ANGII-PE mouse

Mouse model of angiotensin II/phenylephrine-induced cardiac dysfunction and myocardial fibrosis

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The ANGII-PE mouse model exhibits key hallmarks of hypertension-induced cardiac dysfunction including hypertrophy, reduced ejection fraction and development of extensive perivascular/interstitial myocardial fibrosis.

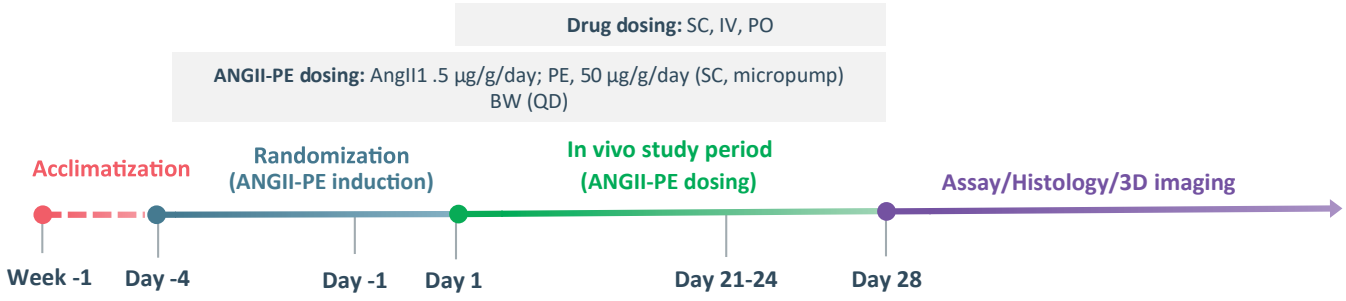
ANGII-PE mouse model is Ideally suited for rapid evaluation of therapeutic drug efficacy using a combination of echocardiography, 3D imaging, quantitative histology and RNA-seq to provide a detailed view of cardiac pathological changes.

Key model traits

- Co-infusion with angiotensin II and α-adrenergic agonist phenylephrine.
- Cardiac hypertrophy with systolic and diastolic dysfunction, including reduced ejection fraction.
- Extensive perivascular and interstitial myocardial fibrosis.
- Therapeutic evaluation of drug efficacy.

Model induction	Chronic dosing of angiotensin II (1.5 ug/d/day) and phenylephrine (50 ug/g/day) using subcutaneous osmotic micropump for total of 28 days.
Strain	Male C57BL/6J mice

Study outline



Model induction
+ ANGII-PE micropump implantation
+ Vehicle micropump implantation

Randomization
+ BW

Echocardiography
+ LV mass
+ LVAW/LVPW
+ EF
+ IVRT
+ E/e'
+ GLS (strain)
+ RPLSR (strain)
+ FS (strain)

Termination
+ Heart weight
+ Plasma

Heart histology
+ Fibrosis (PSR)
+ Optional analyses

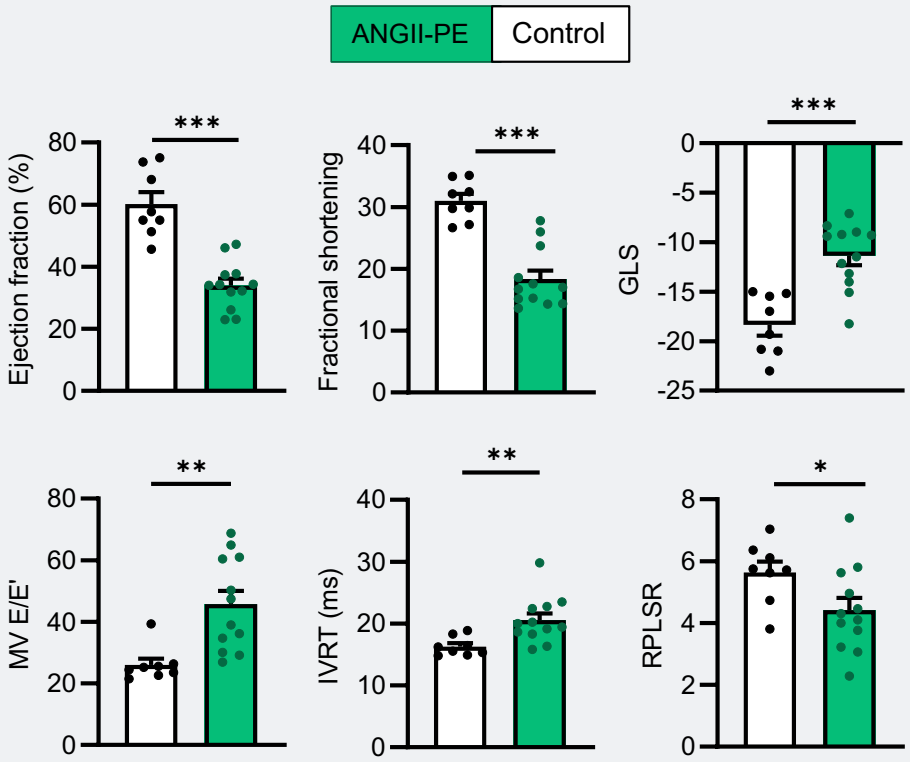
Heart 3D imaging:
+ Hypertrophy

Tissue samples:
+ Heart RNA sequencing
+ Optional analyses

Terminal biochemistry:
+ Plasma NT-proBNP

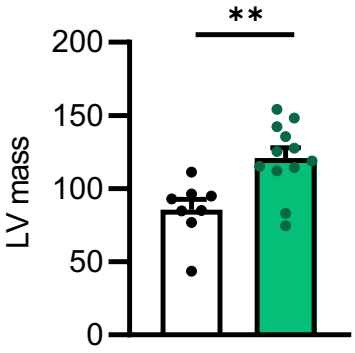
Cardiac dysfunction

The ANGII-PE mouse model develop characteristics of chronic heart failure (HF) as characterized by echocardiography measures and speckle-tracking strain analysis. Systolic dysfunction is evident in reduced ejection fraction (HFrEF), reduced fractional shortening and impaired global longitudinal strain (GLS). Diastolic dysfunction is demonstrated in increased left ventricle filling pressure (MV E/E' ratio), prolonged isovolumetric relaxation time (IVRT) and reduced reverse peak longitudinal strain rate (RPLSR).



Cardiac hypertrophy

The ANGII-PE mouse model develop extensive cardiac hypertrophy. ANGII-PE infused mice demonstrate increased heart weight, left ventricle (LV) mass and wall thickness.



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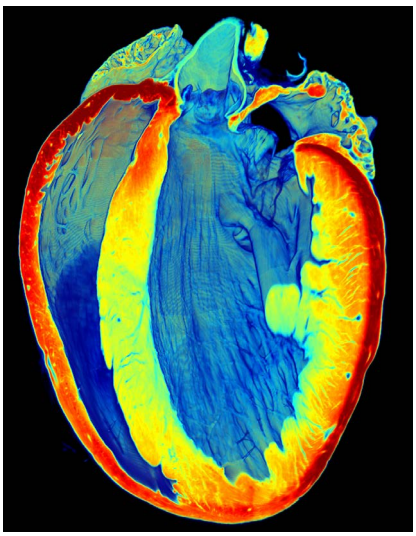

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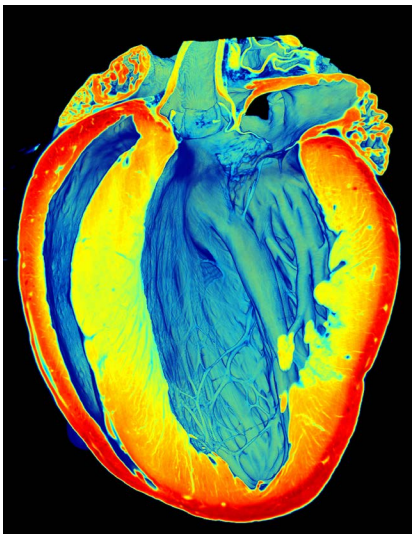

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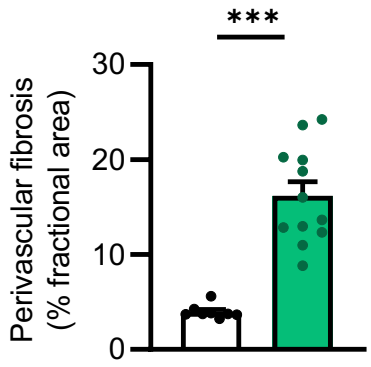

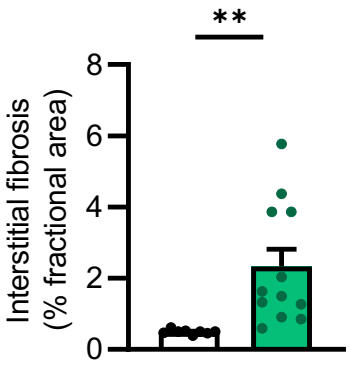

Myocardial fibrosis

The ANGII-PE mouse model develop myocardial fibrosis. ANGII-PE infused mice show prevalent interstitial and perivascular fibrosis, as evaluated by quantitative image analysis of Picro Sirius Red-stained histological sections.

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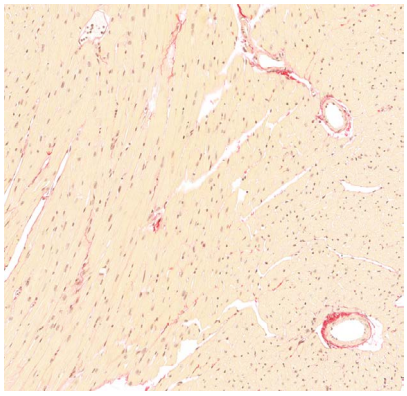

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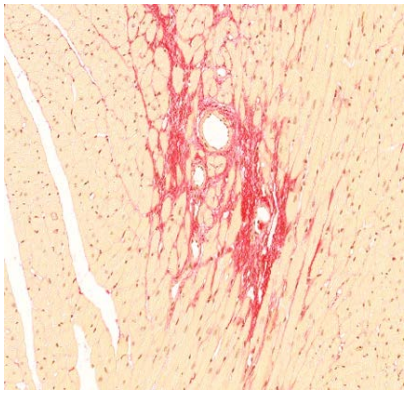
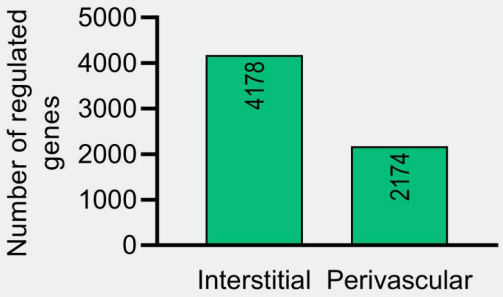


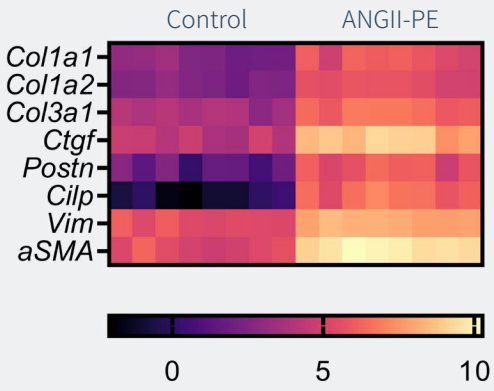
Transcriptomic profile in myocardial fibrosis

The ANGII-PE mouse model develop profound transcriptomic profile for myocardial fibrosis.

ANGII-PE-induced mice demonstrate distinct gene expression signature for perivascular and interstitial myocardial fibrosis, evaluated by laser capture microdissection (LCM) and RNA-sequencing with bioinformatic analysis.



Interstitial fibrosis



Perivascular fibrosis