

Trx-2 KO MICE ARE MORE SENSITIVE TO OXIDATIVE STRESS INDUCED BY DIAQUAT

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Trx-2 is a mitochondria-specific member of the thioredoxin superfamily, and is important in antioxidant defenses against ROS-induced damage in the mitochondria. Previously, we have found that diquat treatment in wild type mice in vivo, affects mitochondria function, modifying aconitase activity, ATP and ROS production. Likewise, the mitochondrial electron transport complexes are also vulnerable to oxidative damage induced by diquat, producing an inhibition of complexes I (30%), II (10%), III (60%), IV (20%) and V (50%), with a time course of activity loss that is unique for each complex. In addition, we found an increase in HNE adducts, nitrotyrosine modifications and carbonyl groups among the oxidative modification induced by diquat. In this study, we evaluated the biological significance of Trx-2 deficiency on mitochondrial function and oxidative damage induced by diquat using Trx-2 KO mice. Wild type and Trx-2 KO mice were injected i.p with DQ (50mg/Kg) and sacrificed at 0 and 6 hrs of treatment. Plasma ALT levels, ATP production and oxidative modifications to proteins were measured. Our results indicates, that Trx-2 KO mice are more sensitive to oxidative stress than wild type mice, showing a reduction in ATP production, an increase in ALT levels and also an increase in carbonyl group formation induced by diquat. Therefore, our studies indicate that Trx-2 KO mice are more sensitive to oxidative stress induced by diquat, and future studies will focus on Trx-2 role in the oxidative damage of specific macromolecules and signal transduction pathways leading to apoptosis. *(Supported by NIH grant R01 AG23843)*