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Różne mechanizmy działania microRNA w procesie translacji

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Streszczenie w języku angielskim

Protein synthesis by translation is a very complex process based on the information found in the mRNA. The process is influenced by several protein factors from the initiation to the termination phase. It can also be affected by microRNAs, i.e. short non-coding RNAs, which work by destabilization of the mRNA or by blocking the translation initiation. The dissertation discusses issues related to the mechanisms of microRNA interactions in the translation process and examines them using reporter genes. The main aim of the work was to study the influence of various microRNAs on the translation process, and mRNA degradation and to examine intercellular differences in this regard. In the process the levels of reporter gene expression and their changes under the influence of microRNA 21, 24, and let-7 were determined at the mRNA and protein levels. The impact of the presence of transcripts containing microRNA binding sites on the expression of genes not regulated by miRNAs was also analyzed. It also examined how complexes containing transcripts regulated and unregulated by miRNAs sediment during centrifugation in a sucrose gradient and how expression levels of the studied reporter genes change, at the mRNA and protein level, after the addition of anti-miR oligonucleotides that inhibit the activity of the tested microRNAs. Finally, a mathematical model was designed to predict the presence of non-polysomal mRNA-protein complexes and their properties. As a result, it was observed that different microRNAs within one cell type had different effects on mRNA and protein levels, but the same microRNAs had different effects within other cell types. In the case of sucrose gradient centrifugation, the accumulation of transcripts in different fractions was observed depending on the type of occurrence of microRNA binding sites. The effect of microRNA on the expression of the studied genes at the mRNA and protein level was also checked after the addition of anti-miR oligonucleotides, such action showed the classic mechanism of action of microRNA and possible other actions, including the protective effect of miRNA on mRNA or increasing the efficiency of the translation process by facilitating translation initiation. The search for complexes other than polysomal by creating mathematical models showed the possibility of such complexes in both light and heavy fractions characterized by different degrees of condensation and in sucrose gradients traveling with different polysomal fractions.