**HEME OXYGENASE-1 DEFICIENCY EXACERBATES ABDOMINAL AORTIC ANEURYSM**

Y.C. Ho, M.L. Wu, **S.F. Yet**

National Health Research Institutes, Zhunan, Taiwan

Despite a protective role of the anti-oxidative and anti-inflammatory heme oxygenase-1 (HO-1) in several cardiovascular diseases has been established, the role of HO-1 in abdominal aortic aneurysm (AAA) formation remains unclear. We subjected mice deficient in apoE or deficient in both HO-1 and apoE to an angiotensin II-infused AAA model. HO-1 was barely detectable in the aorta under normal physiological conditions but markedly induced in the aortic wall after angiotensin II infusion, implicating a role in AAA. HO-1 deficiency increased AAA incidence and rupture rate, increased aortic aneurysmal area and severity, accompanied with severe elastin degradation and medial degeneration. Further analysis revealed that lack of HO-1 markedly enhanced reactive oxygen species levels, smooth muscle cell (SMC) loss, macrophage infiltration, and matrix metalloproteinase (MMP) activity in the aneurysmal aortic wall, resulting in exacerbated AAA formation. In vitro, angiotensin II induced HO-1 expressions in apoE-deficient SMCs and macrophages. Deficiency in both HO-1 and apoE rendered SMCs more susceptible to oxidant-induced cell death, and an enhanced MMP2 activity in response to angiotensin II. In primary macrophages, absence of HO-1 aggravated the responses to angiotensin II by increasing inflammatory cytokine productions and MMP9 activity. Taken together, our results demonstrate that the induction of HO-1 in the aortic wall during AAA progression might be a protective mechanism while deficiency of HO-1 exacerbates AAA via enhanced oxidative stress and inflammation. Increasing HO-1 expression in the aorta might be a promising therapeutic strategy for AAA.