

## Design of copper(II) complexes as potential anticancer drugs

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The fibroblast growth factor receptors (FGFR) are tyrosine kinases that are present in many types of endothelial and tumor cells and play an important role in cell growth, survival, and migration as well as in maintaining tumor angiogenesis (1). FGFR genetic alterations are frequently observed in cancer, suggesting that FGFR inhibition may be a promising therapy in patients harboring these lesions (2). In particular, molecules with structural properties similar to Ponatinib, a known inhibitor of FGFR, that shows a selective interaction for the ATP binding site of the isoform 4 of these receptors (FGFR4), are being considered. Molecular modeling studies have been conducted to design novel potential inhibitors of the FGFR4, starting from the crystallographic structure of Ponatinib complexed with this specific isoform (2), Fig. 1 left. The considered ligands must contain chelating coordination sites for copper(II) ions (Fig. 2 right). In fact, copper (II) complex are considered as promising anticancer agents (3,4). It is expected that, under intracellular hypoxic conditions, the spontaneous reduction to a lower oxidation state of the metal ion should occur, with consequent release of the ligand molecule and the subsequent interaction of the latter with the target biomolecule.

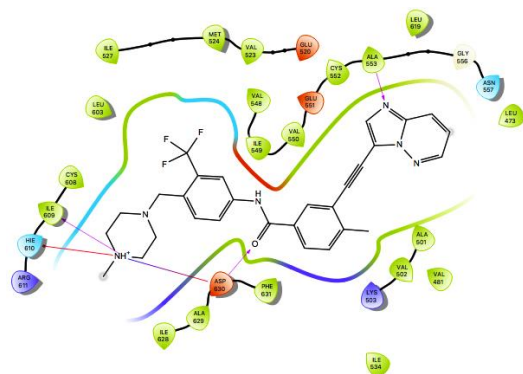


Figure 1

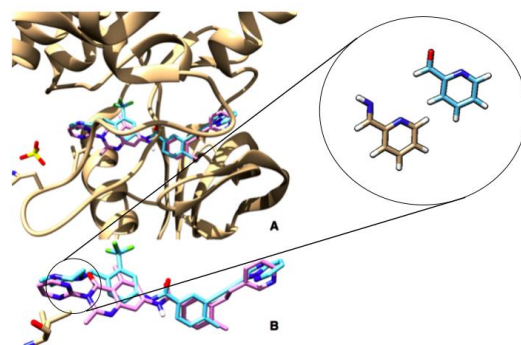


Figure 2

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