQQQQQQQQQ**.....PPPPQPPQLP	*Laf*
MKAFESLKSF**QQQQQQQQQQQQ**.....PPPPPPPLPP	*Ptr, Ppa*
MKAFESLKSF**QQQQQQQQQQQ**.....PPPPPPPPPP	*Csa*
MKAFESLKSF**QQQQQQQQQQQ**.....PPPPPPPPPP	*Mml*
MKAFESLKSF**QQQQQQQQQQQ**.....PPPPPPPPPX	*Nle*
MKAFESLKSF**QQQQQQQQQQQ**.....PPPPPPPQPP	*Cfa*
MKAFESLKSF**QQQQQQQQQQQ**.....PPPPPPQPPQ	*Oar*
MKAFESLKSF**QQQQQQQQ**.....PPPQAPPPPP	*Rno*
MKAFESLKSF**QQQQQQQ**.....PPPQAPPPPP	*Mmu*
Note: oligopeptides encoded by miR-1322 binding polysites are indicated in bold type	

MAGI1 is a family of membrane-bound guanilatkinase (MAGUK), involved in the formation of multiprotein complexes on the inner surface of plasma membrane required for intercellular contacts (http://www.ncbi.nlm.nih.gov). It is shown that MAGI1 can inhibit cellular migration and invasiveness in hepatocellular carcinoma (Zhang, 2011: 381-385). The decrease in MAGI1 expression correlates with an unfavorable prognosis for hepatocellular carcinoma and can serve as a prognostic marker (Zhang, 2012: 93-99). In CDS of mRNA of *MAGI1* gene, 15 sites for binding miR-1322 in region from 1730 to 1772 nucleotide of mRNA were detected. The value of *MAGI1* mRNA and miR-1322 interaction is 83 – 88% of the maximum value of ΔG/ΔGm. Region of MAGI1, which contains miR-1322 binding sites in CDS of mRNA, encodes polyglutamine sequence. Octapeptides flanking polyglutamine in MAGI1 protein are highly conserved in many mammalian species (Table 5). In the sequence of polyglutamine encoded by binding sites, proline inserts are found. The largest number of miR-1322 binding sites in mRNA of *MAGI1* gene was detected in *Pteropus alecto*, *Pan paniscus* and *Macaca fascicularis* – 22 sites (ΔG/ΔGm is equal to 83 – 88%).

MLLT3 is a subunit of transcription elongation complex. MLLT3 is involved in the early regulation of erythroid and megakaryocytic cells (Pina, 2008: 264-273). t(9;11) translocation in *MLL* is the cause of acute myeloid leukemia (Bergerson, 2012: 4512-4523). In CDS region of mRNA of *MLLT3*, 34 miR-1322 binding sites were identified at region from 731 to 836 nucleotides with an interaction value of 83.3 to 88% of the maximum value of ΔG/ΔGm. Region of MLLT3, which contains miR-1322 binding sites in CDS mRNA, encodes polyserin sequence. Polyserin in orthologues MLLT3 proteins is flanked by

conservative amino acids (Table 6). There are identical number of miR-1322 binding sites and flanking regions in mRNA of *MLLT3* of *Mus musculus* and *Homo sapiens*. Therefore to study the regulation of *MLLT3* gene expression by miR-1322 molecule, the choice of *Mus musculus* as an animal model object will be adequat. An increase in the number of binding sites was found in *Macaca mulatta*, *Macaca fascicularis*, *Chlorocebus sabaeus, Pan troglodytes* (36); *Pan paniscus, Gorilla gorilla gorilla* (35). The maximum number of binding sites was found in *Nannospalax galili* – 46.

Table 5 – Oligopeptides of orthologous MAGI1 proteins encoded by miR-1322 binding sites

Region of MAGI1 protein containing the oligopeptide encoded by miR-1322 binding sites	Object
AKRKKQIE**QQQQQQQQQPQQQPQQQQQQQQQQQQQQQQQPQQQ**.EEWTEDH	*Pal*
AKRKKQLE**QQQQQQQQQQQQQQQQQQQQQQQQQQQ**.......TEEWTEDH	*Ppa, Mfa*
AKRKKQLE**QQQQQQQQQQQQQQQQQQQQQQQQQQQ**.........TEEWTEDH	*Csa*
AKRKKQLE**QQQQQQPQQPQQLQQQQQQQQPPP**..........PEEWTEDH	*Nga*
AKRKKQLE**QQQQQQQQQQQQQQQQPQQ**.............TEEWTEDH	*Sbo, Cja*
AKRKKQLE**QQQQQQQQQQQQQQQQQQQQ**.............TEEWTEDH	*Hsa*
AKRKKQLE**QQQQQQQPQPQPQQQQQQPQ**.............EEWTEDH	*Tch*
AKRKKQLE**QQQQQQQQQQQQQQQQQQ**.............TEEWTEDH	*Ggo*
AKRKKQLE**QQQQQQQQQQQPPPQQQQ**.............SEEWAEDH	*Mdo*
AKRKKQLE**QQQQPQQQQQQQQQQQP**.............PEEWTEDH	*Cfa*
AKRKKQLE**QQQQPQQPQQQQQQQQQ**.............PEEWTEDH	*Uma*
AKRKKQLE**QQQQQQQQQQQQQQPPP**.............AEEWTEDH	*Ocu*
AKRKKQLE**QQQQQQQQQQQQQQQQ**.............TEEWTEDH	*Ptr*
AKRKKQLE**QPQQPQQQQPQQQQQ**.............PEEWTEDH	*Ame*
AKRKKQLE**QQQQQQQQQQQQ**.....PEEWTEDH	*Bmu, Pho, Chi, Oar*
AKRKKQIE**QQQQQQQQQQQQ**.....PEEWTEDH	*Eca*
AKRKKQLE**QQQQQQQPQPPQ**.....PEEWTEDH	*Mmu*
AKRKKQLE**QQQQQQQQQQ**.....PEEWTEDH	*Bta*
AKRKKQLE**QQQPQQQQ**.....PEEWTEDH	*Bac*
AKRKKQLE**QQQQQQQQ**.....PEEWTEDH	*Cfe*
Note: oligopeptides encoded by miR-1322 binding polysites are indicated in bold type	

Table 6 – Oligopeptides of orthologous MLLT3 proteins encoded by miR-1322 binding sites

Region of MLLT3 protein containing the oligopeptide encoded by miR-1322 binding sites	Object
DPNRSIHT**ZZSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSS**TSFSKPHK	*Nga*
DPNRSIHT**ZSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSS**....TSFSKPHK	*Mml, Mfa, Ptr, Csa*
DPNRSIHT**ZSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSS**.....TSFSKPHK	*Ppa, Ggo*
DPNRSIHT**ZSSCSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSS**.....TSFSKPHK	*Chi*
DPNRSIHT**ZSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSS**......TSFSKPHK	*Nle, Cja*
DPNRSVHT**ZSCSSSSSSSSSSSSCSSSSSSSSSSSSSSSSSSSSSSSS**......TSFSKPHK	*Mda, Bta*
DPNRSIHT**ZSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSS**......TSFSKPHK	*Hsa, Mmu*
DPNRSVHT**ZSCSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSS**......TSFSKPHK	*Eca*
DPNRSIHT**ZCSSSSSSSSSSSSSSCSSSSSSSSSSSSSSSSSSSSSSS**.......TSFSKPHK	*Cfa, Fca*
DPNRSVHT**ZCSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSS**.......TSFSKPHK	*Laf*

continuation of table 6

Region of MLLT3 protein containing the oligopeptide encoded by miR-1322 binding sites	Object
DPNRSIHT**ZSCSSSSSSSSSSSSSSSSSSSSSSSSSSSS**.....TSFSKPHK	*Ssc*
DPNRSVHT**ZSSSSSSSSSSSSSSSSSSSSS**.....TSFSKPHK	*Pal*
DPNRSIHT**ZSSSSSSSSSSSSSSSSSSS**.....TSFSKPHK	*Rro*
DPNRSIHT**ZSCSSSSSSSSSSSSSSSS**.....TSFSKPHK	*Pho*
DPNRSIHT**ZSSSSSSSSSSS**.....TSFSKPHK	*Cfe*
DPNRSIHT**ZSSSSSSSSSS**.....TSFSKPHK	*Oar*
DPNRSIHT**ZSSSSSSSSS**.....TSFSKPHK	*Sbo*
Note: oligopeptides encoded by miR-1322 binding polysites are indicated in bold type; Z = 7S	

The product of meningioma 1 gene (*MN1*) is a transcriptional coactivator, participates in the development of meningiomas (http://www.ncbi.nlm.nih.gov). Increased MN1 expression is observed in some types of acute myeloid leukemia (Grosveld, 2007: 336-339). Overexpression of MN1 accelerates the development of aggressive leukemia by suppressing p53, which leads to a decrease in apoptosis and resistance to chemotherapy (Pardee, 2012: e4318). In CDS region of mRNA gene of *MN1* gene, 23 binding sites for miR-1322 with interaction energy of 83-87.5%, located from 2519 to 2610 nucleotides were found. The region with polysites encodes polyglutamine sequence (Table 7).

Table 7 – Oligopeptides of orthologous MN1 proteins encoded by miR-1322 binding sites

Region of MN1 protein containing the oligopeptide encoded by miR-1322 binding sites	Object
HPAPDHQS**LQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQR**QNAALMIKQM	*Hgl*
HPAPDHQS**LQQQQQQQQQQQQQQQQQQQQQQQQQQQQQR**.....QNAALMIKQM	*Pab*
HPGPDHQS**LQQQQQQQQQQQQQQQQQQQQQQQQQQQQQR**.....QNAALMIKQM	*Rno*
HPAPDHQS**LQQQQQQQQQQQQQQQQQQQQQQQQQQQQQR**.....QNAALMIKQM	*Ptr*
HPAPDHQS**LQQQQQQQQQQQQQQQQQQQQQQQQQQQQQR**.....QNAALMIKQM	*Hsa, Ggo*
HPAPDHQS**LQQQQQQQQQQQQQQQQQQQQQQQQQQQQQR**.....QNAALMIKQM	*Nle*
HPGPDHQS**LQQQQQQQQQQQQQQQQQQQQQQQQQQQQQR**.....QNAALMIKQM	*Mmu*
HPAPDHQS**LQQQQQQQQQQQQQQQQQQQQQQQQQQQQQR**.....QNAALMIKQM	*Csa*
HPGPDHQS**LQQHQQQQQQQQQQQQQQQQQQQQQR**.....QNAALMIKQM	*Nga*
HPAPDHQS**LQQQQQQQQQQQQQQQQQQQQQQQQQQQQR**.....QNAALMIKQM	*Mml, Mfa, Rro*
HPAPDHQS**LQQQQQQQQQQQQQQQQQQQQQQQQQQQR**.....QNAALMIKQM	*Bac*
HPAPDHQS**LQQQQHQQQQQQQQQQQQQQR**.....QNAALMIKQM	*Ssc*
HPAPDHQS**LQQQQQQQQQQQQQQQQQR**.....QNAALMIKQM	*Fca*
HPAPDHQSM**QQQQQQQQQQQQQQQQR**.....QNAALMIKQM	*Ocu*
HPAPDHQS**LQQQQQQQQQQQQQQQQR**.....QNAALMIKQM	*Lve, Eca*
HPAPDHPS**LQQQQQQQQQQQQQQR**.....QNAALMIKQM	*Chi, Bta*
HPAPDHQS**LQQQQQQQQQQQQQR**.....QNAALMIKQM	*Pal*
HPAQDHQS**LQQQQQQQQQQQQR**.....QNAALMIKQM	*Laf*
Note: oligopeptides encoded by miR-1322 binding polysites are indicated in bold type	

Octapeptides flanking oligopeptides encoded by miR-1322 binding sites in MN1 protein are highly conserved. The number of binding sites for miR-1322 varies among mammalian species. Thus, increase in the number of binding sites occurs in *Pan troglodytes* – 24, in *Rattus norvegicus* and *Pongo abelii* – 25 and *Heterocephalus glaber* – 37. In *Gorilla gorilla gorilla*, the number of binding sites and sequences of polyglutamine-flanking amino acids are identical to those in human MN1. As a model object, in the study of regulation of *MN1* gene expression by miR-1322, *Gorilla gorilla gorilla* (23 binding sites) and *Rattus norvegicus* (25 binding sites) can be chosen. However, the difference in the number of binding sites can influence degree of suppression of MN1 protein translation, which should be taken into account when interpreting experimentally obtained results.

Another target gene of miR-1322 is *THAP11* (THAP domain containing 11), a gene that contains THAP domain. THAP family proteins act as transcription factors that control cell proliferation, apoptosis and epigenetic silencing (http://www.ncbi.nlm.nih.gov). It has been shown that *THAP11* is involved in the regulation of cell proliferation, embryogenesis, and pluripotency of embryonic stem cells (Dejosez, 2008: 1162-1174). Knockdown of *THAP11* in colon cancer SW620 cell line led to a significant decrease in proliferation (Parker, 2012: 1654-1670). Overexpression of *THAP11* changes the expression levels of such transcription factors as c-Myc, c-Myb, GATA-2 and Fli1 (Kong, 2014: e91557). In CDS region of mRNA of *THAP11* gene, 27 miR-1322 binding sites were detected in mRNA region from 548 to 630 nucleotides. *THAP11* gene region, which contains the miR-1322 binding sites in CDS mRNA, encodes polyglutamine. The value of miR-1322 – mRNA of *THAP11* interaction is 83 – 92% of the maximum value of ratio ΔG/ΔGm. Octapeptides flanking polyglutamine in the THAP11 protein of orthologs are highly conserved (Table 8).

Table 8 – Oligopeptides of orthologous THAP11 proteins encoded by miR-1322 binding sites

Region of THAP11 protein containing the oligopeptide encoded by miR-1322 binding sites	Object
PAGAAAAR**RRQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQAS**PSASTAQT	*Ocu*
PAGAAAAR**RRQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQSS**.....PSASTAQT	*Hsa*
PAGAAAAR**RRQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQPS**.....PSASTAQT	*Csa*
PAGAAAAR**RRQQQQQQQQQQQQQQQQQQPPPQQQQQQQPS**.....PSASTAQA	*Ame*
PAGAAAAR**RRQQQQQQQQQQQQQQQQQQQQQQQQQQQQQPS**.....PSASTAQT	*Lve*
PAGAAAAR**RRQQQQQQQQQQQQQQQQQQQQQQQQQQQQQPS**.....PSASTAQA	*Cfa*
PAGAAAAR**RRQQQQQQQQQQQQQQQQQQQQQQQQQQQQQPS**.....PSASTAQT	*Mml, Mfa*
PAGAAAAR**RRQQQQQQQQQQQQQQQQQQQQQQQQQQQQQS**.....PSSSTAQT	*Rro, Rno*
PAGAAAAR**RRQQQQQQQQQQQQQQQQQQQQQQQQQQQQSS**.....PSASTAQT	*Ptr*
PAGAAAAR**RRQQQQQQQQQQQQQQQQQQPQPQQQQSS**.....PSASTAQT	*Eca*
PAGAAAAR**RRQQQQQQQQQQQQQQQQQQQQQQQQQQQSSS**.....PSSSTAQT	*Cja*
PAGAAAAR**RRQQQQQQQQQQQQQQQQQQPPPQQQSS**.....PSASTAQA	*Fca, Pti*
PAGAAAAR**RRQQQQQQQQQQQQQQQQQQQQQQPS**.....PSASTAQT	*Bac*
PAGAAAAR**RRQQQQQQQQQQQQQQQQQQLQQQQPS**.....PSSSTAQT	*Mmu*
PAGAAAAR**RRQQQQQQQQQQQQQQQQQQQQQQAS**.....QSSSTAQT	*Cgr*
PAGAAAAR**RRQQQQQQQQQQQQQQQQQQQQQQSS**.....PSASTAQT	*Ggo*
PAGAAAAR**RRQQQQQQQQQQQQQQQQQQQQQQPS**.....PSASTAQT	*Chi, Bta*
PAGAAAAR**RRQQQQQQQQQQQQQQQQQQPQQPS**.....PSASTAQT	*Pal*
PAGAAAAR**RRQQQQQQQQQQQQQQQQQQQQQQPS**.....PSASTAQT	*Bmu*
PAGAAAAR**RRQQQQQQQQQQQQQQQQQQQQQQSS**.....PSASTAQT	*Pab*
PAGAAAAR**RRQQQQQQQQQQQQQQQQQQQQQQSS**.....PSTSTAQT	*Nga*
PAGAAAAR**RRQQQQQQQQQQQQQQQQQQQQQQPS**.....PSVSATQT	*Hgl*
PAGAAAAR**RRQQQQQQQQQQQQQQQQQQQQQQPS**.....PSASTAQL	*Laf*
Note: oligopeptides encoded by miR-1322 binding polysites are indicated in bold type	

Most species of orthologs in mRNA of *THAP11* gene have a decrease in the number of miR-1322 binding sites. So, 26 miR-1322 binding sites in mRNA of *Chlorocebus sabaeus*, 24 in mRNA of *Lipotes vexillifer*, 23 in mRNA of *Canis familiaris*, 22 in mRNA of *Macaca mulatta* and *Macaca fascicularis,* 21 in mRNA of *Pan troglodytes* and *Pan paniscus*, 18 in mRNA of *Mus musculus*. The maximum number of binding sites was found in *Oryctolagus cuniculus* – 33, which makes it possible to choose it as an animal model for study of pathologies caused by *THAP11*-miR-1322 association.

TBP is a TATA-binding protein and a group of evolutionarily conserved proteins TBP-associated factors or TAFs are part of the TFIID transcription factor. TBP is required for transcription of RNA polymerase II. The TBP contains a sequence of 25-42 glutamine residues. The expansion of the number of repeats of glutamine to 45-66 is associated with development of a neurodegenerative disease – spinal carbellar ataxia 17 (http://www.ncbi.nlm.nih.gov). In CDS region of mRNA of *TBP* gene, 29 sites for miR-1322 binding are identified in region from 451 to 547 mRNA nucleotides. Part of mRNA of *TBP* gene containing miR-1322 binding sites encodes polyglutamine (Table 9). The interaction value of miR-1322 and mRNA of *TBP* gene is 83 – 87% of the maximum values of ΔG/ΔGm. Decapeptides flanking polyglutamine in TBP protein from N-terminal side are highly conserved. In mRNAs of orthologues *TBP* genes, a decrease in the number of miR-1322 binding sites is observed. So, 26 miR-1322 binding sites in mRNA of *Pan troglodytes*, 23 – in mRNA of *Rhinopithecus roxellana*.

Table 9 – Oligopeptides of orthologous TBP proteins encoded by miR-1322 binding sites

Region of TBP protein containing the oligopeptide encoded by miR-1322 binding sites	Object
SLSILEEQQR**QQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQ**AVAAAAVQQS	*Hsa*
SLSILEEQQR**QQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQ**...AVAAAAVQQS	*Ptr*
SLSILEEQQR**QQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQ**.....AVAATAVQQS	*Rro*
SLSILEEQQR**QQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQ**.....AVAAAAVQQS	*Ppa*
SLSILEEQQR**QQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQ**.....AVAAAAVQQS	*Ggo*
SLSILEEQQR**QQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQ**.....AAAAVQQS	*Eca*
SLSILEEQQR**QQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQ**.....AAVAAA.QQS	*Lve*
SLSILEEQQR**QQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQ**.....AVAAAAVQQS	*Nle, Cja*
SLSILEEQQR**QQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQ**.....AAVAA.VQQS	*Chi*
SLSILEEQQR**QQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQ**.....AVAAAAVQQS	*Pab*
SLSILEEQQR**QQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQ**.....AVAAAAVQQS	*Mml,Mfa*
SLSILEEQQR**QQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQ**.....AVAA*AVQQS	*Ocu*
SLSILEEQQR**QQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQ**.....AVAT*SVQQS	*Rno*
SLSILEEQQR**QQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQ**.....AVAT*SVQQS	*Mmu*
Note: oligopeptides encoded by miR-1322 binding polysites are indicated in bold type; *-AAA	

We assume that miRNA targeting can be significant if the gene contains repeats of binding site sequences. We have shown that miR-1322 has polysites in CDS regions of mRNA of dozens of human genes. Experimental verification of functionality of such a large number of sites is laborious. One way to determine the reliability of sites for miRNA is to prove the existence of these sites in mRNA of orthologous genes and to analyze their divergence during evolution. We analyzed the conservation of miR-1322 polysites in CDS mRNAs of *ATN1, BCL6B, HTT, MAGI1, MLLT3, MN1, THAP11, TBP* human genes and their orthologues. The results of the study of the conservation of miR-1322 polysites in CDSs of *ATN1, BCL6B, HTT, MAGI1, MLLT3, MN1, THAP11, TBP* human genes and their orthologues showed that nucleotide sequences of miRNA binding sites in mRNA can be translated in different reading frames with the synthesis of polyQ or polyS. Oligopeptides flanking polyglutamine or polyserin encoded by miR-1322 binding sites are highly conserved. During evolution, the number of miR-1322 binding sites changes, which indicates species dependence of the

efficiency of regulation of these genes expression by miR-1322.

An increase in the number of binding sites for miR-1322 in mRNAs of *ATN1* and *HTT* genes can lead to development of neurodegenerative diseases. Normally, the CAG segment is repeated up to 35 times within these gene, mutant *ATN1* gene contains from 48 to 93 CAG repeats, mutant *HTT* gene contains to 39-75 copies of a trinucleotide repeat (Matilla-Dueñas, 2012: 172-188; Bobori, 2015: 59-65). It can be assumed that trinucleotide repeats in mRNAs can participate in the development of diseases as targets for miR-1322. The energy of interaction between miR-1322 and mRNAs of *ATN1, BCL6B, HTT, MAGI1, MLLT3, MN1, THAP11, TBP* genes is between -84 kJ/mole and -93 kJ/mole. However, when predicting the probability of inhibition degree of gene expression by miRNAs, it is not enough to know only their affinity to mRNAs. Effect of suppression of genes expression directly depends on the ratio of mRNAs and miRNAs molecules concentrations, which must be taken into account when planning experiments and processing data. This can be explained by the scheme:

$$\text{miRNA} + \text{RISC} \leftrightarrow \text{RISC}(\sim\text{miRNA}) \leftrightarrow \text{RISC}(\sim\text{miRNA}) + \text{mRNA} \leftrightarrow \text{RISC}(\sim\text{miRNA}) \approx \text{mRNA} \rightarrow \text{RISC}(\sim\text{miRNA}) + \text{res-mRNA},$$

where RISC (RNA-induced silencing complex) – association of proteins contained in RISC complex without miRNA; RISC(~miRNA) – association of proteins contained in RISC complex without miRNA with miRNA; RISC(~miRNA)≈mRNA – RISC complex with miRNA and mRNA, formed by hydrogen bonds; res-mRNA – restricted mRNA.

The scheme shows following processes: miRNA binds to a group of RISC proteins, forming RISC(~miRNA). Further, RISC(~miRNA) binds to mRNA via hydrogen bonds (≈) and inhibits protein synthesis, or RISC cleaves mRNA, which is further degradated by cytoplasmic restriction enzymes. The stage of binding RISC(~miRNA) to mRNA is reversible and in the absence of their interaction, mRNA can be used for translation. It follows from this scheme that different effects can be observed depending on the ratio of concentrations of miRNAs and mRNAs. Assume that miRNA is completely complementary to binding site in mRNA, that is, it has a high affinity to mRNA. Despite this, at low concentrations of miRNAs compared to mRNAs, the complex will have little effect on inhibition of translation, since miRNAs will bind with a small part of synthesized mRNAs. If concentration of miRNAs is comparable or greater than concentration of mRNAs, protein synthesis will be slowed down or completely inhibited. For example, with an average affinity of miRNA-mRNA interaction, the effect of complete inhibition of protein synthesis can be achieved at miRNA concentrations much greater than mRNAs.

Conclusion

In the mRNAs of orthologous genes of studied animal species, miR-1322 binding sites are identified that encode polyamino acids of glutamine and serine. The number of polyamino acids varies during the evolution of species and there is a tendency to increase the length of polyamino acids in proteins during evolution. Revealed changes in the number of miR-1322 polysites can influence the susceptibility of various species to diseases caused by involvement of described genes. Our analysis allows us to supplement existing knowledge about the role of miR-1322 in key biological processes and to make general contribution to study of diseases associated with *ATN1, BCL6B, HTT, MAGI1, MLLT3, MN1, THAP11, TBP* genes. Moreover, it is possible to propose an adequate experimental animal model for further study of regulation of described genes expression by miR-1322. Based on the analysis of the number of miR-1322-3p binding sites and their physicochemical properties as a model object for studying the regulation of the expression of the described genes, the following can be proposed: for *ATN1-Felis catus* (17 binding sites); for *BCL6B-Gorilla gorilla* (6 binding sites); for *HTT – Sus scrofa* (13 binding sites), for *MAGI1 – Saimiri boliviensis* and *Callithrix jacchus* (15 binding sites); for *MLLT3 – Mus musculus* (34 binding sites), *MN1 – Gorilla gorilla gorilla* (23 binding sites) and *Rattus norvegicus* (25 binding sites), for *THAP11 – Chlorocebus sabaeus* (26 binding sites) and *Oryctolagus cuniculus* (33 binding sites), for TBP – Pan troglodytes (26 binding sites).

Assosiation of miR-1322 with its target genes can serve as markers for some neurodegenerative disorders and types of cancer. For adequate choice of experimental animals, it is necessary to take into account the number of binding sites and interaction characteristics between miRNAs and mRNAs of target genes.

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