Science Translational Medicine
AAAS

www.sciencetranslationalmedicine.org/cgi/content/full/9/390/eaah5084/DC1

Supplementary Materials for

BET bromodomain inhibition suppresses innate inflammatory and profibrotic transcriptional networks in heart failure

Qiming Duan, Sarah McMahon, Priti Anand, Hirsh Shah, Sean Thomas,
Hazel T. Salunga, Yu Huang, Rongli Zhang, Aarathi Sahadevan, Madeleine E. Lemieux,
Jonathan D. Brown, Deepak Srivastava, James E. Bradner,
Timothy A. McKinsey, Saptarsi M. Haldar*

*Corresponding author. Email: saptarsi.haldar@gladstone.ucsf.edu

Published 17 May 2017, *Sci. Transl. Med.* **9**, eaah5084 (2017)
DOI: 10.1126/scitranslmed.aah5084

The PDF file includes:

Fig. S1. Echocardiographic data from sham- and TAC-treated mice at day 53.
Fig. S2. Transcriptomic effects of chronic JQ1 administration in baseline (sham-operated) hearts.
Fig. S3. GSEA and fingerprinting analysis of differentially expressed genes in mouse LV.
Fig. S4. Additional qRT-PCR of exercise-regulated genes in mouse left ventricle.
Fig. S5. qRT-PCR and GSEA in human iPSC-CMs.
Legends for tables S1 to S6

Other Supplementary Material for this manuscript includes the following:
(available at www.sciencetranslationalmedicine.org/cgi/content/full/9/390/eaah5084/DC1)

Table S1 (Microsoft Excel format). Normalized RNA-seq expression data for sham-vehicle and sham-JQ1 groups.
Table S2 (Microsoft Excel format). Normalized RNA-seq expression data for sham-vehicle, TAC-vehicle, and TAC-JQ1 groups.
Table S3 (Microsoft Excel format). Normalized RNA-seq expression data for sham-vehicle, MI-vehicle, and MI-JQ1 groups.
Table S4 (Microsoft Excel format). List of 193 genes in the Venn overlap in Fig. 4A.

Table S5 (Microsoft Excel format). Normalized RNA-seq expression data from human iPSC-CMs for unstimulated, ET-1, and ET-1 + JQ1 groups.
Table S6 (Microsoft Excel format). List of qRT-PCR primers and TaqMan probes.

SUPPLEMENTARY MATERIALS

Supplementary Figures

Figure S1

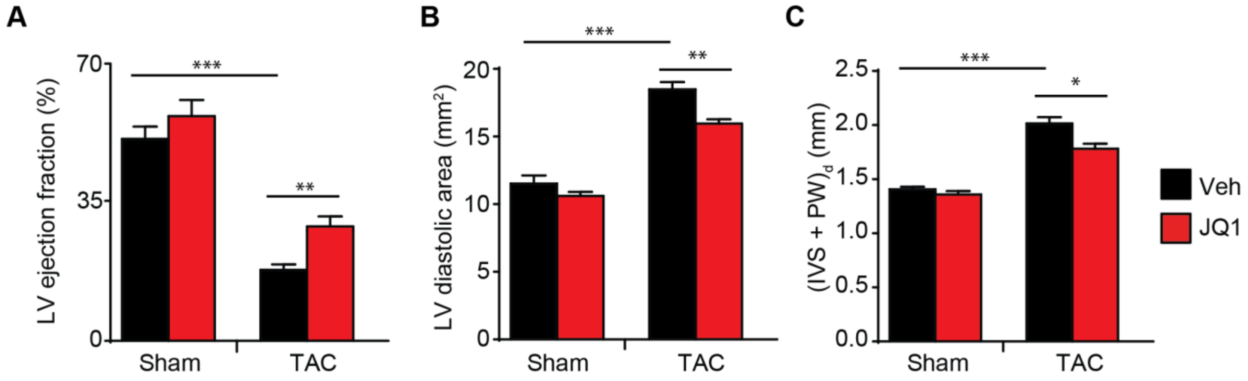
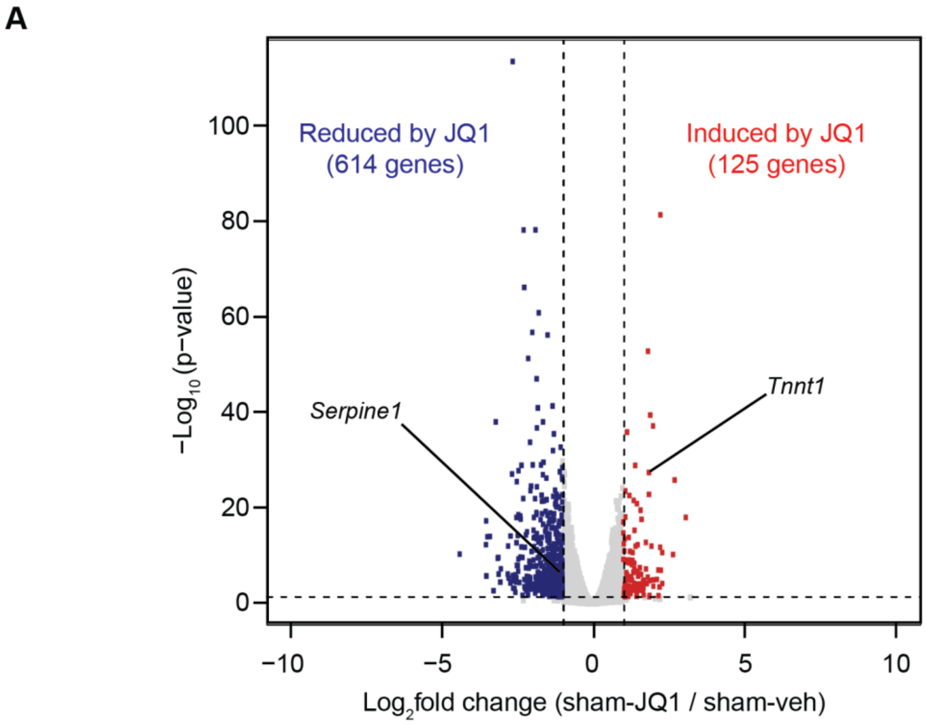


Fig. S1. Echocardiographic data from sham- and TAC-treated mice at day 53. (**A)** LV ejection fraction. **(B)** LV diastolic area. (**C**) LV wall thickness. $(IVS + PW)_d$ is the sum of the thickness of the interventricular septum and posterior LV wall at end diastole. (for A-C, n=10) $*p < 0.05$, $**p < 0.01$, $***p < 0.001$ for indicated comparison. Data shown as mean ± SEM.

Figure S2



B

Reduced by JQ1

Category	Term	% List	FDR
GOTERM_BP_FAT	GO:0006955~immune response	14	<1e-11
GOTERM_BP_FAT	GO:0006952~defense response	14	<1e-7
GOTERM_BP_FAT	GO:0007155~cell adhesion	14	<1e-4
GOTERM_BP_FAT	GO:0045087~innate immune response	8	<1e-5
GOTERM_BP_FAT	GO:0034097~response to cytokine	7	<1e-3
GOTERM_CC_FAT	GO:0031012~extracellular matrix	6	<1e-2
GOTERM_BP_FAT	GO:0030595~leukocyte chemotaxis	4	<1e-4

Induced by JQ1

Category	Term	% List	FDR
INTERPRO	IPR018181:Heat shock protein 70, conserved site	3	<0.05

Fig. S2. Transcriptomic effects of chronic JQ1 administration in baseline (sham-operated) hearts. JQ1 was administered at 50 mg/kg daily intraperitoneally according to the protocol in Figure 1A; RNA-seq was performed on LV tissue at day 53. (**A**) Volcano plot showing genes downregulated by JQ1 (blue) and upregulated by JQ1 (red). The hatched lines represent cutoff criteria for differential expression calls (>2-fold change and adjusted p-value<0.05). Representative genes are called out (black lines). (**B**) Gene ontology analysis using DAVID for the JQ1-downregulated genes (top table) and JQ1-upregulated genes (bottom table). False discovery rate<0.05 was considered statistically significant.

Figure S3

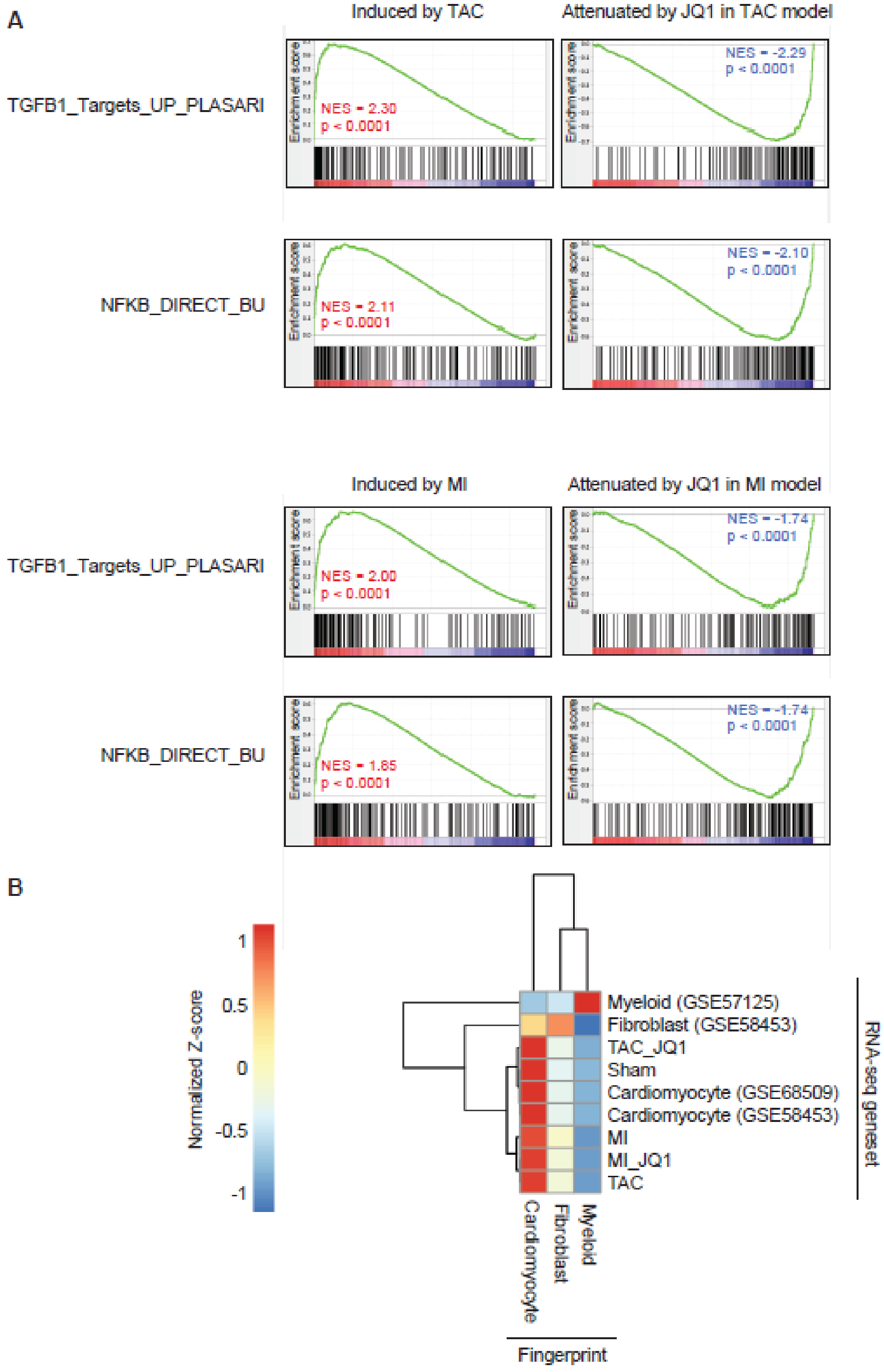


Fig. S3. GSEA and fingerprinting analysis of differentially expressed genes in mouse LV. (**A**) Gene set enrichment analysis for genes induced by stress (TAC, MI) and attenuated by JQ1 against curated signatures of TGF-β and NFκB targets. NES, Normalized enrichment score.

Family-wise error rate p-value < 0.05 was considered significant. (**B**) Heatmap of normalized Z-score from cell-restricted fingerprinting analysis (3 cell types indicated on bottom) of the transcriptomic profiles for indicated groups (right).

Figure S4

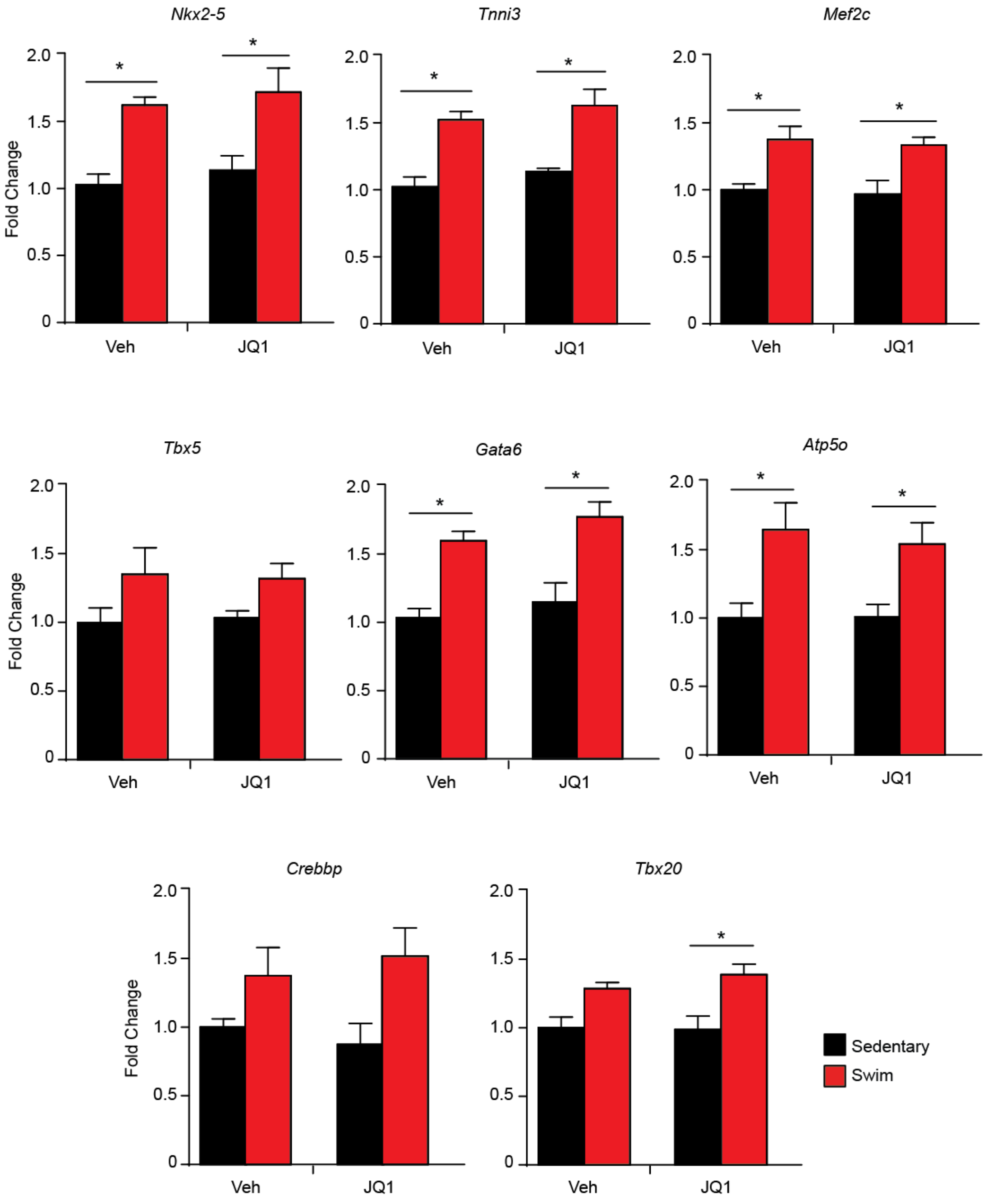


Fig. S4. Additional qRT-PCR of exercise-regulated genes in mouse left ventricle. qRT-PCR for indicated genes in mouse LV tissue (n = 5). *$p < 0.05$ for indicated comparisons. Data shown as mean ± SEM.

Figure S5

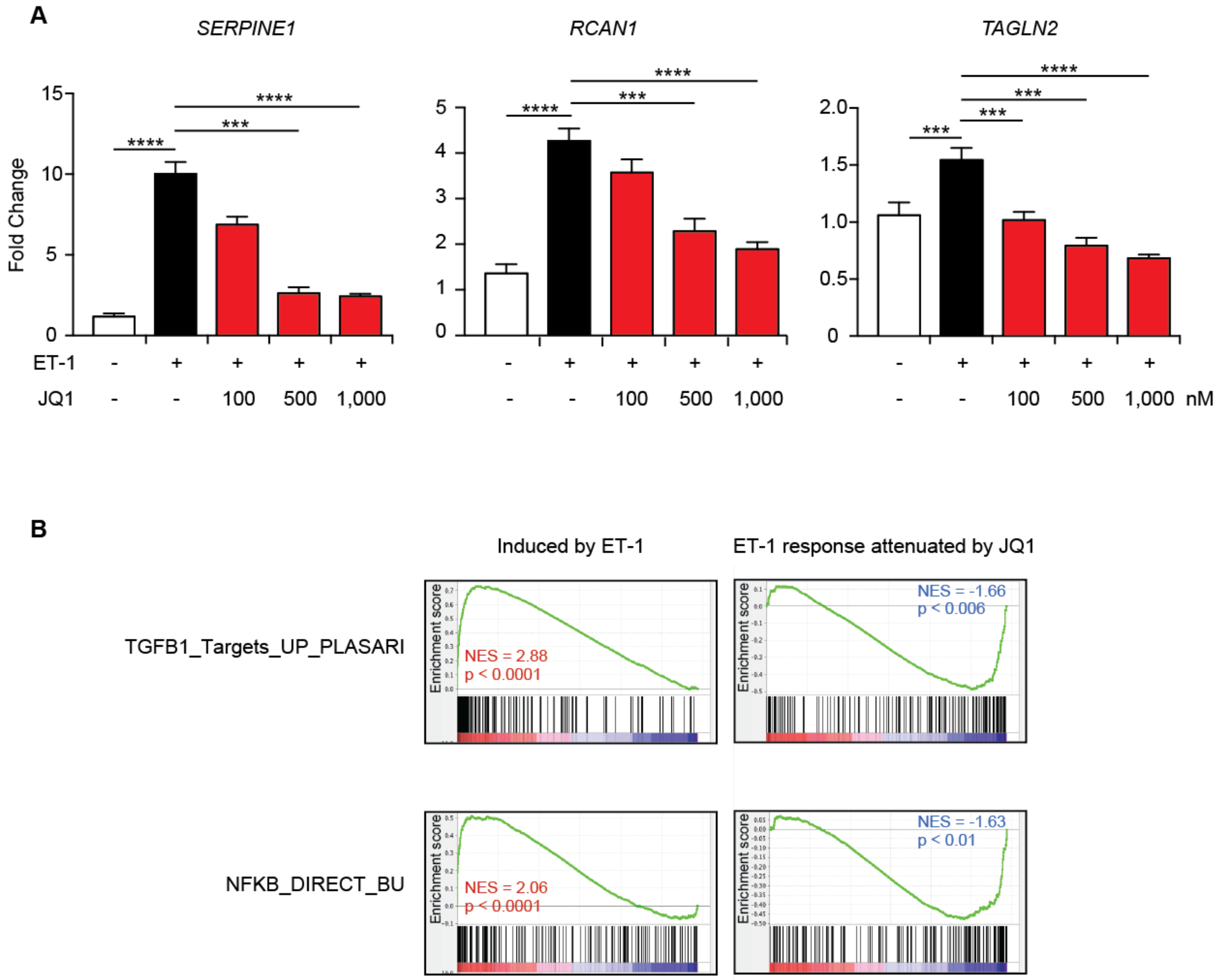


Fig. S5. qRT-PCR and GSEA in human iPSC-CMs. (A) qRT-PCR for indicated genes in iPS-CMs (n = 12). ****p<0.001, ***p<0.01. Data shown as mean ± SEM. (**B**) Gene set enrichment analysis for genes induced by ET-1 and attenuated by JQ1 against curated signatures of TGF-β and NFκB targets. NES, Normalized enrichment score. For GSEA, family-wise error rate p-value < 0.05 was considered significant.

Supplementary Tables

Table S1. Normalized RNA-seq expression data for sham-vehicle and sham-JQ1 groups. Mean FPKM for each experimental group with fold change and adjusted p-value for relevant comparisons is provided in an Excel spreadsheet.

Table S2. Normalized RNA-seq expression data for sham-vehicle, TAC-vehicle, and TAC-JQ1 groups. Mean FPKM for each experimental group with fold change and adjusted p-value for relevant comparisons is provided in an Excel spreadsheet.

Table S3. Normalized RNA-seq expression data for sham-vehicle, MI-vehicle, and MI-JQ1 groups. Mean FPKM for each experimental group with fold change and adjusted p-value for relevant comparisons is provided in an Excel spreadsheet.

Table S4. List of 193 genes in the Venn overlap in Fig. 4A. List of official gene symbols is provided in an Excel spreadsheet.

Table S5. Normalized RNA-seq expression data from human iPSC-CMs for unstimulated, ET-1, and ET-1 + JQ1 groups. Mean FPKM for each experimental group with fold change and adjusted p-value for relevant comparisons is provided in an Excel spreadsheet.

Table S6. List of qRT-PCR primers and TaqMan probes. The list is provided in an Excel spreadsheet.