실험적 항기저막 사구체 신염의 발현에서 재조합 uteroglobin과 transglutaminase 2의 상관 관계

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The Effect of Cross-talk between Transglutaminase 2 and Uteroglobin in the Development of Experimental Crescentic Glomerulonephritis

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Background : Although we have previously reported that recombinant uteroglobin (rUG) prevents the experimental crescentic glomerulonephritis (eGN), the involved mechanism is still unknown. UG is considered to have the immunomodulatory and anti-inflammatory activities, while is one of substrate for transglutaminase 2 (TG2) which is expressed in kidney and promotes the inflammatory process and fibrosis in tissue damage. Here, we tried to test the relationship between the protective effects of rUG and the changes of TG2 expression using a murine eGN model.

Methods and Results : In-vitro expression of TG 2 of mesangial cell lines to exogenous stimuli was evaluated with immunofluorescence staining. eGN was induced by the i.v. injection of rabbit anti-GBM Abs to mice (C57BL/6), and the renal injury was evaluated 7, 14 days afterward. rUG or control vehicle were given intravenously to mice for 3 days after disease induction. TG 2 expressions were evaluated using con-focal microscopy, real time PCR and western blot methods. The in-vitro expression of TG2 in mesangial cell lines by the stimulation with LPS was diminished with the addition of rUG in a dose-dependent manner. TG2 expression was parallel with TGF-beta expression. rUG treatment lessened the severity of eGN, i.e. marked attenuation of mesangial matrix expansion, cell proliferation, and cellular crescents. Proteinuria was significantly reduced in mice treated with rUG compared with disease-control mice at 7 and 14 days after an anti-GBM Ab injection. Confocal microscopic examinations showed that the induced expression of TG 2 by anti-GBM Ab was markedly decreased by rUG, which was also confirmed by real-time PCR and western blot methods. The spatial pattern of TG2 expression was also parallel with TGF-beta expression. Now we try to evaluate the role of TG2 in eGN using a TG2 knock-out system and TG2 inhibitors.

Conclusion : This study suggests that the attenuation of inflammation by UG in eGN may be caused by, at least in part, a productive cross-talk between UG and TG2.