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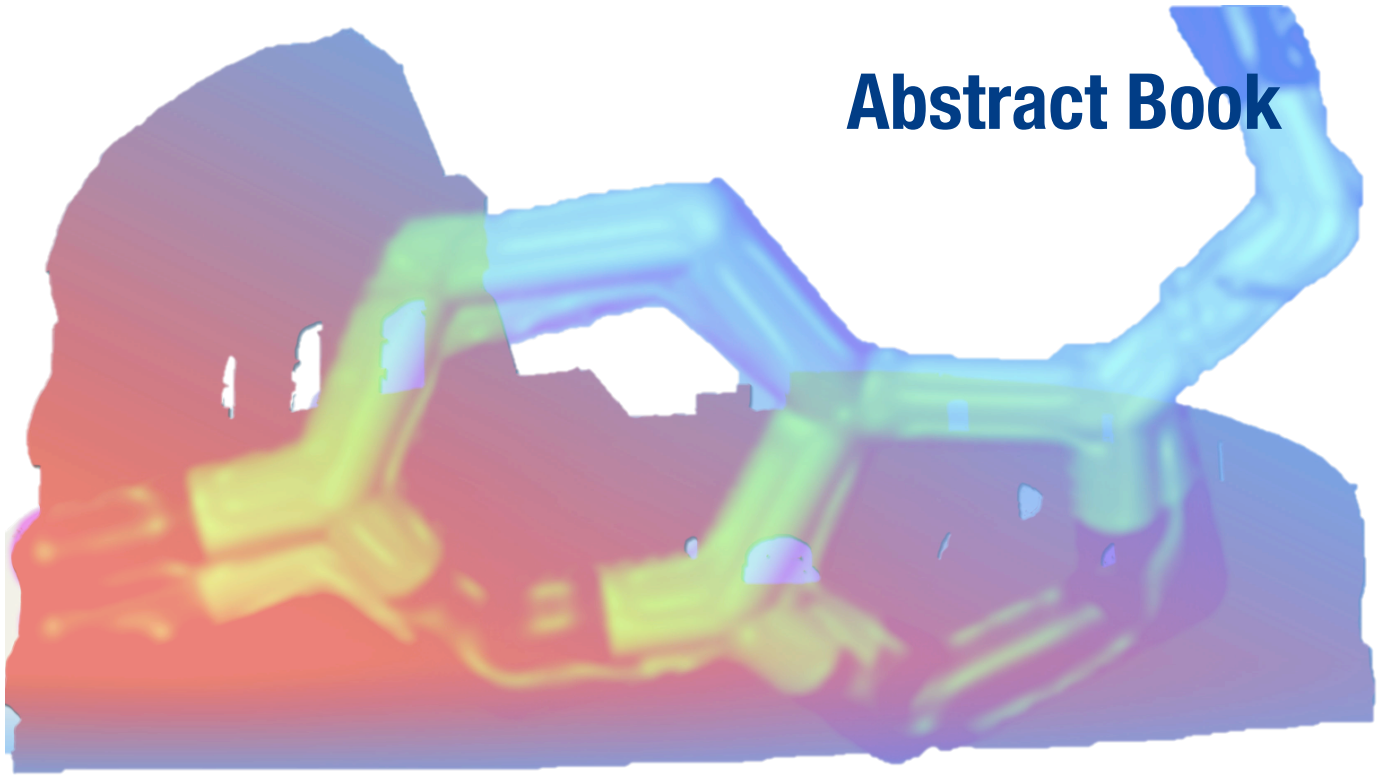

Abstract Book

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SELECTIVE G-QUADRUPLEX STABILIZERS: SALPHEN-LIKE COMPLEXES WITH ANTIPROLIFERATIVE ACTIVITY

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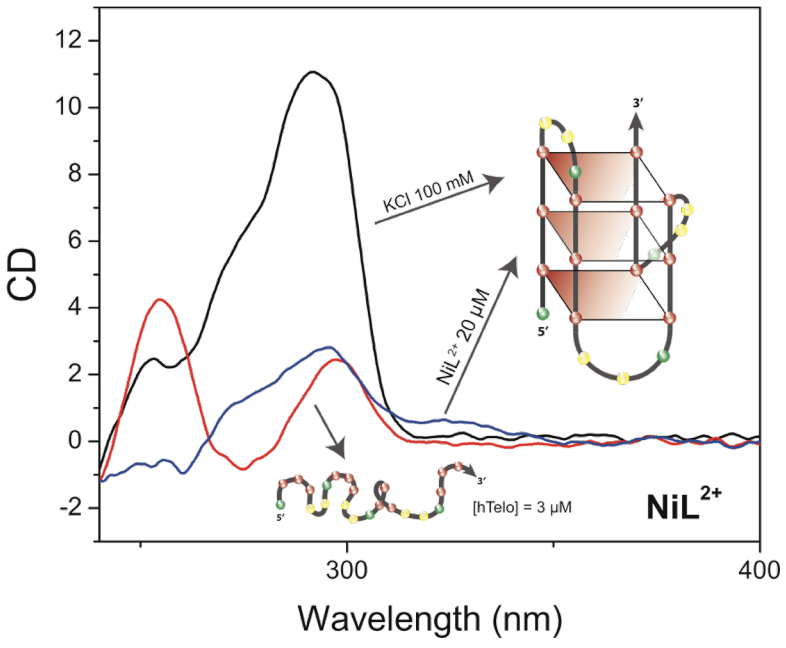
The main goal of anticancer research is to develop therapeutic agents with improved biological activity against cancer cells. Chasing this purpose, recent years have seen an increased interest in the study of small molecules able to bind the deoxyribonucleic acid (DNA) when it assumes secondary structures known as G-quadruplexes (G4) in preference over its B form.[1] G4-DNAs are found in chromosomal DNA mainly in telomeric sequences, but also in some sequences that seem to play important roles in regulating the expression of genes (among them some oncogenes such as *c-myc*).[1,2]

Schiff base complexes derived from *N*,*N*′-bridged tetradentate ligands involving N_2O_2 donor atoms present very favourable features to act as G4 binders. Thus, a series of square-planar and square pyramidal metal complexes, ML^{2+} (M = Ni, Cu, and Zn), have been synthesized and characterized. Their affinity for wild-type *hTelo* and *c-myc* G-quadruplexes DNA and for ct-DNA was investigated by UV absorption spectroscopy, circular dichroism and viscosimetry. The experimental data together with computational approaches collectively suggest that the complexes bind effectively to G-quadruplexes by direct end-stacking with high selectivity with respect to B-DNA. The best G4-DNA stabilizer was found to be NiL^{2+} with a binding constant of about 6.0×10^6 M^{-1}. More interestingly NiL^{2+} is able to induce conformational changes favoring *hTelo* quadruplex DNA formation without the presence of KCl.



The compounds showed concentration- and time-dependent cytotoxity towards HeLa and MCF-7 tumor cell lines. Furthermore, the complexes achieved significant effects on cell cycle distribution with G2/M arrest in HeLa cells and G0/G1 arrest in MCF-7 cells. The distinct cell cycle arrest phase observed in cells treated with the ML^{2+} complexes might be due to the different consequences of DNA binding properties in different cancer cells.

References

1) Balasubramanian, S. *et al. Nat. Rev. Drug Discov.* **2011**, 10, 261–275.
2) Yang, D. *et al*. *Future Med. Chem.* **2010**, 2, 619–646.