

## KSN 2017 Abstract

KSN-17-P309

### ER stress and polyuria in $\alpha$ -galactosidase A deficient mice

\*Ki-hwan HAN<sup>1</sup>, Ji-eun KIM<sup>1</sup>, Sae-jin LEE<sup>1</sup>, Su-youn LEE<sup>1</sup>, Sung-chul JUNG<sup>2</sup>

<sup>1</sup>Department of Anatomy, Ewha Womans University, Korea, South, <sup>2</sup>Department of Biochemistry, Ewha Womans University, Korea, South

**Objectives** : Fabry disease is a lysosomal storage disorder caused by deficiency of the enzyme  $\alpha$ -galactosidase A ( $\alpha$ -Gal A). Misfolded enzymes are retained in the endoplasmic reticulum (ER) and degraded before sorting into lysosomes resulting in lysosomal accumulation of globotriaosylceramide (Gb3). The purpose of this study was to investigate the effects of ER stress on polyuria, initial renal symptoms, in  $\alpha$ -Gal A deficient mice.

**Methods** : Kidney tissues were processed for  $\alpha$ -Gal A enzyme activity assay, Gb3 level quantification, immunocytochemistry, and immunoblot analysis.  $\alpha$ -Gal A deficiency caused significant polyuria that was associated with increased renal Gb3 level.

**Results** : Fabry kidneys showed a significantly increased expression of ER stress proteins, Bip and CHOP. Immunocytochemistry revealed that the expression of Bip and CHOP was induced mainly in glomeruli, outer medullary vascular bundles, and medullary collecting ducts. AQPs are key transport proteins involved in urine concentration in the kidney. Expression of AQP2, 3, and 4 proteins significantly decreased in Fabry kidneys, but the abundance of AQP1 protein remained unchanged. Confocal microscopy demonstrated that AQP2 was abnormally localized in the cytoplasm in medullary collecting ducts. Electron microscopy confirmed the presence of typical lamellar inclusion bodies in collecting duct cells.

**Conclusions** : These findings suggest that ER stress and altered expression of AQPs may play an important role in urinary concentration defect in Fabry disease.

This work was supported by funds from the National Research Foundation of Korea (NRF-2013R1A1A2058028) and intramural research promotion grants from Ewha Womans University School of Medicine.

**Keywords** :  $\alpha$ -Galactosidase A, ER stress, Polyuria, AQPs