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Background : The liver X receptor α (LXR α) has an important role in lipids and carbohydrates metabolism. It regulates the SREBP1 genes which expression is closely related to nephrosclerosis in diabetic animals. We postulated that LXR α would have an important role in the progression of diabetic nephropathy with the increase of nephrosclerosis via an enhancement of the SREBP1 expression.

Methods : We have given TO901317, an agonist of LXR α , through gavage into the type II diabetic mouse model, the db/db mouse (3 control group and 5 TO group), for 2 weeks. With the mesangial cells extracted from C57BL6 mice, we cultured them in the presence of 25 mM glucose with or without TO901317. Also, we transfected siRNA of SREBP1 into the mesangial cells and repeated the culture in high glucose media. We measured the amount of protein and mRNA of LXR α , SREBP1, and collagen IV by Western blot and real time PCR, respectively, and measured the area of 100 glomeruli and the ratio of mesangial matrix area compared to whole glomerular area in each mouse kidney tissue with PAS staining.

Results : After 2 weeks, serum glucose level was lower (601 ± 126 vs 325 ± 119 mg/dL, $p=0.036$) and serum triglyceride level (262 ± 10 vs 623 ± 183 ug/mL, $p=0.012$) were higher in TO group than in control group. In TO group, the mRNA levels of LXR α and SREBP1 were increased at 1.61 folds and 5.60 folds compared to control group, respectively. The mRNA expression of collagen IV in TO group was 1.72 times (SD;0.27 times) compared to that of control ($p<0.05$) and the protein level of collagen IV also increased in TO group. The mRNA expression of TGF β also increased in the kidney tissue of TO group at 1.54 times. The glomerular area was not different between TO and control group but the ratio of mesangial matrix to whole glomerular area was increased in TO (41.2% vs 56.8%, Mann-Whitney test, $p<0.001$). In the mesangial cell cultured with TO 901317, the mRNA expressions of LXR α , SREBP1, and collagen IV were increased at 2.84, 1.34, 13.30 folds compared to in cells cultured without TO901317. The effect of TO 901317 on expression of collagen IV was markedly decreased in cells transfected with siRNA of SREBP1 in which the protein level of SREBP1 was suppressed.

Conclusion : The LXR α enhanced by TO901317 in diabetic mouse and mesangial cells cultured in 25mM glucose increased the mesangial matrix and collagen IV expression. This phenomena may be through regulating expression of SREBP1.

Key Words : LXR, SREBP1, 당뇨병

LXR, SREBP1, Diabetic nephropathy