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Book of Abstracts

CELLS AND
EMBRYOS

FOOD,
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CLINICAL
APPLICATIONS

HEALTH -
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**THE FEATURES OF miRNA BINDING SITES IN CDS
OF AR mRNA AND ITS ORTHOLOGS**

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The androgen receptor gene encodes a protein that is a steroid-hormone activated transcription factor. AR involved in the development of spinal-bulbar muscular atrophy, a number of cardiovascular diseases (hypertension, atherosclerosis, myocardial hypertrophy) and cancer (prostate cancer, breast cancer).

Previously, binding sites for miRNAs in 3'UTR region of AR gene were identified. Whereas the presence of binding sites in the protein-coding region (CDS) of the mRNA of AR gene has not been studied.

Purpose of the study. Identification of binding sites for miRNAs in CDS of AR and its orthologs is necessary to better understand the patterns of regulation of AR expression in the evolution process. The presence of binding sites for miRNAs in orthologous genes can serve as the basis for using animal models for studying the mechanisms by which miRNAs regulate AR gene expression.

The nucleotide sequences of the mRNA of AR human gene and its orthologs were taken from the NCBI GenBank. Of the 2565 miRNAs available in the miRBase database using the MirTarget program, we detected miR-1322, miR-1260a and miR-1260b, which have multiple binding sites in the CDS of mRNA of AR gene. The MirTarget program defines the beginning of miRNA binding sites in mRNA from the first nucleotide of 5'UTR of mRNA, free hybridization energy (ΔG , kJ/mole), and the schemes of miRNA-mRNA interaction.

There are 23 sequentially located miR-1322 binding sites in the CDS of AR mRNA located from 693 to 780 nucleotides. There are 17 and 19 miR-1260a and miR-1260b binding sites located from 1874 to 1928 and from 1869 to 1927 nucleotides, respectively. The binding sites of miR-1322 encode polyglutamine, the binding sites of miR-1260a and miR-1260b encode polyglycine in the AR protein. The free energy of miR-1322 interaction with the mRNA binding sites of AR gene varies from -82.8 to -89.2 kJ/mole. The value of ΔG of the interaction of miR-1260a and miR-1260b with AR mRNA varies from -82.8 to -87.3 kJ/mole and from -81.6 to -91.3 kJ/mole, respectively. For the group of 24 mammalian species, the polyglutamine in the AR protein is flanked by the conservative amino acids AASAAPP GAS and GEDGSPQAHR. Polyglycine in the AR protein is flanked by the conservative amino acids TAEEGQLYGP and EAGAVAPYGY in the group of 22 mammalian species. In proteins of AR orthologs the amount of polygluta-

mine and polyglycine encoded by the binding sites for miR-1322, miR-1260a and miR-1260b changes. Thus, miR-1322 binding sites encode 42 glutamines in *Felis catus*, 25 glutamines in *Oryctolagus cuniculus*, 22 glutamines in *Pan troglodytes*, and 17 glutamines in *Ailuropoda melanoleuca*. In the frequently used model animals *Rattus norvegicus* and *Mus musculus* the position of the miR-1322 binding sites is changed. There are 19 glycines in *Gorilla gorilla gorilla*, 18 glycines in *Pan paniscus* and 17 glycines in *Pan troglodytes* encoded by the miR-1260a and miR-1260b binding sites.

When studying the regulation of *AR* gene expression by miR-1322, miR-1260a and miR-1260b molecules in various pathologies in mammals, the difference in the number and location of multiple binding sites in the mRNA of the *AR* orthologs should be considered.

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