УДК 577.29

DEVELOPING THRESHOLDING DNA NANOMACHINE FOR CANCER DIAGNOSIS AND TREATMENT

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Введение. Cancer group of diseases is considered a leading cause of death worldwide, while many of them can be cured when treated on time [1]. It is not a surprise that nowadays the number of research aimed to develop new effective methods of cancer diagnosis and treatment is increasing. Upon others, DNAzyme-based constructions have gained significant interest as alternatives for cancer treatment. Since the discovery of DNAzymes by Breaker and Joyce in 1994 numerous constructions based DNAzyme have been investigated with more or less efficacy in down regulating the mRNA of some essential genes [2]. The aim of this research is to develop a 7-input DNA nanomachine with threshold activation cleaving synthetic long RNA.

Основная часть. The proposed project relies on designing a 7-input DNA nanomachine based binary DNAzyme (Bi-Dz) connected to a scaffold. The idea behind the 7-input design is to ensure that the mechanism is triggered only when the activator concentration reaches a threshold value. The principle of Bi-Dz is simple: upon binding of the input molecule (miR-92) the catalytic core will form again initiating the cleavage of the target. In case of 7-input DNA nanomachines, we have designed it the way that each strand self-folds and requires 6 miR-92 to unwind the strands in order for the 7^{th} to reform the catalytic core. However, to get such behaviour we should prioritize each input (miR-92) binding site. Prioritising can be achieved by quantifying the thermodynamic favourability of each miR-92 to its binding site to form a stable duplex using Gibbs free energy (ΔG). The main principle of the design, which is six of the input binding sites need to have the same ΔG, while the one forming a catalytic core needs to have ΔG of a lower value to be bind last allowing for correct threshold activation.

Within this research 7-input DNA nanomachines of various designs were created and assembled. Each design showed itself as a functional DNAzyme. The analysis of cleavage activity indicated the cleavage activity of the described DNA nanomachines is conditional and dependent on the input molecule concentration, reaching the peak value at the expected concentration of miRNA.

Выводы. In this project DNAzyme-based 7-input DNA nanomachines are created, for which conditional cleavage activation is achieved. The outlined principle of the design can be a base for future new designs with small adjustments. The results are promising and display 7-input DNA nanomachines as a potential alternative agent in cancer gene therapy in the near future.

Список использованных источников:

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