

Employing siRNA tool and its delivery platforms in suppressing cisplatin resistance: Approaching to a new era of cancer chemotherapy

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Although chemotherapy is a first option in treatment of cancer patients, drug resistance has led to its failure, requiring strategies to overcome it. Cancer cells are capable of switching among molecular pathways to ensure their proliferation and metastasis, leading to their resistance to chemotherapy. The molecular pathways and mechanisms that are responsible for cancer progression and growth, can be negatively affected for providing chemosensitivity. Small interfering RNA (siRNA) is a powerful tool extensively applied in cancer therapy in both pre-clinical (in vitro and in vivo) and clinical studies because of its potential in suppressing tumor-promoting factors. As such oncogene pathways account for cisplatin (CP) resistance, their targeting by siRNA plays an important role in reversing chemoresistance. In the present review, application of siRNA for suppressing CP resistance is discussed. The first priority of using siRNA is sensitizing cancer cells to CP-mediated apoptosis via down-regulating survivin, ATG7, Bcl-2, Bcl-xl, and XIAP. The cancer stem cell properties and related molecular pathways including ID1, Oct-4 and nanog are inhibited by siRNA in CP sensitivity. Cell cycle arrest and enhanced accumulation of CP in cancer cells can be obtained using siRNA. In overcoming siRNA challenges such as off-targeting feature and degradation, carriers including nanoparticles and biological carriers have been applied. These carriers are important in enhancing cellular accumulation of siRNA, elevating gene silencing efficacy and reversing CP resistance.

Keywords: Cisplatin Small interfering RNA Chemoresistance Drug resistance Nanoparticle Biological carrier