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SHP和Smurf2在大鼠肝纤维化中的动态表达及意义

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中文摘要：目的观察小异二聚体伴侣（small heterodimer partner，SHP）和Smad泛素化调节因子-2(Smad ubiquitin regulatory factor-2，Smurf2)在大鼠肝纤维化进展过程中的动态变化及二者之间与TGF-β1的关系的探讨。方法清洁级SD大鼠分两组：正常对照组6只，模型组24只，二甲基亚硝胺（DMN）腹腔注射制备大鼠肝纤维化模型。造模后分别在第2、4、6、8周取大鼠静脉血及肝脏标本，HE和Masson染色并光镜下观察各组大鼠肝组织病理变化；RT-PCR检测SHP、Smurf2、TGF-β1 mRNA在造模过程中的动态变化。结果模型组第4、6周肝纤维化明显；模型组血清ALT、AST、HA升高，并于4周时达高峰；Alb逐步下降，6周时最低，各时间点与对照组相比有统计学差异（P<0.05）。造模后，SHP mRNA表达逐渐增加，第4周达到高峰（0.397±0.016），随后在第6、8周逐渐降低，且明显低于对照组，各模型组与对照组相比有统计学差异（P=0.019，P<0　001，P<0.001,P<0.001）；Smurf2 mRNA在肝纤维化的过程中表达呈进行性增高，8周达到高峰（0.408±0.054），与对照组（0.229±0.024）相比有统计学差异（P<0.001）；TGF-β1 mRNA表达水平逐步增高，于4周时达高峰（0.656±0.036），各模型组与对照组（0.304±0.037）相比具有统计学差异（均P<0.01）。直线相关分析提示SHP与TGF-β1 mRNA呈正相关（r=0.674，P<0.01）。结论SHP、Smurf2在肝纤维化过程中呈升高趋势，分别在第4、8周达到高峰，提示二者可能在肝纤维化发生发展过程中起到重要作用。

中文关键词：小异二聚体伴侣（SHP）　Smad泛素化调节因子（Smurf2）　转化生长因子β1　二甲基亚硝胺　肝纤维化

Dynamic Expression of SHP and Smurf2 in Rats Models of Liver Fibrosis and Its Significance

Abstract: ObjectiveTo explore the expression and significance of small heterodimer partner (SHP)and Smad ubiquitin regulatory factor-2（Smurf2） in rat model of hepatic fibrosis. MethodsSD rats were randomly divided into two group : 6 rats in normal control group and 24 rats in model group.The rat model of HF was established by intraperitoneal injection of dimethylnitrosamine (DMN). After model was made, the rats blood and liver tissue specimens were taken in 2, 6, 4, 8 weeks respectively.Sections of liver tissue were stained with hematoxylin-eosin and Masson and were observed under optical microscope. Gene expression of SHP,Smurf2 and TGF-β1 mRNA in rat liver were determined at different time points with reverse transcription-polymerase chain reaction(RT-PCR). ResultsThe levels of hepatic fibrosis were the most obvious at 4,6 weeks. In model group, ALT and AST、HA increased, reached a peak at 4 weeks; Alb decrease/gradually, and reached the lowest at 6 weeks（22.2±1.2）.And compared with control the difference at rarious time points group had statistically significance.After modeling, SHP mRNA levels began to rise, and reached a peak at 4 weeks(0　397±0.016), then decreased gradually at 6 w and 8 weeks.The difference between experimental subgroups and control group had statistical significance (P=0　019, P<0.001, P<0.001,P<0.001）. Smurf2 mRNA expression increased gradually with the extension of the modeling time, reached a peak at 8 weeks（0.4075±0.05368）, and the discrepancy between it and control group（0.229±0.024）had statistical significance(P<0.001).TGF-β1 mRNA expression increased gradually with the extension of the modeling time, reached a peak at 4 weeks（0　656±0.036）, and the discrepancy between experimental subgroups and control group（0.304±0　037）had statistical significance(P<0.001). Linear correlation analysis showed that SHP was positively correlated with TGF-β1（r=0.674, P<0. 01）. ConclusionDuring the progression of HF,SHP and Smurf2 were trended to increase, and reached a peak at 4 and 8 weeks, respectively.SHP and Smurf2 may play an important role in the development of hepatic fibrosis.

keywords:SHP Smurf2 Transforming growth factor β1 Dimethylnitrosamine hepatic fibrosis