Title : Understanding quadruplex formation by C-rich DNA sequences: the i-motif		
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Research Area: Biophysics		
Methods: Steady-state and time-resolved spectroscopy (UV-absorbance, CD, Fluorescence),		
biochemical methods		

## PhD track subject

Non-canonical nucleic acids structures have emerged during the last decades as critical factors to modulate DNA and RNA transactions. Among them, i-motifs (i-DNA) represent unusual, fourstranded DNA structures present in key regions of the genome. The dynamics of i-DNA structures may be relevant for mediating key biological processes. In this context, we wish to understand the rules that govern the formation of i-DNA, their pH dependency, thermodynamics and folding kinetics by a wealth of complementary techniques ranging from biochemical studies to ultrafast time-resolved spectroscopy.

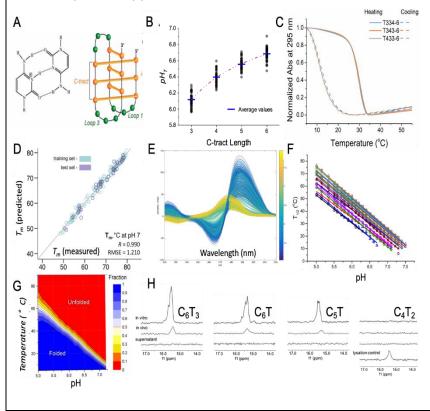


Figure 1: Analysis of i-DNA properties. **(A)** Cytosinecytosine<sup>+</sup> (C:C<sup>+</sup>) base pair (*left*) and schematic representation of an i-motif structure (right) (B) pH of mid-transition as function of C-track length. (C) Melting profiles at neutral pH for three different sequences: а hysteresis phenomenon is clearly visible. (D) Machine learning allows a reliable prediction of i-DNA stability. (E) Superimposition of 2500 CD spectra of various sequences at different pH. (F) Stability of i-DNA forming sequences as a function of pH for 20 different sequences. (G) Example of a phase diagram for an i-DNA forming sequence. (H) In cell and in vitro imino <sup>1</sup>H NMR spectra of four different C-rich motifs;

## References:

- 1. Cheng M, Chen J, Ju H, Zhou J, <u>Mergny JL</u>, Drivers of i-DNA formation in a variety of environments revealed by four-dimensional UV melting and annealing. **J Am Chem Soc**. (2021) <u>143</u>, 7792-7807
- Cheng M, Qiu D, Tamon L, Ištvánková E, Víšková P, Amrane S, Guédin A, Chen J, Lacroix L, Ju H, Trantírek L, Sahakyan AB, Zhou J, <u>Mergny JL</u>. Thermal and pH stabilities of i-DNA: confronting in vitro experiments with models and in-cell NMR data. Angew Chem Int Ed Engl. (2021) <u>60</u>, 10286-10294. doi: 10.1002/anie.202016801
- Iaccarino N, Cheng M, Qiu D, Pagano B, Amato J, Di Porzio A, Zhou J, Randazzo A, <u>Mergny JL</u>. Effects of sequence and base composition on the CD and TDS profiles of i-DNA. Angew Chem Int Ed Engl. (2021) <u>60</u>, 10295-10303. doi: 10.1002/anie.202016822
- 4. <u>Mergny JL</u>, Sen D. DNA Quadruple Helices in Nanotechnology. **Chem Rev.** 2019, 119, 6290-6325. doi: 10.1021/acs.chemrev.8b00629
- 5. <u>Hache F</u>, Changenet P. Multiscale conformational dynamics probed by time-resolved circular dichroism from seconds to picoseconds. **Chirality** 2021, 33, 747. doi: 10.1002/chir.23359