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Electron-Transfer-Based Combination Therapy of Cisplatin with a Molecular Promoter for Cancer Treatment

Wednesday 15 June 2016 10:00 (15 minutes)

Cisplatin is a very widely used platinum-based chemotherapy drug and is the cornerstone agent in treating a variety of cancers, including ovarian cancer, testicular cancer, cervical cancer, bladder cancer, lung cancer, head and neck cancer, lymphoma, and brain tumors. It is one of the few curative anticancer agents. However, its clinical application is often limited by severe toxic side effects and resistance possessed by various cancers.

Our group has recently, through the femtomedicine approach, unraveled a new molecular mechanism of cisplatin. We found that cisplatin is extremely effective for the dissociative electron transfer (DET) reaction [1,2] to produce a reactive radical that causes DNA strand breaks, apoptosis and final clonogenic cell kill.

Based on this DET mechanism, it is proposed that cisplatin may be administered in combination with a biological electron donor PM to enhance the chemotherapeutic efficacy. We have obtained promising results in in vitro tests of a few combinations. Through cell survival experiments, MTT assays and clonogenic assays, it has been shown that our proposed combinations significantly enhance the cell-killing on cancer cells, but surprisingly, not on normal cells. Besides, γ-H2AX staining on treated cells indicates that more double strand breaks can be induced using our combination. In addition, measurements on caspase 3/7 activity clearly show an enhancement in the population of apoptotic cells using our combination. Xenograft mouse models have also proved the anti-cancer effect of our combination. Furthermore, spectroscopic measurement has confirmed the electron transfer reaction between cisplatin and PM. These results show great potential of the DET mechanism to improve the therapy of cancer using cisplatin.

[1] Lu, Q.-B., Kalantari, S., and Wang, C.-R. (2007) Electron transfer reaction mechanism of cisplatin with DNA at the molecular level. Mol. Pharm. 4, 624–8.

[2] Lu, Q.-B. (2007) Molecular reaction mechanisms of combination treatments of low-dose cisplatin with radiotherapy and photodynamic therapy. J. Med. Chem. 50, 2601–4.

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