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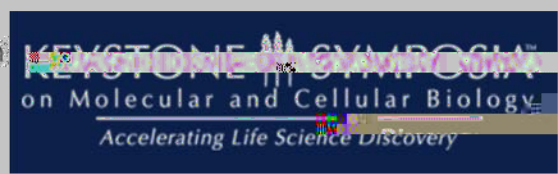
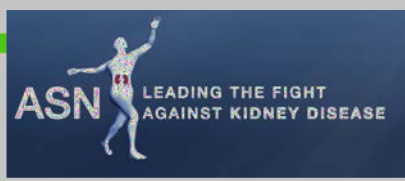


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## Cd40 May Cause Renal Fibrosis in a Hypertensive Model

Haller, Steven

**Objective:** Cd40 plays a crucial role in immunity and inflammation, and is highly expressed in the kidney. We hypothesized that Cd40 may play a crucial role in the development of renal disease.

Haller, Steven

### Design and Methods

Male Dahl salt-sensitive (Dahl S) and mutant rats weighing 180-200g were used. Kidney tissue and renal function was determined by urinary protein excretion. Eight Dahl S rats were used as age-matched controls.

What is referring to Dahl S?

Do you mean...

**Results:** Western blot analysis confirmed that Cd40 expression was significantly higher in Dahl S rats compared to age-matched controls, whereas the *Cd40* mutants did not. There was no difference in systolic blood pressure between Dahl S and *Cd40* mutants. Kidney tissue derived from the *Cd40* mutants showed a significant decrease in collagen type-1 expression compared to the kidney tissue of Dahl S controls ( $p < 0.01$ ). *Cd40* mutants also showed a significant decrease in urinary protein excretion compared to Dahl S controls.

Haller, Steven

### Conclusions

Cd40 is an important mediator of immunity and has been implicated in the development of renal fibrosis. A novel *Cd40* mutant rat model was developed that mimicked the phenotype of renal fibrosis and renal dysfunction independent of blood pressure. Our results indicate that *Cd40* may play a crucial role in the development of hypertensive renal disease.

Haller, Steven

How was it created?

Haller, Steven

How many were used?

What is collagen, a marker of...

Haller, Steven

Used for what?

Haller, Steven

Product of fibrosis?

Haller, Steven

What is renal disease?

Haller, Steven

Conclusion

Haller, Steven

Conclusion

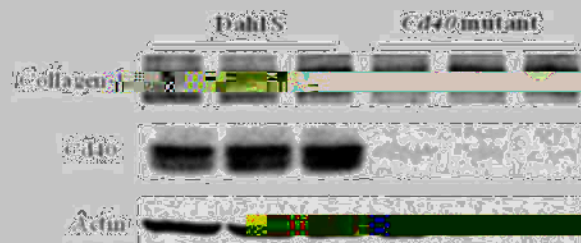


Figure 1. Collagen I Western Blot Analysis of Dahl S and Cd40 mutant rats. The blot shows that Cd40 mutant rats have significantly lower levels of Collagen I expression compared to Dahl S rats.

## Cd40 Mediates Renal Fibrosis in the Dahl Genetically Hypertensive Rat

**Objective:** Cd40 plays a role in the development of renal fibrosis in some injury models. The genetically hypertensive Dahl S rat (S rat) is highly susceptible to the development of renal disease. We sought to create a Cd40 mutant with the genetic background of the S rat to determine the role of Cd40 in the development of hypertensive renal disease.

**Design and Methods:** A novel Cd40 mutant with genetic disruption of Cd40, was created in the Dahl S rat using the zinc-finger nuclease method. Male Cd40 mutant (n=8) and Dahl S rats (n=8) were used. Systolic blood pressure was determined by tail-cuff measurement. Kidney tissue was harvested and renal function was determined by urinary protein excretion (UPE). Eight Dahl S rats were used as controls.

**Results:** Western blot analysis revealed that the Cd40 mutant rats showed cross-reactivity with anti-Cd40 antibody, whereas the Cd40 mutant rats did not. There was no difference in systolic blood pressure between the S rats and Cd40 mutant rats. Kidney tissue derived from the Cd40 mutant rats showed a significant decrease in collagen type I (p<0.01, Figure 1). The Cd40 mutant rats also exhibited a significant decrease in UPE compared to the S rats (115.2 ± 12.4 vs 189.3 ± 12.6 mg/24hrs, p<0.01).

**Conclusions:** A novel Cd40 mutant, using a genetic background of the Dahl S rat, shows a decrease in renal fibrosis and urinary protein excretion. These results indicate that Cd40 may play a critical role in the development of renal fibrosis.

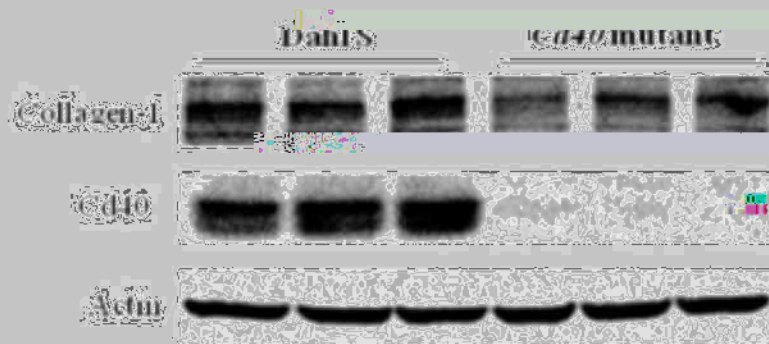


Figure 1. Representative Western blot analysis of kidney tissue from Dahl S and Cd40 mutant animals.

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