The SHC (Spontaneously Hypercholesterolemic) Rat as a Translational Model of FSGS: Renoprotective Effects of Irbesartan

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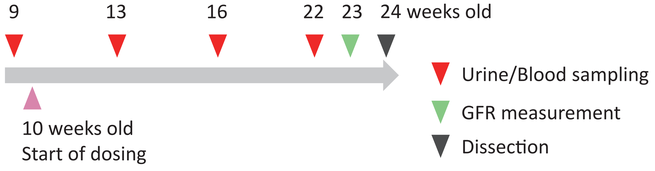
Introduction

- Focal segmental glomerulosclerosis (FSGS) is an important cause of progressive kidney disease.
- Many commonly used animal models are driven by toxic, surgical, or monogenic mechanisms, limiting their relevance to the heterogeneous and multifactorial pathophysiology of human FSGS.
- Therefore, there is a need for translationally relevant models reflecting the multifactorial nature of human FSGS.
- SHC rats spontaneously develop proteinuria, renal dysfunction, and glomerulosclerosis associated with hyperlipidemia and hypertension, recapitulating key features of secondary FSGS.

Objective

To evaluate the renoprotective effects of the clinically effective ARB irbesartan in SHC rats and assess their utility as a translational model of FSGS.

Methods



- Male SHC rats received irbesartan (50 mg/kg/day, p.o.) for 14 weeks.
- Blood and urine samples were collected during treatment.
- GFR was measured, and histological and gene expression analyses were performed at necropsy.
- Statistical analysis: Student's t-test or Wilcoxon test.

Results

1. Model characteristics

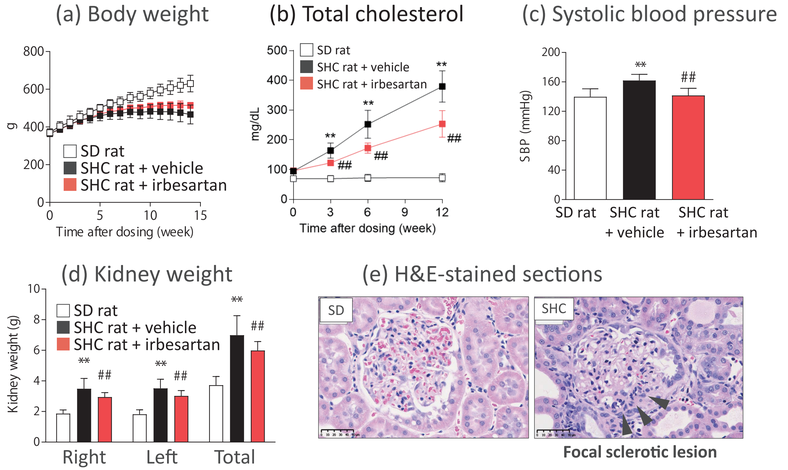
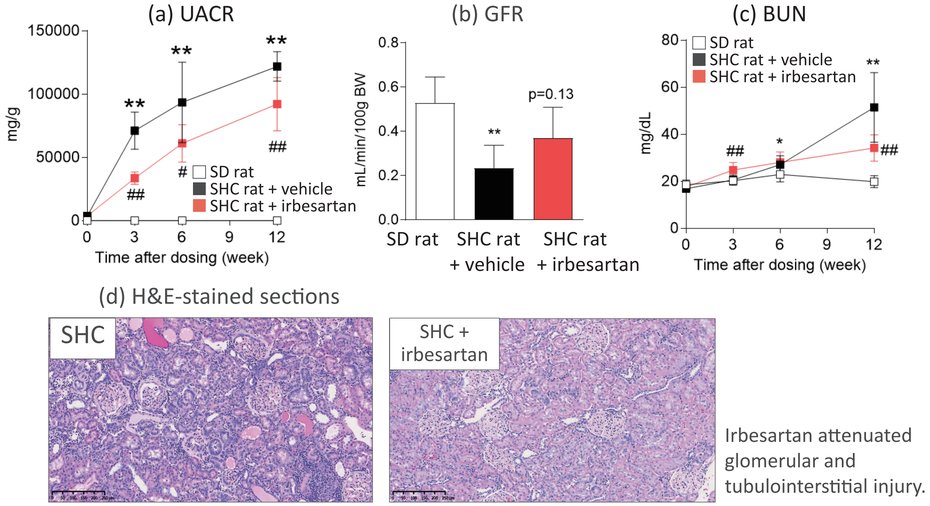


Fig. 1. Characteristics of SHC rats. (a) Body weight. (b) Plasma total cholesterol. (c) Systolic blood pressure. (d) Kidney weight. (e) Representative H&E-stained kidney sections demonstrating focal glomerulosclerotic lesions (arrowheads). Data are presented as mean ± S.D. (n = 6–9). **: p < 0.01 vs. SD rats; ##: p < 0.01 vs. SHC vehicle group.

2. Renoprotective effects of irbesartan



Irbesartan attenuated glomerular and tubulointerstitial injury.

Fig. 2. Renoprotective effects of irbesartan in SHC rats. (a) Urinary albumin-to-creatinine ratio (UACR). (b) Glomerular filtration rate (GFR). (c) Blood urea nitrogen (BUN). (d) Representative H&E-stained kidney sections from SHC rats treated with vehicle or irbesartan. Data are presented as mean ± S.D. (n = 6–9). *: p < 0.05, **: p < 0.01 vs. SD rats; #: p < 0.05, ##: p < 0.01 vs. SHC vehicle group.

3. Potential mechanisms

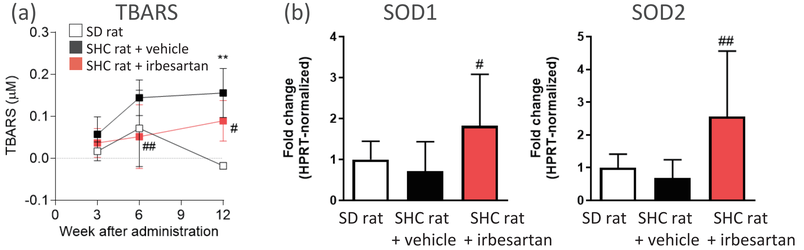


Fig. 3. Effects of irbesartan on oxidative stress and antioxidant gene expression in SHC rats. (a) Plasma TBARS levels. (b) Renal SOD1 and SOD2 mRNA expression. Gene expression levels were normalized to HPRT. Data are presented as mean ± S.D. (n = 6–9). **: p < 0.01 vs. SD rats; #: p < 0.05, ##: p < 0.01 vs. SHC vehicle group.

Summary and Key Message

- **SHC rats responded to irbesartan with improvements in albuminuria, renal function, histopathology, and oxidative stress.**
- **SHC rats recapitulate key features of human FSGS and respond to clinically effective therapy, supporting their utility as a translational model for evaluating novel therapeutics.**

COI disclosure information: We have no financial relationship to disclose for our presentation contents.

Please contact us if you are interested in drug discovery research for kidney diseases!

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