

热休克诱导结直肠癌细胞外泌体的免疫效应

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Immunological Effects of Exosomes from Colorectal Cancer Cells Induced by Shocked Heat

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摘要 目的探讨热休克影响结直肠癌细胞外泌体诱导树突状细胞肿瘤相关蛋白因子的释放和细胞毒效应。方法临床经病理学确诊的结直肠管状腺癌细胞分离培养, 43℃热休克1 h, 四步离心获得细胞上清外泌体。诱导树突状细胞刺激细胞毒反应。酶联免疫测定树突状细胞释放TNF- α 、MIP-1 α 、RANTES, MTT法测定对结直肠癌细胞的杀伤作用。结果结直肠癌细胞热休克获得的外泌体刺激DC分泌TNF- α 、MIP-1 α 、RANTES, 与对照组比较差异有统计学意义 ($P < 0.05$)。热休克促进外泌体诱导的结直肠癌细胞杀伤活性, 与未经热休克培养获得的外泌体诱导组比较差异有统计学意义 ($P < 0.05$), 与结直肠癌细胞裂解物诱导组比较差异具有统计学意义 ($P < 0.01$), 未经热休克培养获得的外泌体诱导组与癌细胞裂解物诱导组比较差异有统计学意义 ($P < 0.05$)。100 $\mu\text{g}/\text{ml}$ 剂量诱导效应强于50 $\mu\text{g}/\text{ml}$ 组。结论热休克培养可以通过促进效应细胞肿瘤相关蛋白因子释放, 增强对结直肠癌细胞的杀伤活性, 有剂量依赖性, 为开拓高效无细胞疫苗来源提供了实验基础。

关键词: 结直肠癌 树突状细胞 外泌体 热休克

Abstract: Objective To investigate the effect of heat shock exosome (H-exo) from colorectal cancer cell on the protein factor secreted by the induced dendritic cells (DC) and the DC stimulating T-cell toxicity. Methods Colorectal tubular adenocarcinoma specimens through the clinical pathology diagnosis were isolated and cultured. After 1 hour heat shock at 43°C, the exosomes was obtained by four-step centrifugation and used to induce DC. The induced DC stimulates cytotoxic T lymphocytes for 24 hours. The production of TNF- α , MIP-1 α , RANTES by DC was assessed by ELISA assay. By the MTT method T-cell toxicity were evaluated. Results We found that the heat shock exosomes (H-Exo) promoted DC to secrete TNF- α , MIP-1 α , RANTES, significant differences compared with control group, $P < 0.05$. To compare with the non-heat shock exosomes (Exo) group, The H-Exo induced cytotoxicity, $P < 0.05$, and with the colorectal cancer cell lysate (Lys) group, was significantly different ($P < 0.01$). To compare with the Exo and Lys group, there was significant difference ($P < 0.05$), and the inductive effect of 100 $\mu\text{g}/\text{ml}$ dose groups was stronger than 50 $\mu\text{g}/\text{ml}$. Conclusion Heat shock of colorectal cancer cells in culture can enhance immunological effects of exosomes with relation to inductive dose.

Key words: Colorectal cancer Dendritic cell Exosomes Heat shocking

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