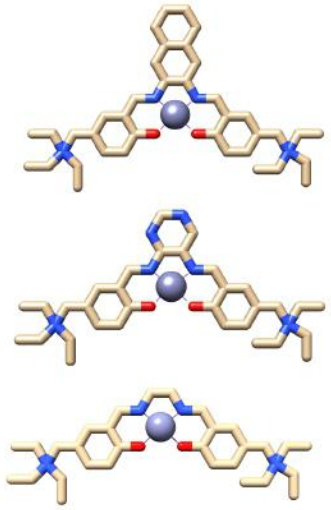
# Duplex and G-quadruplex DNA-binding of synthetic molecules in the search of novel anticancer drugs: experimental and computational studies

Giampaolo Barone[a,b]
[a] *Department of Biological, Chemical and Pharmaceutical Sciences and Technologies, Viale delle Scienze, Edificio 17, 90128 Palermo, Italy.*
[b] *Euro-Mediterranean Institute of Science and Technology (IEMEST), Via Emerico Amari 123, 90139 Palermo, Italy.*

e-mail: giampaolo.barone@unipa.it

Nickel(II), copper(II) and zinc(II) complexes of $N_2O_2$ tetradentate Schiff base ligands strongly interact with B-DNA, usually by groove-binding and/or by intercalation [1]. It has been also shown that the presence of aromatic substituents on the N,N' bridge make them suitable G-quadruplex binders. In this context, we have recently investigated the binding toward duplex and G-quadruplex DNA of nickel(II), copper(II) and zinc(II) complexes of Salen derivatives (see Figure), by spectroscopic and computational approaches [2,3]. The compounds show also biological activity against human cancer cell lines.



Different substituents are currently considered on the N,N'-bridge, in order to increase their selectivity towards telomeric and oncogene promoter G-quadruplexes, targeting their grooves rather than their aromatic ends. The impact of the metal center on the quadruplex binding ability is also taken into account. The competitive binding toward duplex and G-quadruplex DNA in aqueous solution is addressed through circular dichroism, absorption spectroscopy and fluorescence resonance energy transfer (FRET) measurements. Atomic level details of the metal complex-DNA supramolecular systems are obtained through computational investigations, consisting of molecular dynamics (MD) simulations and by density functional theory/molecular mechanics (DFT/MM) calculations, providing support for the interpretation of the binding mechanism

**References**

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