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CIK体内外抗宫颈癌HeLa细胞的作用及其荷瘤小鼠体内分布特点 点此下载全文

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摘要：

目的： 探讨细胞因子诱导的杀伤细胞（cytokine-induced killer cell，CIK）对荧光素酶标记的人宫颈癌HeLa-luc细胞的体内外抗肿瘤作用，了解CIK回输荷瘤小鼠后在不同器官的分布特点。 方法： 由健康志愿者外周血单个核细胞体外诱导培养CIK，流式细胞术检测CIK表面分子的表达，RT-PCR法检测 IFN-γ mRNA的表达，MTT法和瑞氏-姬姆萨染色测定CIK对HeLa-luc细胞的杀伤作用。建立荷HeLa-luc瘤BALB/c裸鼠模型，体内成像系统观察荷瘤小鼠肿瘤大小变化及CIK治疗效果，共聚焦显微镜观察不同器官中CIK的分布情况。 结果： CIK在体外诱导培养14~21 d，其生长达到高峰，此时CD3+CD56+ T细胞的比例增加50倍以上， IFN-γ mRNA表达水平也达到高峰。在效靶比为20∶1、40∶1时，CIK对HeLa-luc细胞的杀伤率分别为（51.16±2.64）%、（72.14±4.21）%，明显高于对照组的（16.33±3 09）%、（21.26±2.71）%（ P <0.05）。CIK治疗5周和8周后，对荷瘤小鼠的抑瘤率分别为47.18%、64.38%。CIK治疗组荷瘤小鼠外周血中IFN-γ水平为（61.92±6 49）pg/ml，明显高于对照组的（34.30±1.78）pg/ml（ P <0.05）。CFSE标记的CIK经腹腔和瘤旁注射入荷瘤小鼠3 h，在肺、肝、脾、外周血、肿瘤中均可观察到绿色荧光；腹腔途径注射24 h时，肿瘤组织中CIK浓度达到高峰（20.56±1.72）%；瘤旁途径注射3 h时，肿瘤组织中CIK达到高峰（25.75±3.45）%。 结论： CIK在体内外对宫颈癌HeLa-luc细胞均有较强的杀伤作用，CIK经不同途径注射荷瘤小鼠后可以广泛分布于全身器官，其到达各脏器的浓度与输注途径及时间密切相关。

关键词：细胞因子诱导的杀伤细胞 宫颈癌 HeLa-luc细胞 IFN-γ 抗肿瘤作用 体内分布

Anti-tumor activity of CIK cells on cervical cancer HeLa cells in vitro and in vivo and their distribution characteristics in tumor-bearing mice Download Fulltext

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Abstract:

Objective ：To study the anti-tumor activity of cytokine-induced killer cells (CIK cells) against HeLa-luc cells (cervical cancer HeLa cells labeling luciferase) in vivo and in vitro , and to analyze the distribution characteristics of CIK cells in different organs in a mouse xenograft model of cervical cancer nude. Methods: CIK cells were induced from peripheral blood mononuclear cells of health volunteers and cultured in vitro. The phenotype of CIK cells were determined by flow cytometry. The expression of IFN-γ mRNA in CIK cells was detected by RT-PCR assay. The killing activity of CIK cells on HeLa-luc cells was determined by MTT assay and Wright-Giemsa’ s staining. HeLa-luc cell-bearing BALB/c nude mouse model was established. Tumor size changes and treatment effect were detected using in vivo Xenogen IVIS Imaging System. The distribution characteristics of CIK cells in different organs were detected by confocal microscopy. Results: CIK cells grew up to the peak after being cultured for 14-21 d. The percentage of CD3+CD56+T cells was increased more 50 times than that of the beginning. The expression level of IFN-γ mRNA in CIK cells was also increased to the peak. When the ratios of effect to target were 20 ：1, and 40 ：1, the cytotoxicity of CIK cells on HeLa-luc cells was (51 16±2.64)% and (72.14%±4.21)%, respectively, and was significantly higher than that of the control group (\[16 33±3.09\]%, \[21.26±2.71\]%, respectively, P <0.05). The inhibitory rate of CIK cells on the tumor was 47.18% and 64.38% at the fifth week and the eighth week, respectively. The level of IFN-γ mRNA in the CIK experiment group (61.92±6.49) pg/ml was significantly higher than that in the control group (34.30±1.78) pg/ml (P <0 05). Green fluorescence can be observed in the lung, liver, spleen, peripheral blood and tumor tissues under the confocal microscope 3 h after CFSE-labeled CIK cells injection via peritoneal cavity and tumor adjacent. 24 h after injection via peritoneal cavity, the highest concentration of CIK cells was 20.56% in the tumor tissues, and 3 h after injection via tumor adjacent, the highest concentration of CIK cells was 25.75% in the tumor tissues. Conclusion: CIK cells show a strong cytotoxicity on cervical cancer HeLa-luc cells in vivo and in vitro. The CIK cells are extensively distributed into different organs after injection via peritoneal cavity or tumor adjacent. The concentration of CIK cells in different organ is closely related to the injection route and time.

Keywords:cytokine-induced killer cell cervical cancer HeLa-luc cell IFN-γ anti-tumor effect distribution pattern in vivo

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