

**Health and Exercise Science Senior Thesis Projects
Spring 2014**

Title of Thesis: The anti-obesity effects of MnTBAP: PAR-2 pathway

Student Name(s): Timothy W. Brodsky and Alexandra Z. Sosinsky

Faculty Sponsor Name(s): T.H. Reynolds, PhD

Abstract

Manganese tetrakis benzoic acid porphyrin (MnTBAP) is a superoxide dismutase mimetic that has been shown to reduce reactive oxygen species (ROS) and improve insulin sensitivity. Protease-activated receptor-2 (PAR-2) signaling has been implicated in the development of diet-induced obesity and insulin resistance. PAR-2 signaling is closely linked with ROS. The purpose of this study was to determine whether the anti-obesity and insulin-sensitizing effects of MnTBAP treatment in dietary-induced obese (DIO) mice were associated with a decreased expression of tissue factor (TF) and PAR-2, and an increased expression of cathepsin G (CtsG) and proteinase 3 (Prot3). Male C57B6 mice were fed a low fat diet (LFD) or a high fat (HFD) for five months. During the last five weeks of the dietary intervention, mice were given intraperitoneal injections of MnTBAP (10 mg/kg/day) or vehicle. MnTBAP treatment significantly decreased body weight (52.8 ± 2 vs. 40.1 ± 2.1 g) and epididymal white adipose tissue (EWAT) weight (2.53 ± 0.11 vs. 1.47 ± 0.13 g) and increased insulin sensitivity. PAR-2 and TF expression were significantly decreased in EWAT from HFD mice treated with MnTBAP. CtsG and Prot3 expression were significantly increased in both LFD and HFD fed mice treated with MnTBAP. Taken together, our data demonstrates that MnTBAP treatment reduces dietary-induced obesity by a mechanism that may involve disruption of the PAR-2 signaling pathway.