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Ranolazine reduces remodeling of the right ventricle and provoked arrhythmias in rats with pulmonary hypertension

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Supplemental Data

Measurements of Cardiac Function in the Isolated Heart. Isovolumic left ventricular (LV) contractile performance in the Langendorff mode perfused heart was assessed using a water-filled balloon inserted into the LV and connected to a physiological pressure transducer (ADInstruments, Colorado Springs, CO).). The balloon volume was adjusted to set the LV end diastolic pressure (EDP) to 7±1 mmHg at baseline. Contractile function of the right ventricular (RV) was measured using a pressure catheter (SPR-407, Millar Instruments, Houston, TX) inserted into the RV. LV and RV mechanical function measurements were performed simultaneously with the ECG and MAP detection.

Systolic pressure (SP) was measured, rate pressure product (RPP, the workload of the ventricles) calculated as [(SP – EDP) x heart rate], and contractility was estimated as +d*P*/d*t* (maximum rate of pressure rise during contraction). Diastolic function was determined as –d*P*/d*t* (maximum rate of pressure fall during relaxation).

Supplemental Table 1: Contractility of left and right ventricles in the isolated heart.

Systolic Pressure (SP), Rate Pressure Product (RPP), and ± dP/dt_{max} in rats treated with sham (n=5), sham+ 0.5% RAN (S+R, n=6), MCT (n=6), and MCT+ 0.5% RAN (M+R, n=6) 4 weeks following the injection of MCT. No significant differences were detected in the LV between treatments. In contrast, in the RV MCT treatment leads to a significant change of contractile function, which are normalized or mitigated by chronic RAN treatment. Data are mean ± S.E.M. One-way ANOVA analysis followed by Tukey post-hoc test was performed to determine significant differences. *P < 0.001 vs. sham; $^{\#}P$ < 0.001 vs. MCT.

	Left Ventricle				**Right Ventricle**			
	Sham	**S+R**	**MCT**	**M+R**	**Sham**	**S+R**	**MCT**	**M+R**
SP (mmHg)	**101 ± 6.5**	**96 ± 3.7**	**111 ± 15.5**	**102 ± 9.3**	**23 ± 3.7**	**18 ± 4.9**	**88* ± 13.2**	**26$^{\#}$ ± 7.5**
RPP (mmHg*min^{-1})	**25200 ± 1960**	**24400 ± 1600**	**23380 ± 4010**	**21020 ± 3520**	**5910 ± 1230**	**3500 ± 910**	**18870* ± 2874**	**3880$^{\#}$ ± 620**
+ dP/dt_{max} (mmHg*s^{-1})	**3760 ± 208**	**3450 ± 318**	**3200 ± 462**	**3640 ± 412**	**810 ± 127**	**615 ± 144**	**2300* ± 341**	**810$^{\#}$ ± 167**
- dP/dt_{max} (mmHg*s^{-1})	**2100 ± 77**	**2015 ± 104**	**1970 ± 314**	**1970 ± 225**	**495 ± 38**	**360 ± 56**	**1430* ± 224**	**517$^{\#}$ ± 75**

Telemetry in Rats with PAH. In one group of rats (n=5) telemetry devices (HD-S21, Data Sciences, New Brighton, MN) were implanted two weeks prior to MCT administration. Systemic pressure, RV pressure, and ECG were continuously recorded and monitored for 8 weeks.

Supplemental Figure 1. Representative tracings of continuous telemetry data (ECG) of one rat with PAH at day 1 and 33 before it experienced VF (**A**). Tracings of ECG, RV pressure (RVP), and blood pressure (BP) at the start of VF and 1 min following VF at day 33 resulting in sudden cardiac death (**B**).