Hidenori Yasuda et al., J Nephrol Ther 2015, 5:4
http://dx.doi.org/10.4172/2161-0959.C1.019

OMICS International
conferenceseries.com

4th International Conference on
Nephrology & Therapeutics
September 14-16, 2015 Baltimore, USA

Congenital nephron reduction with Astrin defect results in progressive renal fibrosis and glomeruloscrelosis

Hidenori Yasuda, Yuki Tochigi, Kentaro Katayama and **Hiroetsu Suzuki**
Nippon Veterinary and Life Science University, Japan

The nephron numbers individually varies in various mammalian species. In any renal diseases with reduced nephron mass, nephrons never regenerate because mature kidneys already lose their stem cells. Recently it has been reported that birth weight is related to nephron mass. The low birth weight leads to reduced nephron numbers and high risks for chronic kidney disease (CKD). Thus, the pathogenesis of CKD caused by nephron reduction is thought to be important for prognosis of such CKD patients. So we focused on hypoplastic kidney (HPK) with 80% nephron reduction in affected rats of HGNII strain. The affected HPK rats have a loss-of-function mutation on the gene encoding a microtubule-associated protein, Astrin. Although it has been reported that Astrin is required for mitotic progression in HeLa cells, *in vivo* function of Astrin especially in renal development and its' involvement to renal diseases have not yet been established. Based on our previous reports (NDT 2005; 20: 1362-9, Pediatric Nephrol 2006; 21: 637-42, Congenit Anom (Kyoto) 2007; 47: 34-44), we have hypothesized that the defect of Astrin might be related with development and prognosis of CKD. In the present study, we immunohistologically examined the progression of CKD in HPK rats at 5-30 weeks of age. In HPK rats at 5 weeks of age, the glomerulus already hypertrophied and exhibited infiltration of macrophages, increased TGF-β and fibronectin levels and desquamation of podocytes (discontinuity of podocin staining in glomerulus). In affected glomerulus at 20 weeks of age afterward, we found high levels of PDGF and its receptor, increases of mesangial cells and extracellular matrixes (ECMs) including collagen type 1, collagen type 4 and fibronectin and epithelial-mesenchymal transition in Bowman's capsule. In the interstitium of HPK, we found increases of PDGF receptor β-positive fibroblasts at all week's examined and α-SMA positive myofibroblasts after 10 weeks afterwards, indicating the transition from fibroblast to myofibroblast. Then we observed age-related accumulation of ECMs with increased levels of PDGF. Consisting with these changes, we observed hematological symptoms of renal dysfunction with age-related deterioration. These results suggested that congenital 80% nephron reduction due to loss of Astrin results in progressive renal fibrosis and glomerulosclerosis and that genetic abnormality of Astrin is one of the possible risk factors for CKD. Recently, it has been reported that Astrin is a negative mTOR regulator of stress response in HeLa cells (Cell 2013; 154: 859-74). We will discuss the possibility that Astrinis related with embryonic pathogenesis of HPK.

hideyasuda4@gmail.com

Notes: