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ҚАЗАҚСТАН РЕСПУБЛИКАСЫНЫҢ
БІЛІМ ЖӘНЕ ҒЫЛЫМ МИНИСТРЛІГІ
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Биология және биотехнология факультеті
Факультет биологии и биотехнологии
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DIFFERENCES OF miRNA BINDING SITES IN mRNAS OF HUMAN AND MOUSE TITIN GENES

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Titin is a protein of human muscle tissue. It is the largest protein in the nature and plays enormous role in providing elasticity and structural integrity of sarcomers. Defects of titin synthesis causes to the development of serious cardiovascular diseases such as dillated cardiomyopathy, heart failure, coronary heart disease, myocardial infarction and etc. Different titin isoforms synthesizes in various types of muscle tissue (heart and sceletal striated musle tissue) and are encoded by different combinations of exons. The interaction between miRNAs and mRNAs of human and mouse titin genes was not studied so it became an aim of our study. Nucleotide sequences of human and mouse titin genes were found in the Genbank (*https://www.ncbi.nlm.nih.gov/genbank/*). Nucleotide sequences of human and mouse miRNAs were found in the miRBase (*www.mirbase.org/*). Free energy of miRNA-mRNA binding (ΔG), $\Delta G/\Delta G_m$ ratio (%), positions and schemes of potential miRNA binding sites were calculated by the program MirTarget. ΔG_m (maximal ΔG) is free energy of miRNA binding with absolutely complementary nucleotide sequence. $\Delta G/\Delta G_m$ ratio was used as comparative critery of miRNA-mRNA interaction rates. It was found that only 18 miRNAs of 6271 human miRNAs bound with mRNA of human titin gene with value of $\Delta G/\Delta G_m$ equal to 90 % and more. All of their's 22 binding sites are one nucleotide longer than miRNA sequences (excluding miR-11-28905-3p and miR-14-24215-3p) because these miRNAs have no complementary pair for one nucleotide of mRNA. ix miRNAs are synthesized in intergenic regions (miR-6861-5p, miR-494-5p, miR-374b-3p, miR-374c-3p, miR-34a-3p and miR-4495) and seven other miRNAs (miR-578, miR-3714, miR-1278, miR-544b, miR-4738-3p, miR-136-3p and miR-4693-5p) are synthesized in 5'UTR, CDS, 3'UTR and introns of protein-coding host genes. The rest five miRNAs (miR-19-36945-3p, miR-1-1585-3p, miR-11-28905-3p, miR-14-24215-3p and miR-12-32366-3p) are novel human miRNAs that were discovered in 2015 [1]. miR-6861-5p and miR-14-24215-3p have three binding sites each. After studying human miRNAs binding with mRNA of human titin gene we found four mouse miRNAs (mmu-miR-34a-3p, mmu-miR-136-3p, mmu-miR-374c-3p and mmu-miR-494-5p) that are similar to corresponding human miRNAs. Only mmu-miR-494-5p bound with mRNA of human titin gene with value of $\Delta G/\Delta G_m$ that is equal 93 %. At the same time only hsa-miR-19-36945-3p from the number of human miRNAs bound with complete sequence of mouse titin gene with $\Delta G/\Delta G_m$ ratio equal 90 % and more (93 %). These results show that regulation of mouse titin gene expression is not adequate model for human but artificial siRNAs that are complementary for miRNA binding sites can bind with mRNA of titin gene and repress expression of this gene.

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