

论文

人单克隆抗体与平阳霉素偶联物治疗乳腺癌实验研究

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摘要:

抗乳腺癌人单抗CMI用DextranT-40为中介体的方法与平阳霉素(PYM)偶联,体外实验显示CMI-PYM偶联物对人乳腺癌细胞的IC<sub>50</sub>(抑制50%克隆生成浓度)为0.35μmol·L<sup>-1</sup>;游离PYM为4.0μmol·L<sup>-1</sup>。裸鼠体内实验证明,局部给予CMI-PYM偶联物(2.5mg·kg<sup>-1</sup>)对移植的人乳腺癌抑制率达95%,等剂量平阳霉素为58%。结果表明人单抗CMI-平阳霉素偶联物对乳腺癌有显著疗效,偶联物对肿瘤的抑制作用比游离平阳霉素更强。

关键词: 人单克隆抗体 平阳霉素 乳腺癌 免疫偶联物

EFFECT OF THE CONJUGATE COMPOSED OF A HUMAN MONOCLONAL ANTIBODY AND PINGYANGMYCIN ON MAMMARY CANCER

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Abstract:

To avoid or reduce the induction of human anti-mouse antibody reaction,it is important to use human antibody for the preparation of therapeutic immunoconjugate. CM1, a human monoclonal antibody directed against mammary cancer, was linked to pingyangmycin(PYM),an antitumor antibiotic identical to bleomycin A5 currently in clinical use, employing Dextran T-40 as an intermediate agent. As determined by clonogenic assay with mammary cancer CAMA cells, the IC<sub>50</sub> values for CM1-PYM conjugate and free PYM were 0.35 μmol·L<sup>-1</sup> and0μmol·L<sup>-1</sup>,respectively. Mammary cancer CAMA was transplanted sc in nude mice. Peritumoral injection of CM1-PYM conjugate at doses of 1.25 mg·kg<sup>-1</sup> and 2.5 mg·kg<sup>-1</sup> inhibited the growth of CAMA xenograft by 86%and 95%(P<0.01), whereas the injection of equivalent doses of free PYM inhibited CAMA xenograft by 49%and 58%(P<.05),respectively. CM1-PYM conjugate showed remarkable suppresstion on CAMA xenograft and the inhibitory effect of CM1-PYM conjugate was much higher than that of free PYM, By histo-pathological examination ,no toxic changes were found in the heart, lung,liver,intestines,kidney,spleen and bone marrow of the CM1-PYM-or PYM-treated animals. These results suggest that local administration of the immunoconjugatecomposed of a human monoclonal antibody and pingyangmycin is highly effective and the conjugate may be useful in therapy for human breast cancer.

Keywords: Pingyangmycin Immunoconjugate Mammary Cancer Human monoclonal antibody

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