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A novel oxidative stress biomarker, APX-501, protein is a promising new biomarker for the initiation and progression of diabetic nephropathy in type 2 diabetic patients

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Objectives : A large body of evidence indicates that oxidative stress is one of the most important mechanism link for the major pathways involved in the development and progression of diabetic vascular complications. Nox (NADPH oxidase)-derived ROS (reactive oxygen species) have been implicated in the development of diabetic nephropathy. Recently we identified that APX-501 protein was synthesized from mesangial cells and podocytes, and found that APX-501 is involved in oxidative stress in the kidney. Therefore, we investigated the role of APX-501 as a new biomarker for diabetic nephropathy in type 2 diabetic patients.

Methods : 131 type 2 diabetic patients and 35 patients with nephrotic syndrome as a control were included and prospectively followed up 6months.The study population were comprised of four groups: a nondiabetic patients with nephrotic range of proteinuria as a control (n=35), a normoalbuminuric diabetic group (n=34), a microalbuminuric diabetic group (n=26) and an overt proteinuria group (n=71). Plasma levels of APX-501 were measured at baseline and 6months later by ELISA. Additionally, we performed animal and in vitro studies using db/db mice to further confirm the role of APX-501 in diabetic nephropathy.

Results : Plasma APX-501 concentrations were significantly higher in the microalbuminuria and overt proteinuria diabetic patients than in the controls. Plasma APX-501 levels showed progressively increased levels in accordance with the stage of diabetic nephropathy. Plasma APX-501 levels were positively correlated with systolic blood pressure, serum creatinine levels and urinary albumin excretion (UAE), and were inversely correlated with eGFR. During 6months follow up period, plasma APX-501 levels showed progressively increased in all diabetic patients. The degree of increment of APX-501 was

were most profound in microalbuminuric and overt proteinuria group. In type 2 diabetic db/db mice, plasma levels and renal expression of APX-501 showed significantly increased according to age compared with those in nondiabetic db/m mice. In cultured cells, high glucose and angiotensin II increased synthesis of APX-501. Furthermore, gene silencing of APX-501 ameliorated the high glucose-induced ECM synthesis and oxidative stress markers.

Conclusions : These findings suggest that APX-501 synthesis is activated in early stage of diabetic environment, and progressively increased in the progression of diabetic nephropathy. APX-501 protein may be a novel new biomarker for diabetic nephropathy in type 2 diabetic patients.

Keywords : APX-501, Oxidative stress, Progression of renal disease, Biomarker