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论文

3-取代芳基氧化吲哚(PH II-7)对肿瘤细胞周期的影响

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摘要：

目的观察3-取代芳基氧化吲哚(PH II-7)对肿瘤细胞周期分布的影响，明确PH II-7的抗敏感肿瘤和耐药肿瘤的共同机制。方法用流式细胞仪检测细胞周期分布，Western印迹分析细胞周期相关蛋白的表达，^{3}H-TdR参入法检测细胞DNA合成，ELISA测定酪氨酸激酶的活性。结果PH II-7对多种肿瘤细胞（包括耐药细胞）的周期分布均有影响，阻滞细胞G_1期至S期的移行，细胞周期相关蛋白CDK2，Rb和c-myc的表达被抑制，Cyclin E的表达升高。PH II-7还可抑制^{3}H-TdR的参入，抑制EGFR的酪氨酸激酶的活性。结论抗耐药肿瘤新药PH II-7是一种细胞周期阻滞剂，可能是通过抑制CDK2而使肿瘤细胞阻滞在G_1期，同时也说明细胞周期阻滞可能是抗耐药肿瘤的新方向。

关键词： 氧化吲哚衍生物 细胞周期 多药耐药 肿瘤细胞株

Effects of 3-substituted aryl oxindole(PH II-7) on cell cycle of tumor cells

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Abstract:

AimTo study the antitumor mechanism of 3-substituted aryl oxindole (PH II-7) and determine its effects on cell cycle distribution of tumor cells. MethodsThe cell cycle distributions were determined with FACS. The cell cycle regulation-related proteins of K562 lysates were analyzed with Western Blot. The inhibition of PH II-7 on DNA synthesis of tumor cells were estimated though ^{3}H-thymidine incorporation and the tyrosine kinase activity of EGFR of A431 lysates was measured with ELISA. ResultsPH II-7 effected cell cycle distribution of several tumor cells, including multidrug resistant tumor cell lines, and accumulation of cells in the G_0-G_1 stages was observed. The cell cycle regulation-related proteins CDK2, Rb and c-myc were inhibited by PH II-7 in a dose dependent manner, whereas the expression of CyclinE was increased after exposure to PH II-7. Furthermore, PH II-7 2.0 mg·L^{-1} was shown to inhibit the incorporation of ^{3}H-thymidine into DNA, and 21.89%-41.29% of the PTK activity of EGFR in A431 lysates was inhibited by PH II-7 2-8 mg·L^{-1} in a dose-dependant manner. ConclusionPH II-7, a new anti-tumor agent, blocks the transition of cell cycle of tumor cells from G_1 to S phase by inhibition CDK2.

Keywords: cell cycle multidrug resistance tumor cell lines oxindoles

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