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Expression of interleukin-6 mRNA and its protein in the liver at the early stage after burns complicated with endotoxemia in rats

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Abstract Objective: To observe the distribution and cell localization of interleukin-6 (IL-6) mRNA in the liver after burns complicated with endotoxemia. Methods: After 156 Wistar rats were randomized into complex, burn, endotoxin-intoxicated and normal control groups, the changes of the content serum IL-6 and the expression and localization of liver IL-6 and IL-6 mRNA were investigated with serum quantification, immunohistochemistry and *in situ* hybridization. Results: Serum IL-6 reached its peak for twice at the 0.5th and 6th (12th h respectively. IL-6 mainly localized in sinusoid endothelial cells and Kupffer cells (KCs) while IL-6 mRNA in KCs, polymorphonuclear neutrophils and macrophages. Conclusion: IL-6 is one of the key cytokines in liver damage after burns complicated with endotoxemia in rats and closely correlated to the synthesis of lipopolysaccharide binding protein in hepatocytes.

Key words burns; endotoxemia; interleukin-6; lipopolysaccharide binding protein; immunohistochemistry; *in situ* hybridization; rat

博士生论文摘要

组织金属蛋白酶抑制剂 TIMP-2基因转染对胃癌细胞 SGC-7901侵袭能力的影响

The effect on invasiveness of gastric carcinoma cell SGC-7901 by transfection of tissue inhibitor metalloproteinase-2 gene

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实验以调查胃癌中 MMPs/TIMPs基因表达变化规律结果为依据,在体内构建了含人全长 TIMP-2 cDNA基因的可能控逆转录病毒表达载体,经转染到具有高侵袭能力的人胃癌细胞 SGC-7901B,检测到 TIMP-2基因整合人细胞基因组 DNA中,在 mRNA和蛋白水平表达有明显增高。表明所构载体正确并具有 TIMP-2蛋白活性,进一步分别从体内、外观察了 TIMP-2基因转染对胃癌细胞系的恶性侵袭表型的影响。

结果表明:① MMP-2、MT-MMP在胃癌患者中呈普遍高表达,与胃癌病程成正比。其中 MMP-2/TIMP-2比率随胃癌病程进展而升高,是较其它 MMPs/TIMPs与胃癌转移更为密切的肿瘤分子标志。② 筛选人胃癌 SGC-7901母系细胞株,获得有不同增殖和侵袭能力的二个亚系,其中 SGC-7901B其软琼脂形成率、Boyden Chamber侵袭能力均明显高于母系,是研究胃癌侵袭的良好细胞模型。③ 利用基因工程技术合成 91bp的 TIMP-2信号肽序列,与 TIMP-2 cDNA连接获得全长 TIMP-2 cDNA,并将 MT-1启动子与 TIMP-2全长可调控逆转录病毒载体。④ 外源基因 TIMP-2成功地整合人受体细胞 SGC-7901B,并在 mRNA水平表达明显增高。蛋白测定表明Ⅳ型胶原酶受到抑制,说明基因转染成功。⑤ TIMP-2基因转染可抑制 LN对肿瘤细胞的粘附,辅展作用,且随着作用时间延长作用更加明显,细胞表面微绒毛稀疏,胞内嵴减少。

6. TIMP-2基因转染使瘤细胞在裸鼠内瘤时间延长,成瘤率、侵袭能力受到抑制。

以上说明 TIMP-2基因转染下调了胃癌细胞恶性侵袭表型,是一个负调控因子。

关键词 基因转染;胃肿瘤;基因治疗;TIMP

中图法分类号 R735.2

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