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ATTI DEL CONGRESSO

CSB-PO-07 Harpin oligonucleotides forming G-quadruplexes: new aptamers with potential anti-HIV activity

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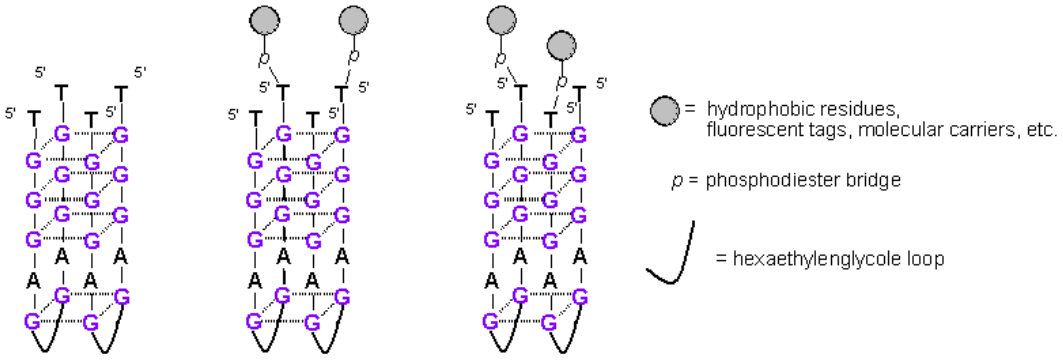
Several G-rich synthetic oligodeoxyribonucleotides (ODNs) have shown promising biological properties, ranging from anticancer to anti-HIV activities. G-quadruplex formation was found to be a crucial prerequisite in determining these biological effects [1]. Aptamers exhibiting anti-HIV activity represent an important class of potential therapeutics [2]. Recently we described the synthesis and characterization of new d(TGGGAG) ODNs, conjugated with different aromatic groups at the 5'-end through a phosphodiester bond [3]. The modified sequences showed a parallel stranded tetramolecular G-quadruplexes CD profile and a pronounced anti-HIV-1 activity.

Herein, with the aim to use d(TGGGAG) as a lead sequence for a more effective anti-HIV agent, we propose the fully automated synthesis of new ODNs containing two d(TGGGAG) sequences whose 3-ends are joint by an hexaethylenglycole loop. CD analysis was undertaken on the 3'-3' linked d(TGGGAG) *hairpins* in comparison with the corresponding unmodified oligomers. Besides, in order to study the influence of the conjugation at the ends of the *harpin* chains on their ability to stabilize quadruplex structures and on their anti-HIV activity, different conjugated oligomers have been studied.



[1] B. Gatto, M. Palumbo and C. Sissi, *Curr. Med. Chem.*, **2009**, *16*, 1248–1265.
[2] H. Hotoda, M. Koizumi, et. al., *J. Med. Chem.*, **1998**, *41*, 3655–3663.
[3] G. Di Fabio, J. D'Onofrio, M. Chiapparelli, B. Hoorelbeke, D. Montesarchio, J. Balzarini and Lorenzo De Napoli, *Chem. Commun.*, **2011**, 2363 – 2365.