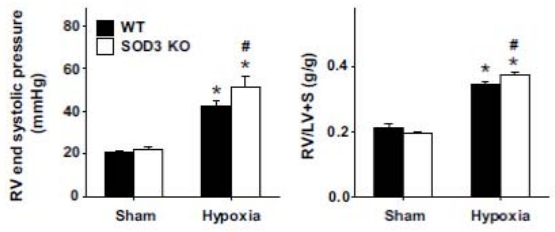
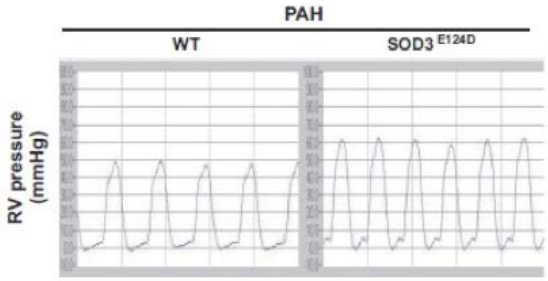
Cardiovascular: Sod3

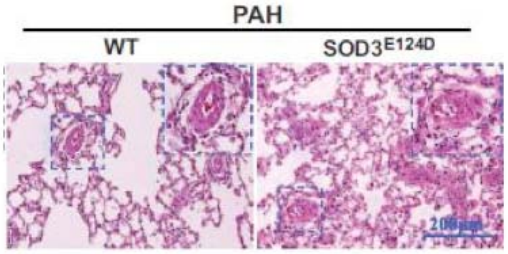
Sod3 TGEM® Rat: Exacerbated Pulmonary Arterial Hypertension and Right Ventricular Hypertrophy & Kidney Disease

Pulmonary artery hypertension (PAH) is a progressive disease with a very poor prognosis characterized by a elevation of pulmonary arterial pressure, ultimately inducing right ventricular (RV) hypertrophy and heart failure. Studies have demonstrated that increased oxidative stress, may contribute to the pathogenesis and the development of idiopathic PAH in patients. The Sod3 TGEM® knockout rat model displays significantly increased oxidative stress and thus RV pressure and pulmonary vascular remodeling, as well as greater RV hypertrophy in response to induced chronic hypoxia as well as monocrotaline (MCT) induction (Xu et al.*Hypertension*. 2011 Aug;58(2):303-9).

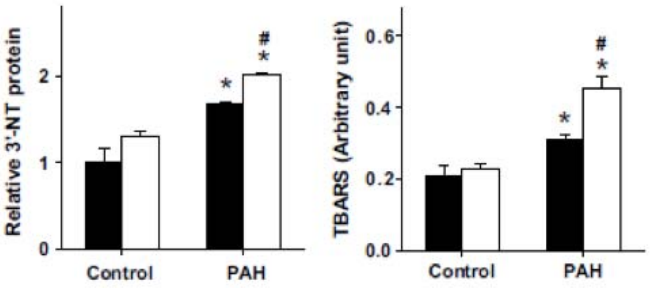




Sod3 TGEM® knockout rats display significantly exacerbated hypoxia-induced increases of RV pressure and hypertrophy



Sod3 TGEM® Knockout Rats display exacerbated MCT-induced pulmonary vascular remodeling with significantly greater increases in fully muscularized small arterioles and decreased nonmuscularized small arterioles.



Sod3 TGEM® Knockout Rat develops significantly increased lung oxidative stress with the presence of significantly increased oxidative stress markers 3'-nitrotyrosine and TBARS.

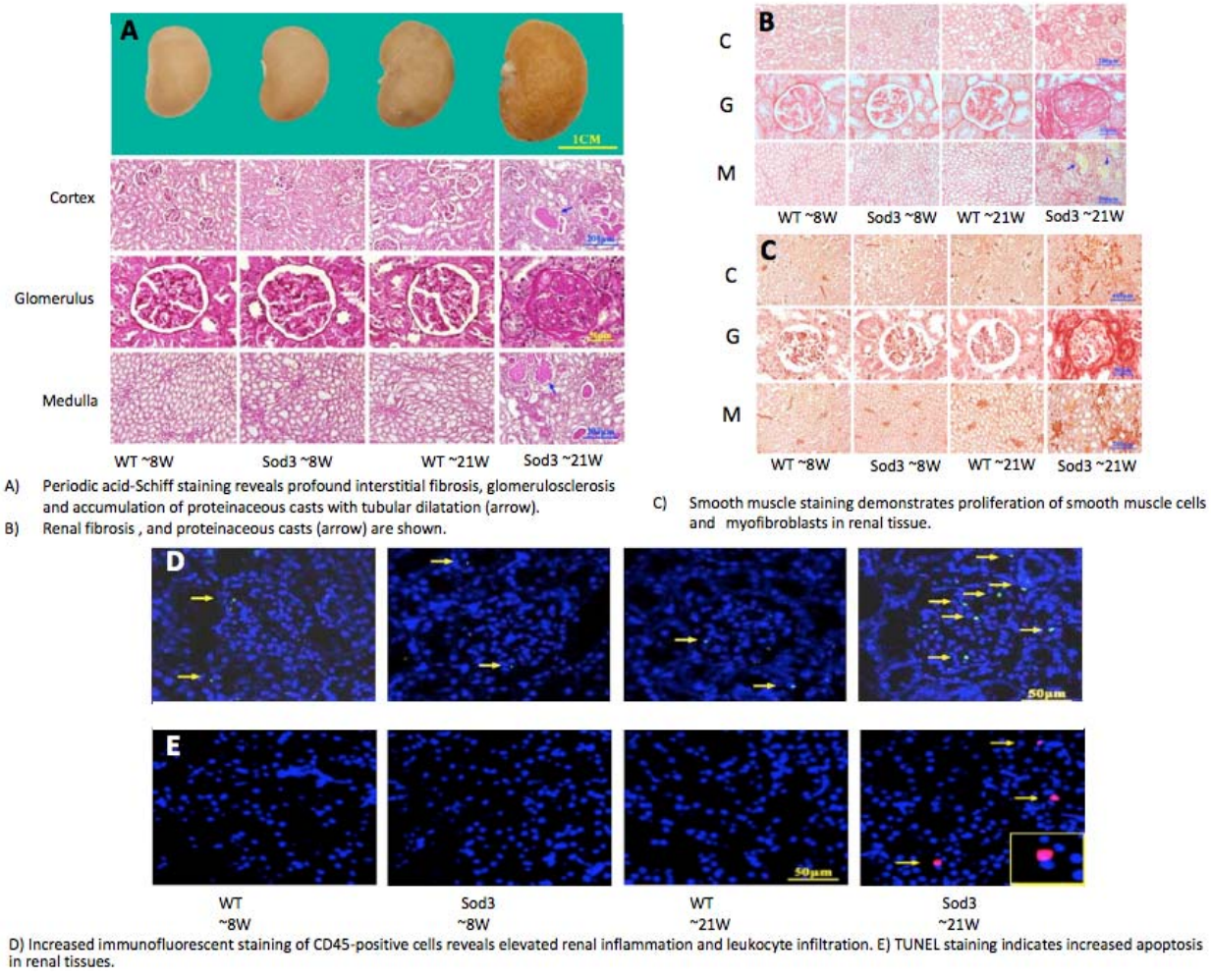
Transposagen's Sod3 TGEM® Knockout Rat model displays more severe hypertension, more remodeling of the pulmonary arteries and more RV hypertrophy and fibrosis in the setting of MCT-induced pulmonary hypertension.

Chronic Kidney Disease Model

A TGEM® Rat Model for chronic kidney disease (CKD) with known etiology is useful for drug discovery and development in CKD. CKD is a progressive disease that worsens with age; therefore, a non-acute CKD rat model is

ideal for relevant studies. The Sod3 TGEM® Rat Model lacks the extracellular superoxide dismutase 3 (Sod3) which is essential for regulating oxidative stress and is highly expressed in renal tissue.

The Sod3 TGEM® Rat Model is phenotypically indistinguishable from wild type littermates at 8 weeks of age. However, by 21 weeks Sod3 TGEM® Rats develop profound CKD characterized by focal necrosis and fibrosis, glomerulosclerosis, massive proteinaceous cast accumulation with tubular dilatation, interstitial fibrosis with hypertension and renal failure with increased serum creatinine.



A) Periodic acid-Schiff staining reveals profound interstitial fibrosis, glomerulosclerosis and accumulation of proteinaceous casts with tubular dilatation (arrow).
B) Renal fibrosis , and proteinaceous casts (arrow) are shown.

C) Smooth muscle staining demonstrates proliferation of smooth muscle cells and myofibroblasts in renal tissue.

D) Increased immunofluorescent staining of CD45-positive cells reveals elevated renal inflammation and leukocyte infiltration. E) TUNEL staining indicates increased apoptosis in renal tissues.

Potential Study Applications:

- Cardiovascular
- Hypertension
- Kidney Diseaase

Access to the Sod3 TGEM® Rat

- Cryopreserved
- Live colony

Sod3 TGEM® Rat Publications:

Reference:	Application:
Chen et al. Hypertension. 2011 Aug;58(2):303-9	**Pulmonary arterial hypertension & Right ventricular hypertrophy**
Xu et al Hypertension-2011-303-9	**Kidney failure**