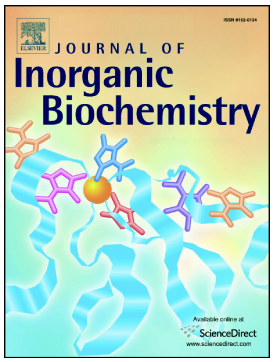

Anticancer copper complex with nucleus, mitochondrion and cyclooxygenase-2 as multiple targets

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PII: S0162-0134(18)30461-6
DOI: doi:10.1016/j.jinorgbio.2018.10.003
Reference: JIB 10577

To appear in: *Journal of Inorganic Biochemistry*

Received date: 3 August 2018
Revised date: 9 October 2018
Accepted date: 12 October 2018

Please cite this article as: Xiangchao Shi, Hongbao Fang, Yan Guo, Hao Yuan, Zijian Guo, Xiaoyong Wang , Anticancer copper complex with nucleus, mitochondrion and cyclooxygenase-2 as multiple targets. Jib (2018), doi:10.1016/j.jinorgbio.2018.10.003

Anticancer copper complex with nucleus, mitochondrion and cyclooxygenase-2 as multiple targets

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Abstract: Copper complexes are hopeful anticancer drugs due to their multifacet biological properties and high biocompatibility. Inflammatory environment plays an important role in tumor progression and affects the body response to chemotherapeutic agents. A copper(II) complex CuLA with a phenanthroline derivative N-(1,10-phenanthrolin-5-yl)-nonanamide (L) and two aspirin anions (A) as the ligands was synthesized. CuLA effectively induces mitochondrial dysfunction and promotes early-apoptosis in SKOV-3 cells; moreover, it suppresses the expression of cyclooxygenase-2, a key enzyme involved in inflammatory response, in lipopolysaccharide stimulated RAW 264.7 cells. By contrast, the analogue complex CuL without aspirin ligand shows similar influences on cellular redox homeostasis and cell cycle progression but relatively low cytotoxic activity due to its mild effect on mitochondrial function; more importantly, it lacks inhibition to cyclooxygenase-2. The results demonstrate that CuLA inhibits cancer cells through dual pathways involving DNA damage and mitochondrial dysfunction. The introduction of aspirin not only enhances the antitumour efficacy but also reduces the inflammatory threat. Copper complexes with both antitumor and anti-inflammatory activities may