Introduction and Aims: Renal fibrosis develops in chronic kidney diseases and represents a major health concern. However, progression rates vary among patients, presumably due to genetic variation. We have previously described strain dependent progression of renal fibrosis in TGFß transgenic mice, being C57Bl6 (B6) mice resistant (Nephrol Dial Transplant Plus 2011, 4 (S2): 421-429). Although renal complement expression has been described in several experimental and human kidney diseases, we hypothesize that the complement activation might strongly depend on genetic variability of mice.

Methods: Kidneys of B6-TGFß and CBAxB6-TGFß male transgenic mice and their wild type controls (B6 and CBAxB6) were investigated at the age of 14 days (n=6/group) for gelatinase zymography, mRNA and protein expression. Data are presented as mean±SD. Statistical significance was evaluated using Kruskal-Walls test.

Results: Survival of CBAxB6-TGFß mice was one tenth of that seen in B6-TGFß mice. Plasma levels of TGF-ß were similarly elevated in both transgenic strains. However, only CBAxB6-TGFß mice had increased urinary protein creatinine ratio (UPCR: CBAxB6-TGFß 12±3 vs B6-TGFß 5±1, p=0.025). In CBAxB6-TGFß mice, we observed severe glomerulosclerosis and tubulointerstitial fibrosis with significant collagen-I mRNA (Collagen-I: CBAxB6-TGFß:5.2±1.5 vs B6-TGFß:1.9±0.2, p=0.01) and collagen-III mRNA overexpression (Collagen-III: CBAxB6-TGFß:4.3±0.9 vs B6-TGFß:1.9±0.3, p<0.05). This was accompanied by 60-fold increase in C3 mRNA (C3: CBAxB6-TGFß:69.3±10.5 vs B6-TGFß:1.3±0.4, p<0.01), 7-fold increase in C4 mRNA (C4: CBAxB6-TGFß:7.4±1.6 vs B6-TGFß:1.5±0.5, p<0.05) and 4-fold increase in C3a-Receptor mRNA expression (C3aR: CBAxB6-TGFß:3.8±0.9 vs B6-TGFß:1.2±0.1, p<0.05). Immunohistochemistry for C3 revealed mostly tubular localization. MMP-9 gelatinase activity was significantly lower in CBAxB6-TGFß kidneys (arbitrary units: CBAxB6-TGFß 8±2, B6-TGFß 12±1, p=0.04).

Conclusions: We conclude that genetic background determines the expression rate of renal complement system components in our model of kidney fibrosis. Altered renal complement expression could, through local effects, influence the progression of chronic kidney disease.