DNA nanostructures involving unusual structures: i-motif and G-quadruplexes.

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Most DNA-based higher order structures are based on DNA duplexes stabilized by Watson-Crick base pairs. However, a number of non-classical pairing patterns are possible between or within DNA strands. These interactions result in the formation of unusual structures, among them Gquadruplexes and i-motifs (Fig. 1). These structures have clear advantages over conventional duplex DNA, such as enhanced thermal stability, conductivity, and sensitivity to chemical stimuli (for a review: (1))

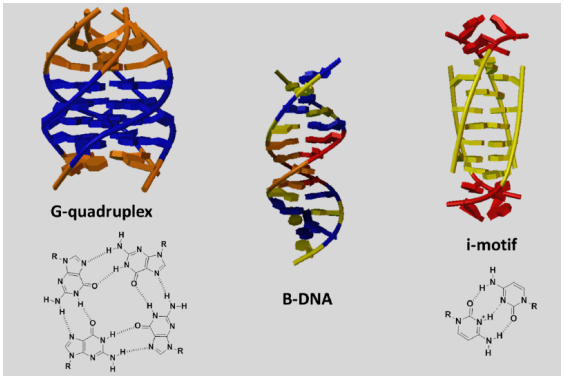

Figure 1: DNA double-helix (center); G-quadruplex and corresponding G-quartet (left) and i-motif and C.C+ base pair (right)

G-quadruplexes (G4) are formed with G-rich DNA and RNA sequences. A major drawback of G4 designs is the lack of control over the assembly process. We recently provided solutions to this problem (2, 3). In addition, we designed biosensors based on Gquadruplex formation (4) and used G4 structures to control DNA origami operations (5). Finally, we recently demonstrated that G-rich DNA sequences may function as a double switch whose function is based on different triggers provided that their secondary (6).

The DNA i-motif is formed under slightly acidic conditions from cytosine rich DNA sequences. We have shown the formation of a "double quadruplex" structure with i-motif and G4 structures on the same strand. The structural switching can be employed as a NOTIF logic gate (7). I-motif DNA structures have actually been extensively used in the fabrication of nanodevices, biosensors and delivery systems, taking advantage of their exquisite pH-sensitivity. Using scaffolding templates, we provide evidence that i-motif can be formed at physiological pH, offering new perspective for the design of DNA-based pHnanosensors acting in a physiological pH range.

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(1) Yatsunyk, Mendoza & Mergny., Acc. Chem. Res. 2014, 47: 1836
(2) Yatsunyk et al, ACS Nano 2013, 7: 5701
(3) Mendoza et al., Chem. Eur. J. 2015, 21: 6732
(4) Lim et al., Chem. Sci. 2015, 6: 4284
(5) Mendoza et al., Nano Letters. 2016, 16: 624
(6) Largy et al., J. Am. Chem. Soc. 2016, in press. DOI: 10.1021/jacs.5b13130.
(7) Zhou et al., Angewandte Chem. Int. Ed. 2013, 52: 7742