中国公共卫生 2014, 30(10) 1265-1267 DOI: 10.11847/zgggws2014-30-10-09 ISSN: 1001-0580 CN: 21-1234/R

论文

海兔素对小鼠H_{22}移植瘤侵袭及免疫调节影响

王青[1], 梁惠[1], 刘颖[2], 戈娜[1], 马爱国[1]

1. 青岛大学医学院医学营养研究所, 山东 青岛 266021;
2. 青岛大学医学院细胞与分子生物学实验室

摘要：

目的 观察海兔素对H_{22}荷瘤小鼠肿瘤生长侵袭的影响及免疫调节作用。方法 昆明小鼠40只，随机分为模型组、海兔素低、中、高剂量组（n=10）。各组小鼠左前腋下皮下接种H_{22}肝癌细胞，建立小鼠H_{22}移植性肿瘤模型，次日除模型组外，海兔素低、中、高剂量组分别以25、50、100 mg/kg海兔素灌胃，于15 d后处死，剥离肿瘤，称重，计算抑瘤率；采用免疫组化法测定肿瘤组织中基质金属蛋白酶-9（MMP-9）、血管内皮生长因子（VEGF）及增殖细胞核抗原（PCNA）表达，酶联免疫吸附试验测定血清中白细胞介素-6（IL-6）、肿瘤坏死因子-α（TNF-α）水平。结果 低、中、高剂量海兔素组小鼠抑瘤率分别为28.31%、33.84%、42.96%，呈量效依赖性；经50、100 mg/kg海兔素处理后，小鼠肿瘤组织中MMP-9表达阳性率分别为（54.29±6.41）%、（29.31±3.15）%，明显低于模型组（74.80±8.06）%；VEGF和PCNA阳性表达逐渐下降，呈剂量效应关系（P<0.05）；中、高剂量海兔素组小鼠血清中IL-6和TNF-α水平[分别为（0.34±0.050）、（0.37±0.04）和（1.26±0.21）、（1.49±0.17）μg/L]，均明显高于模型组，差异有统计学意义（P<0.05）。结论 海兔素可抑制H_{22}小鼠肿瘤增长，其机制可能与海兔素抑制肿瘤组织细胞外基质降解以及新生血管形成，同时提高机体免疫能力有关。

关键词： 海兔素 H_{22}肿瘤 基质金属蛋白酶-9（MMP-9） 血管内皮生长因子（VEGF） 增殖细胞核抗原（PCNA） 白细胞介素-6（IL-6） 肿瘤坏死因子-α（TNF-α）。

Effect of aplysin on invasion and immunomodulatory of hepatocarcinoma 22 in mice

WANG Qing, LIANG Hui, LIU Ying, et al

Institution of Nutrition, Medical College of Qingdao University, Qingdao, Shandong Province 266021, China

Abstract:

Objective To investigate the effect of aplysin on tumor invasion and immunomodulation in mice with hepatocarcinoma-22(H_{22}) implantation.Methods Forty Kunming mice were randomly divided into four groups:model group and aplysin treatment groups(25, 50, 100 mg/kg^{-1}/d^{-1}) and H_{22} cells were inoculated subcutaneously into left anteromedial of the mice of all the groups.Except for the model group, all the mice in the other 3 groups were treated with aplysin of different dosage by gavage on the second day and sacrificed after 15 days.We weighed the tumor tissue and calculated the tumor inhibition rate.The expressions of matrix metalloproteinases-9(MMP-9), vascular endothelial growth factor(VEGF), and proliferating cell nuclear antigen(PCNA) in tumor tissue were determined simultaneously with immunohistochemistry.And the levels of interleukin-6(IL-6) and tumor necrosis factor-α(TNF-α) in serum were measured with enzyme-linked immunosorbent assay(ELISA).Results Aplysin decreased the tumor weight significantly in a dose-dependent manner, with the tumor inhibition rates of 28.31%, 33.84%, and 42.96%, respectively.For the mice with aplysin treatment at the concentrations of 50 and 100 mg/kg^{-1}/d^{-1}, the expressions of MMP-9 were 54.29±6.41% and 29.31±3.15%, and were significantly different from that of model group(74.80±8.06%).The expressions of VEGF and PCNA were obviously inhibited in a dose-effect mamer(P<0.05).In moderate and high-dose asplysin treatment groups, the level of IL-6 in serum were 0.34±0.050 and 0.37±0.04 and the TNF-α were 1.26±0.21 and 1.49±0.17, which were significantly higher than those of model group(P<0.05).Conclusion Aplysin could inhibit tumor growth by suppressing extracellular matrix degradation and angiogenesis and improving the immune capacity in mice.

Keywords: aplysin H_{22} tumor MMP-9 VEGF PCNA IL-6 TNF-α

收稿日期 2013-12-26 修回日期 网络版发布日期 2014-03-28

DOI: 10.11847/zgggws2014-30-10-09

基金项目:

山东省科技发展计划（2012YD15011）；国家“十二五”科技支撑计划（2012BAD33B01）

通讯作者: 梁惠，E-mail：qdlianghui@126.com

作者简介:

参考文献：

[1] 贺娟,梁惠,李元,等.海兔素对D-半乳糖诱导衰老小鼠抗氧化作用[J].中国公共卫生,2009,25(9):1122-1123
[2] Ge N,Liang H,Liu Y,et al.Protective effect of aplysin on hepatic injury in ethanol-treated rats[J].Food Chem Toxicol,2013,doi:10.1016/j.fct.2013.08.071.
[3] 马文龙,梁惠,刘颖.海兔素对人乳腺癌 SK-BR-3 细胞的抑制作用及机制研究[J].天然产物研究与开发,2012,24(9):1201-1205
[4] 刘颖,梁惠,苏爱,等.海兔素对人胃癌细胞 SGC-7901 增殖和凋亡的影响[J].中国药理学通报,2010,26(3):333-337.
[5] 刘颖,梁惠,徐宏伟,等.海兔素对 S180 荷瘤小鼠的抑瘤活性及其免疫作用的实验观察[J].中国药理学通报,2006,22(11):1403-1405.
[6] Chen R,Cui J,Xu C,et al.The significance of MMP-9 over MMP-2 in HCC invasiveness and recurrence of hepatocellular carcinoma after curative resection[J].Ann Surg Oncol,2012,doi:10.1245/s10434-011-1836-1837.
[7] Sze KM,Wong KL,Chu GK,et al.Loss of phosphatase and tensin homolog enhances cell invasion and migration through AKT/Sp-1 transcription factor/matrix metalloproteinase 2 activation in hepatocellular carcinoma and has clinicopathologic significance[J].Hepatology,2011,53(5):1558-1569.
[8] Nart D,Yaman B,Yilmaz F,et al.Expression of matrix metalloproteinase-9 in predicting prognosis of hepatocellular carcinoma after liver transplantation[J].Liver Transpl,2010,16(5):621-630.
[9] 郭荣平,俞武生,韦玮,等.PCNA在接受过术前经导管肝动脉栓塞化疗的肝癌组织中的表达及其预后意义[J].癌症,2008,27(2):201-205.
[10] Satomi Y.Fucoxanthin induces GADD45A expression and G1 arrest with SAPK/JNK activation in LNCap human prostate cancer cells[J].Anticancer Res,2012,32:807-813.
[11] Cheung FWK,Li C,Che CT,et al.Geoditin A induces oxidative stress and apoptosis on human colon HT29 cells[J].Mar Drugs,2010,8:80-90.
[12] Hong JY,Boo HJ,Kang JI,et al.(1S,2S,3E,7E,11E)-3,7,11,15-Cembratetraen-17,2-olide,a cembrenolide diterpene from soft coral *Lobophytum sp*,inhibits growth and induces apoptosis in human colon cancer cells through reactive oxygen species generation[J].Biol Pharm Bull,2012,35:1054-1063.
[13] 梁惠,贺娟,张士璀,等.凹顶藻萜类化合物抑瘤活性及其对免疫作用的研究[J].中国海洋药物,2005(1)：6-9.
[14] 刘克为,梁惠,高华.海藻萜类化合物对H_{22}小鼠IL-6和TNF-α水平的影响[J].中国海洋药物,2009(4):9-12.
[15] 张琪,杨鸣琦,王根辈,等.新城疫病毒和康莱特注射液联合抗肿瘤试验中瘤组织的病理变化及IL-6表达的研究[J].中国兽医杂志,2010,46(10):33-34.
[16] 李卫,刘佳,自家媛,等.α肿瘤坏死因子的研究进展[J].动物医学进展,2010,31(12)：108.
[17] Salako MA,Kulbe H,Ingemarsdotter CK,et al.Inhibition of the inflammatory cytokine TNF-α increases adenovirus activity in ovarian cancer via modulation of cIAP1/2 expression[J].Molecular Therapy,2010,19(3):490-499.

本刊中的类似文章

1．王豫萍, 程明亮, 关丽, 陆爽.蓝莓对免疫性肝纤维化大鼠HGF表达影响[J]. 中国公共卫生, 2012,28(8): 1051-1054
2．江秀娟, 陈俊瑶, 包晓玲.非小细胞肺癌与血清中2种相关因子含量关系[J]. 中国公共卫生, 2010,26(7): 807-808
3．贺娟, 梁惠, 李元, 史大永, 马爱国.海兔素对D-半乳糖诱导衰老小鼠抗氧化作用[J]. 中国公共卫生, 2009,25(9): 1122-1123
4．刘剑英, 钟进义.核辐射接触人员淋巴细胞增殖与凋亡水平检测[J]. 中国公共卫生, 2009,25(2): 238-239
5．张敬, 孟繁萍, 张军, 石红军.氧化损伤相关基因表达在镍致细胞转化中作用[J]. 中国公共卫生, 2009,25(1): 61-63
6．于萍, 钟进义, 赵蓉, 刘辉.葡多酚对小鼠乳腺癌细胞增殖活性抑制作用[J]. 中国公共卫生, 2006,22(12): 1425-1427
7．张明五, 吴皓, 吴逸明, 王新朝.不同温度下紫杉醇对人肺癌A549细胞抑制效应[J]. 中国公共卫生, 2006,22(5): 550-552
8．才秀莲, 李兴升, 李季蓉, 张先平.染锰鼠睾丸增殖细胞核抗原与热休克蛋白表达[J]. 中国公共卫生, 2005,21(11): 1331-1332

反馈人		邮箱地址	
反馈标题		验证码	1105