

## **Cu/Zn SOD TRANSGENIC RATS SHOW REDUCED OXIDATIVE DAMAGE AND INCREASED SURVIVAL**

Y. Ikeno (P), L. Cortez, C. Lew, W. Qi, A. Chaudhuri, 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 Cu/Zn superoxide dismutase (SOD) on oxidative stress and on aging in transgenic rats overexpressing Cu/ZnSOD [Tg(*hSod1*)<sup>+0</sup>]. This study was conducted because substantial evidence suggests that oxidative stress affects aging and various age-related diseases. Although a number of investigators have studied various genetic manipulations in mice, this is the first study to use transgenic rats to study aging. Our results showed that Tg(*hSod1*)<sup>+0</sup> rats had significantly higher Cu/ZnSOD activity compared to wild-type rats without a downregulation of other major antioxidant enzymes. The increase in Cu/ZnSOD activity was associated with lower levels of DNA oxidation, protein oxidation and lipid peroxidation. Tg(*hSod1*)<sup>+0</sup> rats also showed evidence of increased longevity. The survival study, which is ongoing, showed that the survival of Tg(*hSod1*)<sup>+0</sup> and wild-type rats at 25 months was 79% and 47%, respectively. Thus, our findings suggest that increased Cu/ZnSOD activity in Tg(*hSod1*)<sup>+0</sup> rats is correlated to reduced oxidative damage, and associated with increased longevity. These results are in contrast to a previous study with transgenic mice showing that the overexpression of Cu/ZnSOD did not affect lifespan. These data suggest that genetic manipulations might have a differential effect on lifespan in different species. *(Supported by grant from the VA Merit Review)*