

论文

单克隆抗体与平阳霉素偶联物对肿瘤的区域性导向实验治疗

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摘要:

以小鼠H22肝癌腹腔内移植和胸腔内移植肿瘤为模型,观察3A5-PYM偶联物对腔内肿瘤的治疗作用,并以裸鼠移植结肠癌为模型,观察局部注射的治疗作用。结果表明,于小鼠肝癌H22皮下肿瘤局部给药,3A5-PYM在肿瘤中的浓度较游离PYM高,滞留时间也较长。对小鼠腹腔内或胸腔内移植的肿瘤,腔内注射3A5-PYM比游离PYM具有更显著的延长动物生存期的作用。裸鼠皮下移植HT-29人结肠癌,在肿瘤周围注射3A5-PYM比iv或ip给予3A5-PYM显示更高的抑瘤率。提示单抗与平阳霉素偶联物在肿瘤的区域性导向治疗中有较好的疗效。

关键词: 单克隆抗体 平阳霉素 区域性导向治疗 免疫偶联物

USE OF MONOCLONAL ANTIBODY-PINYANGMYCIN CONJUGATE IN EXPERIMENTAL REGIONAL TARGETING THERAPY OF TUMOR

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Abstract:

McAb 3A5, a rat monoclonal antibody, was linked to pingyangmycin (PYM), an antitumor antibiotic identical to bleomycin A5 currently in clinical use, employing Dextran T-40 as an intermediate agent. The 3A5-PYM conjugate retained complete immunoreactivity of McAb-3A5. Determined by clonogenic assay with colon cancer HT-29 cells, the IC<sub>50</sub> values for 3A5-PYM conjugate and free PYM were 0.6 μmol·L<sup>-1</sup> and 10.2 μmol·L<sup>-1</sup>, respectively. Hepatoma H22 ascites was transplanted into the peritoneal or thoracic cavity of mice. On the next day, 3A5-PYM or PYM, were injected into the cavity. Therapeutic effect was evaluated on the survival time of mice. For intraperitoneal tumor, the ILS(%) values were 238% for 3A5-PYM and 40% for PYM. For intrapleural tumor, the ILS(%) values were 384% for 3A5-PYM and 66% for PYM. Murine hepatoma H22 was transplanted sc into mice and 3A5-PYM conjugate or free PYM were injected peritumorally. As determined by antimicrobial assay, the administration of 3A5-PYM showed higher concentration and longer retention time in the tumor than that of free PYM. Tumor fragments of human colon cancer HT-29 were transplanted sc into nude mice. Then 3A5-PYM or PYM was injected iv, ip or pt (peritumorally) 3 days after inoculation, twice a week, with a total of 7 injections. Tumor growth inhibition was evaluated 4 weeks later. The inhibition rates on the growth of colon cancer xenografts were as follows: (1) for iv route, 58% by PYM, 79% by 3A5-PYM; (2) for ip route, 52% by PYM, 61% by 3A5-PYM; and (3) for pt route, 73% by PYM, 96% by 3A5-PYM. These results indicate that 3A5-PYM conjugate is highly effective against targeted human cancer xenograft and mouse tumor when administered peritumorally or intracavitarily.

Keywords: Pingyangmycin Immunoconjugate Regional targeting tumor therapy Monoclonal antibody

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