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论著

TAT-P53融合蛋白的小鼠肝毒性

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摘要 目的 观察TAT类融合蛋白体内抗肿瘤的毒性。方法 成功转染移植B16黑色素细胞瘤的C57小鼠ip给予P53, TAT-P53和TAT-常氧依赖性降解结构域(ODD)-P53蛋白5 mg·kg^{-1}, 共计12 d。全自动血液生化指标分析仪测定血清天冬氨酸转氨酶(AST)、丙氨酸转氨酶(ALT)活性、甘油三酯 (TG)、血浆总蛋白(TP)、白蛋白(Al)、血糖(GLU)、尿素(UREA)、肌酐(Cre)和胆固醇(CHO)。结果 与正常小鼠相比, 模型组AST和ALT活性显著升高, TP水平降低。与模型组比较, 给予P53和TAT-P53 后, 血清AST和 ALT活性升高的现象没有明显改善, 反而比模型组略有上升, TP水平降低的现象也无显著改观, 但TG水平显著升高($P<0.01$);给予TAT-ODD-P53融合蛋白后, AST和 ALT活性升高的现象得到有效逆转, TP接近正常小鼠水平, 同时没有发现TG显著升高的现象。与正常对照组比较, 给予P53, TAT-P53和TAT- ODD-P53组Al, GLU, UREA, Cre和CHO无明显变化。结论 TAT-P53在体内具有潜在的肝毒性, 但无肾毒性。

关键词 TAT类融合蛋白 肝毒性 天冬氨酸转氨酶 丙氨酸转氨酶 甘油三酯 总蛋白

分类号

Hepatic toxicity of TAT-P53 fusion protein in mice

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Abstract

OBJECTIVE To study the potential toxicity of TAT-fused protein drugs. **METHODS** B16 melanoma bearing mice were established via subcutaneously injection of B16 tumor cells in C57 mice. TAT-ODD-P53, TAT-P53 and P53 fusion proteins were used for anticancer therapy at the dose of 5 mg·kg^{-1} by ip injection for 12 d. Twenty-four hours after the last injection, animals were executed and serum samples were harvested for aspartate aminotransferase (AST), alanine aminotransferase (ALT), triglyceride (TG), total protein (TP), albumin (Al), glucose(GLU), urea nitrogen (UREA), creatinine(Cre) and cholesterol(CHO). **RESULTS** The level of AST and ALT in serum in TAT-P53 and P53 treatment groups was higher than that of in normal control group, but was higher in TAT-ODD-P53 treated mice than that of normal mice, and lower than in TAT-P53, P53 and saline buffer treatment groups. The TG level of P53 and TAT-P53 treated mice was higher than that of normal control mice or saline buffer and TAT-ODD-P53 treated tumor bearing mice. Moreover, the TP level from P53, TAT-P53 and saline treated mice was higher than that of normal control and TAT-ODD-P53 treated animals. There was no significant difference in Al, GLU, UREA, Cre and CHO between TAT-ODD-P53, TAT-P53 and P53 fusion protein groups compared with normal control group. **CONCLUSION** TAT-P53 has potential toxicity to the liver.

Key words TAT-fused protein hepatic toxicity aminotransferase alanine aminotransferase triglyceride total protein

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