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论文

脂质体肝实质细胞靶向性研究

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摘要：

目的 脂质体经配体修饰后介导受体细胞,以达靶向给药。方法 肝实质细胞上无唾液酸糖蛋白受体(ASGP-R)的配体无唾液酸胎球蛋白(AF)修饰脂质体得AF-SSL。将ASGP-R重组于脂质双分子膜(BLM)得ASGP-R-BLM,与AF-SSL相互作用,监测BLM膜电参数变化,确定受体-配体间识别反应;用3H标记方法测AF-SSL与肝实质细胞在体内外靶向性;将AF-SSL包抗癌药阿霉素(ADM),考察其抗癌药效。结果ASGP-R-BLM稳定时间随AF-SSL加入量增加而缩短,表现出明显的量效关系,证明在ASGP-R-BLM与AF-SSL之间有特异识别反应;体外AF-SSL与肝实质细胞结合率明显高于无AF修饰脂质体SSL(在第10和90 min时$P<0.05$,在第30和60 min时$P<0.01$);抗肝癌疗效,AF-SSL组大鼠存活期显著长于无AF修饰组,且对心、肾、肺的毒副作用小。结论配体修饰脂质体达到主动靶向对应受体细胞是可行的,本文为脂质体细胞水平靶向给药提供依据。

关键词： 肝实质细胞 脂质体 细胞靶向性 无唾液酸糖蛋白受体 配体介导

Study on the hepatocytic cell targetability of liposomes

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Abstract:

AimTo target for hepatocytic cell, liposomes was modified by special ligand. Methods Sterically stabilized liposomes (SSL) was conjugated with asialofeticin (AF), the ligand of asialoglycoprotein receptor (ASGP-R) of hepatocyte. ASGP-R-BLM is the ASGP-R reconstructed on bilayer lipid membrane (BLM). The recognition reaction between AF-SSL and ASGP-R-BLM can be monitored by the varieties of membrane electrical parameters. The targetability of AF-SSL mediated to hepatocyte was detected by radioisotopic labeled *in vitro* and *in vivo*. The therapeutic effect of antihepatocarcinoma was observed also. ResultsThe lifetime of ASGP-R-BLM decreased with the added amount of AF-SSL. It was demonstrated that there was recognition reaction between AF-SSL and ASGP-R-BLM. The combination of AF-SSL with hepatocyte was significantly higher than that of SSL without AF-modified *in vitro* and *in vivo*. The survival time of rat for AF-SSL carriered ADM (adriamycin) group was much longer and the toxicities on heart, kidney and lung were lower than those SSL carried ADM group. ConclusionIt is possible to actively target the cell with specific receptor by ligand modified liposomes. The result prvide scientific basis of hepatocyte targeted liposomes.

Keywords: cell targetability membrane receptor ligand mediated hepatocyte asialofeticin liposomes

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