

## C57BL/6J-Rosa26-hAGT

**Strain Name:** C57BL/6JGpt-Rosa26<sup>em1Cin(hAGT)</sup>/Gpt

**Strain Type:** Knock-in

**Strain Number:** T058351

**Background:** C57BL/6JGpt

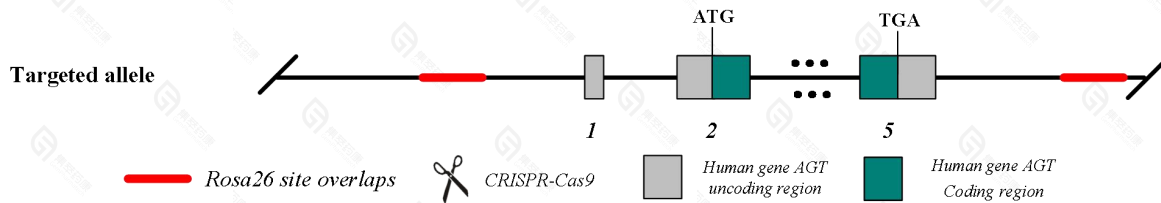
### Description

Angiotensinogen, also known as AGT, is the only precursor of all angiotensin peptides. The AGT protein encoded by this gene is mainly expressed in the liver and is involved in maintaining the homeostasis of blood pressure, fluid and electrolyte<sup>[1]</sup>. As a substrate 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<sup>[2]</sup>. 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<sup>[3]</sup>. It has been reported that AGT can also be directly involved in the regulation of blood pressure. Perivascular adipose tissue (PVAT) is a complete layer of adipose tissue around blood vessels, which has the function of protecting vascular tension. AGT is highly expressed in PVAT, and inhibition of AGT expression in PVAT decreases blood pressure<sup>[4]</sup>. However, 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<sup>[5]</sup>. Studies have also shown that simultaneous overexpression of human angiotensinogen and renin leads to spontaneous hypertension in mice<sup>[6]</sup>.

GemPharmatech used gene editing technology to create the mouse model overexpression human *AGT* gene at *Rosa26* locus, which leads to human angiotensinogen expression in mice without interruption of endogenous mouse *Agt* gene. This genetic engineering mouse model is therefore suitable for preliminary drug screening and efficacy test of cardiovascular disease therapies targeting AGT.

## Strategy



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

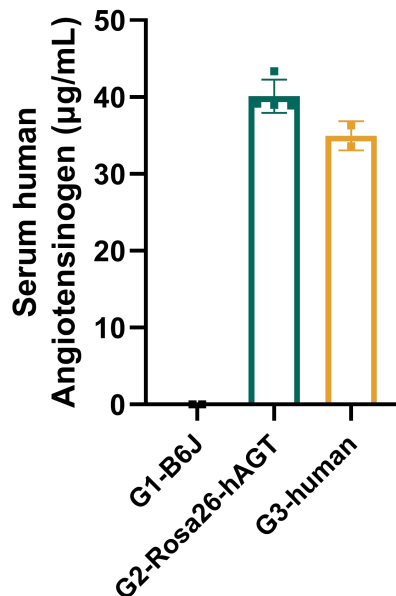
## Applications

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

#### Serum hANGT level test



**Fig 2. Human AGT protein is expressed in C57BL/6J-Rosa26-hAGT mice**

Serum samples from B6J WT mice (G1), Rosa26-hAGT mice (G2) and human (G3) were analyzed using ELISA kit (Abcam, ab287170), which specifically recognizes human AGT. Mice used in this experiment are all of 7-8 w age.

## References

1. Shu, Z., et al., *Angiotensinogen and the Modulation of Blood Pressure*. Front Cardiovasc Med, 2021. **8**: p.645123.



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. Xu, Y., Rong, J., & Zhang, Z., *The emerging role of angiotensinogen in cardiovascular diseases*. J Cell Physiol, 2021. **236**(1): p. 68-78.
5. 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.
6. 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.