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### Targeting Quadruplex Nucleic Acids: From Chemical Biology Tools to Drug Prototypes

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For many years our research efforts have been focused on the design of small molecules for probing nucleic acid structures. Our targets are more specifically tetrahelical secondary structures such as G-quadruplexes (G4) that can be found in Guanine-rich regions. These structures are involved in various genomic dysfunctions and may ultimately cause genetic instability related to cancer development.<sup>1</sup> Our primary aim is to provide chemical biology tools for a better understanding of the roles of these structures. Our secondary aim is to evaluate the anticancer therapeutic potential of quadruplex-targeted agents.

A large number of compounds have been developed for targeting quadruplexes but few display the criteria of selectivity required for in-cell probing.<sup>2</sup> We have contributed to develop the bisquinolinium phenanthroline compounds (PhenDC) that rank amongst the best G4 probes both in terms of affinity and selectivity and which are usable in yeast and mammalian cells.<sup>3</sup> We will give a short overview of recent chemical developments of these agents, of their use for probing quadruplex formation in cells and of their anticancer drug properties.<sup>4-6</sup>

#### References:

- 1- N. Maizels, G4 motifs in human genes *Ann. N.Y. Acad. Sci.* **2012**, 1267, 53.
- 2- D. Monchaud and M.-P. Teulade-Fichou, A Hitchhiker guide to G-quadruplex ligands, *Org. Biomol. Chem.* **2008**, 6, 627.
- 3- a) De Cian et al *J. Amer. Chem. Soc.* **2007**, 129, 1856. b) W.J Chung et al. *Angew. Chem. Int. Ed.* **2014**, 53, 999. c) J. Lefebvre et al. *Angew. Chemie Int. Ed.* **2017**, 56, 11365.
- 4- A. Piazza et al. *Nucleic Acid Res* **2010**, 38, 4337.
- 5- D. Verga et al. *J. Mol. Biol. & Mol. Imaging* **2017**, 4(1), 1029.
- 6- M.-J. Lista et al. *Nature Comm.* **2017**, 7, 435-444.

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