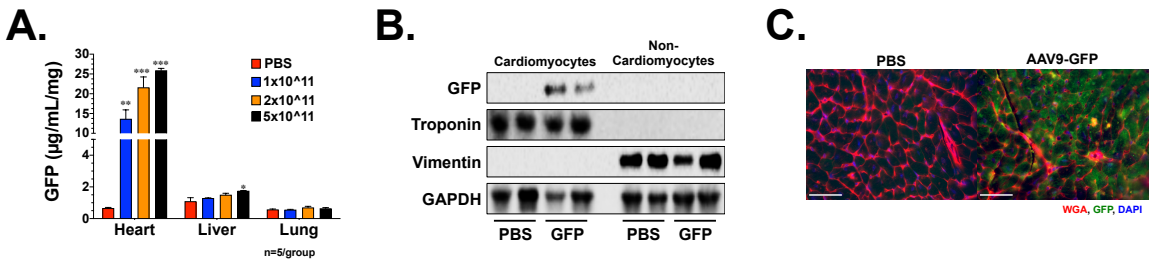
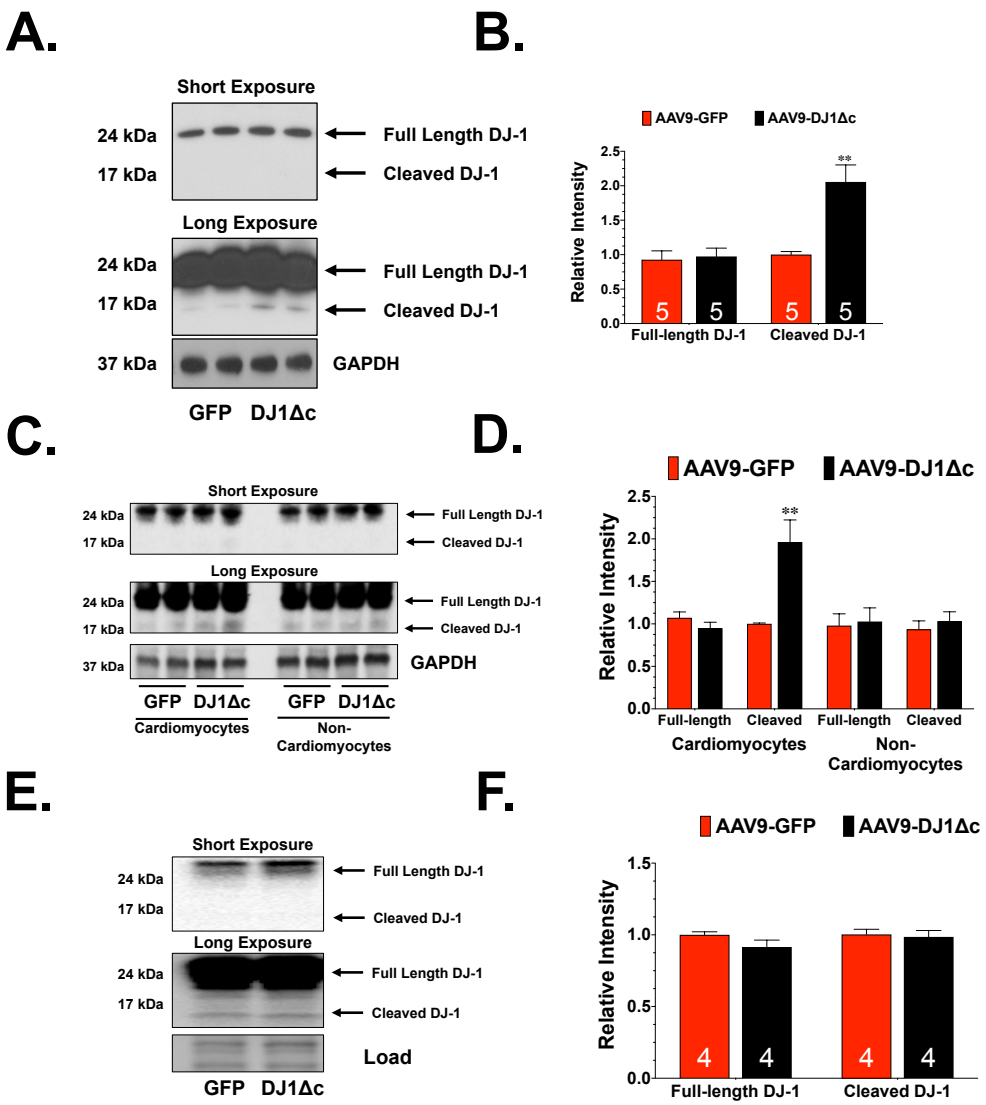
SUPPLEMENTAL MATERIAL

Figure S1. Delivery of AAV9-GFP Increases the Expression of GFP in the heart.



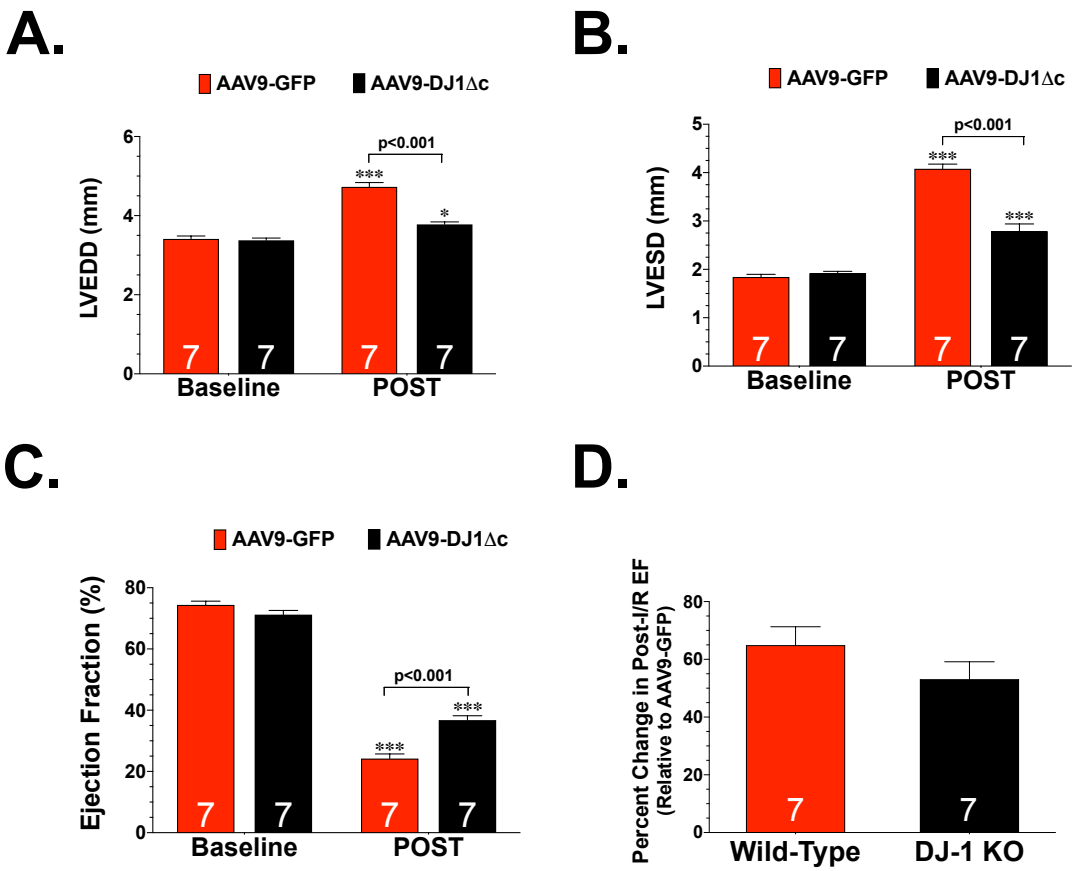
(**A**) GFP levels in heart, liver, and lung tissue collected from mice administered different doses of AAV9-GFP. (**B**) Immunoblots of GFP in cardiomyocytes and non-cardiomyocytes isolated from mice treated with either PBS or AAV9-GFP. (**C**) Representative images of heart sections from PBS and AAV9-GFP treated mice stained with wheat germ agglutinin (WGA), GFP, and DAPI. Scale bar equals 100 µm. Values are means±SEM. One-way Anova with Dunnett. *p<0.0, **p<0.01, and ***p<0.001 vs. PBS.

Figure S2. Delivery of AAV9-DJ1 or AAV9-DJ1Δc Increases the Expression of DJ-1 only in the heart.



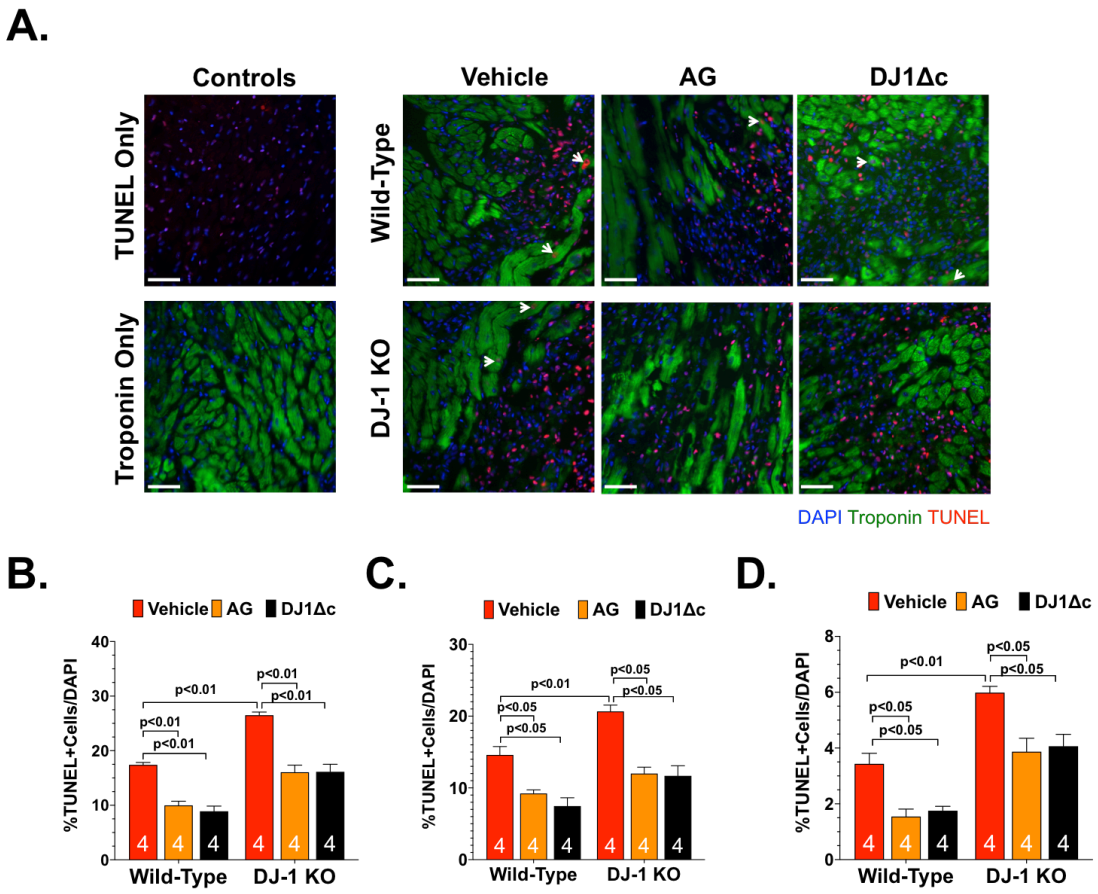
(**A**) Immunoblots and (**B**) densitometric analysis of the expression of the full-length and cleaved forms of DJ-1 from hearts administered AAV9-GFP or AAV9-DJ1Δc. Values are means±SEM. t-test. **p<0.01 vs. AAV9-GFP. (**C**) Immunoblots and (**D**) densitometric analysis of the expression of the full-length and cleaved forms of DJ-1 in cardiomyocytes and non-cardiomyocytes isolated from mice treated with either AAV9-GFP or AAV9-DJ1ΔC (DJ1ΔC). Values are means±SEM. Lane in between cardiomyocytes and non-cardiomyocytes was intentionally left blank. t-test. **p<0.01 vs. AAV9-GFP. (**E**) Immunoblots and (**F**) densitometric analysis of the expression of the full-length and cleaved forms of DJ-1 in livers collected from mice treated with AAV9-GFP, or AAV9-DJ1ΔC. Values are means±SEM. One-way Anova with Tukey.

Figure S3. Delivery of AAV9-DJ1Δc Attenuates Ischemia-Reperfusion Induced Heart Failure in DJ-1 Deficient Mice.



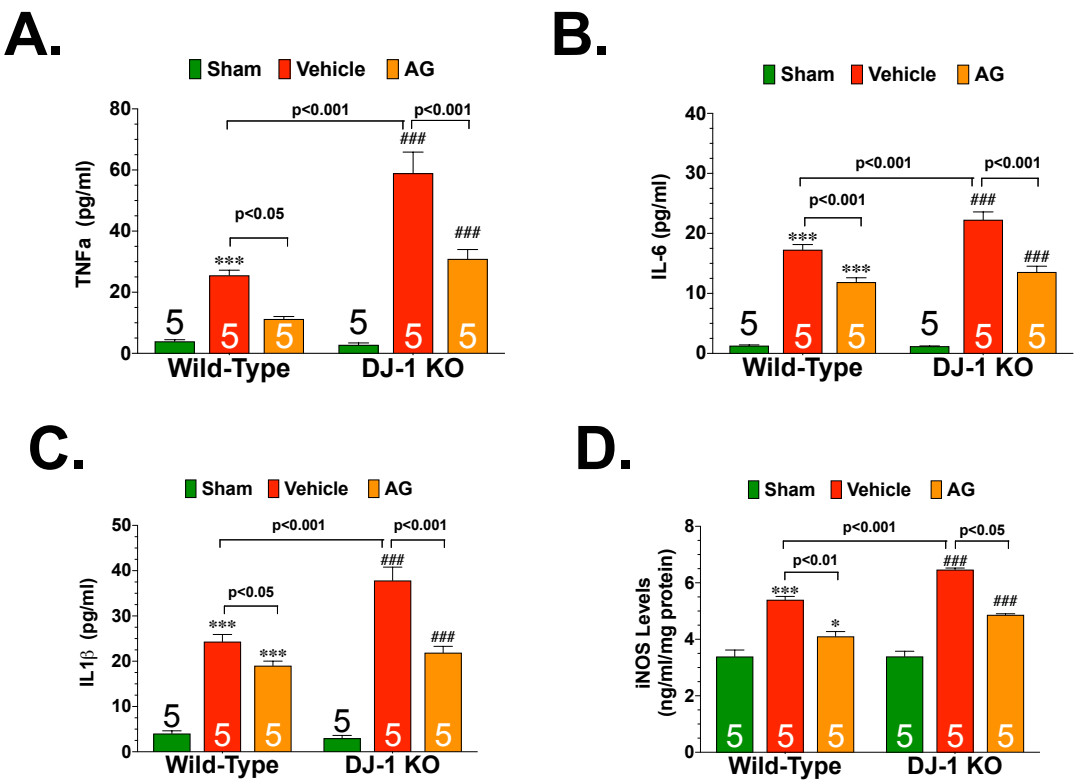
(**A**) Left ventricular end-diastolic diameter (LVEDD), (**B**) LV end-systolic diameter (LVESD), and (**C**) LV ejection fraction. All measurements were performed on hearts from AAV9-GFP (GFP) or AAV9-DJ1Δc treated DJ-1 deficient (DJ-1 KO) mice at 4 weeks of reperfusion. Values are means±SEM. Two-way Repeated Measures ANOVA with Bonferroni. *p<0.05 and ***p<0.001 vs. Baseline. (**D**) Improvements in ejection fraction (EF) observed post-I/R in Wild-Type and DJ-1 KO mice treated with AAV9-DJ1Δc when compared to matched AAV9-GFP treated mice. Values are means±SEM. t-test. *p<0.05 and **p<0.01 vs. AAV9-DJ1.

Figure S4. Aminoguanadine and AAV9-DJ1Δc Reduce Apoptotic Cells in Wild-Type and DJ-1 Deficient Hearts.



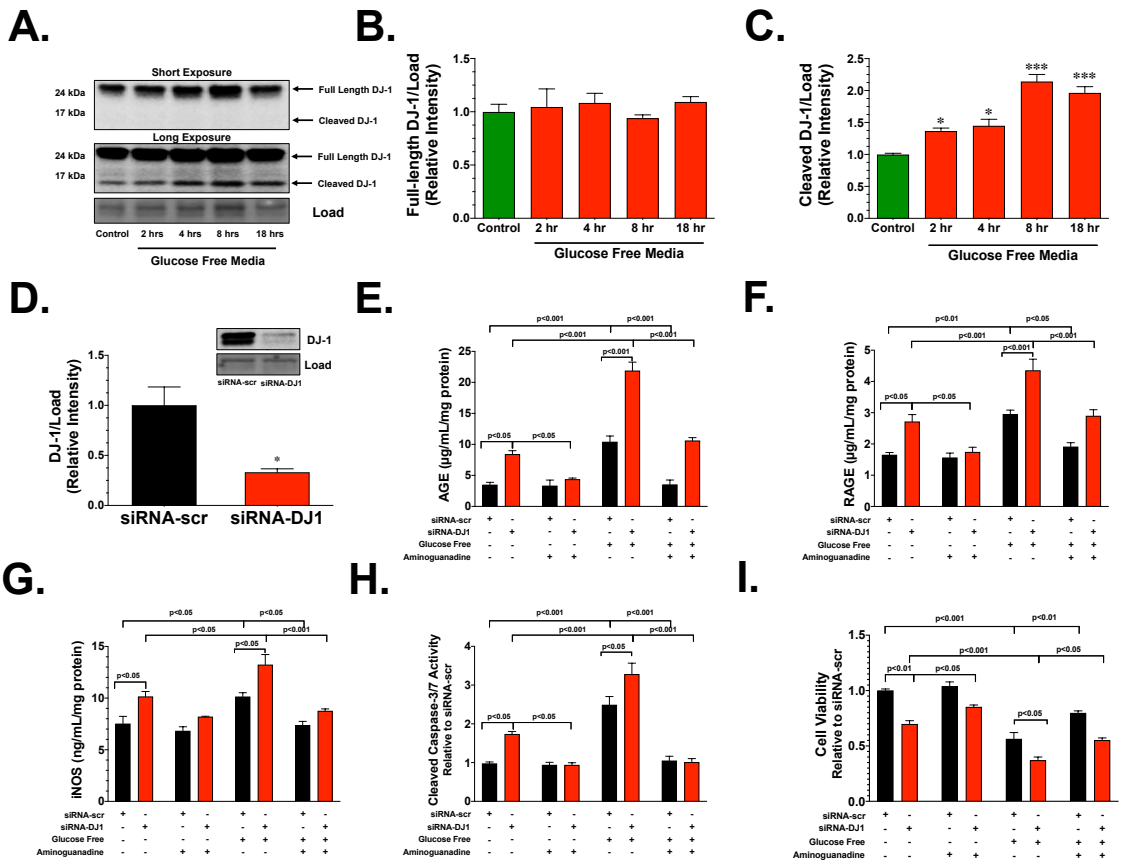
(A) Representative images of heart sections showing TUNEL positive cells (red) in the scar area and infarct border zone. Nuclei are stained with DAPI (blue) and cardiomyocytes are stained with cardiac troponin (green). Arrowheads indicate TUNEL positive nuclei in cardiomyocytes. Scale bar equals 50 μm. Control images to the left represent sections stained with either TUNEL or troponin antibody only. **(B)** Summary of percentage of TUNEL positive cells per nuclei in all cells in the field of interest. **(C)** Summary of percentage of TUNEL positive cells per nuclei in non-cardiomyocyte. **(D)** Summary of percentage of TUNEL positive cells per nuclei in cardiomyocytes. All measurements were performed in heart samples collected at 3 days of reperfusion from Wild-Type and DJ-1 deficient mice (DJ-1 KO) administered vehicle, aminoguanadine (AG; 1g/L), or AAV9-DJ1Δc. Values are means±SEM. Two-way ANOVA with Tukey.

Figure S5. Aminoguanadine Reduces Inflammation and iNOS Levels in Wild-Type and DJ-1 Deficient Hearts.



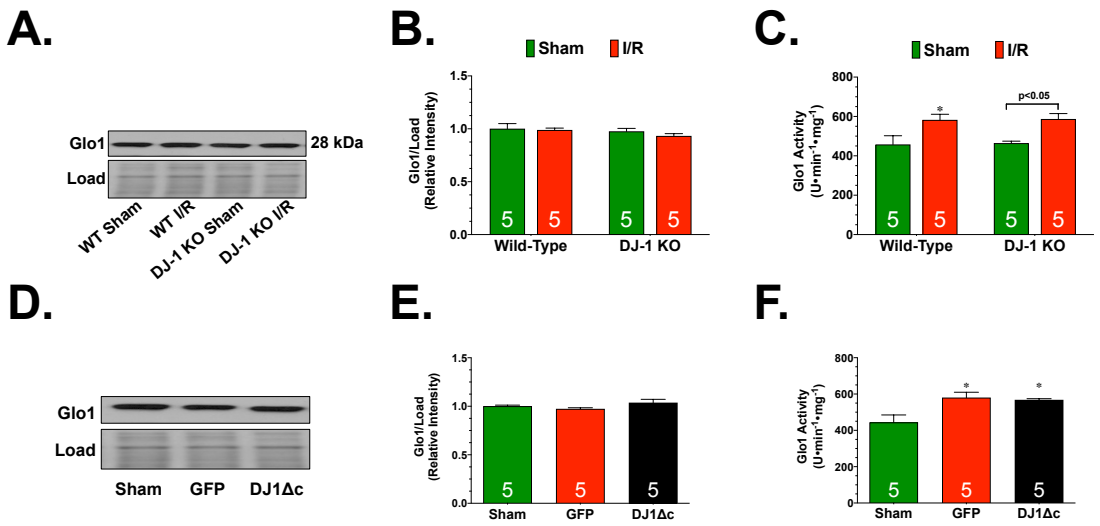
Cardiac levels of (**A**) tumor necrosis factor α (TNFα), (**B**) interleukin 6 (IL-6), (**C**) IL-1β, and (**D**) inducible nitric oxide synthase (iNOS) levels. All measurements were performed in heart samples collected at 3 days of reperfusion from Wild-Type and DJ-1 deficient mice (DJ-1 KO) administered vehicle or aminoguanadine (AG; 1g/L). Values are means±SEM. Two-way ANOVA with Tukey. *p<0.01 and ***p<0.001 vs. Wild-Type Sham. $^{###}$p<0.001 vs. DJ-1 KO Sham.

Figure S6. Knockdown of DJ-1 in H9c2 cells Enhances Glycative Stress and Cell Death in Response to Energy Stress.



(**A**) Immunoblots and densitometric analysis of the expression of the (**B**) full-length and (**C**) cleaved forms of DJ-1 in H9c2 cells exposed to glucose free media for up to 18 hours. Values are means±SEM. One-way ANOVA with Dunnett. *p<0.01 and ***p<0.001 vs. Control. (**D**) Immunoblot and densitometric analysis of DJ-1 from cells transfected with either control siRNA (siRNA-scr) or siRNA to DJ-1 (siRNA-DJ1) for 48 hours. Levels of (E) advanced glycation end-products (AGE), (F) the receptor for AGEs (RAGE), and (G) inducible nitric oxide synthase (iNOS). (H) Cleaved caspase-3/7 activity. Cells were transfected with siRNA-scr or siRNA-DJ1. All measurements were performed in samples exposed to glucose free media for 4 hours in the presence or absence of aminoguanadine (100 μM). Values are means±SEM of three independent experiments of at least three biological replicates.. Two-way ANOVA with Tukey. (**I**) Cell viability was determined in samples exposed to glucose free media for 18 hours. Values are means±SEM of three independent experiments of at least three biological replicates. Two-way ANOVA with Tukey.

Figure S7. DJ-1 Does not Alter the Expression of Activity of Glyoxylase-1.



(A) Immunoblots and (**B**) densitometric analysis of the expression of glyoxylase-1 (Glo1). (**C**) Glo1 activity. Measurements were performed in heart samples collected at 3 days of reperfusion from Wild-Type or DJ-1 deficient mice (DJ-1 KO). Values are means±SEM. Two-way ANOVA with Tukey. *p<0.01 vs. Wild-Type Sham. **(D)** Immunoblots and (**E**) densitometric analysis of the expression of glyoxylase-1 (Glo1). (**F**) Glo1 activity. Measurements were performed in samples collected at 3 days of reperfusion from AAV9-GFP (GFP) or AAV9-DJ1Δc (DJ1ΔC) treated mice. Values are means±SEM. One-way Anova with Tukey. *p<0.05 vs. Sham.