

Endoplasmic Reticulum Stress and Metallothionein

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Many people are susceptible to age-related diseases including type 2 diabetes mellitus, cardiovascular disease, hypertension, hyperlipidemia and cancer. Much attention has been paid to these lifestyle-related diseases because the incidences of the diseases are increasing in the developed countries. Although it has been shown that production of reactive oxygen species (ROS) causes the initiation and promotion of the life style-related diseases, the details are uncertain. Recently, Ozcan et al. (Science 306, 457-461, 2004) reported that obesity causes endoplasmic reticulum (ER) stress, leading to insulin resistance through the suppression of insulin receptor signaling. In addition, zinc deficiency upregulates the mammalian ER stress response indicating requirement for Zn in ER function.

Since metallothionein (MT) contains zinc and has a regulatory role of zinc metabolism and anti-oxidative role, we investigated the nature of stress reaction and a preventive role of against oxidative- and ER stress in the present study. We also investigate the possible effect of MT on the development of obesity was examined using MT-null and wild-type mice fed a high-fat diet.

We observed that ER stress increased induction of MT synthesis, and the enhanced response to ER stress was observed in the liver of in MT-null mice (Kondoh et al., Toxicol. Lett, 148,133-139, 2004). MT and/or Zn liberated from Zn-MT may regulate development of obesity, insulin- and leptin resistance via modulation of ER stress.