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论著

肝癌细胞增殖受M-CSF胞内和胞外自分泌的双重调控

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摘要 目的：研究胞内M-CSF及其受体在肝癌SMMC 7721细胞的表达与性质,探讨胞内M-CSF对SMMC 7721细胞增殖的影响及其机制。 方法： 以高表达M-CSF的人肝癌细胞系（SMMC 7721细胞）为模型，以免疫组化、流式细胞计数、反义技术与蛋白印迹等方法观测胞内M-CSF对SMMC 7721细胞增殖的影响及其机制。 结果： M-CSF 及其受体主要在SMMC 7721细胞的胞质、胞核中表达，胞内的M-CSF的相对分子量为20 000，M-CSFR的相对分子量为120 000；免疫共沉淀分析证明M-CSF在细胞内与M-CSFR以复合物的形式存在；M-CSF的单克隆抗体及其反义寡聚核苷酸能抑制SMMC 7721细胞的增殖、下调cyclinD1/E的表达和上调p16的表达，且M-CSF的单克隆抗体及其反义寡聚核苷酸的联合使用能进一步加强对SMMC 7721细胞抑制作用和增加下调cyclinD1/E和上调p16的表达幅度。 结论： SMMC 7721细胞受M-CSF胞外自分泌和胞内自分泌的双重调控。

关键词 巨噬细胞集落刺激因子； SMMC 7721细胞； 肝肿瘤

分类号 R363

Proliferation of human hepatoma cells are regulated by the intracrine and autocrine loop of the macrophage colony-stimulating factor system

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Abstract

<FONT face=Verdana>AIM: To study the expression and characterization of intracellular macrophage colony-stimulating factor (M-CSF) in human hepatoma cell line, SMMC 7721 cell, and to explore the mechanism by which M-CSF regulates the proliferation of human hepatoma cells. METHODS: The immunohistochemical staining, flow cytometry, antisense technique and Western blotting were used to study the effects and mechanisms of intracellular M-CSF on the proliferation of human hepatoma cells. RESULTS: SMMC 7721 cells highly expressed M-CSF and its receptor. The localization of positive reactions was mainly in cytoplasma and nucleus in SMMC 7721 cells. In cytoplasma and nucleus, one isoforms of M-CSF was found with the molecular weight (MW) of 20 kD, while one type of M-CSFR was discovered with MW of 120 kD. Immunoprecipitation assay showed that these ligands existed in binding with its receptor. Monoclonal antibody (McAb) against M-CSF and antisense oligodeoxynucleotides (ASODN) blocking M-CSF expression inhibited the proliferation of SMMC 7721 cells. McAb and ASODN regulated the expression of cyclin D1/E and p16. Simultaneous administration of both McAb and ASODN inhibited the proliferation of SMMC 7721 cells and modulated the expression of cyclins at greater degrees. CONCLUSION: Our results suggest that an autocrine and an intracrine loop of M-CSF/M-CSFR are present in SMMC 7721 cells. </FONT>

Key words Macrophage colony-stimulating factor SMMC 7721 cells； Liver neoplasms

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