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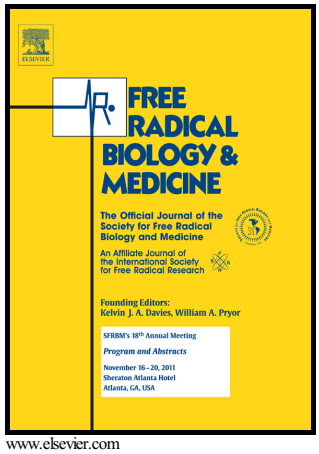

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PII: S0891-5849(16)30409-9
DOI: http://dx.doi.org/10.1016/j.freeradbiomed.2016.08.028
Reference: FRB12982

To appear in: *Free Radical Biology and Medicine*

Received date: 24 June 2016
Revised date: 23 August 2016
Accepted date: 26 August 2016

Cite this article as: Le Zhang, Qing Cheng, Longjie Zhang, Yijun Wang, Gary F. Merrill, Tal Ilani, Deborah Fass, Elias S.J. Arnér and Jinsong Zhang, Serum thioredoxin reductase is highly increased in mice with hepatocellular carcinoma and its activity is restrained by several mechanisms, *Free Radical Biology and Medicine,* http://dx.doi.org/10.1016/j.freeradbiomed.2016.08.028

Serum thioredoxin reductase is highly increased in mice with hepatocellular carcinoma and its activity is restrained by several mechanisms

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Abstract

Increased thioredoxin reductase (TrxR) levels in serum were recently identified as possible prognostic markers for human prostate cancer or hepatocellular carcinoma. We had earlier shown that serum levels of TrxR protein are very low in healthy mice, but can in close correlation to alanine aminotransferase (ALT) increase more than 200-fold upon chemically induced liver damage. We also found that enzymatic TrxR activity in serum is counteracted by a yet unidentified oxidase activity in serum. In the present study we found that mice carrying H22 hepatocellular carcinoma tumors present highly increased levels of TrxR in serum, similarly to that reported in human patients. In this case ALT levels did not parallel those of TrxR. We also discovered here that the TrxR-antagonistic oxidase activity in serum is due to the presence of quiescin Q6 sulfhydryl oxidase 1 (QSOX1). We furthermore found that the chemotherapeutic agents cisplatin or auranofin, when given systemically to H22 tumor bearing mice, can further inhibit TrxR activities in serum. The TrxR serum activity was also inhibited by endogenous electrophilic inhibitors, found to increase in tumor-bearing mice and to include protoporphyrin IX (PpIX) and 4-hydroxynonenal (HNE). Thus,