ABSTRACT

The project aims to investigate unorthodox quadruplex structures and their interaction with two specific ligands. G quadruplexes have emerged as a prominent class of nucleic acid secondary structures that are relevant for disease therapeutics and diagnosis. Thousands of ligands have been designed till date that recognize quadruplexes and may lead to stabilization or destabilization of the structure upon binding. We intend to visualize such changes using dimeric carbocyanine G quadruplex-selective dyes that have been developed in our laboratory as visualization can aid in understanding functional aspects of G quadruplexes in our genome. We also aim to study the interplay between the dye and the ligand upon binding to G quadruplex structures. The ligand olaparib is an anti-cancer drug and PARP inhibitor which binds to PARP's (DNA damage repair protein) catalytic domain thus inhibiting PARP to recruit other repair proteins to the site of damaged DNA. PARP is known to bind to G rich regions in telomere. Thus, there is an indirect quadruplex interaction of olaparib. Our results indicate promising ability of our dyes to reflect the changes occurring in cells upon treatment with the anti-cancer drug and also some interplay which is more evident in a specific topology of G quadruplex compared to the other. This interplay is also dependent on the order of binding of the drug and dye to the quadruplexes.

Keywords: G quadruplex, dimeric carbocyanine, quadruplex selective dye, visualization, PARP, olaparib.