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论著

CD147单克隆抗体对HCE1多细胞球体紫杉醇耐药的影响

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摘要：

目的：研究CD147单克隆抗体在人宫颈鳞癌细胞株HCE1多细胞球体模型中对紫杉醇天然耐药的影响，探讨CD147单克隆抗体是否可以逆转HCE1多细胞球体天然耐药及其对P-糖蛋白（P-gp）的影响。方法：运用液体重叠法和旋转法建立HCE1多细胞球体模型。以单层细胞作为对照，观察CD147单克隆抗体干预前后HCE1多细胞球体形态学变化。WST-1法检测不同浓度的CD147单克隆抗体干预前后，紫杉醇对HCE1多细胞球体的抑制率，计算半数抑制浓度（half maximal inhibitory concentration, IC50）和多细胞耐药指数（index of multicellular resistance，MCRI），并绘制浓度抑制率曲线。用对照组，CD147单抗,紫杉醇及紫杉醇+CD147单抗分别干预单层细胞及多细胞球体，流式细胞学检测细胞周期及凋亡率。用免疫组织化学法分别检测药物干预前后单层细胞及多细胞球体中CD147和P-gp的表达。结果：成功建立了HCE1多细胞球体紫杉醇天然耐药模型。CD147单克隆抗体能使HCE1多细胞球体解聚。CD147单克隆抗体能增强HCE1多细胞球体对紫杉醇的敏感性。5，10，20 μg/mL CD147单克隆抗体组 IC50分别为（40.31±3.73），（32.43±1.56），（30.69±1.01） μg/mL，5和10 μg/mL CD147单抗组呈剂量依赖性（P<0.05）而10和20 μg/mL CD147单抗组无明显剂量依赖性（P>0.05），其凋亡率接近单层细胞（P>0.05）。CD147单克隆抗体引起多细胞球体G1/G0期阻滞，和紫杉醇联用，分别在G1/G0和G2/M 2个调控点共同阻滞HCE1细胞生长。HCE1多细胞球体各组中CD147和p-gp表达呈一致性。结论：成功建立宫颈鳞癌HCE1多细胞球体紫杉醇天然耐药模型；CD147的表达与宫颈鳞癌HCE1多细胞球体对紫杉醇的耐药呈正相关，阻断CD147可部分逆转HCE1多细胞球体对紫杉醇的天然耐药；CD147介导的HCE1多细胞球体的紫杉醇天然耐药可能与P-gp有关。

关键词： 宫颈癌;多细胞球体;CD147;P-糖蛋白;紫杉醇

Effect of CD147 monoclonal antibody on paclitaxel resistance in HCE1 multicellular spheroids

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Abstract:

ObjectiveTo investigate the effect of CD147 monoclonal antibody (mAb) on the natural resistance to paclitaxel (TAX) in the human cervical cancer line (HCE1) multicellular spheroid (HCE1/MCS) model and if CD147 mAb can reverse the HCE1/MCS resistance to TAX. MethodsHCE1/MCS was obtained by liquid overlay and rotating technique. HCE1/MCS morphological changes were observed before or after the interference of CD147 mAb. The effects of TAX on HCE1/MCS (including inhibition ratio, IC50 and index of multicellular resistance) before or after CD147 mAb treatment were determined by the method of WST-1 and the inhibition ratio curve was mapped. Cell cycle and apoptosis were detected by flow cytometer (FCM). The expression of CD147 and P-gp of both HCE1/MC and HCE1/MCS was detected by immunocytochemistry. ResultsHCE1/MCS was established successfully. CD147 mAb could inhibit HCE1/MCS from forming spheroids. CD147 mAb could enhance the sensitivity of HCE1/MCS to TAX. IC50 in different concentrations of CD147 mAb (5，10，20 μg/mL) HCE1/MCS group were (40.31±3.73), (32.43±1.56), and (30.69±1.01) μg/mL. CD147 mAb resulted in G1/G0 arrest in HCE1/MCS. CD147 mAb of low concentrations (0-10 μg/mL) caused a dose-dependent inhibition of HCE1/MCS (P<0.05). Combined with TAX, CD147 mAb could also induce HCE1/MCS cell cycle arrest in both G1/S and G2/M stage. The expression of CD147 and P-gp was consistent in HCE1/MCS groups. ConclusionCD147 plays an important role in muliticellular resistance of cervical cancer and inhibition of CD147 can synergistically reverse the multicellular drug resistance (MCR) in cervical cancer. The MCR of HCE1/MCS mediated by CD147 is related to P-gp.

Keywords: cervical cancer multicellular spheroids CD147 P-glycoprotein paclitaxel

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