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제2형 당뇨모델 mice에서 Toll like receptor signaling의 억제가 신장에 미치는 효과

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Renal Effects of Inhibiton of Toll Like Receptor Signaling in Type-2 Diabetic Mice

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Chronic inflammation caused by high concentration of glucose and free fatty acids (FFAs) is one of the major pathogenesis of type2 DM. Recent evidences suggest that the activation of toll-like receptor (TLR) signaling, which is involved in various innate immune responses, induces peripheral insulin resistance and mediates central insulin and leptin resistance. The present study was performed to investigate the renal effects of TLR signaling blockade in the diabetic mouse.

One group of db/db mice was treated for 3 months with a potent immunomodulator GIT27, which targets the function of macrophages through inhibition of TLR4 and TLR2/6-mediated signaling pathways. Another group of db/db mice and db/m group were treated with control vehicle. GIT27 treated db/db mice showed decrease in HbA1c at 3 months (8.81±1.61 vs 11.72±1.21, p=0.02), improved glucose tolerance, decrease in kidney/body weight (7.74±1.09 vs 9.10±0.82 ($x10^{-3}$), p=0.04) and fat/body weight (38.03±5.14 vs 45.45±1.33 ($X10^{-3}$), p< 0.01), lower lipid profile without impact on body weight, insulin levels, food consumption. GIT27 treatment also markedly decreased urinary albumin excretion (30.24±17.38 vs 6.88±10.50ug/d, p=0.02) and proinflammatory cytokine synthesis(IL-2, TNF-α, p<0.05). Tissue lipid metabolism(cholesterol, triglyceride, lipid peroxidase) and glomerulosIcerosis were also improved in GIT treatment group. In cultured podocytes, free fatty acids stimulation with high glucose increased TLR4 expression and proinflammatory cytokines, which effects were abolished by treatment with GIT27. It suggested that Inhibition of TLR signaling pathway improved glucose tolerance, lipid profile and proteinuria in diabetic db/db mouse.

Key Words: 염증, 제2형 당뇨, 톨 유사 수용체
Inflammation, type 2 DM, Toll like receptor