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论著

高复制HBV转基因小鼠模型对抗乙型肝炎病毒药物的效应研究

刘光泽[1，2], 孔祥平[2], 任向荣[2], 李秀梅[2], 胡莲美[2], 黄黎珍[1], 顾为望[1△]

1南方医科大学实验动物中心, 广东 广州510515； 2解放军第458医院肝病重点实验室, 广东 广州510602

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摘要

目的：研究高复制HBV转基因小鼠模型对抗乙肝病毒药物的效应评价。 方法： 选用抗乙肝药物拉咪呋啶、大剂量重组乙肝蛋白疫苗、α-1b型干扰素和RNA干扰在转基因小鼠进行药效及作用机制评价。 结果：拉咪呋啶、重组乙肝疫苗、α-1b型干扰素均可使HBV转基因小鼠血清中HBV DNA滴度显著降低。其中后两者还可提高机体脾细胞IL-2和IFN-γ的水平及使分泌IFN-γ脾细胞Elispot斑点数明显增加。将RNA干扰表达载体pU6-siHBV质粒尾静脉注入小鼠体内。注射后5 d血清HBsAg下降56.7%,抑制作用持续14 d。肝脏免疫组化显示HBcAg阳性细胞明显减少，但血清HBV DNA定量无明显降低。 结论： 本近交系高复制HBV转基因小鼠模型对抗乙肝药物药效学评估是可靠、可行的。

关键词 HBV转基因小鼠； 肝炎,乙型； 疫苗, 合成； 干扰素α； RNA干扰

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Use of high-level HBV replication transgenic mice for evaluating drugs treating hepatitis B virus

LIU Guang-ze[1,2], KONG Xiang-ping[2], REN Xiang-rong[2], LI Xiu-mei[2], HU Lian-mei[2], HUANG Li-zhen[1], GU Wei-wang[1]

1Laboratory Animal Centre, Southern Medical University, Guangzhou 510515, China; 2 Infectious Disease Centre of PLA, 458th Hospital of PLA, Guangzhou 510602, China. E-mail: guww100@163.com

Abstract

<P><FONT face=Verdana>AIM: To study the high-level HBV replication transgenic mice for evaluation of </FONT><FONT face=Verdana>drugs treating hepatitis B virus. METHODS: The HBV transgenic mice were treated respectively with lamivudine, large dose </FONT><FONT face=Verdana>recombinant hepatitis B protein vaccine, α-1b interferon, siRNA to evaluate their </FONT><FONT face=Verdana>pharmacodynamics and mechanism of action. RESULTS: HBV DNA titre was reduced significantly in transgenic mice which were treated with </FONT><FONT face=Verdana>lamivudine (100 mg·kg_{^{⁻¹}}·d⁻¹), recombinant hepatitis B protein vaccine (HBsAg 6 </FONT><FONT face=Verdana>μg/mouse), α-1b interferon (50 μg /mouse), respectively. Recombinant hepatitis B protein </FONT><FONT face=Verdana>vaccine and α-1b interferon promoted the level of IL-2 and IFN-γ and increased the </FONT><FONT face=Verdana>Elispot number of spleen cells secreting IFN-γ in the treated transgenic mice. HBV </FONT><FONT face=Verdana>transgenic mice were treated with RNAi expression vector pU6-siHBV against HBV through vena </FONT><FONT face=Verdana>caudalis by hydrodynamics technique. Five days later, the level of serum HBsAg was reduced </FONT><FONT face=Verdana>by 56.7% and the inhibition lasted at least 14 days.The HbcAg (+) cells were decreased </FONT><FONT face=Verdana>obviously by immunohistochemistry detection in liver tissue, but the RNAi did not reduce </FONT><FONT face=Verdana>the serum HBV DNA titre.
CONCLUSION: These inbreeding high-level HBV replication transgenic mice are reliable and </FONT><FONT face=Verdana>feasible for evaluating the anti-HBV drugs and have its economical and convenient </FONT><FONT face=Verdana>superiority.</FONT></P>

Key words HBV transgenic mice Hepatitis B Vaccines synthetic Interferon-alpha RNA interference

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通讯作者 顾为望 guww100@163.com