MS7-P7 X-ray crystallographic and photophysical studies of DNA i-motifs

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An i-motif is a four stranded structure made of cytosine-rich DNA sequences. Its sequence is usually in the format of $C_{2\text{-}5}L_{1\text{-}9}C_{2\text{-}5}L_{1\text{-}9}C_{2\text{-}5}L_{1\text{-}9}C_{2\text{-}5}$, where C is cytosine and L represents any other base. The conformational change from the C-rich single strand DNA to i-motif takes place between pH 5 and 6.7. These acidic conditions help two parallel i-motif duplexes "zip" together in an antiparallel orientation by protonating N3 in cytosines to create hemiprotonated $C\text{-}C^+$ base pairs (fig. 1).[1]

The i-motif can form as either an inter- or an intramolecular structure. However, only six i-motif crystal structures have been reported on the NDB; all of which are tetramolecular, even though i-motifs *in vivo* would exist as unimolecular. The c-Myc, Bcl-2 and hTERT i-motifs are all unimolecular and are present in the promoter regions of their respective oncogenes.[2] Like the guanine rich G-quadruplex, the presence of a cytosine rich sequence has also been detected within the promoter region of the human telomeric and centromeric DNA, making i-motifs an attractive subject for gene transcription modulation.

UV and synchrotron radiation CD (srCD; beamline B23 at Diamond Light Source) spectroscopy were used to study the structural stability of intramolecular i-motifs. Our results showed that i-motifs with shorter loop lengths exhibit the highest stability.[3] Crystallisation trials based on these initial results will be discussed along with previously recorded i-motif crystals grown in new conditions. We will also be reporting the diffraction of $d(CCCT)_4$ crystals at 0.68 Å at beamline I02, illustrating the advances in modern-day DNA crystallography via synchrotron radiation. Combination of results from the mentioned instrumental approaches shows that these methods are actually complementary.

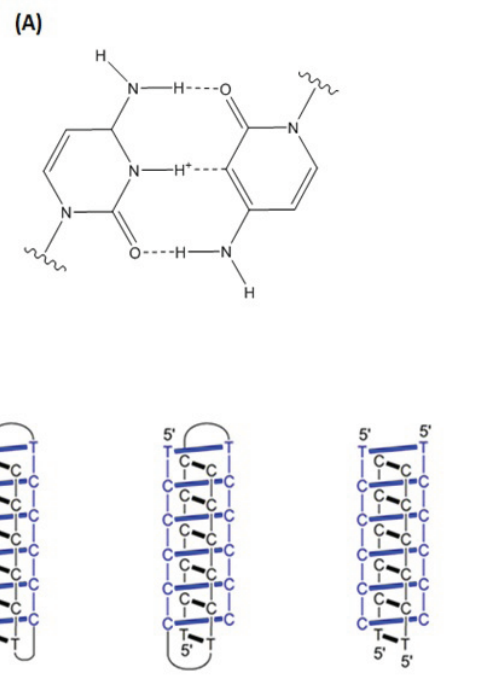

Figure 1. (A) $C\text{-}C^+$ base pairing in i-motifs. (B) Schematic diagrams of unimolecular (left) bimolecular (middle) and tetramolecular (right) i-motifs.

Keywords: i-motif, DNA, srCD

References

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