

Supplementary Materials for

G α_s -Biased β_2 -Adrenergic Receptor Signaling from Restoring Synchronous Contraction in the Failing Heart

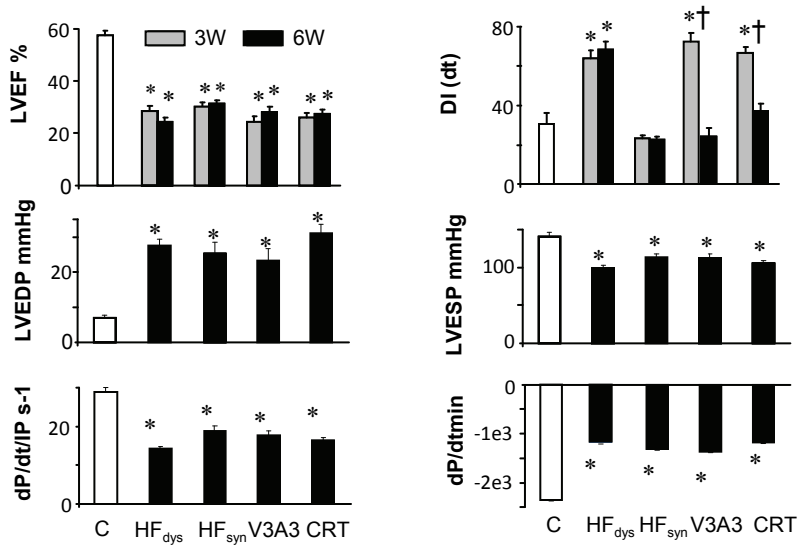
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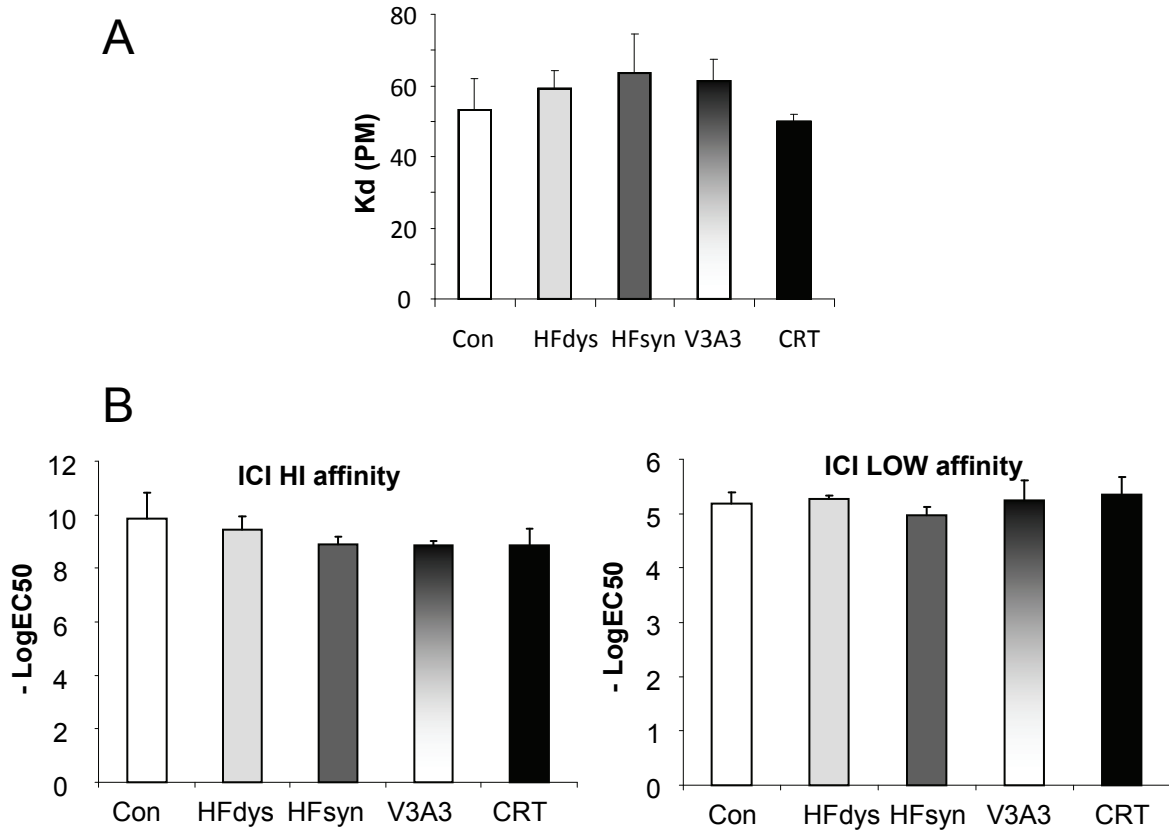
The PDF file includes:

- Fig. S1. Global ventricular function in five experimental models.
- Fig. S2. β -Receptor binding affinity for normal control and four HF models.
- Fig. S3. (A) Effect of β_1 -AR stimulation on myocyte sarcomere shortening and peak calcium transient in the five experimental models. (B) Gene expression of β_1 -AR and β_2 -AR assessed by quantitative PCR.
- Fig. S4. Activation of PKA by fenoterol, as indexed by AKAR3 in myocytes isolated from the five experimental models.
- Fig. S5. Myocardial protein expression of β -arrestin1 and β -arrestin2 in control and four HF models.
- Fig. S6. Full gel electrophoresis for RGS3 protein analysis, displaying both long- and short-form expression changes.
- Fig. S7. mRNA expression of RGS2 and RGS3 from control and four HF models.
- Fig. S8. Protein expression of G $\alpha_i(1,2,3)$, GRK2, RGS4, and β -arrestin1; in AVA versus HF_{syn}.



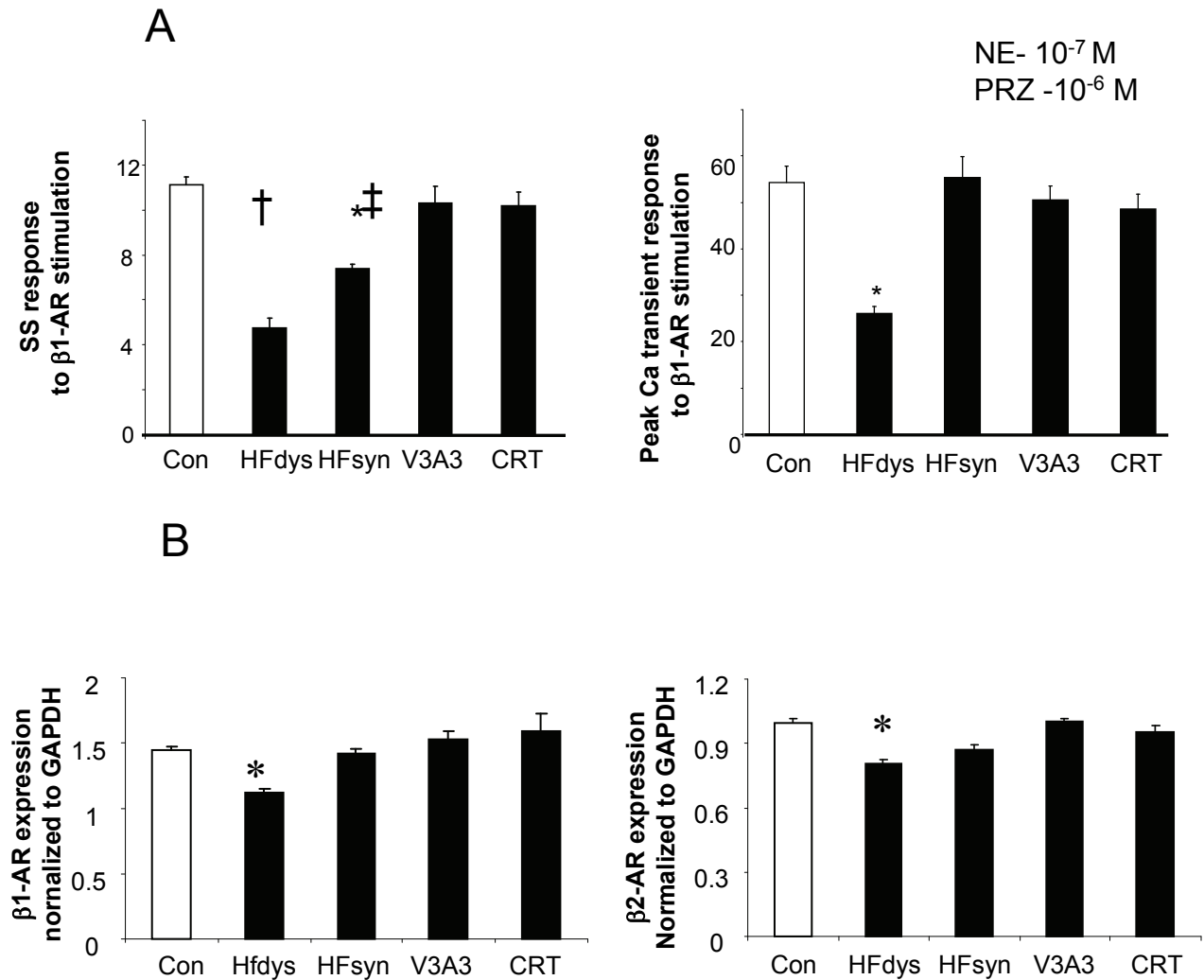
Global ventricular function in five experimental models. Dyssynchrony index (DI) shows the differences between the always dyssynchronous, always synchronous, and 2 resynchronized models, a value of ~30 is typical of the normal heart. LV ejection fraction (LVEF) at 3 and 6 week time points is depressed compared to normal hearts, with very modest differences among models that do not reach statistical significance in a 1-way ANOVA. Similarly, LV end-diastolic pressure (LVEDP), end-systolic pressure (LVESP), contractile function (dP/dt_{max}/IP) and relaxation (dP/dt_{min}) are abnormal in each HF model compared to control, with no major differences among the models. * p<0.01 versus Control, †p<0.001 versus 6-wk data.

Figure S1



β -receptor binding affinity for normal control and four HF models. A) Beta receptor binding affinity (Kd) was unaltered among the five different models. B) Both high and low affinity binding was assessed, and also found to be unaltered among the models.

Figure S2

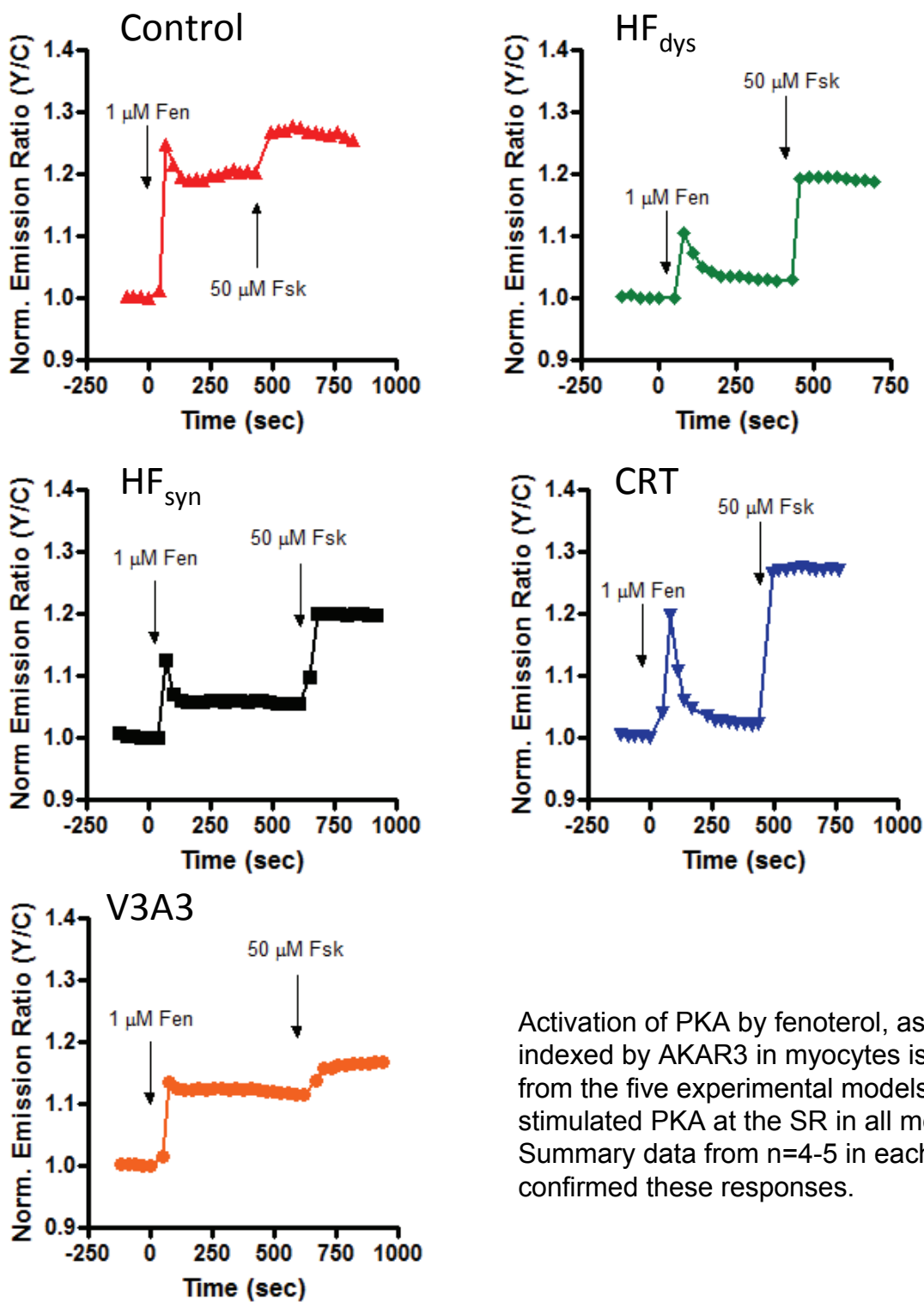


(A) Effect of β_1 -AR stimulation on myocyte sarcomere shortening and peak calcium transient in the five experimental models.

Maximal sarcomere shortening and calcium transient response to selective beta-1 stimulation (combined norepinephrine, NE, and prazosin PRZ). Both responses were reduced in HFdys, with less sarcomere shortening decline in HFsyn. Responses in resynchronization models were similar to control.

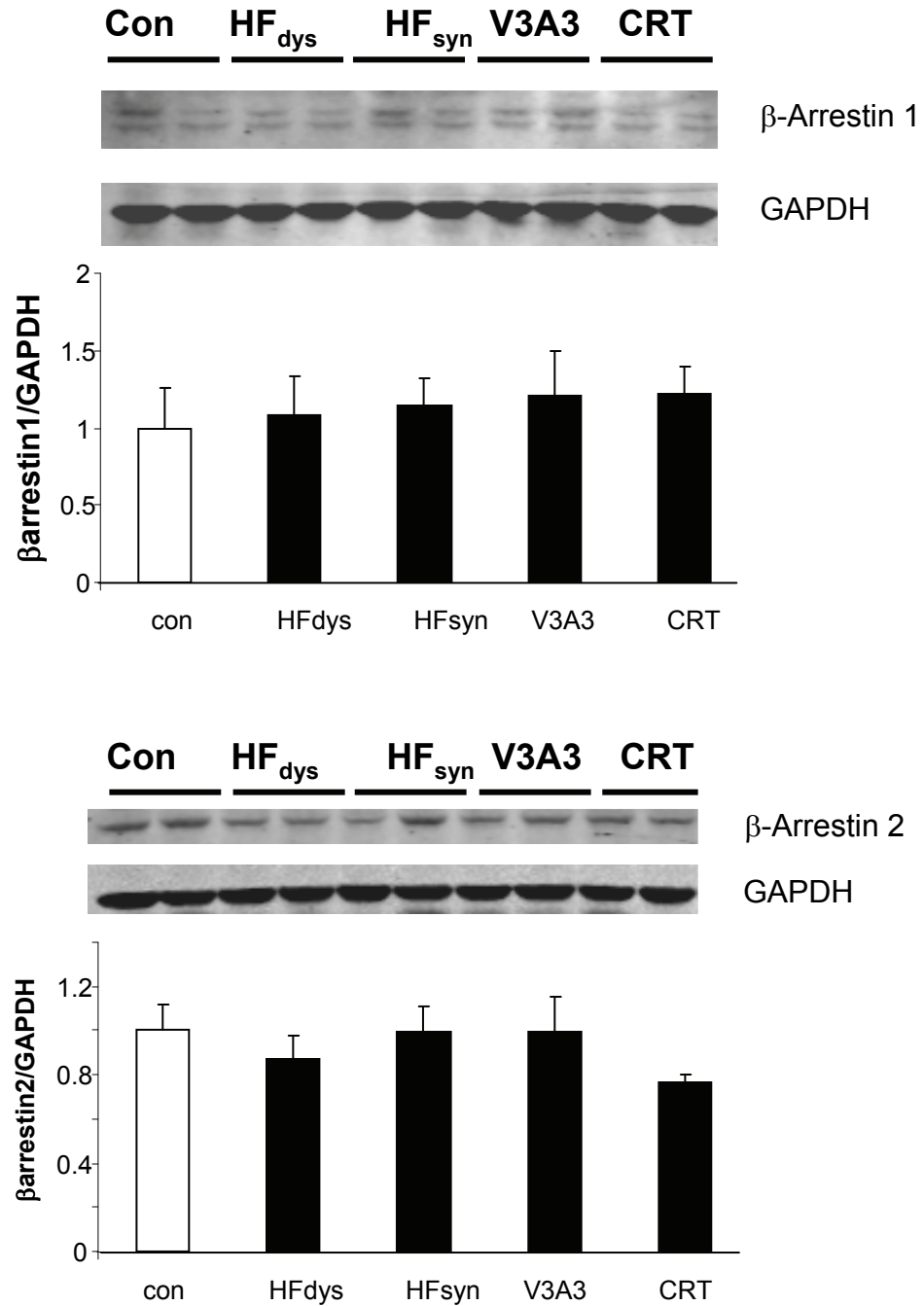
(B) Gene expression of β_1 -AR and β_2 -AR assessed by quantitative PCR. Reduction was observed only in HFdys. * [p<0.05 versus other groups; † p<0.05 versus Con)

Figure S3



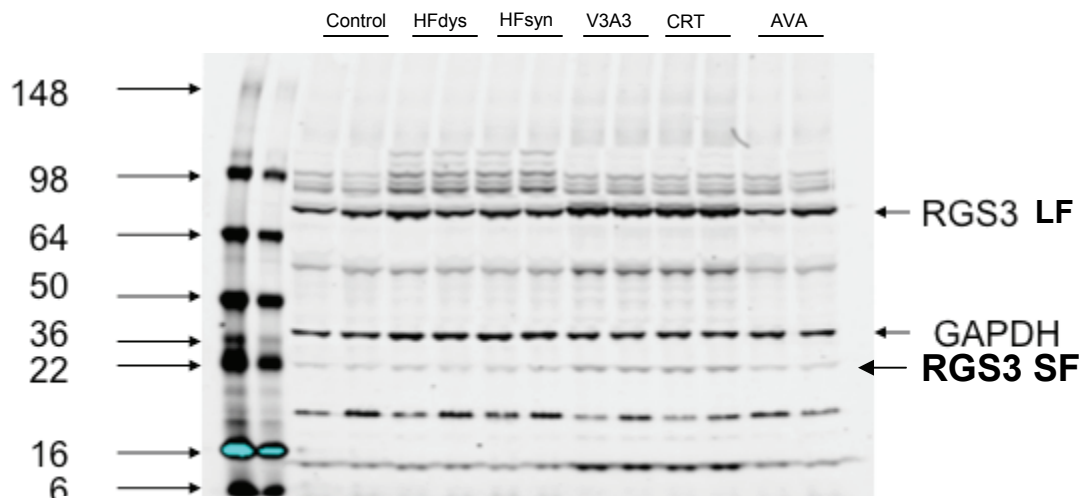
Activation of PKA by fenoterol, as indexed by AKAR3 in myocytes isolated from the five experimental models. Fenoterol stimulated PKA at the SR in all models. Summary data from n=4-5 in each group confirmed these responses.

Figure S4



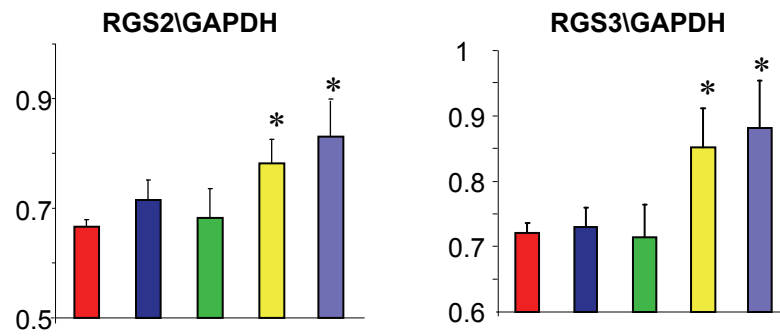
Myocardial protein expression of β -arrestin1 and β -arrestin2 in control and four HF models. There were no significant changes among the models of heart failure or in comparison with normal control. (n=4 dogs for each group).

Figure S5



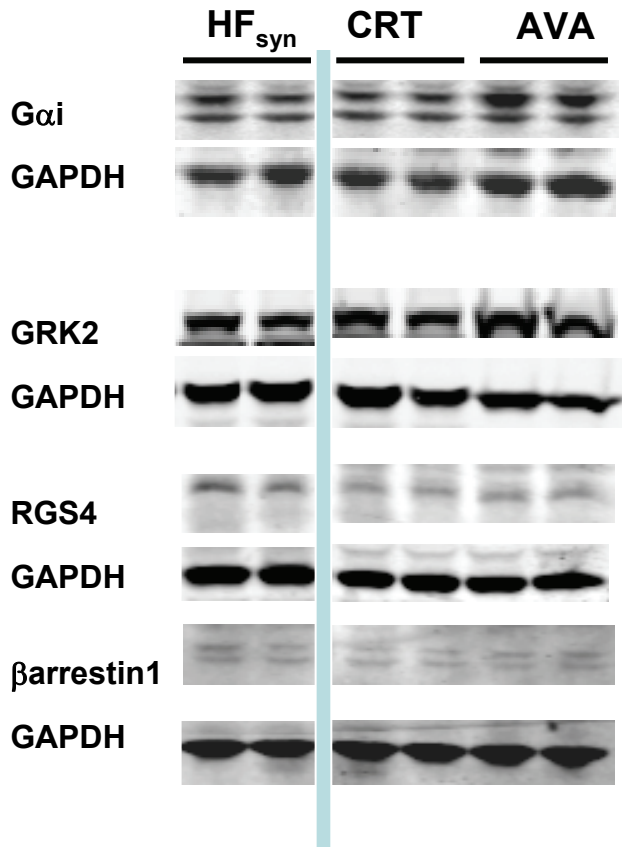
Full gel electrophoresis for RGS3 protein analysis, displaying both long- and short-form expression changes. RGS3 long form (LF, 70 kDa), and short form (SF, 25 kD). The long form band is displayed in Figure 6.

Figure S6



mRNA expression of RGS2 and RGS3 from control and four HF models. RGS2 and RGS3 expression rose with both resynchronization models, but not in the other HF models, while RGS4 increased similarly in all HF models. * $p < 0.05$ versus Control

Figure S7



Protein expression of $G\alpha_i(1,2,3)$, GRK2, RGS4, and β -arrestin1; in AVA versus HF_{syn}. None of these proteins were expressed at levels different from the other HF models. Data shown here contrast to HFsyn – the model closest to AVA.

Figure S8