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Effects of F’, F-ANA and LNA Modification on the Stability of DNA G-quadruplex

Introduction and Objective

Quadruplex is formed by G-tetrads (Fig. a) stacking and it forms at Guanine-rich region. G-quadruplex is reported to have anti-cancer and anti-HIV effect [1]. T0 quadruplex (Fig. b) studied in this project is in (4+0) conformation and has very high symmetry [2]. F’, F-ANA and LNA (Fig. d-f) are modified sugars and they are highly stable in biological condition, easy to synthesize and soluble in water. Thanks to these beneficial properties, F’, F-ANA and LNA are promising candidates for DNA and RNA based drug design [3-5]. In this project, The effects of F’, F-ANA and LNA modifications on thermal stability of G-quadruplex were studied on the platform of T0 G-quadruplex and characterized by UV melting.

Results

- F’ does not alter thermal stability of modified quadruplex.
- F-ANA can stabilize most positions.
- LNA strongly destabilizes 3’ layer turning points but can strongly stabilize other positions.
- 3’ layer turning is more stringent than 5’ layer turning.
- Reason for LNA’s strong de-stabilizing effect for 3’ layer turning points: extra rigid bridge caused LNA cannot accommodate the strain of loop turning.

When the loop strain is released, the Tm of T0-nT and T9-LNA-nT converges.

Conclusion

- F-ANA and LNA can site-specifically stabilize T0 but F’ modification does not have strong influence.
- LNA strongly destabilize the 3’ layer of T0 quadruplex because of the strain caused by short loop.

Reference


Project Title: Structural Basis for the Design of Anticancer Drugs Targeted to Quadruplex DNA and RNA

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