**ENDOTHELIAL DYSFUNCTION IN HYPERTENSION, DIABETES AND OBESITY**

X. Huang, J.J. Corbalan, **T. Malinski**

Ohio University, Athens, OH, USA

Background: The functional endothelium is a main source of nitric oxide (NO), a regulator of vascular homeostasis. The shear stress controls NO release from endothelium, and maximum concentration of NO production can vary significantly from about 100 nmol/L to 500 nmol/L. The highest level of NO is produced by endocardium. In hypertension, diabetes mellitus and obesity, endothelial nitric oxide synthase (eNOS) expression increases while paradoxically bioavailability of NO decreases. This effect can be due to increased production of superoxide which rapidly reacts with NO to produce peroxynitrite (ONOO–). A major source of superoxide in dysfunctional endothelium is NADPH oxidase and eNOS itself.

Methods and Results: We used a nanotechnological/nanomedical approach (nanosensors with diameter < 300 nm) to monitor in vivo and in vitro, real time (microseconds), in situ concentrations of NO, superoxide and ONOO– produced by dysfunctional endothelium in animal models of hypertension (Spontaneous Hypertensive rats), diabetes (streptozotocin-induced diabetes in Wistar-Kyoto rats) and obesity (Zucker rats). We introduced a parameter R, where R = [NO]/[ONOO–], the ratio of NO concentration to ONOO– concentration, to measure a degree of endothelial dysfunction. The R is above 5.0 in normal endothelium. In hypertension, obesity and diabetes mellitus, a severe imbalance between NO and nitroxidative stress was observed with R < 2, and under severe diabetes R < 0.5.

Conclusions: The [NO]/[ONOO–] ratio reflects a functional state of the endothelium and can be used as a diagnostic tool to evaluate damage of vasculature at different disease stages.