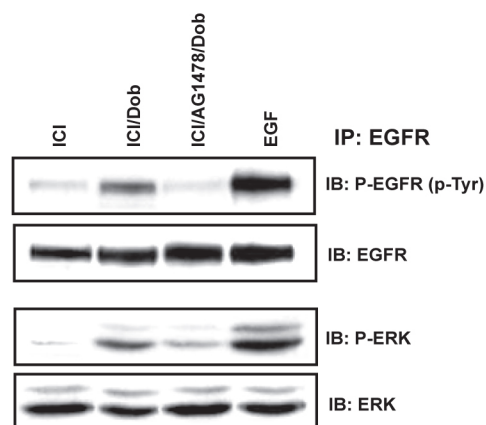


Supplementary Figure 1

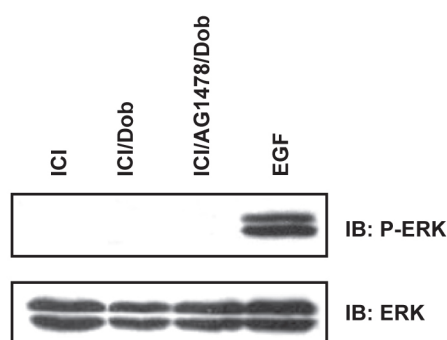
D Adult Cardiomyocytes

A U2S Sarcoma Cells

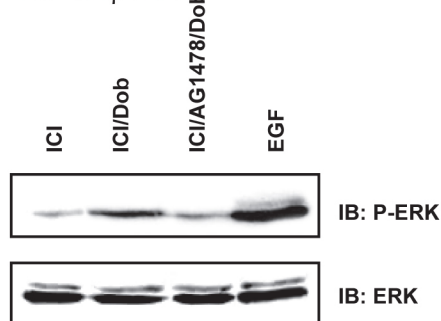


B HEK 293 cells

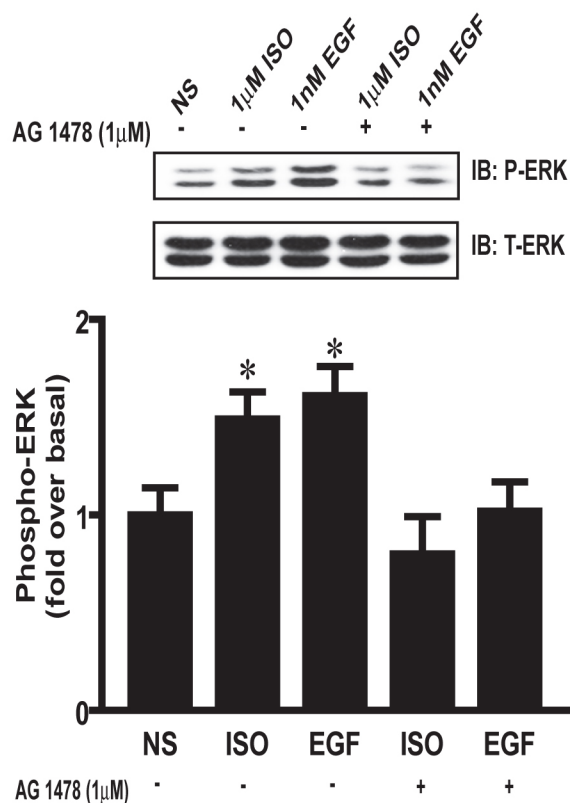
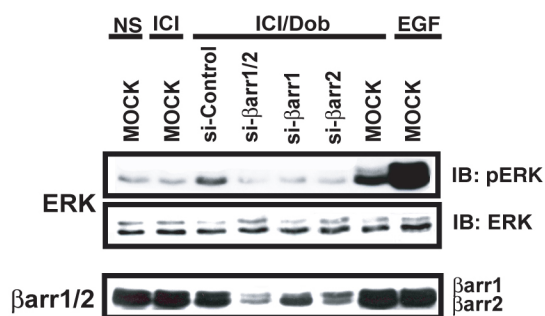
Untransfected cells



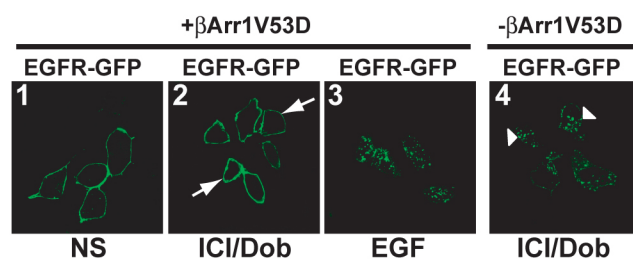
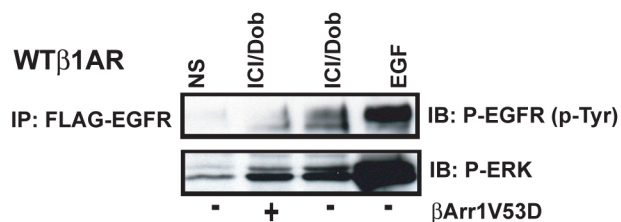
Tx: WT β 1AR



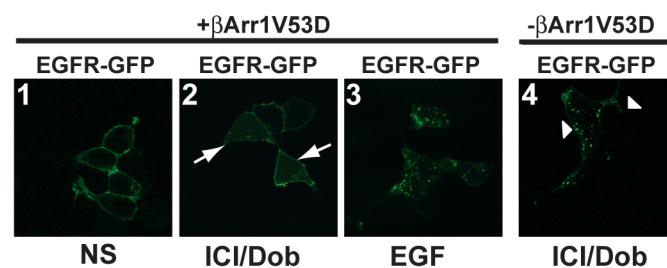
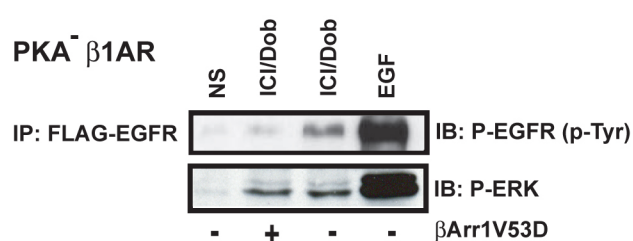
C WT β 1AR, EGFR (transient transfection)



E

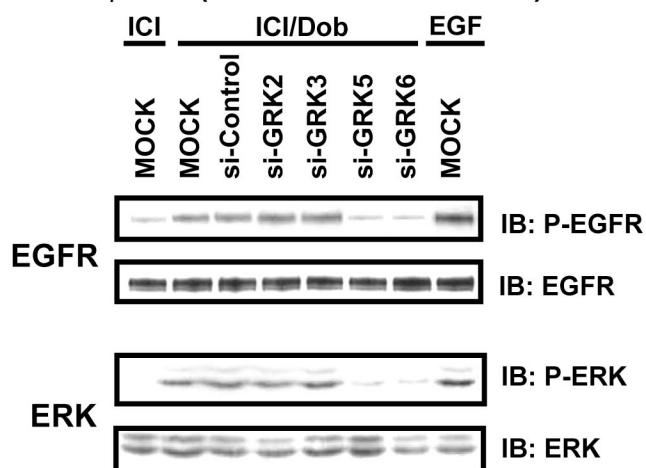


F



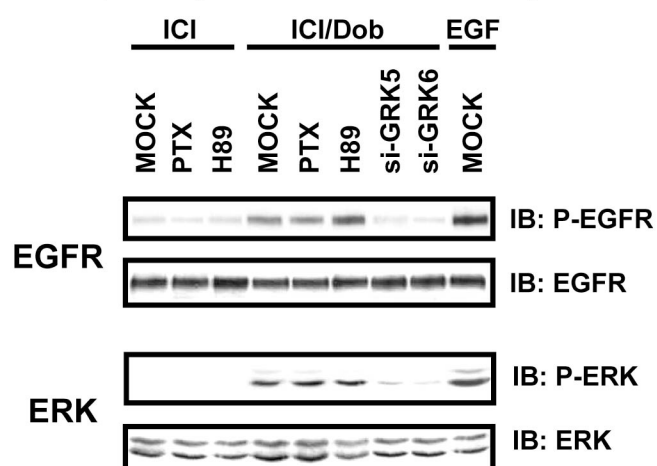
A

WT β 1AR (transient transfection)



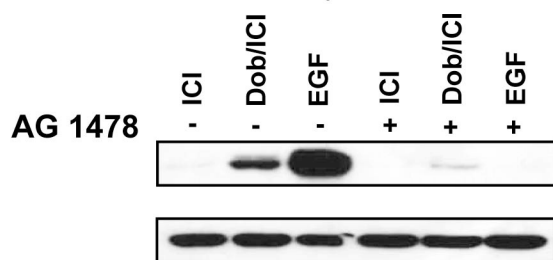
B

WT β 1AR (transient transfection)

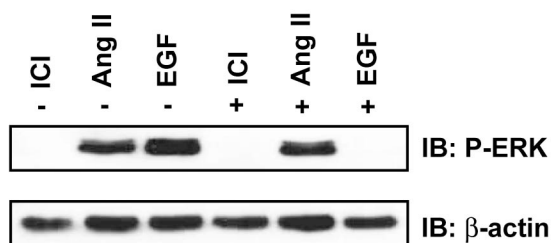


C

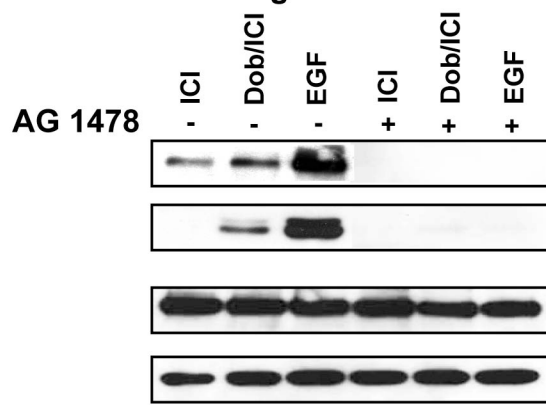
Stable WT β 1AR



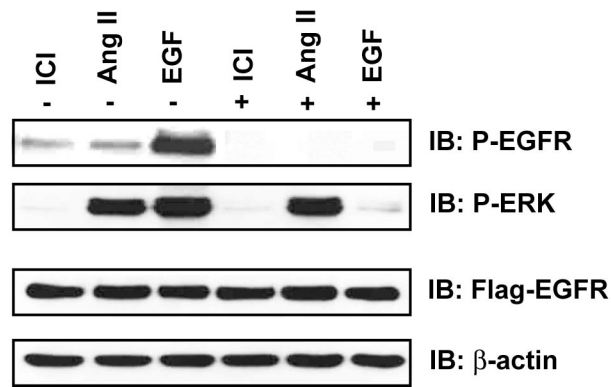
Stable WT AT1R

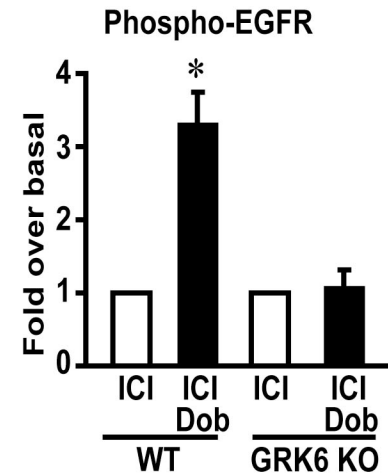
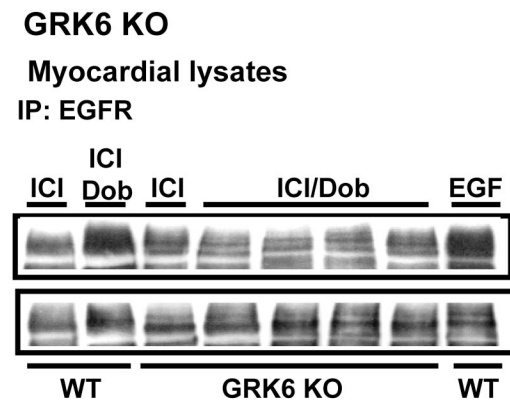
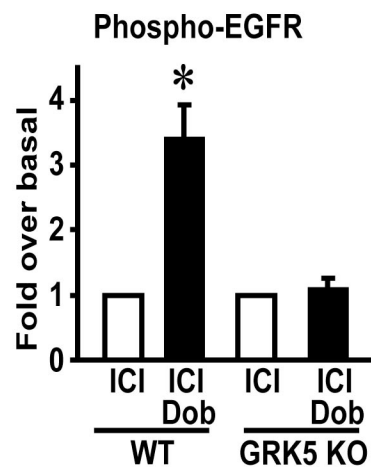
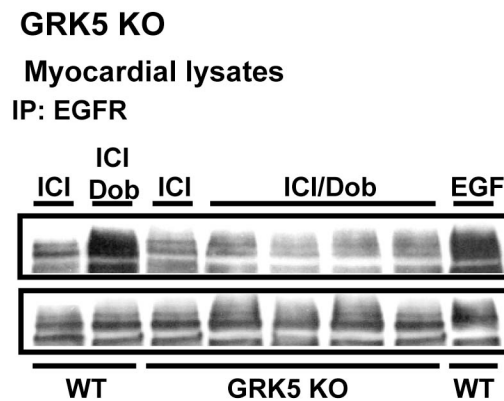
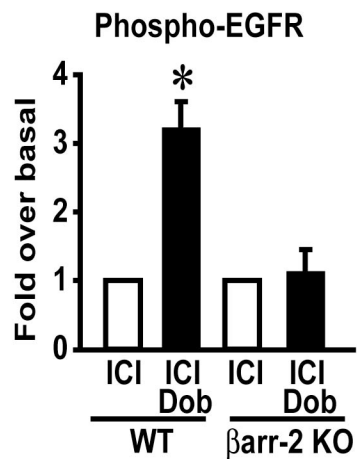
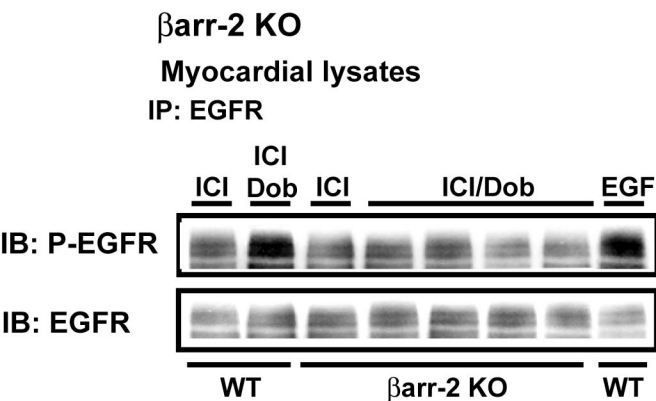


Stable WT β 1AR
Txn: Flag-EGFR



Stable WT AT1R
Txn: Flag-EGFR





A**3rd intracellular loop****C-terminal tail**

WT $\beta 1AR$ 290-LANGRSSKRRPSRLVALREQKALKT-314

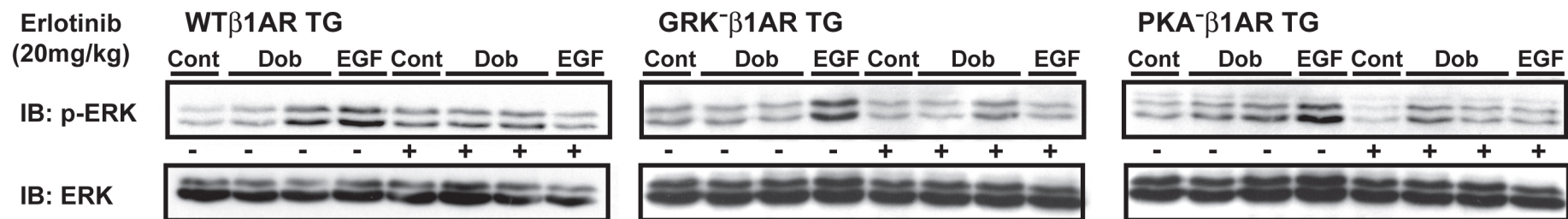
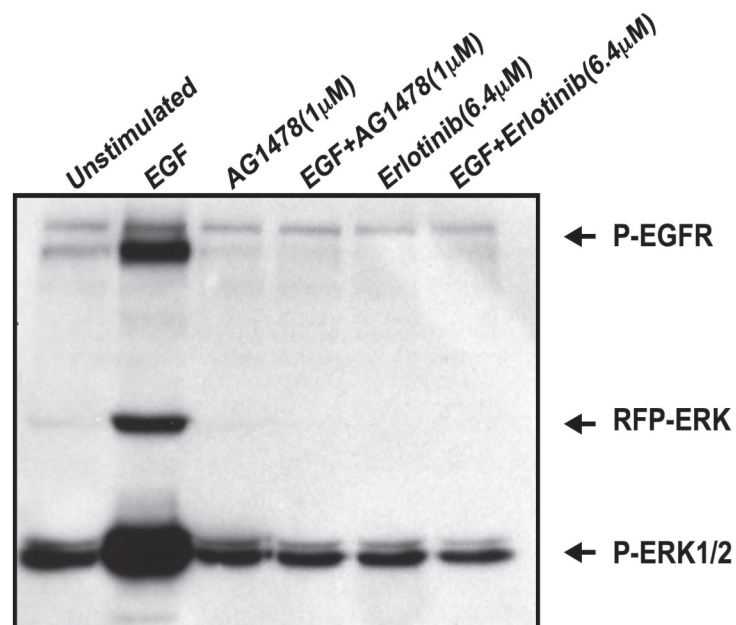
400-ASGCLARAGPPPSPGAPSDDDDDDAGTTPPARLLEPWTGCNCGGTTTVDSDDLDEPGRQGFSSSESKV-465

GRK⁻ $\beta 1AR$ 290-LANGRSSKRRPSRLVALREQKALKT-314

400-ASGCLARAGPPPA**P**GAP**AD**DDDDDDAGA**AA**PPARLLEPWAGCNGG**AA**AVDADAALDEPGRQGF**AA**EAKV-465

PKA⁻ $\beta 1AR$ 290-LANG**RAA**KRRP**AR**LVALREQKALKT-314

400-AAGCLARAGPPPSPGAPSDDDDDDAGTTPPARLLEPWTGCNCGGTTTVDSDDLDEPGRQGFSSSESKV-465

B**C**

Supplementary Table 1. Echocardiographic measurements in NTG, WT and mutant β 1AR TG mice

	5-6month old				12month old			
	NTG	β 1AR TG			NTG	β 1AR TG		
		WT	GRK ⁻	PKA ⁻		WT	GRK ⁻	PKA ⁻
	(n=21)	(n=13)	(n=14)	(n=11)	(n=21)	(n=13)	(n=14)	(n=7)
LVEDD, mm	3.1±0.1	2.8±0.1	3.2±0.1	3.1±0.1	3.5±0.1	3.3±0.1	3.6±0.2	3.3±0.1
LVESD, mm	1.1±0.0	1.0±0.1	1.0±0.1	1.1±0.1	1.6±0.1	1.5±0.1	1.7±0.2	1.3±0.1
IVS, mm	0.9±0.0	0.8±0.0	0.8±0.0	0.8±0.0	0.9±0.0	0.8±0.0	0.9±0.0	0.9±0.0
LVPW, mm	0.7±0.0	0.7±0.0	0.7±0.0	0.8±0.1	0.8±0.0	0.7±0.0	0.7±0.0	0.9±0.1
FS, %	62.9±1.4	66.5±1.7	68.8±2.5	63.7±2.4	54.5±1.5	54.9±1.5	54.3±3.2	61.4±2.5
Vcfc, circ/s	4.1±0.1	4.7±0.1	4.5±0.2	4.6±0.2	3.6±0.1	3.8±0.1	3.7±0.2	3.9±0.2
Heart Rate, bpm	658±12	646±16	663±12	623±22	672±9	670±11	677±9	648±30

Left ventricular end diastolic dimension (LVEDD), left ventricular systolic dimension (LVESD), intraventricular septum (IVS), left ventricular posterior wall (LVPW), fractional shortening (FS), heart rate corrected mean velocity of circumferential fiber shortening (Vcfc). Statistical analysis was performed using t-test with Bonferroni correction for multiple comparisons. No statistical difference was found for any of the β 1AR TG mice compared to NTG mice at 5-6 months or 12 months.

Supplementary Table 2. Serial echocardiographic measurements with chronic ISO

	β 1AR TG							
	NTG (n=21)		WT (n=9)		GRK ⁻ (n=14)		PKA ⁻ (n=9)	
	pre	post	pre	post	pre	post	pre	post
Vehicle treatment								
Serial echocardiography								
LVEDD, mm	3.1±0.1	3.0±0.1	3.1±0.1	3.2±0.1	3.3±0.1	3.1±0.1	3.0±0.1	3.2±0.1
LVESD, mm	1.1±0.1	1.1±0.1	1.3±0.1	1.2±0.1	1.3±0.2	1.2±0.1	1.0±0.1	1.0±0.1
IVS, mm	0.8±0.0*	0.8±0.0*	0.7±0.0	0.6±0.0	0.8±0.0*	0.9±0.0*	0.8±0.0*	0.8±0.0*
LVPW, mm	0.8±0.0*	0.7±0.0	0.6±0.0	0.6±0.0	0.8±0.1*	0.7±0.0	0.7±0.1	0.7±0.0
FS, %	65.6±1.7	64.5±1.7	60.2±2.0	62.7±2.3	61.1±2.6	61.9±1.7	67.0±2.2*	67.8±2.3
Vcfc, circ/s	5.0±0.2	4.8±0.3	4.2±0.2	4.5±0.3	4.7±0.3	4.5±0.2	4.7±0.4	4.1±0.3
Heart Rate, bpm	624±15	678±9	641±21	682±18	605±26	684±9	622±37	673±11
Morphometry								
LV/BW, mg/g		3.5±0.1*		2.8±0.1		3.4±0.1*		3.2±0.2
	β 1AR TG							
	NTG (n=21)		WT (n=9)		GRK ⁻ (n=13)		PKA ⁻ (n=9)	
	pre	post	pre	post	pre	post	pre	post
ISO treatment								
Serial echocardiography								
LVEDD, mm	3.1±0.1	3.1±0.1	3.2±0.1	3.3±0.1	3.1±0.1	3.6±0.1**†	3.2±0.1	3.4±0.1
LVESD, mm	1.2±0.1	1.0±0.1	1.1±0.1	1.2±0.1	1.3±0.1	1.8±0.1**†	1.3±0.1	1.3±0.1
IVS, mm	0.8±0.0	0.9±0.0	0.7±0.0	0.9±0.0	0.9±0.0*	1.0±0.0	0.8±0.1	0.9±0.1
LVPW, mm	0.8±0.0	0.8±0.0	0.7±0.1	0.9±0.0	0.8±0.1	0.8±0.0	0.7±0.1	0.8±0.1
FS, %	61.9±1.1	67.6±1.8*	64.1±1.9	62.4±1.8	60.2±2.2	50.4±1.8**†	60.8±1.7	61.5±1.7
Vcfc, circ/s	4.7±0.2	4.9±0.2	4.3±0.2	4.4±0.2	4.6±0.2	3.5±0.2*†	3.8±0.2*	3.9±0.1
Heart Rate, bpm	637±15	697±13	661±26	724±16	622±23	681±19	558±41*	671±29
Morphometry								
LV/BW, mg/g		3.9±0.1		3.9±0.1		4.5±0.1*		4.2±0.2

Abbreviations as in Table 1. Repeated 2 way ANOVA with Newman-Keuls test for echocardiography, and Bonferroni correction for LV/BW. *, p<0.05 versus WTTG, **, p<0.01 versus NTG, WTTG and PKA-TG, †; p<0.001 post versus pre.