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Title: *Structural RNA conjugated with gold nanoparticles as a tool for gene expression regulation*

English abstract

Now, especially after the global emergence of the first mRNA vaccine against SARS-CoV-2, the importance of RNA research has never been more pronounced. Our understanding of the RNA has steadily deepened since the discovery and subsequent differentiation of the two types of nucleic acids, DNA and RNA. The ribonucleic acid (RNA) is particularly interesting due to its exceptional naturally occurring spatial properties responsible for multiplicity of RNA functions falling way beyond the Central Dogma of Molecular Biology. This quality of RNA led to development of the RNA architectonics, which relies on the RNA motifs used to create RNA nanostructures. As we were gaining the ability to determine and rationally design RNA structures, we also learned to replicate some of the natural processes. Consequently, the new RNA-based technologies that can be applied as therapeutics, sensors or diagnostic tools were introduced and all those can be gathered under the umbrella term of RNA nanotechnology. With the development of modern diagnostics, it has been found that an increasing number of diseases have a genetic cause that leads to impaired protein function. Such abnormalities in protein expression may cause disorders such as: cancers or Alzheimer's disease, likely caused by misfolded protein forming agglomerates, etc. The ability to regulate gene expression holds a promise to treat genetic malfunctions by suppression of defective gene with the RNA interference (RNAi). The use of RNA derived constructs is valuable and offers multiplicity of possible architectures that can be further utilized to design molecular device for a given target.

The purpose of presented thesis is to develop a structural RNA (tectoRNA) conjugate with spherical gold nanoparticle (AuNP). This approach combines two fields of nanotechnology and has a potential to create a uniform platform for a delivery of regulatory elements. Nanotechnology of nucleic acids has been studied since the basis or rational design of DNA was introduced. The use of RNA is of particular interest due to its established role in regulating gene expression through RNAi. The second area of nanotechnology implemented in this project is the nanotechnology of noble metals,

specifically gold. Gold nanoparticles are known for their specific properties, which make them often used for bio-imaging, resonance scattering, energy transfer, biosensors and to study for instance cell endocytosis. Here, we developed a new generation of spherical nucleic acids in which AuNPs are conjugated to a structural RNA trimer carrying three regulatory sequences and a thiol linker. Similar approach was previously used to make spherical nucleic acids, where the AuNP was conjugated with regulatory siRNAs. Introduction of the tectoRNA constructs into a spherical layout gives a chance to increase the local concentration of regulatory elements, implement proportional amounts of different regulatory sequences and finally improve regulatory effect of such molecules. It can therefore become a superior system for delivery of regulatory elements, that gives a solution for future drug design, where RNA-AuNP construct has a capacity to bring abundance of regulatory sequences to the cell.