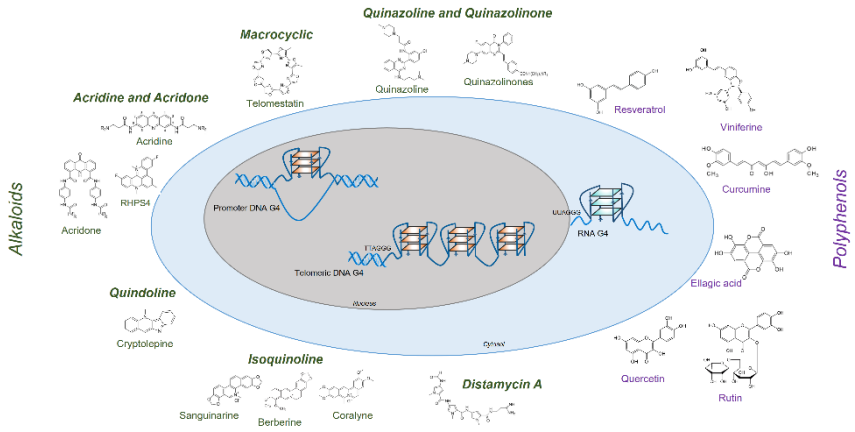
Nucleic acids as target of natural small molecules

Dr. Federica Moraca

Universitá "Federico II" di Napoli

Abstract

Deoxyribonucleic (DNA) and Ribonucleic (RNA) acids are perhaps the most important macromolecules in cell biology. Specifically, DNA is the repository of the genetic information in the cell, whereas RNA carries out a broad range of functions from reading to translating genetic information that underpins all cell life [1]. Besides their canonical base-pairing structures and biological functions, it has been widely demonstrated that both DNA and RNA nucleic acids can adopt also non-canonical higher-order structures called G-quadruplexes (G4s) formed through self-recognition of guanines into stacked tetrads so called G-quartet [2-3]. Several biophysical and structural studies evidence such G4 formation in regulatory regions, such as human telomeres, oncogene-promoter regions, untranslated regions of mRNA, exerting a varity of cellular processes ranging from transcription and translation to the genome instability and cancer, thus emerging as a new class of molecular targets for drug development [4]. Indeed, targeting nucleic acids by small molecules has been the focus of many effective therapeutic strategies, in order to develop new more effective compounds, particularly natural product based [5]. Natural small molecules binding G4s have proven, in fact, to be a new class of anticancer agents. Notably, alkaloids and polyphenols are an important source of G-quadruplex ligands and have significant bioactivities in anticancer therapy [6-7]. Taken togheter, all these evidences highlight the importance of natural products as innovative source with anticancer properties and as starting point for natural-inspired drug discovery.



1. Minchin S.; Lodge, J. *Essays Biochem.*, 63, (2019) 433-456.
2. Biffi, G.; Di Antonio, M.; Tannahill, D. et al. *Nat. Chem.*, 6, (2014) 75–80.
3. Biffi, G.; Tannahill, D.; McCafferty, J. et al. *Nat. Chem.,* 5, (2013) 182–186.
4. Varshney, D.; Spiegel, J. *et al. Nat. Rev. Mol. Cell. Biol.*, 21, (2020) 459-474.
5. Basu, A.; Kumar, G.S.; *Biochim. Biophys. Acta Gen. Subj.*, 1862, (2018) 1995-2016.
6. Xiong, Y.X.; Huang, Z.S. *et al. Eur. J. Med. Chem.,* 97, (2015) 538-51.
7. Pattanayak, R.; Basak, P. *et al. Int. J. Biol. Macromol.,* 89, (2016) 228-37.