262~267.舒尼替尼体内诱导耐药鼻咽癌细胞表达NKG2DLs增强NK细胞的抑瘤作用[J].黄宇贤,王 杨,李玉华,宋朝阳,陈土珍,周 璇,涂三芳,何颖芝,郭坤元.中国肿瘤生物治疗杂志,2010,17(3)

舒尼替尼体内诱导耐药鼻咽癌细胞表达NKG2DLs增强NK细胞的抑瘤作用 点此下载全文

黄宇贤 王 杨 李玉华 宋朝阳 陈土珍 周 璇 涂三芳 何颖芝 郭坤元

南方医科大学 珠江医院 血液科，广东 广州 510282;广东省人民医院 肺癌研究所，广东 广州 510080;南方医科大学 珠江医院 血液科，广东 广州 510282;南方医科大学 珠江医院 血液科，广东 广州 510282;南方医科大学 珠江医院 血液科，广东 广州 510282;南方医科大学 珠江医院 血液科，广东 广州 510282;南方医科大学 珠江医院 血液科，广东 广州 510282;南方医科大学 珠江医院 血液科，广东 广州 510282

基金项目：国家自然科学基金资助项目（No. 30973454）；广东省自然科学基金重点项目（No. 9251051501000007）

DOI：10.3872/j.issn.1007-385X.2010.3.004

摘要：

目的：探讨体内条件下舒尼替尼对耐药鼻咽癌CNE2/DDP细胞NKG2DLs（natural killer group 2 member D ligands)表达的诱导作用，及其对NK细胞抗肿瘤活性的影响。方法：建立ABCG2 high CNE2/DDP和ABCG2 low CNE2/DDP细胞裸鼠皮下移植瘤模型，分如下8组：A、E组分别接种ABCG2 high 、ABCG2 low CNE2/DDP细胞，B、F组分别接种舒尼替尼处理的 ABCG2 high 、 ABCG2low CNE2/DDP 细胞，C、G组分别接种ABCG2 high 、ABCG2 low CNE2/DDP细胞后再输注NK细胞；D、H组接种舒尼替尼处理的ABCG2 high 、ABCG2 low CNE2/DDP细胞后再输注NK细胞。检测各组裸鼠成瘤时间、成瘤率、肿瘤体积和抑瘤率。免疫组织化学法检测移植瘤组织中NKG2DLs的表达。结果：A、B、C、D和E、F、G、H组肿瘤出现时间分别为(5.43±1.00)、(8.50±0 35)、(11 10±1.25)、(13.56±1.23) d和 (9.00±1.00)、(12.30±0.78)、(14.50±0.50)、(17.25±0.77) d，其中舒尼替尼与NK细胞联合处理组（D 和H 组）成瘤时间最晚（ P <0.01）。A、B、C、D和E、F、G、H组肿瘤质量分别为(2.63±0 89)、(1.00±0 03)、(0 65±0.08)、(0.21±0.27) g和(2.79±0.83)、(1.18±0.77)、(0.96±0.50)、(0.86±0.82) g，其中舒尼替尼与NK细胞联合处理组肿瘤质量最小（ P <0 01）；舒尼替尼与NK细胞联合处理的D组和H组的抑瘤率分别为92%和69%。舒尼替尼上调移植瘤组织中NKG2DLs的表达，且ABCG2 high CNE2/DDP细胞移植瘤中的NKG2DLs表达率高于 ABCG2 low CNE2/DDP 细胞。结论：舒尼替尼可在体内诱导CNE2/DDP移植瘤组织表达NKG2DLs，增强NK细胞的抗肿瘤作用。

关键词：舒尼替尼 自然杀伤细胞 NKG2D配体 鼻咽肿瘤 裸鼠移植瘤

Sunitinib enhances inhibitory effect of NK cells against xenografts in nude mice by up regulating NKG2DLs expressions in multidrug resistant nasopharyngeal carcinoma cells Download Fulltext

HUANG Yu-xian WANG Yang LI Yu-hua SONG Chao-yang CHEN Tu-zhen ZHOU Xuan TU San-fang HE Ying-zhi GUO Kun-yuan

Department of Hematology, Zhujiang Hospital, Southern Medical University, Guangzhou 510282, Guangdong, China;Lung Cancer Institute, Guangdong General Hospital, Guangzhou 510080, Guangdong, China;Department of Hematology, Zhujiang Hospital, Southern Medical University, Guangzhou 510282, Guangdong, China;Department of Hematology, Zhujiang Hospital, Southern Medical University, Guangzhou 510282, Guangdong, China;Department of Hematology, Zhujiang Hospital, Southern Medical University, Guangzhou 510282, Guangdong, China;Department of Hematology, Zhujiang Hospital, Southern Medical University, Guangzhou 510282, Guangdong, China;Department of Hematology, Zhujiang Hospital, Southern Medical University, Guangzhou 510282, Guangdong, China;Department of Hematology, Zhujiang Hospital, Southern Medical University, Guangzhou 510282, Guangdong, China

Fund Project:Project supported by the National Natural Science Foundation of China (No. 30973454), and the Key Program of Natural Science Foundation of Guangdong Province (No. 9251051501000007)

Abstract:

Objective:To investigate the effect of sunitinib on NKG2D ligands (NKG2DLs) expressions and its influences on anti tumor effect of NK cells. Methods: ABCG2 high CNE2/DDP and ABCG2 low CNE2/DDP cell implanted mouse tumor models were established and were divided into the following 8 groups. A, E: inoculated with ABCG2 high CNE2/DDP or ABCG2 low CNE2/DDP cells; B, F: inoculated with sunitinib stimulated ABCG2 high CNE2/DDP cells or ABCG2 low CNE2/DDP cells; C, G: inoculated with ABCG2 high CNE2/DDP cells or ABCG2 low CNE2/DDP cells and NK cells;and D, H: inoculated with sunitinib stimulated ABCG2 high CNE2/DDP cells or ABCG2 low CNE2/DDP cells and NK cells.Tumor formation times and rates, tumor volumes, and tumor inhibitory rates were observed in different groups. NKG2DLs expressions in implanted tumor tissues were examined by immunohistochemistry assay. Results: Tumor formation times in A, B,C, D, E, F, G, and H groups were (5.43±1.00), (8.50±0.35), (11.10±1.25), (13.56±1.23), (9 00±1 00), (12.30±0.78),(14.50±0.50), and (17.25±0.77) d, respectively, with those in sunitinib and NK cell combination groups (D and H groups) being the longest ones (P <0.01). Tumor masses in A, B, C, D, E, F, G, and H groups were (2.63±0.89), (1.00±0.03), (0.65±0.08), (0.21±0.27), (2 79±0.83), (1.18±0.77), (0.96±0.50), and (0.86±0.82) g, respectively, with those in sunitinib and NK cell combination groups (D and H groups) being the lightest ones (P <0.01); the tumor inhibitory rates in sunitinib and NK cell combination groups (D and H groups) were 62% and 69%. Sunitinib up regulated NKG2DLs expressions in implanted tumor tissues, with those in ABCG2 high CNE2/DDP cells higher than those in ABCG2 low CNE2/DDP cells. Conclusion: unitinib can up regulate NKG2DLs expressions in CNE2/DDP cell implanted tumor tissues in vivo and enhance anti tumor effect of NK cells.

Keywords:sunitinib natural killer cell natural killer group 2 member D ligand (NKG2DL) nasopharyngeal neoplasmas xenograft in nude mice

主管单位：中国科学技术协会 主办单位：中国免疫学会、中国抗癌学会
地址：上海市杨浦区翔殷路800号 邮政编码：200433 京ICP备06011393号-2
本系统由北京勤云科技发展有限公司设计