

Abstract

The ability of nucleic acids to fold into higher-order non-canonical structures has been postulated and later proven to play an indispensable role in many biological and biomedical processes, such as control of promoter activity and genome instability. G-quadruplexes represent a family of structures adopted by both DNA and RNA sequences rich in guanine. Due to their overrepresentation in regions implicated in essential cellular processes, mutations in G-quadruplex forming sequences often result in development of various diseases, including cancer. Several approaches with the potential to elucidate therapeutical response by manipulating G-quadruplex structures found in promoter and telomeric regions have been suggested.

This dissertation thesis summarizes results from two projects focused on covalent and non-covalent interactions of biologically relevant G-quadruplexes with small molecules. First, we aimed to design stable G-quadruplex decoys by incorporation of pyrene-conjugated nucleotide in the sequence of the *c-kit2* G-quadruplex located in the *KIT* proto-oncogene. If successful, G-quadruplex decoys are expected to sequester essential transcription factors and thus suppress *KIT* expression and consequently cell growth and cancer progression. We provide structural details of three thermally stable G-quadruplex decoys, which vary in accessibility of outer G-quartets. Our results serve as guideline for design of G-quadruplex decoys derived from other biologically relevant G-rich sequences. Secondly, we studied binding of a novel osmium polypyridyl probe to the structure of G-quadruplexes derived from promoter of the *cMYC* proto-oncogene and from human telomere. Our NMR studies revealed that the enantioselectivity of binding is greatly dependent on the G-quadruplex topology. We show the importance of combining structural and photophysical studies to characterize the impact of binding on G-quadruplex structure and on the luminescence response.