Anti-Cancer Drug Delivery Modeling in Nanomedicine with Combinatorial Image Analysis and Non-Linear Regression

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January 6, 2021

Abstract

Purpose: The field of cancer nanomedicine has made significant progress, but its clinical translation is impeded by many challenges, such as the difficulty in analysing intracellular anticancer drug release by the nanocarriers due to the lack of suitable tools. Here, we propose the development of a combinatorial imaging and analysis technique to evaluate anticancer drug such as doxorubicin HCl (DOX) released by a nanocarrier inside the HCT116 colon cancer cells and its subsequent intracellular accumulation. Procedure: Fluorescent cell images were captured and subjected to combined image analysis and machine learning based procedures to assess and quantify the delivery and retention rate of DOX inside the cancer cells by multifunctional CNT-DOX-Fe3O4nanocarrier. Results: We show that DOX in HCT116 cells was higher for multifunctional CNT-DOX-Fe3O4nanocarrierthan free DOX, indicating efficient and steady release of DOX as well as superior retentive property of the nanocarrier. Initially (1 h and 4 h) the luminance intensity of DOX in the cell cytoplasm delivered by CNT-DOX-Fe3O4nanocarrier was ˜0.34 times and ˜0.42 times lesser than that of free DOX delivered normally. However, at 24 h and 48 h post treatment the luminance intensity of DOX for CNT-DOX-Fe3O4nanocarrier was ˜1.98 times and 1.92 times higher than that of free DOX. Furthermore, the luminance intensity of DOX for CNT-DOX-Fe3O4in the whole cell was ˜1.35 times and ˜1.62 times higher than that of free DOX at 24h and 48 h, respectively. Conclusions: The high-throughput nature of our image analysis workflow allowed us to automate the process of DOX retention analysis, and enabled us to devise machine learning-based modeling to predict the percentage of anticancer drug retention in cells. The development of models to automatically quantify and predict intra-cellular drug release in cancer cells could benefit personalized treatments by optimizing the design of nanocarriers.

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