Antibody targeting anti-parallel topology of human telomeric G-quadruplex DNA

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Genomic DNA has the capacity to form alternative structures to the canonical double helix. Among them G-quadruplexes (G4s) are tetrahelix structures that arise from G-rich genomic regions and result from the self-assembly of guanine residues into quartets, which are further stabilized by π-stacking interactions and coordination with metal cations such as K^+ or Na^+. Numerous *in vitro* studies have shown that G4s are highly susceptible to adopt multiple topologies, which exist in dynamic equilibrium. G-quadruplexes are known to play crucial roles in various cellular processes, including transcription regulation, DNA replication, and telomere maintenance. Dysregulation of G4 structures has been linked to several diseases, such as cancer and neurodegenerative disorders.

To investigate the structural and functional properties of G4 DNA in cells, few G4 antibodies have been identified. Most of them, including commercially available BG4, recognize the G4 structure versus duplex DNA but are not specific for a particular topology, in particular to to differentiate between parallel and antiparallel G4 conformations[1]. To develop new antibodies specific to antiparallel conformation, we have used constrained antiparallel G4 telomeric biomolecular system[2] which has been found highly stable allowing the selection of antibodies using phage display method.

In this communication, we will show the use of Elisa and Bio-Layer Interferometry for the studies of the affinity of two selected antibodies and we have demonstrated that these two new antibodies are highly selective for G4 telomeric DNA versus duplex and single-stranded DNA. Furthermore these antibodies have been used for cell imaging to detect telomeric G4 DNA.

References:

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