C57BL/6J-H11-hREN

Strain Name: C57BL/6JGpt-*H11*$^{em1Cin(hREN)}$/Gpt
Strain Type: Knock-in
Strain Number: T058352
Background: C57BL/6JGpt

Description

Renin is the only enzyme which mediate the conversion from Angiotensinogen to Angiotensin I. Renin is expressed and secreted by paragglomerular complex granulosa cells, and it plays essential roles in maintaining the homeostasis of blood pressure, fluid and electrolyte[1]. As an important catalytic enzyme of the renin-angiotensin system, AGT plays an important role in diseases such as essential hypertension, early eclampsia, and obesity-related hypertension.

Essential hypertension accounts for more than 95% of the hypertensive population and is a major risk factor for cardiovascular disease morbidity and mortality in humans[2]. Numerous studies have shown that the overactivated renin-angiotensin system is the main cause of hypertension, renin catalyzes the hydrolysis of angiotensinogen to produce angiotensin I. The C-terminal two amino acid residues of angiotensin I are cleaved via angiotensin converting enzyme (ACE) to form angiotensin II. Angiotensin II has a highly effective vasoconstrictor effect, thereby raising blood pressure and triggering hypertension[3]. The regulation of Renin expression and secretion is highly influenced by renal arteriole blood pressure and cation concentration in initial urine like sodium or calcium ions[1].Studies have shown that the interaction between angiotensinogen and renin is highly specific, since human renin cleaves only human angiotensinogen but not mouse or rat angiotensinogen[4]. Studies have also shown that simultaneous overexpression of human angiotensinogen and renin leads to spontaneous hypertension in mice[5]。

GemPharmatech used gene editing technology to create the mouse model overexpression human *REN* gene at *H11* locus, which leads to human Renin expression in mice without interruption of endogenous mouse *Ren* gene. This genetic engineering mouse model is therefore suitable for preliminary drug screening and efficacy test of cardiovascular disease therapies targeting Renin.

Strategy

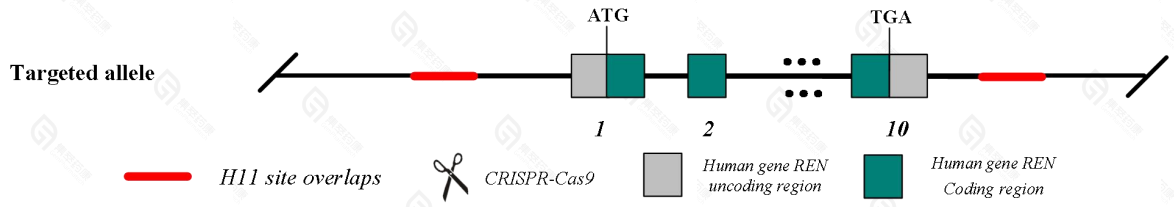

Fig.1 Schematic diagram of C57BL/6J-Rosa26-hAGT model strategy.

Applications

1. Efficacy evaluation and drug screening of human hypertension-related drugs
2. Study on the mechanism of hypertension

Data support

1. Detection of AGT protein expression

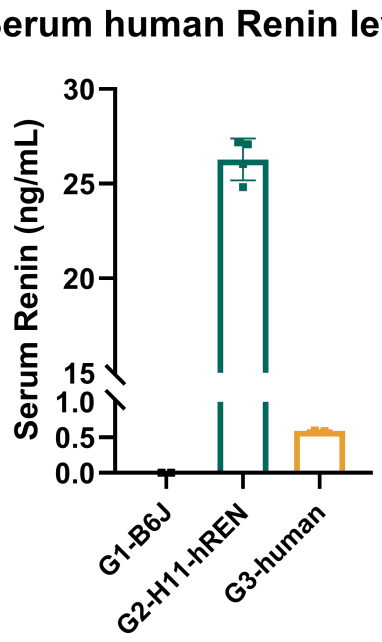

Fig 2. Human Renin protein is expressed in C57BL/6J-H11-hREN mice

Serum samples from B6J WT mice (G1), H11-hREN mice (G2) and human (G3) were analyzed using ELISA kit (Abcam, ab246545). Mice used in this experiment are all of 7-8 w age. The results indicated human Renin protein expression and secretion in H11-hREN mice.

References

1. Schweda, F., et al., *Renin release*. Physiology, 2007.**22**: p. 310-319.

2. Hata, A. *Role of angiotensinogen in the genetics of essential hypertension*. Life Sci, 1995. **57**(26): p. 2385-2395.
3. Lu, H., et al., *Structure and functions of angiotensinogen*. Hypertens Res, 2016. **39**: p. 492–500.
4. Ganten, D., et al., *Species specificity of renin kinetics in transgenic rats harboring the human renin and angiotensinogen genes*. Proc Natl Acad Sci USA, 1992. **89**: p. 7806–10.
5. Merrill, D., C., et al., *Chronic hypertension and altered baroreflex responses in transgenic mice containing the human renin and human angiotensinogen genes*. J Clin Invest, 1996. **7**(4): p. 1047-1055.