Title: Spectroscopic study of key biomolecular interactions for therapeutic applications of modified oligonucleotides

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Abstract: This dissertation thesis is focused on study of biomolecular interactions that are crucial for therapeutic applications of modified oligonucleotides. Interactions of nucleic acids, in particular hybrid DNA: RNA duplexes with fully complementary sequences, as well as DNA: RNA duplexes with a central mismatch were studied. The molecular model was created. With this model the influence of five different chemical modifications in the DNA strand to its binding ability was studied. Structural changes were characterized by Raman spectroscopy using a precise differential and double differential spectra. These data were supplemented by thermodynamic parameters computed from melting curves obtained by UV absorption spectroscopy. Furthermore, the Raman spectroscopy was applied on study of conformation changes in the RNase L protein. These changes in the conformation occur after ligand binding, which in this case, either natural or modified short oligonucleotide. Measurement of RNase L was performed using a special experimental technique – DCDR spectroscopy.

Keywords: Biomolecular interactions, proteins, nucleic acids, Raman spectroscopy, Antisense