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分子靶向药物诱导耐药鼻咽癌CNE2/DDP细胞NKG2DLs的表达 点此下载全文

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摘要：

目的：探讨不同分子靶向药物对高表达与低表达ATP结合转运蛋白G超家族成员2（ATP binding cassette superfamily G member 2，ABCG2）的人耐药鼻咽癌CNE2/DDP细胞（分别简写为ABCG2 high CNE2/DDP和ABCG2 low CNE2/DDP）表面NKG2D配体（natural killer group 2 member D ligands，NKG2DLs）表达的诱导作用及其对NK细胞杀伤敏感性的影响。方法：免疫磁珠法分选ABCG2 high CNE2/DDP、ABCG2 low CNE2/DDP细胞及NK细胞。流式细胞术检测分选细胞的纯度和不同分子靶向药物（硼替佐米、索拉非尼、舒尼替尼）处理前后ABCG2 high CNE2/DDP和ABCG2 low CNE2/DDP细胞NKG2DLs的表达率。LDH释放法检测不同药物处理前后ABCG2 high CNE2/DDP和ABCG2 low CNE2/DDP细胞对NK细胞杀伤的敏感性。结果：ABCG2 high CNE2/DDP 和ABCG2 low CNE2/DDP细胞表面ABCG2的表达率分别为（91.40±2.32）%和（1.70±0.24）%。分选后NK细胞中CD3 -CD16 +CD56 +细胞的比例达90%以上。药物处理前，ABCG2 high CNE2/DDP和ABCG2 low CNE2/DDP细胞 MICA、MICB、ULBP1、ULBP2和ULBP3呈弱表达；经不同分子靶向药物处理后，5种NKG2DLs的表达率均明显上升(P<0 01)，以舒尼替尼处理后NKG2DLs的表达率升高最明显。随着NKG2DLs表达的上调，ABCG2 high CNE2/DDP和ABCG2 low CNE2/DDP细胞对NK细胞杀伤的敏感性也随之升高。结论：不同分子靶向药物可诱导耐药鼻咽癌CNE2/DDP细胞NKG2DLs的表达，以舒尼替尼的诱导作用最强，且肿瘤细胞NKG2DLs的表达与其对NK细胞杀伤敏感性之间存在线性关系。

关键词：分子靶向药物 三磷酸腺苷（ATP）结合转运蛋白G超家族成员2（ABCG2） 鼻咽癌细胞株 NKG2D 配体 自然杀伤细胞

Molecular targeted agents induce NKG2DLs expressions in multidrug resistant nasopharyngeal carcinoma CNE2/DDP cells Download Fulltext

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Abstract:

Objective:To investigate molecular targeted agent induced expressions of natural killer group 2 member D ligands (NKG2D ligands, NKG2DLs) in multidrug resistant nasopharyngeal carcinoma cell line CNE2/DDP with high or low ATP binding cassette superfamily G member 2 expression (ABCG2 high CNE2/DDP cells or ABCG2 low CNE2/DDP cells) and its effects on their cytotoxic sensitivities to NK cells. Methods: ABCG2 high CNE2/DDP cells, ABCG2 low CNE2/DDP cells and NK cells were isolated by magnetic activated cell sorting. Purity of the isolated cells and expression rates of NKG2DLs on ABCG2 high CNE2/DDP and ABCG2 low CNE2/DDP cells before and after treatment with different molecular targeted agents (bortezomib, sorafenib, sunitinib) were examined by flow cytometry (FCM). Cytotoxic sensitivities of ABCG2 high CNE2/DDP and ABCG2 low CNE2/DDP cells were measured by LDH releasing assay. Results: Expression rates of ABCG2 on ABCG2 high CNE2/DDP and ABCG2 low CNE2/DDP cells were (91.40±2.32)% and (1.70±0 24)%, respectively. More than 90% of the isolated NK cells were CD3 -CD16 +CD56 + cells. Expressions of 5 types of NKG2DLs (MICA, MICB, ULBP1, ULBP2 and ULBP3) on untreated ABCG2 high CNE2/DDP and ABCG2 low CNE2/DDP cells were relatively low, but their expressions were significantly up regulated after treatment with different molecular targeted agents (bortezomib, sorafenib, sunitinib), with the highest NKG2DLs expressions found in the sunitinib treated group cells. In addition, cytotoxic sensitivities of ABCG2 high CNE2/DDP and ABCG2 low CNE2/DDP cells to NK cells were increased with the up regulated expressions of NKG2DLs. Conclusion: Different molecular targeted agents can up regulate NKG2DLs expressions in human multidrug resistant nasopharyngeal carcinoma cells, with sunitinib showing the highest induction ability. A linear correlation exists between NKG2DLs expressions and tumor cell cytotoxic sensitivities to NK cells.

Keywords:molecular targeted agent ATP binding cassette superfamily G member 2 (ABCG2) nasopharyngeal carcinoma cell line natural killer group 2 member D ligands (NKG2DLs) natural killer cell

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