STRAIN-DEPENDENT RENAL COMPLEMENT EXPRESSION IN KIDNEY FIBROSIS OF TGF-ß TRANSGENIC MICE

Gábor Kökény, Amelia Foss, Morgan Karetnick, János Szebeni, Ágnes Németh, Krisztina Fazekas, Szabina Czirok, László Rosivall, Miklós M. Mózes

Institute of Pathophysiology, Semmelweis University, Faculty of Medicine,Budapest, Hungary

E-mail: kokeny.gabor@med.semmelweis-univ.hu

BACKGROUND

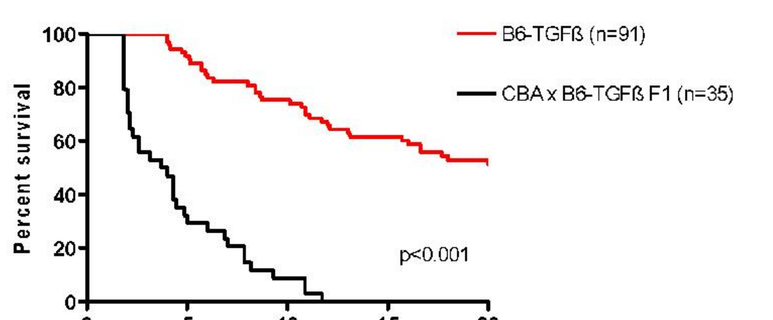
Renal fibrosis develops in chronic kidney diseases. However, progression rates vary among patients, presumably due to genetic variation. We have previously described strain dependent progression of renal fibrosis in TGFß transgenic mice, being C57Bl6 (B6) mice resistant *(Nephrol Dial Transplant Plus 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

Animal model:

Kidneys of B6-TGFß and CBAxB6-TGFß (F1) male transgenic mice and their wild type B6 and CBAxB6 (F1) controls were investigated at the age of 14 days (n=6/group).

Mating scheme:



Performed analyses:

- Matrix metalloprotease (MMP) activity assay
- Renal gene expression levels (qPCR)
- C3 protein expression (immunohistochemistry)
- C3 and C3aR protein expression (immunoblot)

Statistics:

Data are presented as mean+SD. Kruskal-Wallis test was performed (SPSS 10).

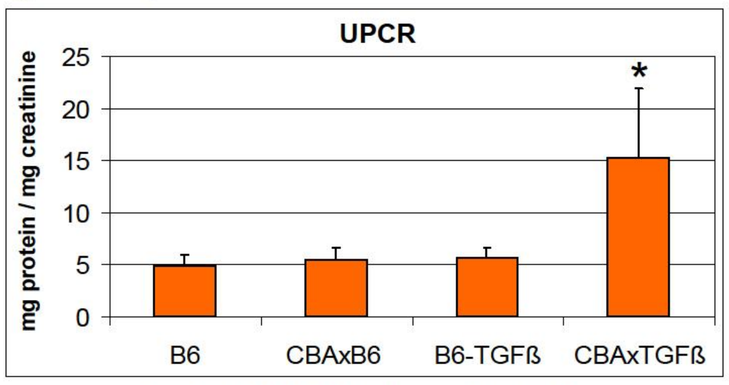
RESULTS

Survival

Survival of CBAxB6-TGFß mice was one tenth of that seen in B6-TGFß mice.

Proteinuria (UPCR)

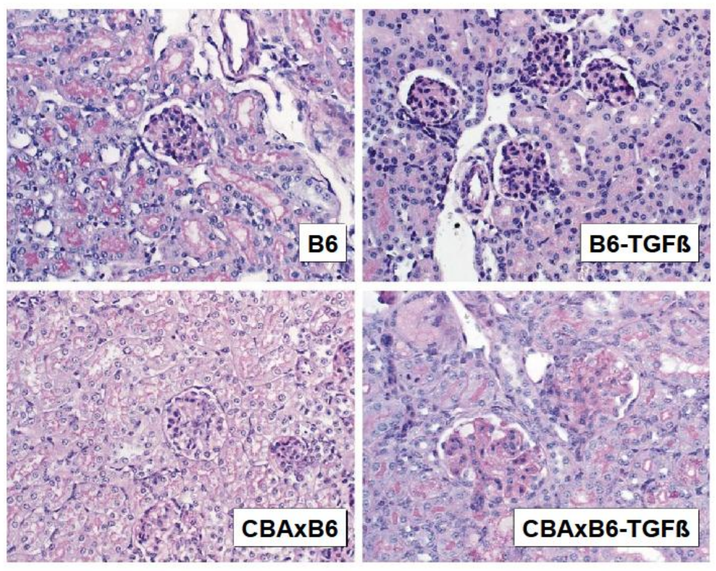
CBAxB6-TGFß mice had increased proteinuria (p=0.025)



* p<0.05 CBAxB6-TGFß vs B6-TGFß

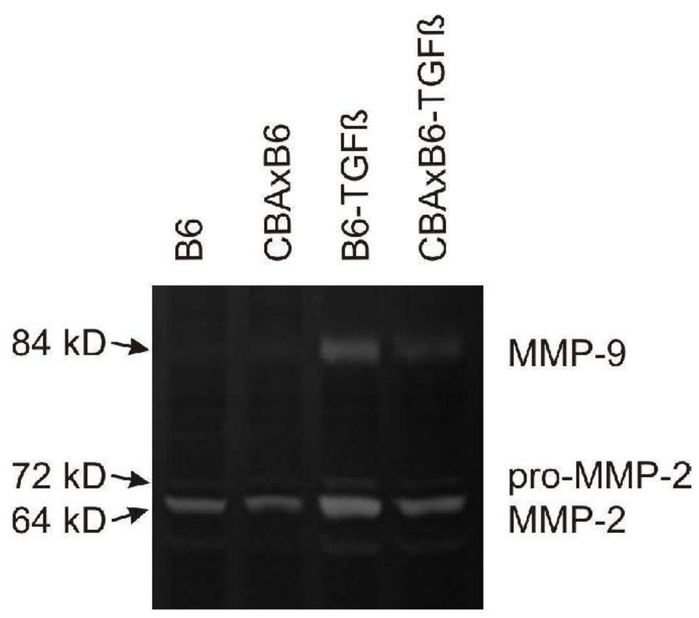
Histology

CBAxB6-TGFß kidneys depicted severe glomerulosclerosis and tubulointerstital damage as compared to B6-TGFß and control mice.

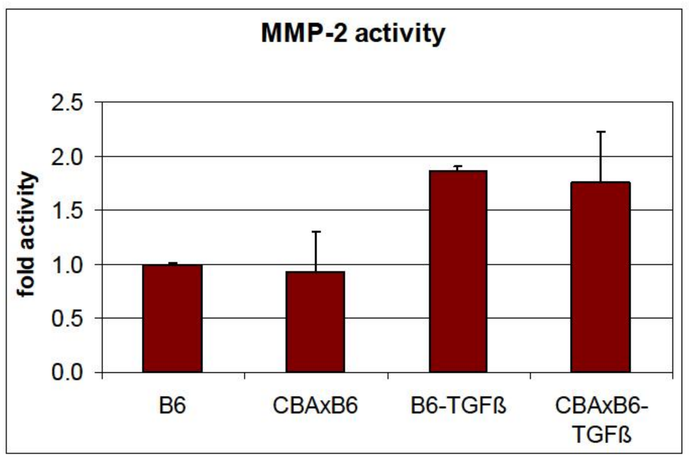


Zymography

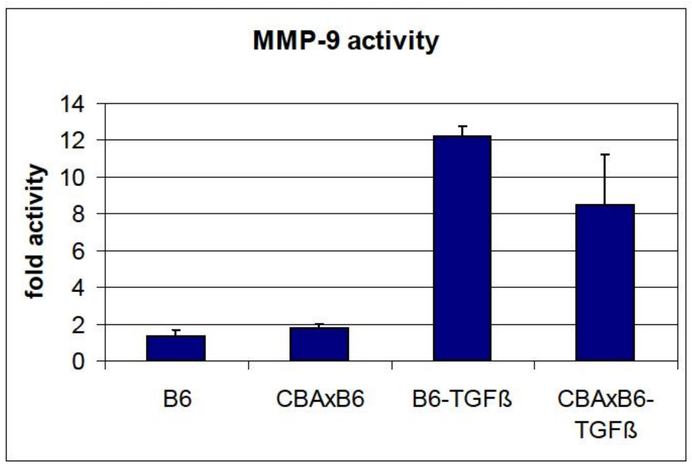
Kidneys of both transgenic strains showed elevated MMP-2 and MMP-9 activity as compated to controls.



Representative gelatinase zymography

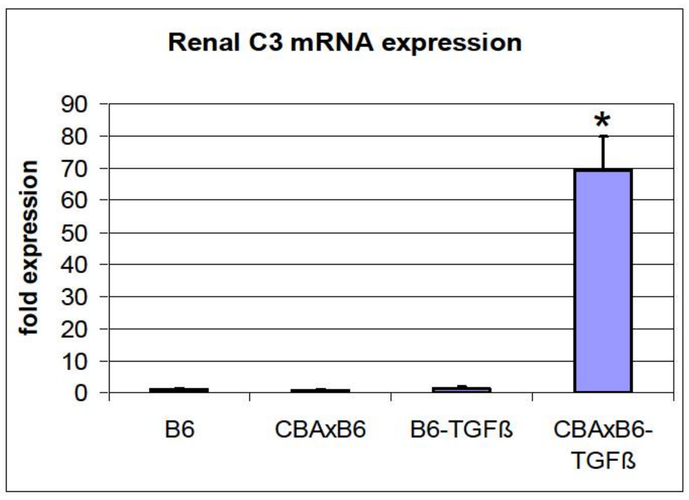


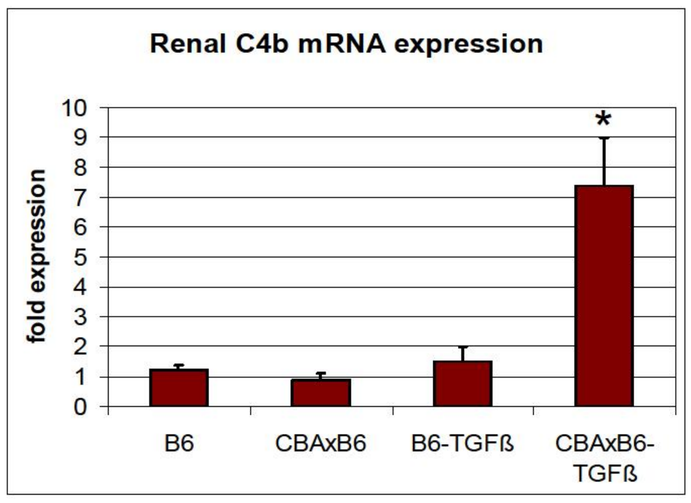
MMP-9 activity was lower in CBAxB6-TGFß kidneys as compared to B6-TGFß.

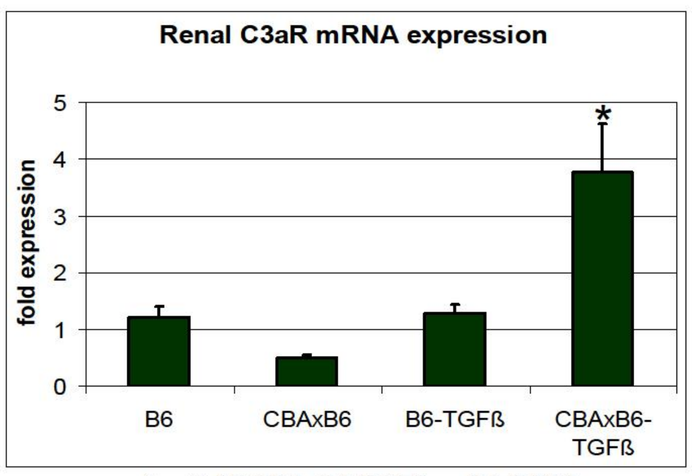


Renal complement expression

CBAxB6-TGFß kidneys showed markedly elevated mRNA expression of C3, C4b and C3aR.

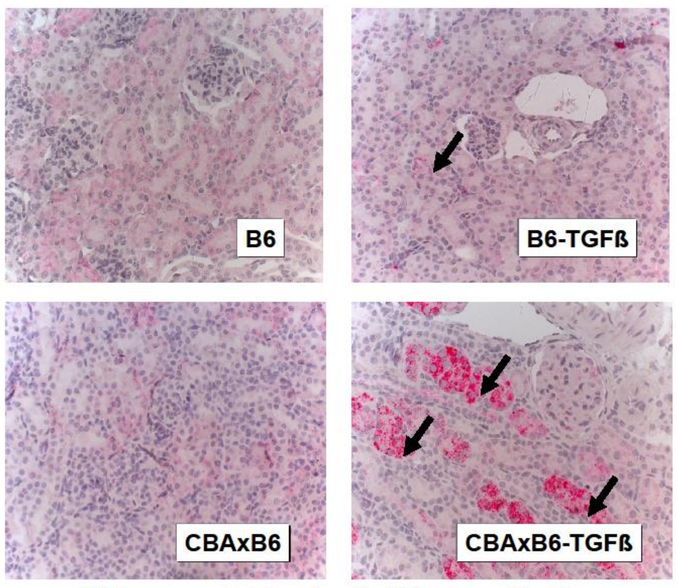






* p<0.05 CBAxB6-TGFß vs B6-TGFß

CBAxB6-TGFß kidneys depicted markedly more C3 positive tubular cells (see below).



C3 immunostaining (red), 400x magnification

CONCLUSION

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.

SUPPORT

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