

[1]秦霞,邱宗荫,邱峰,等.人肺腺癌耐药细胞株A549/CDDP中相关泛素化蛋白质研究[J].第三军医大学学报,2012,34(09):866-869.

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## 人肺腺癌耐药细胞株A549/CDDP中相关泛素化蛋白质研究

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Title: Ubiquitination-associated proteins in human lung adenocarcinoma cisplatin-resistant cell strain A549/CDDP

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关键词: A549细胞; A549/CDDP细胞; 丙酮酸激酶M2; 肿瘤耐药; 泛素化; SUMO化

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摘要: 目的 研究肺腺癌中与耐药相关的泛素化或类泛素化蛋白质及其与耐药的关系。方法 从经顺铂处理和未处理的A549细胞及其耐顺铂细胞株中分离泛素化、类泛素化蛋白质,通过1D SDS-PAGE和Chip HPLC-MS/MS分析鉴别蛋白,Western blot法验证质谱结果;MTT法检测细胞对顺铂的耐药性。结果 鉴定出发生类泛素化修饰蛋白质-PKM2,并发现其在耐药细胞株中低表达;以蛋白酶体抑制剂MG132干预细胞后,PKM2表达上调;CDDP和MG132联合作用细胞后,细胞耐药性下降。结论 细胞中PKM2表达水平与肿瘤细胞耐药程度呈负相关,PKM2受蛋白质类泛素化修饰-SUMO化修饰调节,提示PKM2可能与肿瘤耐药的发生密切相关。

Abstract: Objective Post-translational modification of protein was the most important regulatory mechanism of cell protein in playing biological functions. This study aimed to research ubiquitination or neddylation associated proteins in tumor drug resistance. Methods We employed 1D SDS-PAGE and Chip HPLC-MS/MS to separate and identify ubiquitinated or neddylated proteins from the lysates of CDDP treated or untreated A549 and A549/CDDP cells. Western blotting and confocal laser scanning microscopy were used to validate those results. The sensitivity of cisplatin to cells was determined by MTT assay. Results A SUMO protein pyruvate kinase M2 (PKM2) was identified which located in the cytoplasm and nucleus. The expression of PKM2 was milder in the A549/CDDP cells than in A549 cells, but it was up-regulated when A549/CDDP cells were treated with proteasome inhibitors MG132. Drug resistance was decreased when the A549 and A549/CDDP cells were treated with CDDP combined with MG132. Conclusion The expression of PKM2 is negatively correlated with drug resistance in tumor cells. The expression of PKM2 is

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regulated by SUMO which was a neddylation modification, suggesting that PKM2 might be involved in the development of drug resistance.

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秦霞, 邱宗荫, 邱峰, 等. 人肺腺癌耐药细胞株A549/CDDP中相关泛素化蛋白质研究[J]. 第三军医大学学报, 2012, 34(9): 866-869.

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