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The Development of Hepatocellular Carcinoma in Thioredoxin Reductase 1 Deficient Liver Cells

We examined diethylnitrosamine- (DEN) induced hepatocellular carcinoma (HCC, liver cancer) in either normal mice or mice lacking the thioredoxin system, one of the major cellular antioxidant systems, in liver cells. Utilizing a previously established thioredoxin reductase-1 (txnrd1) conditional-knockout model, forty-one male mice whose liver cells were wild-type, heterozygous, or homozygous for disruption of txnrd1 were challenged with DEN at two-weeks of age. Mice were sacrificed eight months later and macroscopically visible tumors were analyzed. Wild-type mice averaged 13.9 tumors, whereas heterozygous and homozygous mice averaged 10.8 and 4.8 tumors, respectively. Contrary to expectations based on the "oxidation model of carcinogenesis", these results indicated that mice deficient in txnrd1 were resistant to DEN-induced HCC. Ongoing studies are being conducted to investigate the mechanisms underlying this protection.