

## Endogenous Estrogen-Mediated Heme Oxygenase Regulation in Experimental Menopause

Anikó Pósa, Renáta Szabó, Anett Csonka, Médea Veszélka, Anikó Magyariné Berkó, Zoltán Baráth, Rudolf Ménesi, Imre Pávó, Mariann Gyöngyösi, Ferenc László, Krisztina Kupai, and Csaba Varga

### Abstract

Estrogen deficiency is one of the main causes of age-associated diseases in the cardiovascular system. Female Wistar rats were divided into four experimental groups: pharmacologically ovariectomized, surgically ovariectomized, and 24-month-old intact aging animals were compared with a control group. The activity and expression of heme oxygenases (HO) in the cardiac left ventricle, the concentrations of cardiac interleukin-6 (IL-6) and tumor necrosis factor- (TNF- $\alpha$ ), the myeloperoxidase (MPO) activity in the cardiac left ventricle, and the effects of heme oxygenase blockade (by 24-hour and 1-hour pretreatment with tin-protoporphyrin IX, SnPP) on the epinephrine and phentolamine-induced electrocardiogram ST segment changes in vivo were investigated. The cardiac HO activity and the expression of HO-1 and HO-2 were significantly decreased in the aged rats and after ovariectomy. Estrogen depletion was accompanied by significant increases in the expression of IL-6 and TNF- $\alpha$ . The aged and ovariectomized animals exhibited a significantly elevated MPO activity and a significant ST segment depression. After pretreatment with SnPP augmented ST segment changes were determined. These findings demonstrate that the sensitivity to cardiac ischemia in estrogen depletion models is associated with suppression of the activity and expression of the HO system and increases in the secretion of proinflammatory cytokines and biomarkers.

„This research was supported by the European Union and the State of Hungary, co-financed by the European Social Fund in the framework of TÁMOP-4.2.4.A/ 2-11/1-2012-0001 ‘National Excellence Program’.”