**INCREASED RENAL ENAC SUBUNITS AND SODIUM RETENTION IN RATS WITH CHRONIC HEART FAILURE**

**H. Zheng**, X.F. Liu, K.P. Patel

University of Nebraska Medical Center, Omaha, NE, USA

One hallmark of chronic heart failure (CHF) is sodium and fluid retention. One of the key elements involved in renal sodium retention is activation of epithelial sodium channels (ENaC) of principal cells in the collecting tubule. Recently, it has been shown that proteolytic cleavage has an important role in activating ENaC by cleaving at specific sites within the finger domains of ENaC subunits. We hypothesized that renal sodium dysfunction in CHF rats is through the activation of protease-ENaC pathway. The left coronary ligation-induced model of heart failure in the rat was used. Real-time PCR and Western blotting demonstrated that the mRNA and protein abundance of alpha, beta and gamma-subunits of ENaC were significantly increased in the cortex and outer medulla of the kidneys from CHF compared to the sham-operated rats. Furthermore, there was a significant increase in diuretic and natriuretic responses to ENaC inhibitor benzamil in the rats with CHF. We also found that several urinary serine proteases (furin, prostasin and plasmin) were significantly increased in CHF compared to the sham rats. Whole-cell patch-clamp result shows the protease-rich urine increased the sodium inward current in M-1 cells compared to the sham urine incubation. On the contrary, the urine collected from sham rats did not activate ENaC activity in M-1 cells. These results suggest that the increased expression of renal ENaC subunits may contribute to the renal sodium and water retention observed during CHF. Proteases in the renal tubule have important roles in activating ENaC in rats with CHF.