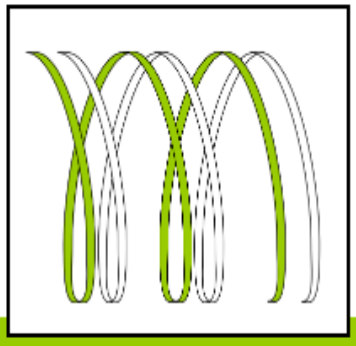
Institute for Information Transmission Problems of the Russian Academy of Sciences (Kharkevich Institute)

9th Moscow Conference on Computational Molecular Biology MCCMB'19
Moscow, 27-30 July 2019



MCCMB 2019

Proceedings of the International Moscow Conference on Computational Molecular Biology

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Acknowledgements

Program

ISBN 978-5-901158-31-9

Moscow
IITP RAS
2019

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Characteristics of miRNA interaction with CDS mRNA genes associated with CAG trinucleotide repeat disorders development

Belkozhayev A.M.

Al-Farabi Kazakh National University, department of Biotechnology, Kazakhstan, Almaty, al-Farabi Ave.,71. e-mail: ayaz_jarkent@mail.ru

Niyazova R.E.

Al-Farabi Kazakh National University, Scientific Research Institute of Biology and Biotechnology Problems, Kazakhstan, Almaty. al-Farabi Ave.,71. e-mail: raiguln@mail.ru

Several inherited neurodegenerative disorders are caused by CAG trinucleotide repeat expansions, which can be located either in the coding region or in the untranslated region (UTR) of the respective genes [1]. The profile of miRNAs in CAG trinucleotide repeat disorders is scarcely described, however miRNA dysregulation has been identified in these diseases and miRNA - related interference with gene expression is considered to be involved in their pathogenesis. Therefore, the search features of miRNA binding with genes associated with the development of CAG trinucleotide repeat disorders is significant [2].

In the present work, miRNA binding sites were predicted by the MirTarget program, which determines: a) the initiation of miRNA binding to mRNA; b) localization of miRNA binding sites in 5'UTR, CDS and 3'UTR mRNA; c) free hybridization energy (ΔG, kJ/mol); and d) schemes of nucleotide interactions between miRNA and mRNA [3]. Binding sites in CDS mRNAs of 102 human genes are borrowed from the NCBI (http://www.ncbi.nlm.nih.gov). The nucleotide sequences of 2567 human miRNAs were taken from the miRBase database (http://mirbase.org). For analyzing and formatting sequences of genes we used the sequence manipulation suite program (https://bioinformatics.org/sms). By using the software of RNA fold web server (http://rna.tbi.univie.ac.at), we predicted the secondary structures of a fragment of single-stranded RNA sequences with miRNAs binding sites.

The obtained results indicate that binding sites of three miRNAs (miR-1322, miR-1281, miR-4258) were found in CDS mRNA genes of 22 the candidate genes with CAG repeats. mRNAs of *ATN1, ATXN1, ATXN2, BRD4 CELF3, EP400, FOXP2, GIGYF2, HTT, MAML3, MN1, MEF2A, NCOR2, SMARCA2, TNRC6B, TOX3, TNRC6A, RUNX2, MLL2* and *ZNF384* genes interact with miR-1322 which CAG codons repeated from 7 to 27. The binding sites of miR-1281 in mRNA of *EGR1* gene is located in coding regions with CAG repeats. Moreover, mRNA of *PHOX2B* gene binds with miR-4258, respectively with CAG repeats.

There are a lot of repetitions of $(CAG)_{27}$ codons in *ATXN1* gene and miR-1322 binds in regions with these repeats with a start in 1578 nt. mRNA of *MAML3* gene has $(CAG)_{24}$ repeat and miR-1322 binding sites located from 2220 nt. In mRNA of *MN1* and *SMARCA2* genes codons

$(CAG)_{23,18}$ repeated and miR-1322 binds in regions with these repeats from 2534 and 766 nt. The binding sites contain nucleotide repeats CAG, which correspond to oligopeptides polyglutamine. The average free energy of miRNA binding sites in mRNA of all targets genes is equal to -113 kJ/mole. Comparatively, from our results CAG repeats have high energy compared to other trinucleotide repeats. miR-1181 and miR-1908-3p have free binding energy more than -112 kJ/mole, which gives the reason anticipate to use their interaction with the corresponding target genes as biomarkers for the development of the neurological diseases.

By these genes taking into account that they contained CAG repeats in their coding regions and excessive recurrence of these dysfunctions may lead to the emergence of hereditary neurodegenerative disease, detected these associations of miRNAs and genes could be used as markers for the diagnosis of hereditary neurodegenerative disease.

1. R. Nalevade, N. Griesche, D. Rayan. (2013) Mechanisms of RNA - induced toxicity in CAG repeat disorders, *Cell Death & Disease*, 4:752.
2. L. Dumitrescu, B. Popescu. (2015) MicroRNAs in CAG trinucleotide repeat expansion disorders: an integrated review of the literature, *CNS Neurol Disord Drug Targets*, 14(2):176-93
3. A. Ivashchenko, O. Berillo, A. Pyrkova, R. Niyazova.(2014) MiR-3960 binding sites with mRNA of human genes, *Bioinformation*, 10:423-427.