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西妥昔单抗对耐药鼻咽癌CNE2/DDP细胞和NK细胞的双重免疫调节作用 点此下载全文

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摘要：

目的：探讨西妥昔单抗(cetuximab)对耐药鼻咽癌CNE2/DDP细胞NKG2D配体（natural killer group 2 member D ligands，NKG2DLs）的表达及NK细胞分泌IFN γ的影响。方法：流式细胞术检测高、低表达ABCG2（ATP binding cassette superfamily G member 2)的耐药鼻咽癌CNE2/DDP细胞（简称ABCG2 low CNE2/DDP细胞和ABCG2 high CNE2/DDP细胞）表面 EGFR 的表达水平，以及西妥昔单抗处理前后两种CNE2/DDP细胞表面NKG2DLs的表达水平。西妥昔单抗处理前后的两种CNE2/DDP细胞分别与NK细胞共培养，ELISA检测上清中IFN γ的分泌水平，LDH释放法检测NK细胞对不同组CNE2/DDP靶细胞的杀伤。结果：ABCG2 high CNE2/DDP和ABCG2 low CNE2/DDP细胞表面EGFR的表达率分别为（43.60±2.01）%和（47.20±2 07）%。西妥昔单抗上调ABCG2 high CNE2/DDP和ABCG2 low CNE2/DDP细胞表面MICA、MICB、ULBP1和ULBP2的表达，但下调 ABCG2 high CNE2/DDP 细胞表面ULBP3的表达。西妥昔单抗处理两种CNE2/DDP细胞后，与NK细胞的共培养体系中IFN γ的分泌水平明显上调（ P <0 01）；西妥昔单抗增强两种CNE2/DDP细胞对NK细胞杀伤的敏感性（ P <0.01）。结论：西妥昔单抗可上调耐药鼻咽癌CNE2/DDP细胞NKG2DLs的表达，间接刺激NK细胞分泌IFN γ，具有双重免疫调节作用。

关键词：西妥昔单抗 鼻咽肿瘤 多药耐药 NKG2D 配体 自然杀伤细胞

Dual immunological regulation effects of cetuximab on multidrug resistant nasopharyngeal carcinoma CNE2/DDP cells and NK cells Download Fulltext

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Abstract:

Objective: To investigate the effects of cetuximab on NKG2D ligands (NKG2DLs) expressions in multidrug resistant nasopharyngeal carcinoma CNE2/DDP cells and IFN γ production in NK cells. Methods: EGFR expressions on CNE2/DDP cells with high and low ABCG2 expression (ABCG2 high CNE2/DDP cells and ABCG2 low CNE2/DDP cells) and NKG2DLs expressions on ABCG2 high and ABCG2 low CNE2/DDP cells before and after cetuximab treatment were detected by flow cytomertry. ABCG2 high and ABCG2 low CNE2/DDP cells were co cultured with NK cells before and after cetuximab treatment, and then IFN γ levels in the supernatants of different groups were detected by ELISA. Cytotoxicity of NK cells against CNE2/DDP cells was measured by LDH releasing assay in different groups. Results: EGFR expressions in ABCG2 high and ABCG2 low CNE2/DDP cells were (43.60±2.01)% and (47.20±2.07)%, respectively. The expressions of MICA, MICB, ULBP1, and ULBP2 on ABCG2 hgh and ABCG2 low CNE2/DDP cells were up regulated by cetuximab stimulation, while ULBP3 expression on ABCG2 high CNE2/DDP cells was down regulated by cetuximab stimulation. IFN γ levels in co culture systems were significantly increased after ABCG2 low and ABCG2 high CNE2/DDP cells were treated with cetuximab (P <0.01). Cetuximab enhanced cytotoxic sensitivities of ABCG2 high and ABCG2 low CNE2/DDP cells in response to NK cells (P <0.01). Conclusion: Cetuximab exerts a dual immunological regulation by up regulating NKG2DLs expressions on nasopharyngeal carcinoma CNE2/DDP cells and stimulating IFN γ production by NK cells indirectly.

Keywords:cetuximab nasopharyngeal neoplasms multidrug resistance natural killer group 2 member D ligand (NKG2DL) natural killer cell

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