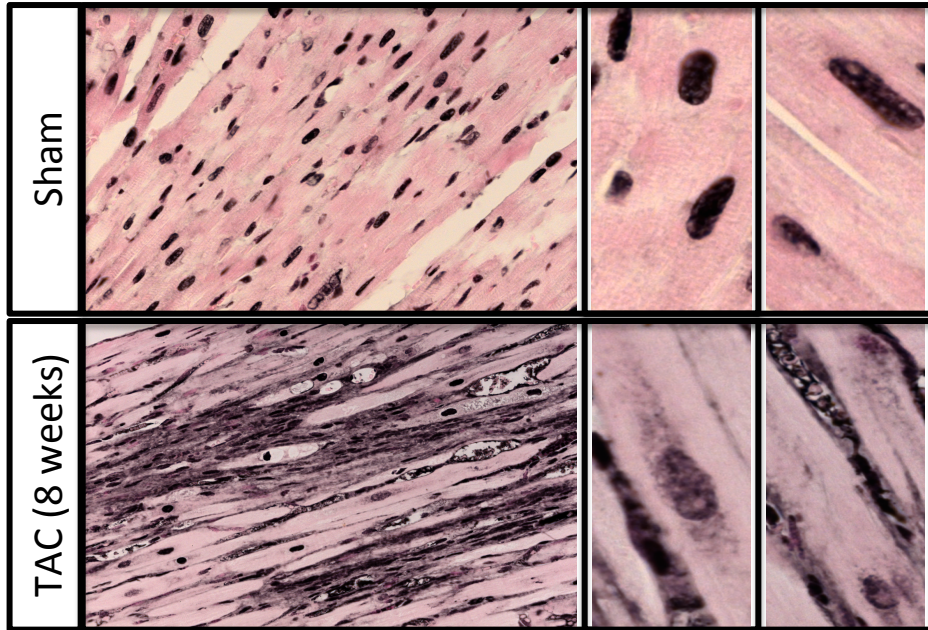
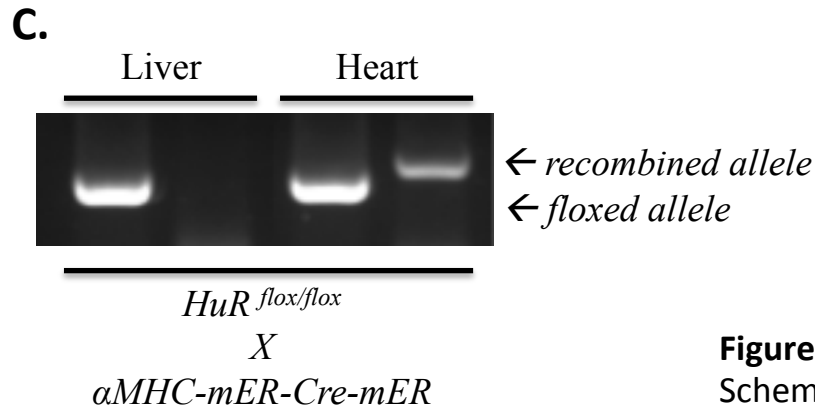
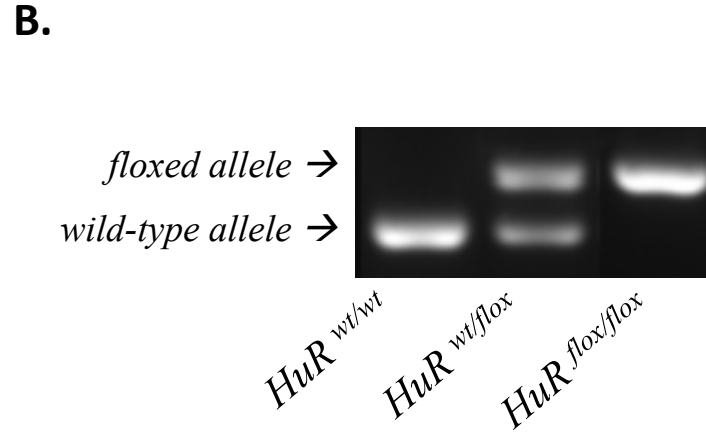
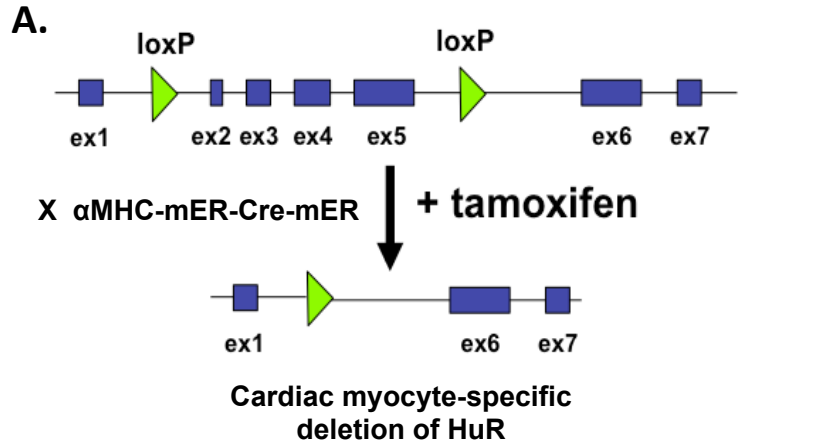


**Figure S1: HuR is activated in a mouse model of cardiac hypertrophy**



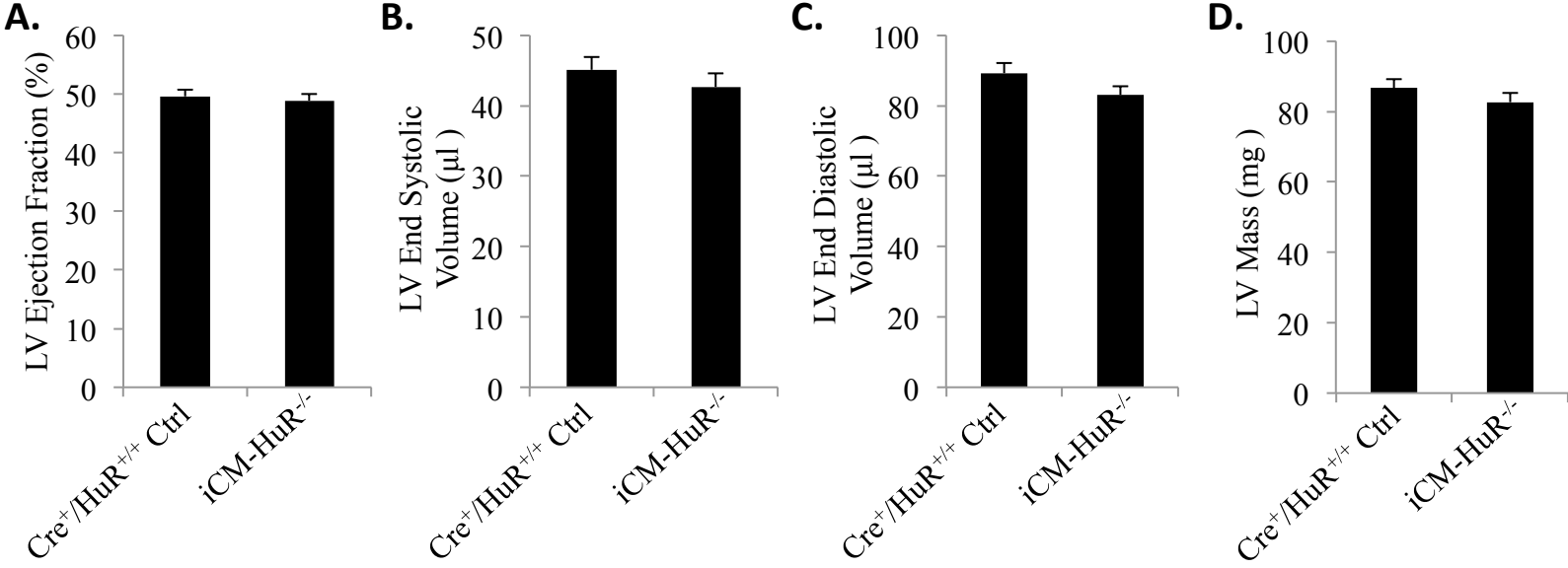
**Figure S1: HuR is activated in a mouse model of cardiac hypertrophy.** DAB stain of HuR (brown) on hearts isolated from c57bl/6 wild type mice 8 weeks post-TAC.

**Figure S2: Creation of a cardiac-specific HuR-deletion mouse.**



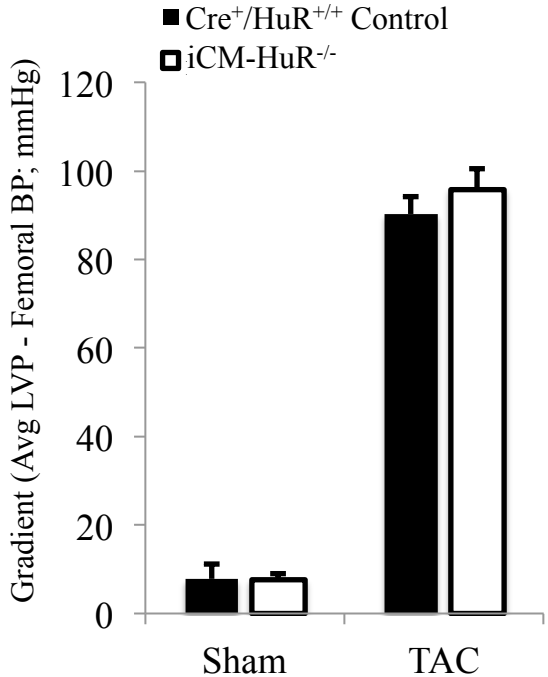
**Figure S2: Creation of a cardiac-specific HuR-deletion mouse. (A)** Schematic of the genetic deletion of HuR using the lox-Cre system and tamoxifen injections to delete exons 2-5 of the HuR gene. **(B)** Genotyping to show the iCM  $HuR^{-/-}$  mice are homozygous for the HuR knockout. **(C)** Genotyping to show the use of the  $\alpha$ MHC-mER-Cre-mER is a cardiac specific knockout of HuR.

**Figure S3: Basal cardiac function is not affected by cardiac-specific HuR deletion.**



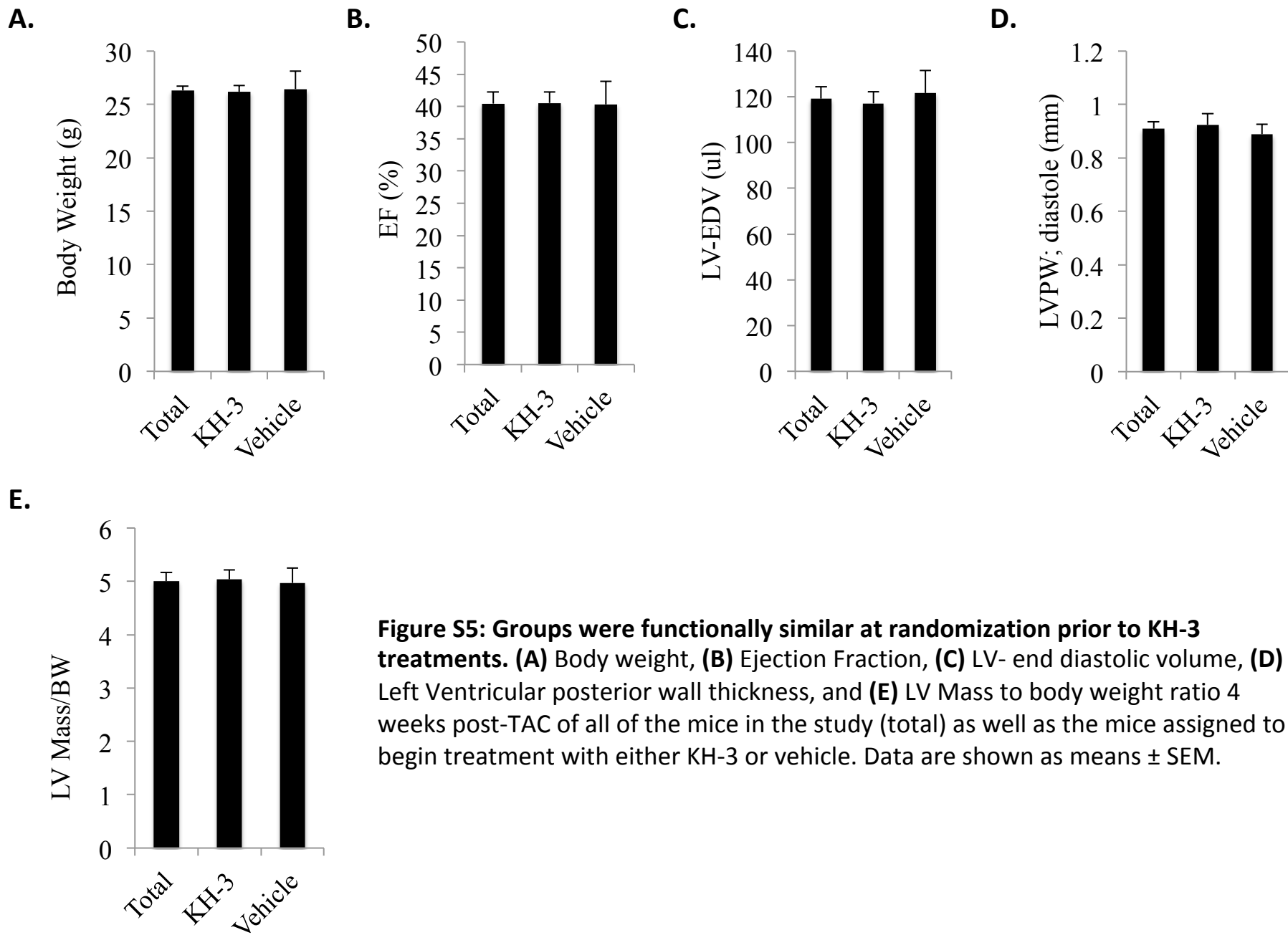
**Figure S3: Basal cardiac function is not affected by cardiac-specific HuR deletion.** (A) LV Ejection Fraction, (B) LV End systolic volume, (C) LV End diastolic Volume, and (D) LV mass, as determined by a baseline echocardiogram, of control and *iCM-HuR<sup>-/-</sup>* mice after tamoxifen treatment, pre-TAC or sham surgery. Data are shown as means ± SEM.

**Figure S4: All mice had equal pressure gradients following TAC.**

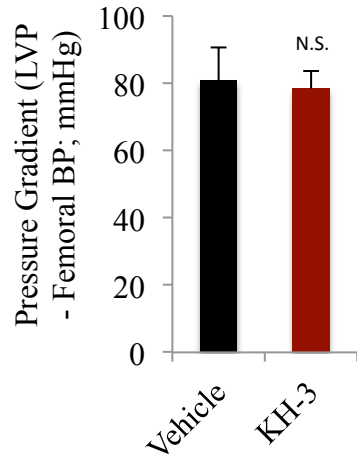


**Figure S4: All mice had equal pressure gradients following TAC.** The pressure gradient (determined by subtracting the femoral blood pressure from the left ventricular pressure) in control and iCM-HuR<sup>-/-</sup> mice 11 weeks post-TAC or sham surgery. Data are shown as means ± SEM.

**Figure S5: Groups were functionally similar at randomization prior to KH-3 treatments**

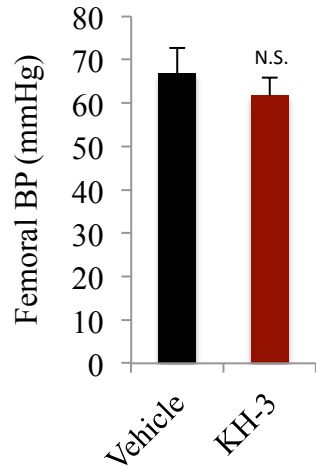


**Figure S6: KH-3 and Vehicle Treated mice had similar LV Pressure Gradients**



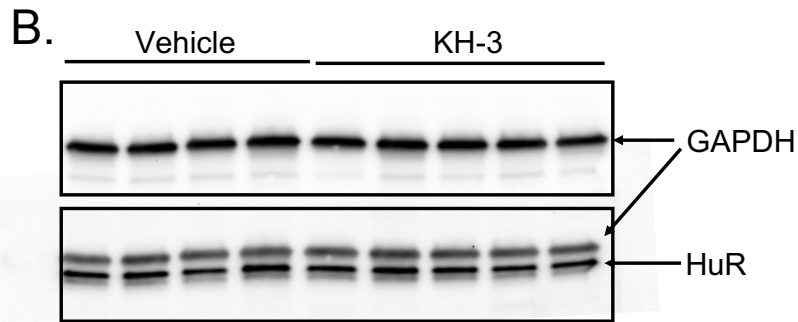
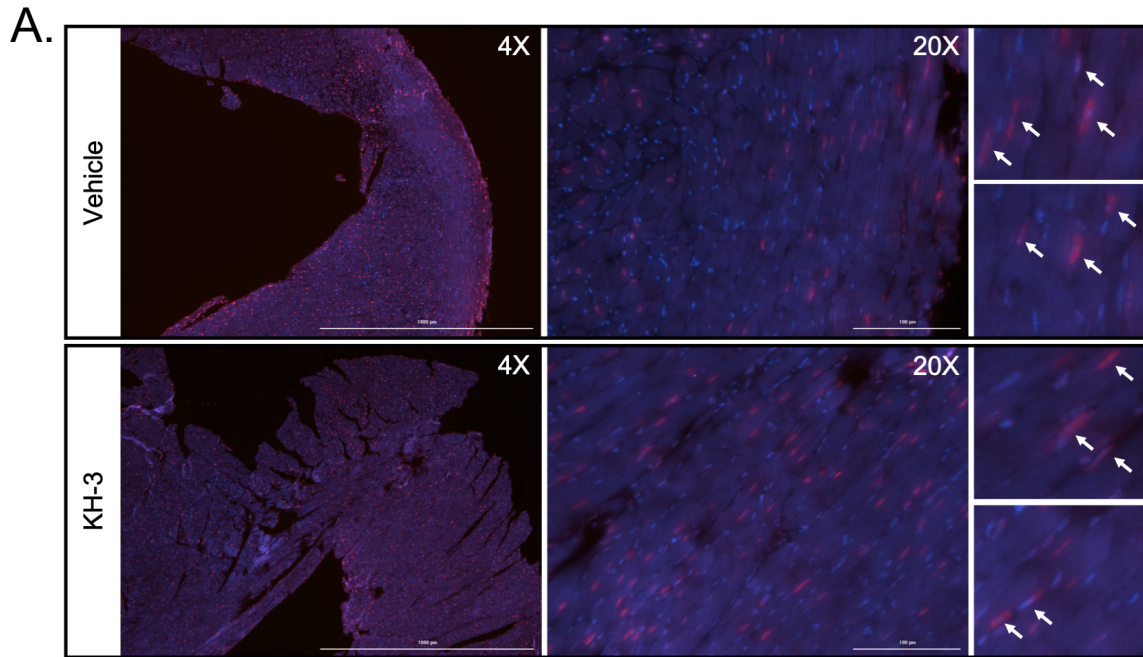
**Figure S6: KH-3 and Vehicle Treated mice had similar LV Pressure Gradients.** Pressure gradient (determined by subtracting the femoral blood pressure from the left ventricular pressure) of mice in the KH-3 treated group and vehicle treated group 11 weeks post-TAC surgery. Data are shown as means  $\pm$  SEM.

**Figure S7: KH-3 treatment shows no effect on vascular function**



**Figure S7: KH-3 treatment shows no effect on vascular function.** The femoral blood pressure in the KH-3 treated group and the vehicle treated group 11 weeks post-TAC surgery. Data are shown as means  $\pm$  SEM.

**Figure S8: KH-3 treatment does not alter HuR activation or expression.**



**Figure S8: KH-3 treatment does not alter HuR activation or expression.** HuR activation 11 weeks post TAC was observed in both the vehicle treated mice and the KH-3 treated mice, as seen by IHC images of HuR (pink) translocation from the nucleus (blue), indicated by the white arrows. 4X scale bar: 1000 $\mu$ m, 20X scale bar: 100 $\mu$ m (**A**). HuR expression was also not affected, as shown by western blot. GAPDH serves as a loading control (**B**).

**Table S1. List of transcripts with differential expression in control and iCM-HuR<sup>-/-</sup> mice at baseline (sham vs. sham groups).**

Gene Symbol	Fold change Control Sham vs. iCM-HuR <sup>-/-</sup> sham	Fold change Control TAC vs. Control sham	Fold change iCM-HuR <sup>-/-</sup> TAC vs. Control TAC	EDGE test: Control Sham vs. iCM-HuR <sup>-/-</sup> sham - FDR p-value correction	EDGE test: Control TAC vs. Control sham - FDR p-value correction	EDGE test: iCM-HuR <sup>-/-</sup> TAC vs. Control TAC - FDR p-value correction
Gm2004	6.614081665	0.143812725	7.500592491	2.39441E-11	7.4527E-21	8.32112E-07
Erdr1	2.26930477	1.260510604	0.814820813	3.66737E-09	1	1
Myh7	1.951617245	7.642820538	0.604527738	5.80995E-05	1.80051E-30	1
Gm6563	16.6366068	1.258468812	0.311801266	0.000192565	1	1

**Table S4. List of TAC-dependent transcripts associated with TGF-β signaling**

Gene Symbol	Fold change Control Sham vs. iCM-HuR-/- sham	Fold change Control TAC vs. Control sham	Fold change iCM-HuR-/- TAC vs. Control TAC	EDGE test: Control Sham vs. iCM-HuR-/- sham - FDR p-value correction	EDGE test: Control TAC vs. Control sham - FDR p-value correction	EDGE test: iCM-HuR-/- TAC vs. Control TAC - FDR p-value correction	Proportion recovery in iCM-HuR-/-
Wnt2	2.512397092	3.576714394	0.418059389	1	0.000567535	0.126757062	0.8077866
Sfrp1	0.957582485	2.130545831	0.631505055	1	1.13897E-08	0.002123649	0.694439224
Cx3cr1	1.215485065	4.120171764	0.537162952	1	3.44339E-25	0.124988228	0.61117409
Postn	1.038619123	11.02058296	0.454874387	1	1.4745E-104	0.000463449	0.599526201
Wnt5a	1.044970712	0.858478909	1.096346918	1	0.00700897	1	0.584448552
Nox4	0.811463742	2.751560787	0.665368852	1	4.33976E-08	0.898534215	0.525678556
Runx1	0.992008327	2.150464655	0.721635952	1	0.000211493	1	0.520321978
Ankrd1	0.683197624	4.61846843	0.594886149	1	8.9519E-31	0.230078079	0.517071123
Ppargc1a	1.024019504	0.686965411	1.233462973	1	8.25062E-08	0.571945689	0.512342702
Dbn1	1.064109719	2.778381031	0.720734881	1	3.44551E-15	0.425168052	0.436298462
Col1a1	1.05390113	3.074522377	0.708000403	1	1.05238E-31	0.254161195	0.432754694
Col4a2	1.052540506	2.440936445	0.763232849	1	5.22721E-23	0.44258734	0.401081929
Tgfb1	1.111777604	1.777558079	0.841935418	1	3.33827E-05	1	0.361347894
Scx	1.008578331	2.394636735	0.800610274	1	7.41887E-10	1	0.342358659
Sox6	0.98376547	0.790460208	1.088101093	1	0.000149998	1	0.332349326
Pde3a	0.979841158	0.834402594	1.063322226	1	0.000165065	1	0.319064354
Clec3b	0.992447759	0.533196549	1.253506362	1	1.57494E-08	0.956298346	0.289562378
Penk	1.077521446	0.393160678		1	0.000102721	1	0.196035399
Serpine1	0.967053287	2.904976651	0.873805893	1	9.77661E-09	1	0.192438545
Star	0.975232788	4.338111431	1.047469829	1	5.82943E-20	1	-0.061690394

**Table S6. Genes changed between wild-type and iCM-HuR<sup>-/-</sup> mice post-TAC that were not changed between wild-type sham v. TAC.**

Gene Symbol	Fold change Control Sham vs. iCM-HuR <sup>-/-</sup> sham	Fold change Control TAC vs. Control sham	Fold change iCM-HuR <sup>-/-</sup> TAC vs. Control TAC	EDGE test: Control Sham vs. iCM-HuR <sup>-/-</sup> sham - FDR p-value correction	EDGE test: Control TAC vs. Control sham - FDR p-value correction	EDGE test: iCM-HuR <sup>-/-</sup> TAC vs. Control TAC - FDR p-value correction
Gm26508	1.12585456	0.708899021	5.105226079	1	1	2.13544E-05
1810014B01Rik	0.666041988	1.017804266	1.508020325	0.27706062	0.870051505	0.007000991
Gm4070	0.932590917	0.972219266	1.444875281	1	0.736706296	0.004995474
Gm11716	1.380071303	1.371832634	0.571916506	1	0.533021528	0.002123649
Gm28372	0.9419528	0.348142859	6.356475918	1	0.357631079	0.009414619
Gm13304	1.015651987	1.673026159	0.591111171	1	0.02941837	0.002878905