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缺氧微环境对TSST-1诱导的抗CEA+结肠癌LoVo细胞免疫治疗的调控 点此下载全文

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摘要：

目的：研究缺氧微环境对靶向性表达的超抗原中毒性休克综合征毒素-1（toxic shock syndrome toxin-1，TSST-1）激活人外周血淋巴细胞（peripheral blood lymphocyte，PBL）对CEA+结肠癌LoVo细胞杀伤作用的调控。 方法：包装、收集前期构建的缺氧反应元件（hypoxia-response elements，HRE）和癌胚抗原启动子CEAp联合调控的逆转录病毒载体pLEGFP-N1-5HRE-CEAp-TSST-1-linker-CD80TM（简称pLEGFP-N1-5HCTC），感染CEA+LoVo细胞及CEA-宫颈癌HeLa细胞，获取稳定表达跨膜型超抗原TSST-1-linker-CD80TM蛋白(TC融合蛋白)的肿瘤细胞。用缺氧模拟试剂CoCl 2模拟缺氧微环境，RT-PCR和Western blotting分别检测缺氧调控下 TSST-1 的表达水平。将健康人PBL与pLEGFP-N1-5HCTC感染后的肿瘤细胞共培养，3H-TdR掺入法检测缺氧调控下PBL的增殖能力，MTT法检测缺氧调控下PBL对肿瘤细胞的杀伤效应。 结果：pLEGFP-N1-5HCTC病毒成功感染CEA+LoVo细胞（5HCTC/LoVo），RT-PCR和Western blotting证实，缺氧可上调5HCTC/LoVo细胞中 TSST-1 mRNA和蛋白的表达，CEA-HeLa细胞在常氧和缺氧条件下均无 TSST-1 的表达。缺氧可上调5HCTC/LoVo细胞诱导的人PBL的增殖（7.3×103 vs 3.1×103cpm，P<0.05），缺氧环境下PBL对5HCTC/LoVo细胞的杀伤率明显高于常氧环境（82.69% vs 53.50%，P<0.01）；CEA-HeLa细胞不能刺激PBL增殖，PBL对其也无抑制作用。 结论：缺氧微环境可显著上调靶向性表达的超抗原TSST-1诱导的对CEA+LoVo细胞的杀伤作用。

关键词：缺氧微环境 中毒性休克综合征毒素-1（TSST-1） CEA+结肠癌细胞 LoVo细胞 HeLa细胞 逆转录病毒 外周血淋巴细胞

Hypoxia microenvironment regulates immunotherapy effect of TSST-1 on CEA positive colon cancer LoVo cells Download Fulltext

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Abstract:

Objective : To evaluate the regulation of hypoxia microenvironment on cytotoxicity effect of peripheral blood lymphocyte (PBL) activated by the superantigen of toxic shock syndrome toxin-1 (TSST-1) against CEA+ human colon cancer cell line LoVo. Methods: The recombinant retroviral vector pLEGFP-N1-5HRE-CEAp-TSST-1-linker-CD80TM (pLEGFP-N1-5HCTC) containing a CEA promoter and 5 copies of the hypoxia-response elements (HRE) enhancer, which was constructed in our previous study, was packaged and collected. pLEGFP-N1-5HCTC was then transducted into CEA+LoVo cells or CEA- human cervical carcinoma HeLa cells, and LoVo or HeLa cells with stable expression of transmembrane superantigen fusion gene TSST-1-linker-CD80TM protein (TC fusion protein) were obtained. Hypoxia microenvironment was simulated by CoCl 2, and RT-PCR and Western blotting were employed to examine the expression of TSST-1 regulated by hypoxia. Human PBL was extracted and co-cultured with transgene tumor cells infected with pLEGFP-N1-5HCTC retrovirus; 3H-TdR assay was employed to detect the proliferation of PBL regulated by hypoxia; and the cytotocixity effect of PBL regulated by hypoxia against the transgene tumor cells was detected by MTT assay. Results: CEA+LoVo cells infected with recombinant retrovirus pLEGFP-N1-5HCTC were obtained (5HCTC/LoVo). The expression of TSST-1 mRNA and protein in 5HCTC/LoVo cells was further increased with hypoxia, which was confirmed by RT-PCR and Western blotting. There was no TSST-1 expression in CEA-HeLa cells under either hypoxic condition or normoxic condition. The proliferation of PBL activated by 5HCTC/LoVo cells was increased with hypoxia (7.3×103 vs 3.1×103 cpm, P<0 05); and the cytotocixity of PBL on 5HCTC/LoVo cells was more effective in hypoxia condition than in normoxic condition (82.69% vs 53.50%, P<0.01). There was no proliferation of PBL activated by CEA-HeLa cells, and PBL also could not inhibit the proliferation of CEA-HeLa cells. Conclusion: Hypoxia microenvironment can increase the cytotocixity effect of targeting expressed superantigen TSST-1 on CEA+LoVo cells.

Keywords:hypoxia environment toxic shock syndrome toxin-1 (TSST-1) CEA-positive tumors cells LoVo cell HeLa cell retrovirus peripheral blood lymphocyte

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