311~315.苹果酸舒尼替尼诱导高表达三磷酸腺苷结合转运蛋白G超家族成员2的耐药鼻咽癌细胞高表达NKG2D配体[J].黄宇贤,郭坤元,王 杨,陈锦章,宋朝阳.中国肿瘤生物治疗杂志,2008,15(4)

苹果酸舒尼替尼诱导高表达三磷酸腺苷结合转运蛋白G超家族成员2的耐药鼻咽癌细胞高表达NKG2D配体 点此下载全文

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摘要：

摘 要 目的: 探讨苹果酸舒尼替尼(sunitinib malate, SU11248)对高表达三磷酸腺苷结合转运蛋白G超家族成员2(ATP-binding cassette superfamily G member 2,ABCG2)耐药鼻咽癌细胞CNE2/DDP(ABCG2high CNE2/DDP)表达NKG2D配体的诱导作用。方法: 利用免疫磁珠技术分离ABCG2highCNE2/DDP细胞及同种异体反应性自然杀伤细胞(allo-reactive natural kill cell, Allo-NK)，流式细胞技术检测分离后细胞的纯度及苹果酸舒尼替尼处理前后ABCG2highCNE2/DDP细胞NKG2D配体表达率，LDH释放测定法检测苹果酸舒尼替尼处理前后ABCG2highCNE2/DDP细胞对Allo-NK细胞的杀伤敏感性。结果: ABCG2highCNE2/DDP细胞分离后ABCG2的表达率为(91.40±2.32)%，Allo-NK细胞分选后CD3－CD16+CD56+细胞的纯度达90%以上。经苹果酸舒尼替尼处理后,ABCG2highCNE2/DDP细胞的NKG2D配体MICA、MICB、ULBP1、ULBP2、ULBP3的表达率由药物处理之前的(2.92±0.33)%、(4.27±0.33)%、(5.80±0.62)%、(11.10±3.15)%、(7.75±1.14)%分别上升到(89.12±4.56)%、(66.10±2.22)%、(67.56±4.19)%、(69.37±8.83)%、(63.28±3.31)%。在效靶比为10∶1、20∶1时，苹果酸舒尼替尼处理前后Allo-NK细胞对ABCG2highCNE2/DDP细胞的杀伤率分别为(15.32±13.86)%、(27.26±6.81) % 及(41.12±4.12)%、(57.25±2.37)%，处理后的杀伤率有明显的提高(F=15.58， P＝0.000)。结论: 苹果酸舒尼替尼通过诱导高表达NKG2D配体(MICA/B、ULBP1-3)，使ABCG2high CNE2/DDP细胞对Allo-NK细胞的杀伤敏感性明显增强。

关键词：苹果酸舒尼替尼 三磷酸腺苷结合转运蛋白G超家族成员2 鼻咽癌细胞 自然杀伤细胞 NKG2D

Sunitinib malate induced high expression of NKG2D ligands in nasopharyngeal carcinoma cell ABCG2 high CNE2/DDP Download Fulltext

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Abstract:

Abstract Objective: To investigate the inducing effects of sunitinib malate on expression of NKG2D ligands in nasopharyngeal carcinoma cell ABCG2 high CNE2/DDP. Methods:ABCG2 high CNE2/DDP cells and Allo NK cells were isolated by magnetic activated cell sorting (MACS). Flow cytometry was used to evaluate the purity of isolated cells and the expression of NKG2D ligands on target cells before and after incubation with sunitinib malate. Then the cytotoxic sensitivity of treated and un treated ABCG2 high CNE2/DDP cells to Allo NK cells were measured by LDH releasing assay. Results: The positive rate of ABCG2 in ABCG2 high CNE2/DDP cells was (91.40±2.32)%. More than 90% of isolated Allo NK cells were proven to be CD3 -CD16 +CD56 + cells. The expression of MICA, MICB,ULBP1, ULBP2 and ULBP3 on ABCG2 high CNE2/DDP cells incubated with sunitinib malate increased from (2.92±0.33)%, (4 27±0.33)%, (5.80±0.62)%, (11.10±3.15)%, and (7.75±1.14)% to (89.12±4.56)%, (66.10±2 22)%, (67.56±4.19)%, (69.37±8.83)%, and (63.28±3.31)%, respectively. At the E : T ratios of 10 : 1 and 20 : 1, the cytotoxic sensitivities of ABCG2 high CNE2/DDP cells to Allo NK cells increased from (15.32±13.86)% and (27.26±6.81)% to (41.12±4.12)% and (57.25±2.37)%, respectively, after treatment with sunitinib malate, with significantly difference found in the cytotoxic sensitivities of target cells in each group before and after sunitinib malate treatment (F =15 58, P =0.000). Conclusion: Sunitinib malate can up regulate expression of NKG2D ligands (MICA/B, ULBP1 3) in ABCG2 high nasopharyngeal carcinoma cells, which results in higher cytotoxic sensitivity to Allo NK cells.

Keywords:sunitinib malate ATP binding cassette superfamily G member 2(ABCG2) nasopharyngeal neoplasms cells natural killer cell (NK) NKG2D

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