CD44 Disruption Attenuates Murine Hepatic Ischemia/Reperfusion Injury

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Purpose: Hepatic ischemia/reperfusion (I/R) injury, which is a pathophysiologic process by various inflammatory activation during the reperfusion, remains an important clinical problem associated with liver transplantation and major liver surgery. Neutrophil adhesion and migration are critical in hepatic ischemia and reperfusion injury (I/R). Despite very strong preclinical data, recent clinical trials failed to show a protective effect of anti-adhesion therapy in reperfusion injury. Therefore, the aim of this study was to assess the role of CD44 in neutrophil infiltration and liver injury during early and late phage of liver I/R.

Method: Male wild-type (C57BL/6) mice (8~12 week old) underwent 60 minutes of partial liver ischemia followed by various periods of reperfusion (6, 15, 24, 48, 72 h and survival study). Liver injury was assessed by plasma level of alanine aminotransferase (ALT) and histopathology. To assess a potential role of CD44 in neutrophil infiltration and liver injury during liver I/R were analyzed by biomolecular and immunohistochemical study. Results were expressed as the mean±SEM. Group comparisons were performed using Student’s t test or analysis of variance. Differences were considered significant at p<0.05.

Result: Reperfusion caused significant hepatocellular injury as it was determined by plasma ALT levels and liver histopathology. The injury was associated with a marked neutrophil recruitment and CD44 expression into the ischemic livers. Administration of anti-CD44 to mice reduced the infiltration of neutrophil into the ischemic tissue, associated with liver function preservation.

Conclusion: These results support critical functions for CD44 in neutrophil recruitment and activation leading to liver damage. Moreover, they provide the rationale for targeting to CD44 as a potential therapeutic approach in liver I/R injury.