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РЕСПУБЛИКИ КАЗАХСТАН
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FEATURES OF THE BINDING OF miR-1322 WITH mRNAs OF GENES ENCODING POLYGLUTAMINE-CONTAINING PROTEINS

Abstract. Many genes encode proteins containing polyglutamine tract, which function is not studied well. It has been established that polyglutamine expansion causes some diseases. Using the MirTarget program, we found that nucleotide sequences in the mRNA of *ATXN1, ATXN2, ATXN7, KCNN3, MEF2A* and *POLG* genes are miR-1322 binding sites. This miRNA can bind with the sites in mRNA and suppress genes expression. There are 22, 16, 8, 17, 9 and 9 miR-1322 binding sites in mRNAs of *ATXN1, ATXN2, ATXN7, KCNN3, MEF2A, POLG* genes, res-+pectively. These polysites encode polyglutamine from 10 to 29 amino acid residues in length. Most of the studied proteins are transcription factors and inhibition of their synthesis can cause neurodegenerative, cardiovascular and oncological diseases. MiRNA binding sites in mRNAs of orthologues genes indicate the emergence of regulation of the studied genes expression by miR-1322 many millions of years ago. Animals containing miR-1322 target genes can serve as experimental models to study the role of polyglutamine in the development of diseases.

Keywords: miR-1322, mRNA, gene, polyglutamine, disease.

Introduction. miRNAs are small non-coding RNAs that are able to regulate gene expression at post transcription level by binding with mRNAs. The role of miRNAs in different biological processes is actively being investigated. It has been shown that these molecules can act as intracellular and intercellular signaling regulators. It has been established that miRNAs bind to mRNAs in 3′-untranslated regions (3′UTRs), 5′-untranslated regions (5′UTRs) and coding domain sequences (CDSs) [1, 2]. Moreover, some miRNAs have binding sites (BS) in 5′UTRs, CDSs, and 3′UTRs [3]. The efficacy of miRNA-mediated repression increased with the number of sites [4]. It is assumed that miRNA binding to mRNA can be significant if the gene contains repeats of site sequences in coding region. Bioinformatics is actively used to fully understand, manage and analyze biological data [5]. It is possible to predict inter-actions between miRNAs and mRNAs and their properties by using different programs [6]. It has been shown that among 17,494 mRNA sequences of human genes miR-1322 has BS in 1,058 genes [7]. Most of them are located in repeat-rich coding regions of mRNAs. Depending on reading frames these BS encode polyGlu, polyAla or polySer. The objective of this study is to research the properties of miR-1322 BS in mRNAs of *ATXN1, ATXN2, ATXN7, KCNN3, MEF2A* and *POLG* and their orthologues. These genes are involved in several diseases. Cytosine-adenine-guanine (CAG) repeat expansions in the coding regions of *ATXN1, ATXN2,* and *ATXN7* are the cause of spinocerebellar ataxias (SCAs) [8]. It has been shown that *KCNN3* may play an important role in the pathogenesis of atrial fibrillation [9]. In other study the *KCNN3* and other small conductance calcium-activated potassium channels are proposed as promising therapeutic targets for neurodegenerative disorders such as Parkinson's disease [10] It has been shown that *MEF2A* might be involved in myocardial infarction, neurodegenerative disorders and in hepatocellular carcinoma development [11, 12]. It has been shown that *POLG* can play a significant role in Parkinson's disease and tumor promotion [13, 14]. Studying of regulation mechanisms of these genes expression is a

promising area for detection and treatment of some neurodegenerative, cardiovascular and oncological diseases.

Materials and methods. The nucleotide sequences of mRNAs of *ATXN1, ATXN2, ATXN7, KCNN3, MEF2A* and *POLG* human genes (Homo sapience – *Hsa*) and their orthologous genes (*Acinonyx jubatus – Aju, Ailuropoda melanoleuca – Ame, Balaenoptera acutorostrata scammoni – Bac, Bos mutus – Bmu, Bos taurus – Bta, Castor Canadensis – cca, Callithrix jacchus– Cja, Canis familiaris – Cfa, Capra hircus – Chi, Chlorocebus sabaeus – Csa, Cricetulus griseus – Cgr, Equus caballus – Eca, Felis catus – Fca, Gorilla gorilla – Ggo, Loxodonta africana – Laf, Lipotes vexillifer – Lve, Macaca fascicularis – Mfa, Macaca mulatta – Mml, Monodelphis domestica – Mdo, Mus musculus – Mmu, Nannospalax galili – Nga, Nomascus leucogenys – Nle, Ornithorhynchus anatinus – oan, Oryctolagus cuniculus – Ocu, Ovis aries – Oar, Pan paniscus – Ppa, Pan troglodytes – Ptr, Pteropus alecto – Pal, Pongo abelii – Pab, Pantholops hodgsonii – Pho, Rhinopithecus bieti – Rbi, Rhinopithecus roxellana– Rro, Rattus norvegicus – Rno, Saimiri boliviensis boliviensis – Sbo, Sarcophilus harrisii – sha, Sus scrofa – Ssc)* were downloaded from NCBI GenBank (http://www.ncbi.nlm.nih.gov). Nucleotide sequence of human mature miR-1322 was downloaded from the miRBase database (http://mir-base.org). The miR-1322 binding sites in CDS region of mRNAs of *ATXN1, ATXN2, ATXN7, KCNN3, MEF2A*, *POLG* genes were predicted using the MirTarget program. This program defines the features of binding: a) the localization of miRNA BS 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). miRNA BS interacting with mRNAs with ΔG/ΔGm ratio of 85% or more were considered. Described BS are polysites arranged in series. The program determines position of BS 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 [3].

Results and discussion. Using MirTarget program, miR-1322 binding polysites in CDS region of mRNAs of *ATXN1, ATXN2, ATXN7, KCNN3, MEF2A*, *POLG* genes were detected. mRNAs and miR-1322 interaction characteristics are given in the table 1. Free energy of hybridization (ΔG) of miR-1322 with mRNAs of *ATXN1, ATXN2, ATXN7, KCNN3, MEF2A*, *POLG* genes is within -87÷-93 kJ/mole. Probability of the interaction between mRNA and miRNA is increases with the increase in length of polysites. ΔG/ΔGm of miR-1322 binding polysites ranged from 85 to 92%.

Table 1 – Characteristics of miR-1322 polysites in mRNAs of *ATXN1, ATXN2, ATXN7, KCNN3, MEF2A*, *POLG* genes

Gene	The position of the beginning of binding site, nt	ΔG/ΔGm, %	Oligopeptides
ATXN1	1559 - 1592 (12) 1604 - 1631 (10)	85.4 ÷ 91.7 87.5 ÷ 89.6	QQQQQQQQQQQQHQHQQ QQQQQQQQQQQQQQH
ATXN2	657 - 714 (16)	87.5 ÷ 89.6	QQQQQQQQQQQQQQQQQQQQQQQQPP
ATXN7	637 - 658 (8)	85.4 ÷ 89.6	QQQQQQQQQPP
KCNN3	401- 425 (7) 512 - 539 (10)	87.5 ÷ 91.7 87.5 ÷ 91.7	QQQQQQQQQQQPP QQQQQQQQQQQQQP
MEF2A	1836 - 1860 (9)	85.4 ÷ 89.6	GFQQQQQQQQQQP
POLG	405 - 428 (9)	85.4 ÷ 87.5	RQQQQQQQQQQQQPQ

Expansion of a polyglutamine tract within the ATXN1 causes lethal neurodegenerative disorder SCA1 [15]. Understanding the normal function of *ATXN1* is essential to decipher the pathogenesis mechanisms in SCA1. Normal alleles of *ATXN1* have a size range of 19–36 repeats, whereas pathological alleles have 39–82 repeats. Two clusters of miR-1322 polysites have been predicted in CDS of mRNA of *ATXN1*: 12 BS for miR-1322 at the position from 1559 to 1611 and 10 miR-1322 BS from 1604 to 1650 nucleotides, respectively. The region of ATXN1, which contains miR-1322 binding is flanked by conserved oligopeptides in a number of orthologs (table 2). ΔG/ΔGm value of miR-1322 interaction with the mRNA BS of *ATXN1* is in the range of 85 to 92%. All orthologs in mRNA of *ATXN1* have a decrease

Table 2 – Oligopeptides of orthologous ATXN1 proteins encoded by miR-1322 binding sites

LSQTPGHKAE**QQQQQQQQQQQQHQHQQQQQQQQQQQQQQH**LSRAPGLITP	*Hsa*
LSQTPGHKAE**QQQQQQQQQQQQHQHQQQQQQQQQQQQH**...LSRAPGLITP	*Ppa*
LSQTPGHKAE**QQQQQHQQQQQQQHQQQQQQQQQQQH**.....LLSRAPGLITP	*Pab*
LSQTPGHKAE**QQQQQQQQQQQHQHQQQQQQQQQQQH**......LSRAPGLITP	*Ptr*
LSQTPGHKAE**QQQQQQQQQQQQQQQQHH**.............LSRAPGLITP	*Mfa*
LSQTPGHKAE**QQQQQQQQQQQQQQQQH**H.............LSRAPGLITP	*Mml*
LSQTPGHKAE**QQQQQQQQQQQQQQQH**...............LSRAPGLITP	*Nle*
LSQTPGHKAE**QQQQQQQQQQQQHH**HH...............LSRAPGLITP	*Rro*
LSQTPGHKAE**QQQQQQQQQQQQH**H.................LSRAPGLITP	*Ggo*
LSQTPGHKAE**QQQQQQQQQQQQHH**.................LSRAPGLITP	*Csa*
Note: in the Table 2 and hereinafter the bold type indicates amino acids encoded by miR-1322 binding sites	

in the number of miR-1322 BS (table 2). Most orthologues mRNAs containing miR-1322 BS were revealed among primates and contained only first set of two miR-1322 polysites.

The protein encoded by the *ATXN2*, contains a polyglutamine tract, long expansion (greater than 33 repeats) of which result in SCA2. Intermediate-length expansions (27-33 glutamines) contribute to susceptibility to amyotrophic lateral sclerosis [16]. In CDS mRNA of *ATXN2* gene, 16 miR-1322 BS were identified in the region from 657 to 733 nucleotides of mRNA with an interaction value ΔG/ΔGm of 87.5-89.6%. The region of mRNA of *ATXN2*, which contains miR-1322 BS in CDS, encodes polyGlu. For the group of orthologues, polygGlu in ATXN2 protein is flanked by conservative decapeptides (table 3). Most species of *ATXN2* gene orthologs in mRNA contains decrease in the number of miR-1322 BS, except *P. troglodytes* containing 19 miR-1322 BS. *F. catus, N. leucogenys* have only five amino acids in ATXN2 protein sequences before polyglutamine tract. While studying the regulation of *ATXN2* expression by miR-1322 in mammals, difference in the number of miR-1322 polysites in mRNA of *ATXN2* gene orthologs should be taken into account.

Table 3 – Oligopeptides of orthologous ATXN2 proteins encoded by miR-1322 binding sites

YGPLTMSLKP**QQQQQQQQQQQQQQQQQQQQQQQQQPP**PAAANVRKPG	*Ptr*
YGPLTMSLKP**QQQQQQQQQQQQQQQQQQQQQQQQQPP**...PAAANVRKPG	*Hsa*
.....MSLKP**QQQQQQQQQQQQQQQQQQQQQPP**......PPAAANVRKPG	*Nle*
YGPLTMSLKP**QQQQQQQQQQQQQQQQQQQQPP**........PPAAANVRKPG	*Csa*
YGPLTMSLKP**QQQQQQQQQQQQQQQQQQPP**...........AAANVRKPG	*Mml,Mfa*
YGPLTMSLKP**QQQQQQQQQQQQQQQPQPP**...........AAANVRKPG	*Cja*
YGPLTMSLKP**QQQQQQQQPQPQP**.................AAANARKPG	*Bta*
YGPLTMSLKP**QQQQQQQQQQPQP**.................AAANARKPG	*Chi*
.....MSLKP**QQQQQQQQQPP**...................AAANARKPG	*Fca*
YGPLTMSLKP**QQQQQQQQQQPP**...................AAANARKPG	*Aju*

ATXN7 is a transcription factor that appears to be critically important for chromatin remodeling at the level of histone acetylation and deubiquitination [17]. It has been determined that the diseased allele associated with SCA7 contains 37-306 CAG, compared to 4-35 in the normal allele [18]. MRNA of *ATXN7* contains eight miR-1322 BS with ΔG/ΔGm ratio of 85 to 90%. miR-1322 BS are found in 12 mammalian species mRNAs of *ATXN7* orthologs (table 4). mRNA of human *ATXN7* contains the greatest number of miR-1322 BS. A decrease in the number of miR-1322 BS in mRNAs of orthologs was observed. So, there are seven miR-1322 BS in mRNA of *O. cuniculus*, six miR-1322 BS in mRNA of *P. abelii* and *Ch. sabaeus*, Five miR-1322 BS are predicted in mRNA of *M. musculus*, Variable in lenghth polyalanine sequence flanks polyGlu from the N-terminal in ATXN7 protein. Amino acid sequence flanking the BS from C-terminus of ATXN7 is also variable in orthologous proteins.

Table 4 – Oligopeptides of orthologous ATXN7 proteins encoded by miR-1322 binding sites

RAAAA.GGAAAAAA**RQQQQQQQQQQPP**PPQPQRQQHPPPPPRR	*Hsa*
RAAAAAGGAAAA..**RQPQQQQQQQPP**...QPQRQQ...PPPRR	*Ocu*
RAAAAAGGAAAAAA**RQQQQQQQQPP**...SQPQRQPPPPPPPPPPRR	*Cfa*
RAAAAAGGAAAAAAR**RQQQQQQQP**....SQPQRQHSPPPPPRR	*Cja*
RAAAAAGGAAAAAA**RQQQQQQQPP**.....QPQRQQQPPPPPRR	*Pab*
RAAAA.GGAAAAAA**RQQQQQQQPP**.....QPQRQQQPPPPPPR	*Csa*
RRAA..GGAAAA..**RQQQQQPQP**.....LQPQRQHPPL...RR	*Mmu*
RAAAAAGGAAAAAG**RQQQQQPP**.......QSQRQQQPPPPPRR	*Nle*
RAAAAGGAAAAAAR**RQQQQQPP**.......QPQRQQQPPPPPPR	*Mml*
RAAAAAGGAAAAAA**RQQQQQPP**.......QPQRQ..PPPP.RR	*Chi*
RAAAA.GGAAAAAA**RQQQQQPP**.......QPPQPQRQPPP.RR	*Ssc*
RRAA..GGAAAA..**RQQQQP**QP......LQLQRQ..HPPP.RR	*Rno*

KCNN3 belongs to the KCNN family of potassium channels and contains two CAG repeat regions in CDS. It has been shown that *KCNN3* SNP polymorphism significantly increases the risk of atrial fibrillation [19]. SK channels are promising therapeutic targets for Parkinson's disease [9]. It has been established that both polyGlu regions are encoded by miR-1322 BS. These two sets of polysites consist of seven and ten BS (ΔG/ΔGm is equal to 87.5 – 91.7%) located in *KCNN3* mRNA from 401 to 444 nt and from 512 to 558 nt, respectively (table 5, 6).

Table 5 – Oligopeptides of orthologous KCNN3 proteins encoded by miR-1322 binding sites located from 401 to 444 nt

KCPCPSSGDE**QQQQQQQQQQQQQQQQQQQPP**PPPAPPATPQQPPGPPL	*Laf*
KCPCPSSGDE**QQQQQQQQQQQQQQQQQQQPP**..PPAPPAAPQQPLGPSL	*Ggo*
KCPCPSSGDE**QQQQQQQQQQQQQQQQQPP**....PPAPPAAPQQPLGPSL	*Ptr*
KCPCPSSGDE**QQQQQQQQQQQQQPP**.......PPAPPAAPQQPLGPSL	*Hsa*
KCPCPSSGDE**QQQQQQQQQQQQQPP**.......PPAPPAAPQQPLGPSL	*Pab*
KCPCPSSGDE**QQQQQQQQQQQQPP**........PPAPPAAPQQPLGPSL	*Mml*
KCPCPSSGDE**QQQQQQQQQQQQPP**........PPAPPAAPQQPLGPSL	*Mfa*
KCPCPSSGDE**QQQQQQQQQQQQPP**........PPAPPAAPQQPLGPSL	*Csa*
KCPCPSSGDE**QQQQQQQQQQQQPP**........PPAPPAAPQQPLGPSL	*Nle*
KCPCPSSGDE**QQQQQQQQQQQPP**......PPPPPAPPAAPQQPPGPPQ	*Eca*
KCPCPSSGDE**QQQQQQQQQQPP**.......PPPPAPPAAPQQPPGPSL	*Sbo*
KCPCPSSGDE**QQQQQQQQQQPP**........PPPPAPPAAPQQPPGPSL	*Cja*
KCPCPSSGDE**QQQQQQQPP**..........PPPPAPPAAPQQPPGPPL	*Bta*
KCPCPSSGDE**QQQQQQPP**............PPPAPPAAPQQPPGPLL	*Nga*
KCPCPSSGDE**QQQQQQPP**............PPSAPPAVPQQPPGPLL	*Rno*
KCPCPSSGDE**QQQQQQPP**............PPPAPPAVPQQPPGPLL	*Mmu*

The change in the number of miR-1322 BS was identified in both GAU repeat-rich sequences of *KCNN3* mRNA. The increase in the first miR-1322 binding polysites was revealed in orthologues *KCNN3* mRNAs of *L. africana, G. gorilla. P. troglodytes.* The identical number of miR-1322 BS has been found in mRNAs of *P. abelii* and *H. sapiens.* The greatest number of second miR-1322 binding polysites among orthologs was found in mRNAs of *N. galili* and *P. troglodytes.* Oligopeptides flanking polyGlu sequence encoded by miRNA BS are quite conserved in many mammalian species; however, there are changes in length of polyproline sequences flanking first set of polyGlu from C-terminus of KCNN3.

Table 6 – Oligopeptides of orthologous KCNN3 proteins encoded by miR-1322 binding sites located from 512 to 558 nt

GPLLQPQPPQL**QQL**QQQQQQQQQQQQQQQQQQQQ**P**PHPLSQLAQL	*Nga*
GPSLQPQPPQL**QQQQQQQQQQQQQQQQQQQQQ**P..PHPLSQLAQL	*Ptr*
GPSLQPQPPQL**QQQQQQQQQQQQQQQQQQQQ**P....PHPLSQLAQL	*Mml, Mfa*
GPLLQPQPPQL**QQQQQQQQQQQQQQQQQQQQ**...APLHPLPQLAQL	*Rno*
GPLLQPQPPQP**QQQQ**S**QQQQQQQ**S**QQQQQQ**...APLHPLPQLAQL	*Mmu*
GPSLQPQPPQL**QQQQQQQQQQQQQQQQ**P.....PHPLSQLAQL	*Ggo*
GPSLQPQPPQL**QQQQQQQQQQQQQQQQ**P.....PHPLSQLAQL	*Hsa*
GPSLQPQPPQL**QQQQQQQQQQQQQQQ**P.....PHPLSQLAQL	*Pab*
GPPLQPQPPQL**QQQQQQQQQQQQ**P.....HPLSQLAQL	*Lve*
GPSLQPQPPQL**QQQQQQQQQQQ**P.....PHPLSQLAQL	*Csa*
GPPLQPQPLQL**QQQQQQQQQQQ**P.....PHPLSQLAQL	*Ssc*
GPPLQPQPPQL**QQQQQQQQ**P.....PHPLSQLAQL	*Bac, Eca*
GPPLQPQPPQL**QQQQQQQPQ**.....HPLSQLTQL	*Bmu*
GPSLQPQPPQL**QQQQQQQ**X**P**.....PHPLSQLAQL	*Sbo*
GPPLQPQPPQL**QQQQQQQ**P.....PHPLSQLTQL	*Oar, Bta, Chi*
GPSLQPQPPQL**QQQQQQQ**P.....PHPLSQLAQL	*Nle, Cja*
GPPLQPQPPQLP**QQQQQQ**P.....PHPLSQLQSQ	*Laf*

The protein encoded by *MEF2A* gene is a DNA-binding transcription factor of MEF2 family. MEF2A protects primary neurons from oxidative stress-induced cell damage and may be involved in various neurodegenerative-related diseases [20]. *MEF2A* is associated with myocardial infarction [21]. Overexpression of *MEF2A* is associated with hepatocellular carcinoma [22]. There are nine miR-1322 BS located in CDS of mRNA of *MEF2A* with ΔG/ΔGm of 85.4 to 89.6%. polyGlu encoded by miR-1322 BS are flanking by conserved olygopeptides PRDRMTPS from N-terminus and RQEMGRSPVDS from C-terminus of MEF2A (table 7).

Table 7 – Oligopeptides of orthologous MEF2A proteins encoded by miR-1322 binding sites

PRDRMTPS**GFSQQQQQQQQQQQQQQQQQQQQQQQ**.....ARQEMGRSPVDS	*Sha*
PRDRMTPS**GFPQQQQQQQQQQQQQQQQQQQQQPQQQQ**.....SSRQEIGRSPVDS	*Oan*
PRDRMTPS**GFPQQQQQQQQQQQQQQQQQQQQQQQ**.....ARQEMGRSPVDS	*Mdo*
PRDRMTPS**GFQQQQQQQQQQQQQQQQQQQQQP**PQPPPPPPQPPQPQPRQEMGRSPVDS	*Nga*
PRDRMTPS**GFQQQQQQQQQQQQQP**....PPQPPPQPQPQPPQPQPRQEMGRSPVDS	*Rro*
PRDRMTPS**GFQQQQPQQQQQQQQP**.....PPPPQPQPQPPQPQPRQEMGRSPVDS	*Nle*
PRDRMTPS**GFQQQQQQQQQQSQP**.....PQPQPQPQPRQEMGRSPVDS	*Eca*
PRDRMTPS**GFQQQQQQQQQQQP**.....PPPPQPQPQPPQPQPRQEMGRSPVDS	*Hsa*
PRDRMTPS**GFQQQQQQQQQQQP**.....PPPPPQPPQPQPRQEMGRSPVDS	*Cgr*
PRDRMTPS**GFQQQQQQQQQQP**.....PQPQPQAQQPQPRQEMGRSPVDS	*Sbo*
PRDRMTPS**GFQQQQQQPQQQP**.....PPQPPQPQPRQEMGRSPVDS	*Mmu*

However, there are variable amino acid sequences containing proline and glutamine residues between polyGlu and RQEMGRSPVDSL. The maximum number of miR-1322 BS among MEF*2A* orthologues were found in *S. harrisii (22), O. anatinus (22), M. domestica (21). M. musculus* has 8 BS for miR-1322 in mRNA of *MEF2A* that should be taken into account while studying the regulation of *MEF2A* expression by miR-1322 using *M. musculus.*

The protein encoded by *POLG* is the catalytic subunit of mitochondrial DNA polymerase. POLG contains a polyglutamine tract. Nine miR-1322 BS were found in mRNA of *POLG*. This region encodes polyGlu sequence in the protein. The miR-1322 BS are located from 205 to 227 nt in *POLG* mRNA, ΔG/ΔGm is equal to 85.4 – 87.5%. There is a decrease in number of miR-1322 polysites among *POLG*

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

SSSVPASDPSDGQRR.**RQQQQQQQQQQQQPQ**QPQVLSSEGGQL	*Hsa*
SSSVPASDPSDGQRRR**RQQQQQQQQQ**P**QQPQ**.QPQVLSSEGGQL	*Ggo*
SSSVPASDPSDGQRRR**RQQQQQQQ**P**QQPQ**...QPQVLSSEGGQP	*Ptr*
SSSVPASDPSDG.RR.**RQQQQQQQQQPQ**....QPQVPSSEGGQL	*Nle*
SSSVPASDPSDGQRR.**RQQQQQQQQPQ**.....QPQVLSSEGGQL	*Ppa*
SSSVPASDPSDEQRRR**RQQQQQQQQPQ**.....QPQVPSSEGGQL	*Pab*
SSSVPASDPSDG.RRR**RQQQQQQQQPQ**.....QQPQVPSSEDGQL	*Rbi*
SSSVPASDPSDG.RRR**RQQQPQQQPQ**.........VPSSEDGQL	*Rro*

orthologues. It was identified that miR-1322 polysites exist in *POLG* mRNA in *G. gorilla, P. troglodytes, N. leucogenys, P. paniscus, P. abelii, R. bieti* and *R. roxellana.* Therefore, in further studying of regulation of *POLG* expression by miR-1322 only some animals could be used as experimental model.

Conclusion. miR-1322 BS were found in mRNAs of *ATXN1, ATXN2, ATXN7, KCNN3, MEF2A* and *POLG*. These binding sites are identified to encode polyGlu. in the orthologous proteins of studied animal species. The number of polyGlu amino acid residues varies during the evolution of species and it was established a tendency of increasing in the length of polyGlu sequence in the proteins during evolution. *In vitro* experiments and clinical research are needed to be conducted for further validation of the interaction between miR-1322 and mRNAs of *ATXN1, ATXN2, ATXN7, KCNN3, MEF2A* and *POLG*. The obtained results demonstrate the possibility of an involvement of miR-1322 in diseases caused by these genes. Our analysis of physicochemical properties of BS allows us to propose an adequate experimental animal for study of regulation of *ATXN1*, *ATXN2, ATXN7, KCNN3, MEF2A* and *POLG* expression by miR-1322.

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MIR-1322 ЖӘНЕ ПОЛИГЛУТАМИНІ БАР АҚУЫЗДАРДЫ КОДТАЙТЫН ГЕНДЕРДІҢ АРАСЫНДАҒЫ БАЙЛАНЫСУ САЙТТАРДЫҢ ЕРЕКШЕЛІКТЕРІ

Аннотация. Көптеген гендер полиглутаминдік трактi бар ақуыздарды кодтайды, олардың қызметі толық анықталмаған. Ұзын полиглутаминдік тізбектің синтезі кейбір аурулардың себебі болып табылатынын көрсетілген. MirTarget бағдарламасын пайдалана отырып, *ATXN1, ATXN2, ATXN7, KCNN3, MEF2A* және *POLG* гендерінің mRNA-ындағы нуклеотидтік тізбектер miR-1322-ның байланысу сайттары екендігі анықталды. Бұл miRNA mRNA-рымен байланыса алады және геннің экспрессиясын тежейді. *ATXN1, ATXN2, ATXN7, KCNN3, MEF2A, POLG* гендердің mRNA-сында 22, 16, 8, 17, 9 және 9 miR-1322 байланысу сайттары бар. Бұл полисайттар, ұзындығы 10-29 амин қышқылдық қалдықтарынан тұратын, полиглутаминді кодтайды. Зерттелген ақуыздардың көпшілігі транскрипциялық факторлар болып табылады, және олардың синтезінің тежеуі нейродегенеративті, жүрек-тамыр және онкологиялық ауруларға алып келуі мүмкін. Ортологиялық гендердің мРНК-да miR-1322 байланысу сайттардың болуы, зерттелген гендердің экспрессиясын реттеуінің миллиондаған жылдар бұрын пайда болғаның көрсетеді. МиР-1322-ның нысана-гендері бар жануарлар, аурулардың дамуындағы полиглутаминнің рөлін зерттеу үшін, тәжірибелік модель ретінде болуы мүмкін.

Түйін сөздер: miR-1322, mRNA, ген, полиглутамин, ауру.

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ОСОБЕННОСТИ САЙТОВ СВЯЗЫВАНИЯ miR -1322 С ГЕНАМИ, КОДИРУЮЩИМИ ПОЛИГЛУТАМИН-СОДЕРЖАЩИЕ БЕЛКИ

Аннотация. Многие гены кодируют белки, содержащие полиглутаминовый тракт, функция которого до конца не изучена. Было показано, что синтез удлиненной последовательности полиглутамина является причиной некоторых заболеваний. С помощью программы MirTarget нами было обнаружено, что нуклеотидные последовательности в мРНК генов *ATXN1, ATXN2, ATXN7, KCNN3, MEF2A* и *POLG* являются сайтами связывания miR-1322. Эта miRNA может связываться с сайтами в mRNA и подавлять экспрессию генов. В mRNAs генов *ATXN1, ATXN2, ATXN7, KCNN3, MEF2A, POLG* содержатся соответственно 22, 16, 8, 17, 9 и 9 сайтов связывания miR-1322. Эти полисайты кодируют полиглутамин длиной от 10 до 29 аминокислотных остатков. Большинство изученных белков являются транскрипционными факторами, и ингибирование их синтеза может вызывать нейродегенеративные, сердечно-сосудистые и онкологические заболевания. Наличие сайтов связывания miR-1322 в mRNA ортологичных генов указывают на возникновение регуляции экспрессии изученных генов много миллионов лет назад. Животные, содержащие гены-мишени miR-1322, могут служить в качестве экспериментальных моделей для изучения роли полиглутамина в развитии заболеваний.

Ключевые слова: miR-1322, mRNA, ген, полиглутамин, заболевание

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CONTENTS