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The role of VSIG4 in the diabetic nephropathy

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Diabetic nephropathy is a leading cause of end stage of renal diseases in the world. Inflammation has been known to be related to the pathogenesis of the diabetic nephropathy. V-set Ig domain containing 4 (VSIG4), which is one of the B7 superfamily, is a receptor for complement 3 and mainly expressed in macrophage. Recently, VSIG4 has been reported to regulate T cell function and to be related to the fibrosis in several diseases. We investigated the expression of VSIG4 under high glucose condition in cultured HK2 cells and in type 2 diabetic animal model.

HK2 cells were incubated with high glucose condition of 30mmol/L D-glucose. The expression of VSIG4 mRNA was measured by semi-quantitative PCR. To determine intrarenal expression of VSIG4, six-week-old male diabetic db/db mice and non-diabetic bb/m mice were examined. The expression of VSIG4 protein was determined by immunohistochemical staining. The expression of VSIG4 protein was graded 0-3 semiquantitatively based on intensity of staining and the percentage of positive grid field.

The VSIG4 mRNA expression was increased in the high glucose condition. The expression was time dependently increased at 6, 12 72 hours. The VSIG4 protein measured by Western blotting showed similar pattern.

We investigated renal expression of VSIG4 at 20 weeks in the db/db and db/m mice. The db/db mice presented significantly higher body weight and glucose level compared to db/m mice: body weight (g) 61.0 ± 2.05 vs. 33.25 ± 1.31 , $p < 0.01$; fasting glucose level (mmol/L) 36.7 ± 1.8 vs. 7.8 ± 0.1 , $p < 0.01$. The serum creatinine was not different between two groups, but urinary amount of albumin is significantly higher in diabetic mice than control mice. The expression of VSIG4 mRNA was significantly 69% higher in the db/db mice than in the db/m mice. The expression VSIG4 protein was also highly expressed in diabetic mice. The VSIG4 protein was mainly expressed in distal tubule: 2.67 vs. 1.5, $p < 0.018$. In the proximal tubule, the expression was weaker but significantly different between two groups: 1.0 vs. 0.33, $p < 0.025$. However, there was no expression in the glomeruli.

In conclusion, the expressions of VSIG4 mRNA and protein are upregulated in diabetic milieu. VSIG4 would be involved in the pathogenesis of diabetic nephropathy.