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# THE PROPERTIES OF MIRNA INTERACTION WITH 5' AND 3' UTR MRNA GENES HAVING NUCLEOTIDE REPEATS

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Several diseases are caused by above – threshold expansion of certain trinucleotide repeats occurring in a protein-coding or non-coding region [1]. miRNAs are regulators of the expression of genes involved in the development of nucleotide repeat disorders. The expression of many genes is regulated by the binding of their mRNA with miRNA, so it is required to identify which candidate genes of nucleotide repeat disorders and to what extent can interact with miRNA.

In this work we have been studied the characteristics of miRNAs binding sites located in 5' UTR and 3' UTR mRNA genes having nucleotide repeats.

miRNA binding sites were predicted by the MirTarget program, which determines: a) the start of the initiation of miRNA binding to mRNAs; b) the localization of miRNA binding sites in 5' UTRs, CDSs and 3' UTRs of the mRNAs; c) the free energy of interaction miRNA and the mRNA ($\Delta G$, kJ/mole); d) the schemes of nucleotide interactions between miRNAs and mRNAs [2].

The nucleotide sequences of human genes mRNAs have been downloaded from NCBI (http://www.ncbi.nlm.nih.gov). Nucleotide sequences of human 2567 miRNAs have been downloaded from the miRBase database (http://mirbase.org).

100 candidate genes with nucleotide repeats have 897 miRNAs binding sites in the 5’UTR and 3’UTR mRNA. The $\Delta G/\Delta Gm$ values equal to 87 % or more. From this results only 19 miRNAs have binding sites in 20 mRNAs of genes with a free interaction energy greater than -120 kJ/mol.

Binding sites of 11 miRNAs have been found in 5'UTR mRNAs of 13 candidate genes: *ABCC1, ADNP, ATP11B, ACADM, ARID3A, ASXL1, ARID1A, ARHGAP17, ASH1L, ASTN2, ARRB1, ANKRD11* and *AMFR*. The mRNAs of *ARL4C, ADARB1, ATXN7L1, ACSL6, AKT2, AGPAT6* and *APBB1IP* genes have ten miRNAs binding sites in 3'UTR.

Only three genes of the 20 candidate genes with a free interaction energy greater than -120 kJ/mol predicted as targets of two or more miRNAs: *APBB1IP* (miR-4763–3p, miR-3960, miR-328–5p); *ASTN2* (miR-4763–3p, miR-4707–5p); *AGPAT6* (miR-1273d, miR-1226–5p). Among miRNAs that bind with high energy to mRNA genes with nucleotide repeats, we choose four miRNAs that have binding sites in mRNAs of two or more genes: miR-619–5p *(ACSL6, AKT2*); miR-6089 (*ACADM, ARID3A, ASXL1*); miR-4787–5p (*AGPAT6, ARHGAP17, ASH1L*); miR-4763–3p (*APBB1IP, ASTN2*).

The mRNAs of *AGPAT6, ARHGAP17* and *ASH1L* genes having nucleotide repeats (GGAGUU**GCCGCCGCCGCC**CCCAC)$_{GCC4}$, (GGG**CCGCCGCCG**CCA**CCGCCG**C)$_{CCG5}$ and (GGAGCU**GCCGCCGCCACCGCC**GC)$_{GCC4}$ in 3' and 5' UTRs are a targets of miR-4787–5p. The obtained results of the mRNA of *ASXL1* and *ARID1A* genes indicated that the miR-6089 and miR-6081 bind with **(CCGCCGCCG**CCCCUCCCCCACCGCC)$_{CCG3}$/ (GGCGCCUCG**GCCGCCGCCGCCGCC**U)$_{GCC5}$ repeats in 5' UTR. miR-3960 and miR-1908–3p bind with mRNA of *APBB1IP* and *ARRB1* genes in sites with (CCC**CCGCCGCCGCCGCCG**CC)$_{CCG5}$ and (**CGGGGGCGGCGGCGGCGG**CCGG)$_{CGG5}$ repeats in 3' UTR and in 5'UTR, respectively.

mRNAs of non-polyglutamine disorders genes (*ATXN10, AFF2*, *CNBP*, *DMPK*, *FMR1*, *FXN*, *JPH3* and *PPP2R2B*) have 202 miRNAs binding sites in 5'UTR and 3'UTR. The ΔG/ΔGm values equal to 87 %. *AFF2* and *FMR1* mRNAs bind with miR-3960 and miR-4258 in regions with nucleotide repeat sequences. miR-3960 and miR-4258 bind with **(GCCGCCGCCGCCGCCGCCGCCGCCGCCGCCGCCGCCGCCGCC)**$_{GCC15}$ and **(CGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG)**$_{CGG19}$ repeats with ΔG/ΔGm values equal or more than 85 % in 5'UTR.

Thus, miRNAs binding sites with mRNA genes of having nucleotide repeats have been predicted. Studying the binding characteristics of miRNA and genes will help identify associations of miRNAs with genes with nucleotide repeats for recommending for the diagnosis of nucleotide repeat expansion disorders.

## REFERENCES

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