Rat model of cardiac fibrosis and systolic dysfunction

A rat model for testing protective or therapeutic therapies targeting cardiomyopathy.

Isoprenaline induces myocardial changes evident 4 weeks after treatment

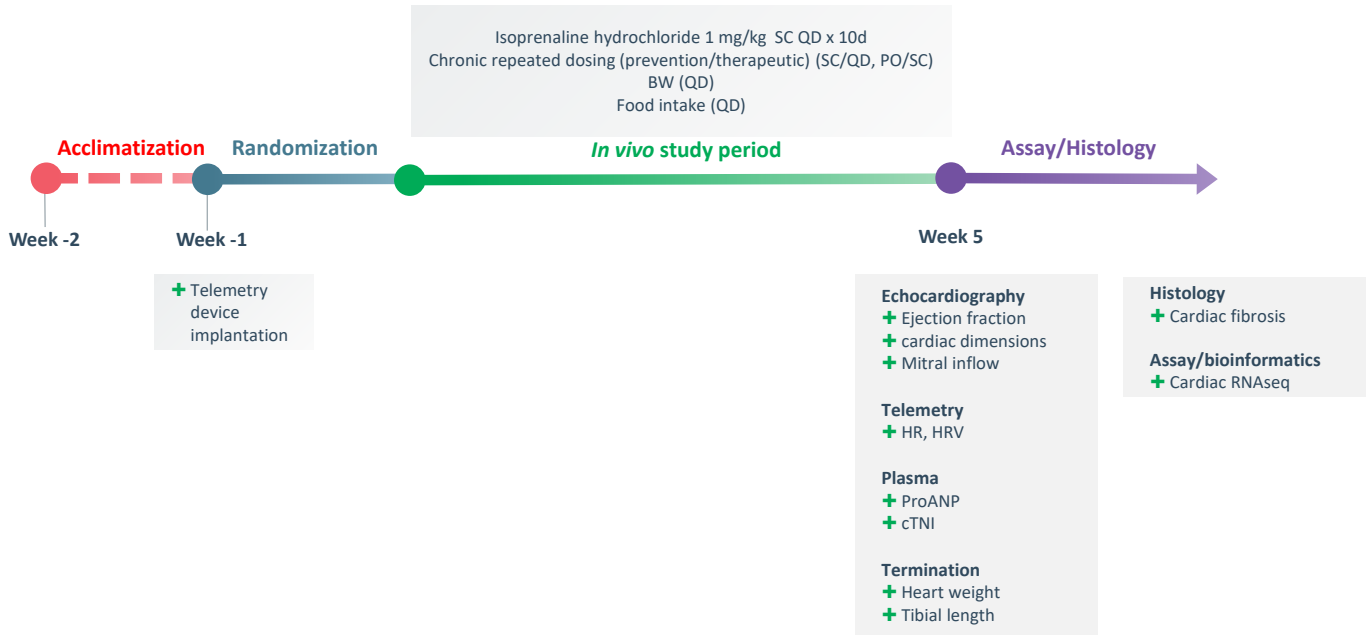
Treatment with low-dose isoprenaline for 10 days induces reduced systolic function and myocardial fibrosis evident even after 4 weeks. The model thus offers the possibility to evaluate the preventive and/or therapeutic drug efficacy in cardiomyopathic conditions induced by tachycardia and inadequate myocardial oxygen supply.

Key model traits

- Even low-dose isoprenaline induces reduced cardiac function and subendocardial fibrosis.
- The isoprenaline dose can be individually adjusted to reflect mild or more advanced cardiomyopathy.
- Evaluation of functional and morphological changes using echocardiography, telemetry, RNA sequencing and clinically relevant plasma markers.

Model induction	Altromin Chow (1234). Optional combination with high fat diets, including high fat Western diet.
Strain	NTac:SD

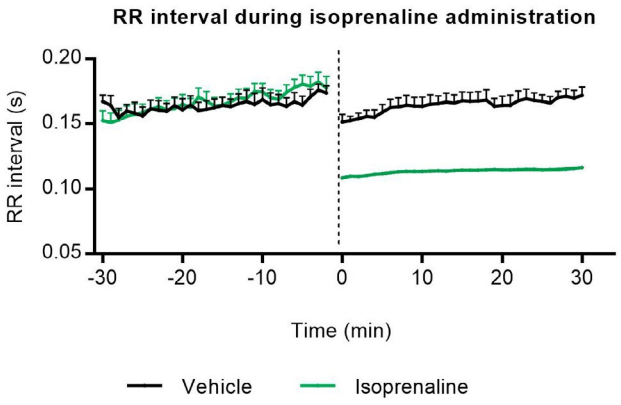
Study outline



Isoprenaline induces profound tachycardia

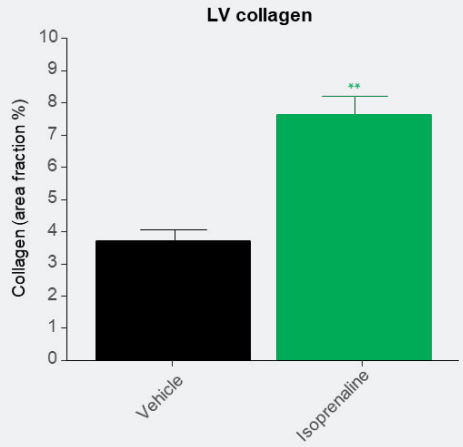
Low-dose isoprenaline reduces the time elapsing between two successive R-waves recorded by telemetry before and after first dose (t=0) (right) and heart rate, its reciprocal, increases (below).

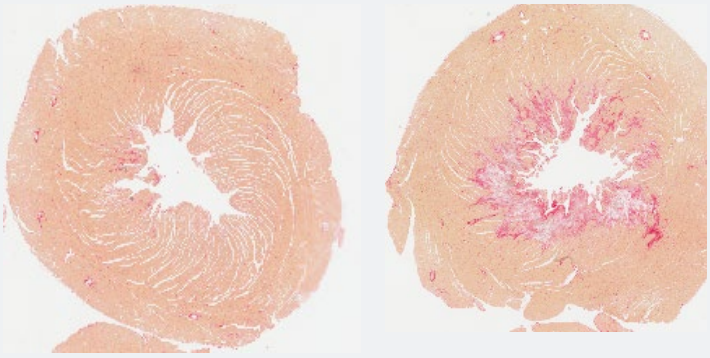
Beats per minute	Before first dose	After first dose
Vehicle	368 ± 14	368 ± 13
Isoprenaline	360 ± 14	529 ± 3



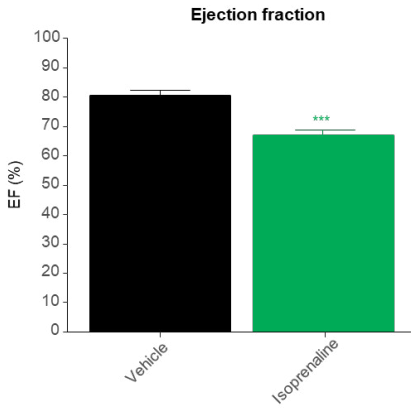
Left ventricular fibrosis

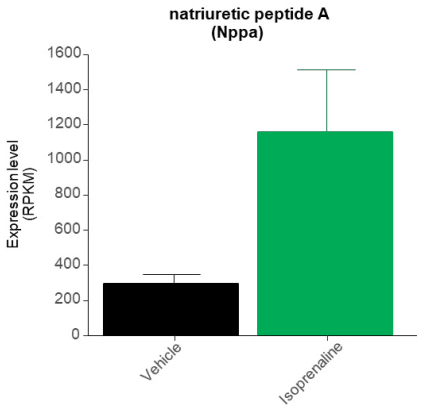
Low-dose isoprenaline induces subendocardial fibrosis evident even 4 weeks after treatment.





PSR stained hearts from a vehicle-treated rat (left) and isoprenaline-treated rat (right).





Left ventricular function

Low-dose isoprenaline induces reduced systolic function assessed by echocardiography and increased gene expression markers of increased cardiomyocyte stretch.