

# 学 位 論 文 の 要 旨

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<p>主論文の題名</p> <p>Comparative Study on the Cytoprotective Effects of Activated Protein C Treatment in Nonsteatotic and Steatotic Livers under Ischemia-Reperfusion Injury</p> <p>主論文の要旨</p> <p>Activated protein C (APC) has cytoprotective effects on liver ischemia-reperfusion injury (IRI). However, it is unclear whether APC is beneficial in steatotic liver IRI. We compared the cytoprotective effects of APC in non-steatotic and steatotic liver IRI.</p> <p><b>Methods:</b> Mice were fed either normal diets (ND mice) or high fat diets (HF mice), were treated with APC or saline (control) and were performed IRI. In an in vitro study, primary steatotic hepatocytes were either untreated, or were treated with APC, then incubated with H<sub>2</sub>O<sub>2</sub>.</p> <p><b>Results:</b> APC significantly reduced serum transaminase levels and the inflammatory cells infiltration compared with control at 4 h in ND mice, while at 24 h in HF mice. APC inhibited sinusoidal endothelial injury in ND mice, but not in HF mice. In contrast, APC activated adenosine monophosphate-activated protein kinase (AMPK) phosphorylation in HF mice, but not in ND mice. In the in vitro study, APC significantly increased AMPK phosphorylation, ATP concentration and survival rates of hepatocytes compared with control.</p> <p><b>Conclusion:</b> During IRI in normal liver, APC attenuated initial damage by inhibiting inflammatory cell infiltration and sinusoidal endothelial injury, but not in steatotic liver. However, in steatotic liver, APC might attenuated late damage via activation of AMPK.</p>			