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[1]朱季香,何长龙,郭艳,等.HCV核心蛋白氨基酸替换与干扰素应答的关系[J].第三军医大学学报,2013,35(09):880-885.

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HCV核心蛋白氨基酸替换与干扰素应答的关

导航/NAVIGATE

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Title: Relationship between amino acid substitutions of

hepatitis C virus core protein with antiviral response to

pegylated interferon

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关键词: 核心蛋白; 丙型肝炎病毒; 氨基酸变异; 病毒学应答

Keywords: core protein; hepatitis C virus; amino acid substitutions;

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摘要: 目的 研究慢性丙型肝炎病毒核心蛋白氨基酸替换与干扰素疗效的

关系。 方法 纳入HCV RNA阳性的慢性丙型肝炎患者108 例,依据干扰素治疗结局分为持续病毒学应答组(76例)、非持续病毒学应答组(32例)。逆转录巢式PCR(RT-nested-PCR)扩增核心蛋白区,分析其氨基酸替换模式及其与干扰素疗效的关系。 结果高频替换(频率>10%)发生于Core蛋白第70、75、91、106、110、

147、187位氨基酸残基,各位点之间存在广泛的连锁替换;两组间Core

蛋白第70位的Q/non-Q替换(P=0.004)、91位的M/non-M替换

(*P*=0.039)、110位的T/non-T替换(*P*=0.025)具有显著差异;70Q、91M、110T替换更倾向于发生不应答治疗结局,*OR*值及95%*Cl*分别为0.288

(0.120~0.693)、0.413 (0.177~0.966)、0.346 (0.133~0.896),同时携

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有上述2个以上的"抵抗型"替换者,治疗4周时HCV RNA水平下降更缓慢(*P*=0.001)。 结论 HCV Core区第70、91、110三个位点可作为Core区预测干扰素疗效的优选氨基酸位点。

Abstract:

To investigate the relationship between amino Objective acid substitutions in hepatitis C virus core region with the virological response (VR) to pegylated interferon. Methods The substitution pattern of amino acid in core region and whether it is associated with VR to pegylated interferon were analyzed retrospectively in a subset of HCV RNA-positive, chronically infected patients who were inpatients or outpatients of our department from December 2008 to October 2012. A total of 108 patients were enrolled and divided into 2 groups based on their final VR to pegylated interferon, sustained VR (SVR) group (n=76), and non-SVR group (n=32). Serum viral RNA was extracted and fulllength core gene was amplified through nested reversetranscription polymerase chain reaction (RT-PCR). Results Hypermutated sites (with mutation frequency exceeding 10%) occurred at positions 70, 75, 91, 106, 110, 147 and 187 amino acids of the core protein. The proportion of Glutamine (Q) and non-Q at position 70, methionine (M) and non-M at position 91, threonine (T) and non-T at position 110 of the core protein were significantly different between SVR and non-SVR group (P=0.004, 0.039 and 0.025, respectively). Q at position 70, M at position 91 and T at position 110 were correlated with non-SVR with OR=0.288, 0.413, 0.346 and 95%*CI*=0.120-0.693, 0.177-0.966, 0.133-0.896, respectively. Patients carried 2 or more undesirable substitutions mentioned above simultaneously tended to attain slower viral decrease after 4 weeks' treatment (P=0.001). Conclusion substitutions at positions 70, 91 and 110 of HCV core protein should be used as predictors of VR to pegylated interferon.

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