Assembly and applications of unusual nucleic acid structures

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G-rich and C-rich DNA and RNA can exploit non-canonical nucleobase interactions to form multi-strand unusual nucleic acid structures such as G-triplex (G3) and G/C tetraplexes (G-quadruplex (G4) and i-motif (C4)). There are now compelling evidences demonstrating that those structures form in key regulatory regions of genomes and transcriptomes where they can be involved in normal and pathological cellular processes. Therefore, the identification of chemical probes and drug candidates capable of specifically binding and/or stabilizing those structures is of great interest. On the other hand, the particular features of those unusual nucleic acid structures have been exploited to develop potent aptamers, catalysts and probes.

Herein, I will present our recent efforts to assemble peptide-DNA conjugates that can fold into stable and well-defined G3 and G4 structures and the use of those structural mimics to 1/ benchmark the affinity/specificity of state-of-the-art G4 binding ligands, 2/ identify the cellular binding partners of G4 via pull-down assays, 3/ design G4 based antiviral aptamers and enzyme mimicking catalysts. I will also discuss our on-going efforts to develop G4-specific ligands through combinatorial approaches.