

DOES OVEREXPRESSION OF THIOREDOXIN 1 INCREASE RESISTANCE TO OXIDATIVE STRESS AND AFFECT AGING AND PATHOLOGY?

Y. Ikeno (P), C. Lew, L. Cortez, A. Chaudhuri, Q. Ran, W. Qi, R. Levine, J. Yodoi, and A. Richardson

Department of Cellular and Structural Biology, and the Barshop Institute for Longevity and Aging Studies, The University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, TX 78229, USA

We examined the effect of increased levels of thioredoxin 1 (Trx1) on resistance to oxidative stress and on aging in transgenic mice overexpressing Trx1 [Tg(hTrx)+/0]. This study was conducted because substantial evidence suggests that oxidative stress affects aging, and Trx1 has antioxidant properties. Our results showed that Tg(hTrx)+/0 mice had significantly higher Trx1 expression (protein and biological activity) compared to wild-type mice and without a downregulation of other antioxidant enzymes. The increase in Trx1 expression was associated with increased resistance to oxidative stress in vitro (hydrogenperoxide treatment of mouse embryonic fibroblast) and in vivo (diquat treatment). Oxidative damage to protein (carbonyl groups and methionine sulfoxide levels) was lower in the livers of Tg(hTrx)+/0 mice compared to wild-type mice. Tg(hTrx)+/0 mice also showed signs of slower aging. For example, Tg(hTrx)+/0 mice showed lower incidences of tumors compared to wild-type mice at 26 months of age. The survival study, which is ongoing, showed the survival of Tg(hTrx)+/0 and wild-type mice at 30 months was 67% and 52%, respectively. Thus, our findings suggest that increased levels of Trx1 in Tg(hTrx)+/0 mice are correlated to increased resistance to oxidative stress, and are associated with less pathology and a higher survival rate. These results support the hypothesis that the overexpression of Trx1 plays a protective role against oxidative stress, and therefore may have an impact on aging and age-related diseases. (*Supported by grant from the VA Merit Review*)