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Introduction and Aims: Diabetic nephropathy (DN) is a low grade inflammatory disease triggered by metabolic disorder. Inflammation has played an important role in the early stage of DN pathogenesis. Inflammatory cytokines, such as C-reactive protein (CRP), have contributed to inflammation through binding immunoglobulin G Fc receptors (FcγRs) on the surface of cells. We previously found that the expression of FcγRs with an immunoreceptor tyrosine-based activation motif (ITAM-FcγRs) increased in the kidney of diabetic CRP-Tg mouse induced by STZ. The present study investigated the potential role of ITAM-FcγRs in the early stage of DN.

Methods: Diabetes was induced by streptozotocin in Sprague Dawley (SD) rats for assessment of kidney injury at 2, 4, and 8 weeks by real-time PCR, immunohistochemistry, and western blot analysis. In vitro, the pathogenic effect of ITAM-FcγRs was investigated using glomerular mesangial cells cultured with high glucose and/or ITAM-FcγRs antibody.

Results: Compared with control, urinary albumin excretion was significantly increased in diabetic SD rats at 2, 4, and 8 weeks after STZ injection. Diabetic rats developed severe renal inflammation with enhanced infiltration of macrophages and T cells, and upregulation of pro-inflammatory cytokines (IL-1β, TNFα). Enhanced renal inflammation in diabetic rats was associated with upregulation of ITAM-FcγRs (FcγRI and FcγRIII), and over-activation of the nuclear factor κB signaling pathway. In vitro, high glucose significantly upregulated pro-inflammatory cytokines (IL-1β, TNFα) via FcγRI /III. FcγRI /III were induced by high glucose, which further promoted high glucose-mediated renal inflammation.

Conclusions: These findings suggested that ITAM-FcγRs (FcγRI /III) may be mediators in the early stage of DN. Enhanced activation of nuclear factor κB signalling pathway may be the mechanism by which ITAM-FcγRs promote renal inflammation under diabetic conditions.