Identification of Proteins Interacting with Cytoplasmic High-Mobility Group Box 1 during the Hepatocellular Response to Ischemia Reperfusion Injury.

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Abstract

Ischemia/reperfusion injury (IRI) occurs inevitably in liver transplantations and frequently during major resections, and can lead to liver dysfunction as well as systemic disorders. High-mobility group box 1 (HMGB1) plays a pathogenic role in hepatic IRI. In the normal liver, HMGB1 is located in the nucleus of hepatocytes; after ischemia reperfusion, it translocates to the cytoplasm and it is further released to the extracellular space. Unlike the well-explored functions of nuclear and extracellular HMGB1, the role of cytoplasmic HMGB1 in hepatic IRI remains elusive. We hypothesized that cytoplasmic HMGB1 interacts with binding proteins involved in the hepatocellular response to IRI. In this study, binding proteins of cytoplasmic HMGB1 during hepatic IRI were identified. Liver tissues from rats with warm ischemia reperfusion (WI/R) injury and from normal rats were subjected to cytoplasmic protein extraction. Co-immunoprecipitation using these protein extracts was performed to enrich HMGB1-protein complexes. To separate and

identify the immunoprecipitated proteins in eluates, 2-dimensional electrophoresis and subsequent mass spectrometry detection were performed. Two of the identified proteins were verified using Western blotting: betaine-homocysteine S-methyltransferase 1 (BHMT) and cystathionine γ-lyase (CTH). Therefore, our results revealed the binding of HMGB1 to BHMT and CTH in cytoplasm during hepatic WI/R. This finding may help to better understand the cellular response to IRI in the liver and to identify novel molecular targets for reducing ischemic injury.

Beteiligte Forschungseinheiten

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