

## **Role of NADPH Oxidase and Renin-Angiotensin System in Intermittent Hypoxia-Induced Inflammation in Rat Adrenal Medulla**

*Yu Liu, and Man Lung Fun<sup>1</sup>*

*Department of Physiology, the University of Hong Kong*

We have shown that intermittent hypoxia (IH) associated with recurrent apnea induces oxidative stress and inflammation in rat adrenal medulla. However the pathogenic mechanism is not clear at present. We hypothesized that the expression of NADPH oxidase (NOX) induced by renin-angiotensin system (RAS) plays a role in the tissue inflammation during chronic IH. Adult SD rats were exposed to air [normoxic (Nx) control] or IH treatment (8 hrs/day) which mimicked a severe recurrent sleep apneic condition for 14 days. Injections of apocynin, an inhibitor of NOX, (25 mg/kg i.p.) or vehicle were performed before the IH treatment every day. the mRNA levels of NOX subunits p22-phox, NOX-2 and NOX-4 and the protein expressions of IL-6, TNF- $\alpha$  and COX-2 were examined by RT-PCR and ELISA. the protein expressions of NOX-4 and RAS components (AGT, AT1 and AT2) were examined by Western blot. Our results showed that the protein expression of IL-6, TNF- $\alpha$  and COX-2 were significantly higher in the IH group than that of the Nx and apocynin-treated hypoxic (AIH) group. the mRNA levels of p22-phox, NOX-2 and NOX-4 were also increased markedly in the IH group, when compared with other two groups. in addition, IH treatment significantly induced the protein expression of NOX-4. Furthermore, the protein expressions of AGT, AT1 and AT2 were increased in the IH group, indicating that the up-regulation of NOX may be induced by the increased RAS expression. in conclusion, we showed that NOX plays a pathogenic role in the IH-induced local inflammation in rat adrenal medulla.