Photophysics of Thienoguanosine Tautomers: Application to the labeling of HIV-1 (-) Primer Binding Site sequence

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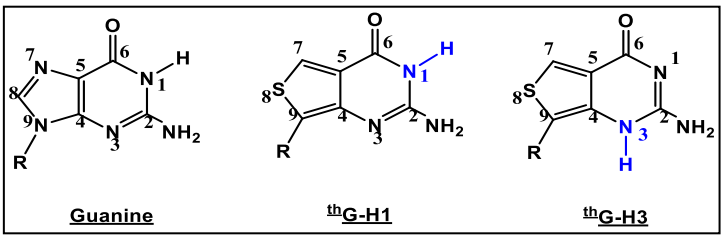

Figure 1. Structures of guanosine (G) and the two emissive tautomers of thienoguanosine (thG-H1 and thG–H3).

The design and successful implementation of fluorescent nucleobase analogues is a precarious art because it requires minimal structural and functional perturbation upon substitution in oligonucleotides. Newly developed fluorescent Guanosine analog, Thienoguanosine (thG) [1] Fig. 1, showed respectable quantum yield as free probe and incorporated in single and duplex structures, and also faithfully mimicked the W-C base pairing.[2] Dwelling into photophysics of free thG nucleoside revealed the existence of two ground state tautomers with shifted absorption and emission spectra.[3] They were identified as thG-H1 and thG-H3 keto-amino tautomers by DFT calculation. Microenvironment sensitivity of both the tautomers revealed that the equilibrium between the two tautomers is dependent on the hydrogen bond ability of the solvent. When incorporated in (-)PBS, the (-)DNA copy of HIV-1 primer binding site, both tautomers are observed. But in duplex (-)/(+)PBS, dthG-H1 tautomer is favored forming a stable W-C base pairing which was also supported by MD calculations showing that dthG-H1 forms three canonical hydrogen bonds. Meanwhile, comparison of matched with mismatched (-)/(+)PBS duplexes further revealed that the relative emission of thG-H3 can be used to detect single molecule polymorphism.

Refrences:

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