DUSP16 promotes cancer chemoresistance through regulation of mitochondria-mediated cell death

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1. 簡述論文的概要與重大發現：抗藥性是治療大多數人類腫瘤的主要障礙。癌症抗藥性是一種受多種機制影響的複雜現象。抗藥性可能從宿主因素內在產生，也可能通過癌細胞的遺傳或表觀遺傳改變而獲得。抗藥性可能賦予癌細胞調節藥物流出率、DNA 損傷修復過程以及影響細胞存活和死亡的信號通路的能力。

   DUSP16 最初被確定為一種抑制 p38 和 JNK 的蛋白質，在癌細胞中的過表達導致化療治療後對細胞死亡的抵抗力增加。從機制上講，DUSP16 抑制 JNK 和 p38 活化，從而減少線粒體中 BAX 的積累，從而減少細胞凋亡。

   這項研究中，我們表明具有較高 DUSP16 表達的癌細胞對化療處理後的細胞死亡具有更強的抵抗力。DUSP16 在癌細胞中的過表達導致在體外和體內用順鉑、卡鉑、奧沙利鉑、氟尿嘧啶等化療藥物治療後細胞死亡減少。DUSP16 水平與治療敏感性之間的相關性與 JNK/p38 活化、線粒體中 BAX 積累、細胞色素 *c* 釋放和半胱天冬酶 9/3 活化的變化有關。

2. 對論文內容的提問：DUSP16 會讓 cell 的細胞凋亡降低，但如果把 DUSP16 給抑制掉，雖然可以幫助減少抗藥性的產生，但會不會對細胞或其他細胞會不會有其他作用?因為 DSUP16 功能可能不只是造成抗藥性。

3. 論文的缺點與評論：本研究闡明了 DSUP16 在癌症裡所引導的抗藥性機制，並將 DUSP16 確定為化療療效的預後標誌物，並作為克服癌症化療抗藥性的治療靶點。

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DUSP16 promotes cancer chemoresistance through regulation of mitochondria-mediated cell death

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Drug resistance is a major obstacle to the treatment of most human tumors. In this study, we find that dual-specificity phosphatase 16 (DUSP16) regulates resistance to chemotherapy in nasopharyngeal carcinoma, colorectal cancer, gastric and breast cancer. Cancer cells expressing higher DUSP16 are intrinsically more resistant to chemotherapy-induced cell death than cells with lower DUSP16 expression. Overexpression of *DUSP16* in cancer cells leads to increased resistance to cell death upon chemotherapy treatment. In contrast, knockdown of *DUSP16* in cancer cells increases their sensitivity to treatment. Mechanistically, DUSP16 inhibits JNK and p38 activation, thereby reducing BAX accumulation in mitochondria to reduce apoptosis. Analysis of patient survival in head & neck cancer and breast cancer patient cohorts supports DUSP16 as a marker for sensitivity to chemotherapy and therapeutic outcome. This study therefore identifies DUSP16 as a prognostic marker for the efficacy of chemotherapy, and as a therapeutic target for overcoming chemoresistance in cancer.

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