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论著`

p38 MAP激酶在山冈霙吾碱肝细胞毒性中的作用

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摘要 目的 探讨丝裂原活化蛋白激酶p38(p38MAP 激酶)在山冈霙吾碱肝细胞毒性中的作用。方法 采用Western杂交方法观察山冈霙吾碱（100 μmol·L^{-1}，分别作用1, 5, 15, 30及60 min）对p38MAP激酶激活的影响； 10 μmol·L^{-1} p38MAP激酶抑制剂SKF86002 预处理15 min后，分别观察其对山冈霙吾碱（100 μmol·L^{-1}）诱导p38MAP激酶磷酸化（30 min, Western杂交法）及细胞毒性（MTT法，36及48 h; 台盼蓝染色法, 36 h）的影响。结果 Western blot结果显示，100 μmol·L^{-1}山冈霙吾碱明显诱导p38 MAP激酶的磷酸化激活，5～30 min时处于较高水平；SKF86002预处理可以明显抑制山冈霙吾碱诱导的p38 MAP激酶磷酸化；MTT染色法和台盼蓝染色实验均发现SKF86002预处理能部分降低山冈霙吾碱诱导的肝细胞毒性〔MTT，36 h: (0.210±0.008) *vs* (0.170±0.003), 48 h: (0.33±0.03) *vs* (0.200±0.003)；台盼蓝染色(80±2)% *vs* (72±7)%; n=8, $P<0.05$〕。结论 p38MAP激酶可能参与了山冈霙吾碱诱导的肝细胞毒性作用。

关键词 山冈霙吾碱 肝细胞 p38 MAP激酶

分类号 R996.2

p38 MAP kinase involved in clivorine-induced hepatocytes toxicity

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Abstract

AIM To explore the role of p38 mitogen-activated protein kinase (p38 MAPK) in clivorine-induced cellular toxicity. **METHODS** Western blot was performed to observe the effect of clivorine(100 μmol·L^{-1}, for 1, 5, 15, 30 and 60 min) on the phosphorylation of p38 MAPK in L-02 hepatocytes. Pretreated with SKF86002 (a specific inhibitor of p38 MAPK) for 15 min, the effects of clivorine (100 μmol·L^{-1} for 30 min)on p38 MAPK phosphorylation and cellular toxicity were measured by Western blot, MTT(for 36 and 48 h) and trypan blue assay (for 36 h), respectively. **RESULTS** Clivorine (100 μmol·L^{-1}) significantly induced the phosphorylation of p38 MAPK, and remained at high level from 5-30 min. Pretreated with SKF86002 (10 μmol·L^{-1}) significantly decreased the phosphorylation of p38 MAPK. SKF86002 also partly improved clivorine-induced cellular toxicity〔MTT, 36 h: (0.210±0.008) *vs* (0.170±0.003, 48 h: (0.33±0.03) *vs* (0.200±0.003); trypan blue assay: (80±2)% *vs* (72±7)%; n=8, $P<0.05$). **CONCLUSION** p38 MAPK signaling pathway may play important roles in the clivorine-induced hepatocytes toxicity.

Key words clivorine hepatocyte p38 MAP kinase

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