光觸發微脂粒系統之研發

Liposomal doxorubicin phototriggered release system

中文摘要

目前所使用的 Liposomal-Doxorubicin 雖然在臨床使用上的確具有降低副作用的效果，但是當微脂粒累積在腫瘤組織之後，由於釋放速率過慢，造成單位時間細胞內的 Doxorubicin (Dox) 濃度過低，因而限制了藥效。本實驗方向爲研發一種具有光觸發釋放能力的 Liposomal-Doxorubucin-Hematporphyrin (LDH)，利用紅光激發包覆在微脂粒脂雙層中的光感物質 Hematporphyrin (Hp)，使其產生自由基及單態氧，造成磷脂質脂肪酸鏈的過氧化作用，進而使微脂粒的穩定度降低，使包覆在微脂粒的 Dox 能夠釋放出來。

實驗採取傳統的薄膜水合法，並添加 Cholesterol (ch)，利用此方式可以穩定地同時包覆 Hp 以及 Dox，在不同配方的釋放速率結果發現，當配方中添加越多的 Cholesterol，添加越少的 L-α-Phosphatidylcholine (Egg PC)，藥物釋放的速率越慢，所製備的微脂粒在經過 635 nm 的紅光觸發後的確可以提高藥物釋放的速率，以及脂雙層的通透性，由細胞毒性測試結果證實，觀察到 A431 細胞在經過實驗所製備的 LDH 處理兩小時之後，結果發現在 LDH 那組給予光照的能量越高，對於細胞的毒性也越大

英文摘要

Using the Liposomal-Doxorubicin has indeed lowered the cardiac toxicity of Doxorubicin. However, release from the liposomes after accumulated in the cancerous tissue was too slow and resulted in low concentrations of doxorubicin in the target cells, and thus limits the effect of the treatment.

In this study, we used the red light to activate the Hematoporphyrin encapsulated in the lipid bilayer in the Liposomal-Doxorubicin-Hematoporphyrin system. After being activated, singlet oxygen as well as free radicals were formed and resulted in peroxidation of tht lipids, de-stablized the liposomes, and subsequently released the encapsulated Doxorubicin.

Liposomes were prepared by the traditional film-hydration method. Cholesterol was added to stabilize Hematoporphyrin and Doxorubicin in the liposomes. Release results showed that by increasing the cholesterol concentration or decreasing the L-α-Phosphatidylcholine (Egg PC) in the formulation, drug release was slower accordingly. After irradiated by 635 nm red light, drug release from the liposomes was faster and the bilayer permeability of the liposomes was increased. Cell toxicity

tests indicated that the toxicity was higher when the dosed cultured cells were exposed to higher light irradiation.