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ATTI DEL CONGRESSO

CSB-PO-08 Synthesis and characterization of a mini-library of new conjugated d(TGGGAG) oligonucleotides with potential anti-HIV activity.

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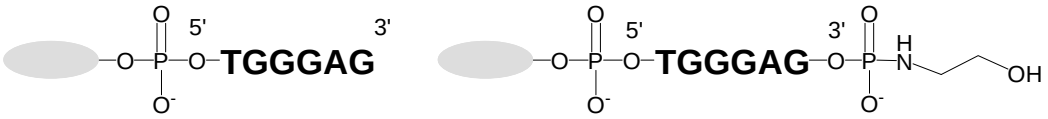
In the search for ODNs endowed with relevant antiviral properties, Hotoda and coworkers [1] investigated a series of G-quadruplex-forming ODNs, finally focusing on modified d(TGGGAG) ODNs conjugated with aromatic residues at the 5-end. These were found to exhibit potent anti-HIV activity associated with low cytotoxicity when carrying at the 5′-end bulky aromatic residues. Recently we described a general approach to obtain a mini library of new d(TGGGAG) ODNs, conjugated with different aromatic groups at the 5'-end through a phosphodiester bond [2]. Several modified sequences showed pronounced anti-HIV-1 activity and they showed high binding affinities for the HIV-1 envelope gp120 and gp41. In these structures the 5-end residues play a major role on the G-quadruplex stability, dramatically enhancing stability of the quadruplex complexes (ΔTm>20°C).

With the final goal to expand the repertoire of accessible end-modified G-rich ODNs, and to get a more complete picture of their structure-activity relationships, we describe herein the synthesis and characterization of a mini-library of new d(5'TGGGAG3') carrying hydrophobic groups at the 5'-end and 2-hydroxyethylphosphate group at the 3'-end, connected through phosphodiester and phosphoramidate bonds, respectively. In order to study the influence of the conjugation at the ends of the oligonucleotide chains on their ability to form quadruplex structures, a CD analysis was undertaken on the conjugated oligomers in comparison with the corresponding unmodified d(TGGGAG) oligomer.



[1] H. Hotoda, M. Koizumi, R. Koga, et al. *J. Med. Chem.*, **1998**, *41*, 3655–3663.
[2] G. Di Fabio, J. D'Onofrio, M. Chiapparelli, B. Hoorelbeke, D. Montesarchio, J. Balzarini and Lorenzo De Napoli, *Chem. Commun.*, **2011**, 2363 – 2365.
[3] J. D'Onofrio, D. Montesarchio, L. De Napoli, G. Di Fabio, *Org. Lett.*, **2005**, *7*, 4927-4930.