A metal ion-drug-induced self-assembly nanosystems for augmented chemodynamic and chemotherapy synergetic anticancer therapy

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1. 簡述論文概要與重大發現：

奈米技術和化學動力療法(CDT)是當前癌症治療的熱門領域，而這項研究將兩者結合在一起，並與現有的化學療法結合，以實現化學動力療法與化療的協同抗癌療效。該奈米載體由碳點(Carbon dot)和富含銅離子的化合物組成，具有良好的穩定性和生物相容性。通過一系列體外和體內實驗，發現這種奈米載體能夠釋放大量的羥氧自由基（·OH），從而引起 4T1 細胞的氧化損傷和凋亡。此外，與化療藥物 doxorubicin(DOX)聯用後，該奈米載體還能促進藥物的轉運和攝取，並且增強了其抗腫瘤效果。該研究的重大發現是利用金屬離子和藥物誘導自組裝奈米載體，可以實現化學動力療法和化療藥物的協同抗癌效果。這種協同治療策略具有較好的安全性和生物相容性，未來可能成為一種重要的抗癌治療方法。

2. 對論文內容的提問：

A. 雖然這篇文章展示了這種基於金屬離子和藥物誘導的自組裝奈米載體對抗腫瘤的有效性，但是其在體內的毒性和生物相容性是否受到考慮？

B. 文章中未提到該奈米載體的成本和製造難度，這些因素是否會限制其在臨床上的應用？

3. 對論文的缺點與評論：

這篇文章的優點包括提出了一個新穎的利用化學動力療法和化學療法的聯合治療策略，並使用碳點作為載體以增強治療效果。此外，作者通過各種實驗驗證了該策略的有效性，並且解釋其作用機制。而這篇文章的缺點包括樣本量較小，以及缺乏進一步的體內實驗證明其安全性和有效性。此外，作者沒有進一步探討這種治療策略對其他癌症的應用，因此其廣泛應用的可行性需要進一步研究。

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ABSTRACT

The complexities in the integration of carrier materials and functional materials make it challenging to promote nanoprobes for clinical translation. Carrier-free self-assembled nanosystems have been proposed as a promising strategy for synergetic anticancer therapy. In this study, carbon dots, copper ions, and doxorubicin (DOX) were assembled into nanoparticles (CCD) to achieve augmented chemodynamic therapy (CDT). The assembled CCD NPs were biodegradable and responsive to GSH and acidic pH in the tumor microenvironment resulting in the release of the DOX, Cu^{2+}, and carbon dots. The intracellular H_2O_2 level was elevated by DOX activated the nicotinamide adenine dinucleotide phosphate oxidases. The GSH was depleted by Cu^{2+}, and the generated Cu^{+} as well as peroxidase-like carbon dots could catalyze the intracellular H_2O_2 to produce cytotoxic ·OH to achieve enhanced CDT effects. Chemotherapy effects were enhanced through increasing drug sensitivity and inhibiting drug efflux after the intracellular redox balance was broken by CCD NPs. The in vivo experiments revealed that CCD NPs possessed the excellent biocompatibility and synergistic anti-tumor ability, which could completely inhibit the growth of 4T1 tumors. As a novel carrier-free nanoprobes, CCD NPs with responsiveness to the tumor microenvironment may have great potential in cancer chemodynamic therapy with high specificity.

1. Introduction

Chemotherapy remains the main strategy of cancer treatment besides surgery and radiotherapy. Chemotherapy is able to eliminate residual lesions that failed to remove by radiotherapy and surgery, prolonging the survival of patients [1]. The chemotherapy drugs DOX and cisplatin are widely used in clinical, but their application is limited by severe side effects and multidrug resistance. Therefore, improving the efficiency of drug delivery and overcoming multidrug resistance are essential for chemotherapy [2]. The developments of nanotechnology hold new promises for drug delivery and enhanced chemotherapy efficacy. For example, nanomedicine can achieve targeted drug delivery, reducing drug damage to normal tissues and increasing drug accumulation at tumor sites [3]. In addition, combining chemotherapy with photothermal therapy (PTT), photodynamic therapy (PDT) and chemodynamic therapy (CDT) can enhance the effects of chemotherapy [4,5]. The glutathione (GSH) depletion and reactive oxygen species (ROS) generation at the tumor microenvironment by nanomaterials can break the redox balance of the tumor microenvironment to overcome multidrug resistance [6,7].

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