

Supplemental Fig. 1: **a**, Volcano plot comparing advanced HF to non-failing donor (n=9 donor, n=41 HF). **b-e**, Heat map of genes involved in cell signaling pathways, Ion channel physiology, ECM organization and metabolism respectively (n=9 donor, n=41 HF). **f**, Ingenuity pathway analysis (IPA) of advanced HF myocardium compared to donor (n=9 donor, n=41 HF).

Supplemental Fig. 2: **a-d**, Heat map of genes involved in cell signaling pathways, ECM organization, Ion channel physiology and metabolism respectively in AEBP1 OE compared to GFP US (n=4 each). **e**, Ingenuity Pathway Analysis (IPA) of AEBP1 OE HCF compared to GFP US control (n=4 each).

Supplemental Fig. 3: **a-d**, Heat map of genes involved in cell signaling pathways, metabolism, Ion channel physiology and ECM organization pathways respectively in AEBP1 KD compared to GFP S (n=3 each). **e**, Ingenuity Pathway Analysis (IPA) of AEBP1 KD HCF compared to GFP S control (n=3 each).

Supplemental Fig. 4: **a-d**, Heat map of genes involved in cell signaling pathways, metabolism, Ion channel physiology and ECM organization pathways respectively in Sham compared to 4-days post MI (4dpMI) myocardium (n=5 each). **e**, Ingenuity Pathway Analysis (IPA) of Sham compared to 4dpMI myocardium (n=5 each).

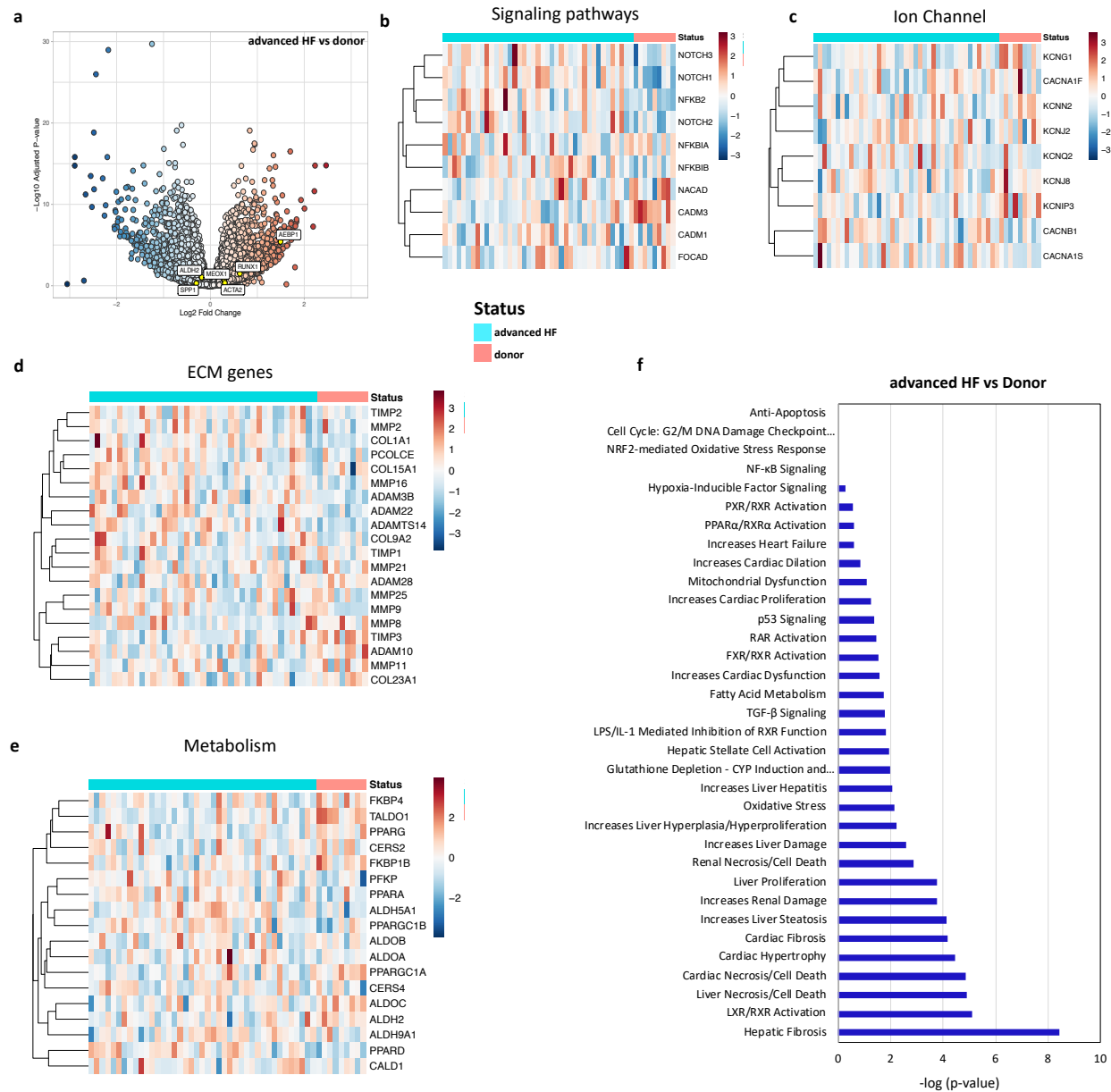
Supplemental Fig. 5: **a**, Representative immunohistochemistry data showing AEBP1 expression in systemic fibrosis model (n=5 each). **b-d**, Longitudinal echocardiography data showing left ventricular ejection fraction (EF%), fractional shortening (FS%) and end-diastolic diameter (LVEDD) respectively (n=5 each). p-value: Multiple two-tailed t-test.

Supplemental Fig. 6: **a**, Representative immunohistochemistry data of GFP and AEBP1 OE in cultured human non-failing donor myocardial slices (n=3 each). **b-d**, Quantification of cell surface area, cell length to width ratio (LWR) and width to length ratio (WLR) from immunohistochemistry (n=3 donor, multiple images/patient). **f**, ECM percentage measured from WGA signal intensity (n=3 donors, multiple images/patient). p-value: Two-tailed unpaired t-test.

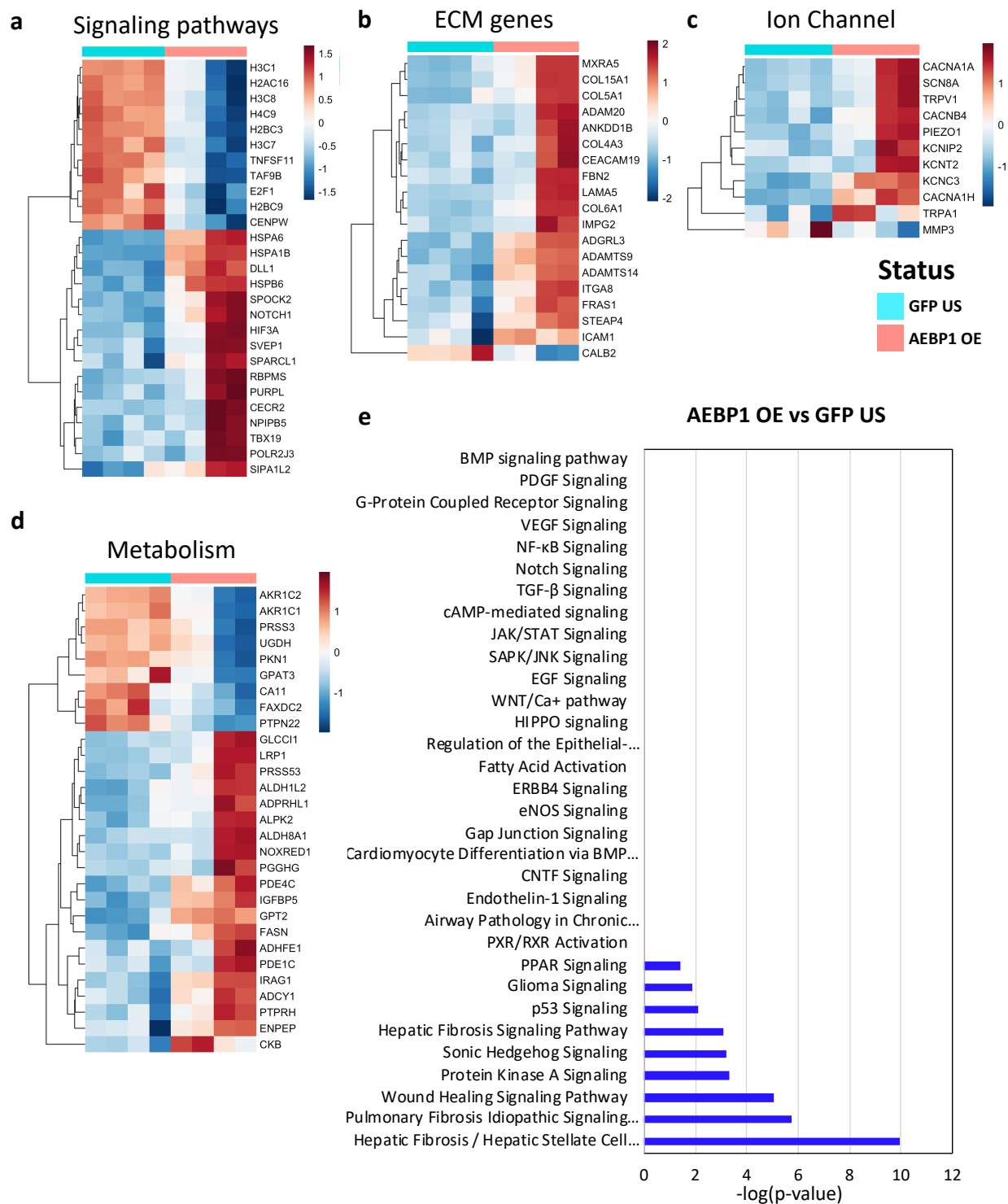
Supplemental Fig. 7: CITE-Seq data from non-failing donor (n=6), patient with acute myocardial infarction (AMI, n=4) and chronic HF (ICM- ischemic cardiomyopathy (n=6) and NICM- non-ischemic cardiomyopathy (n=6)) showing AEBP1 expression in fibroblasts.

Supplemental Fig. 8: AEBP1 is crucial for cardiac fibroblast activation and AEBP1 KD can serve as a potential anti-fibrotic therapy.

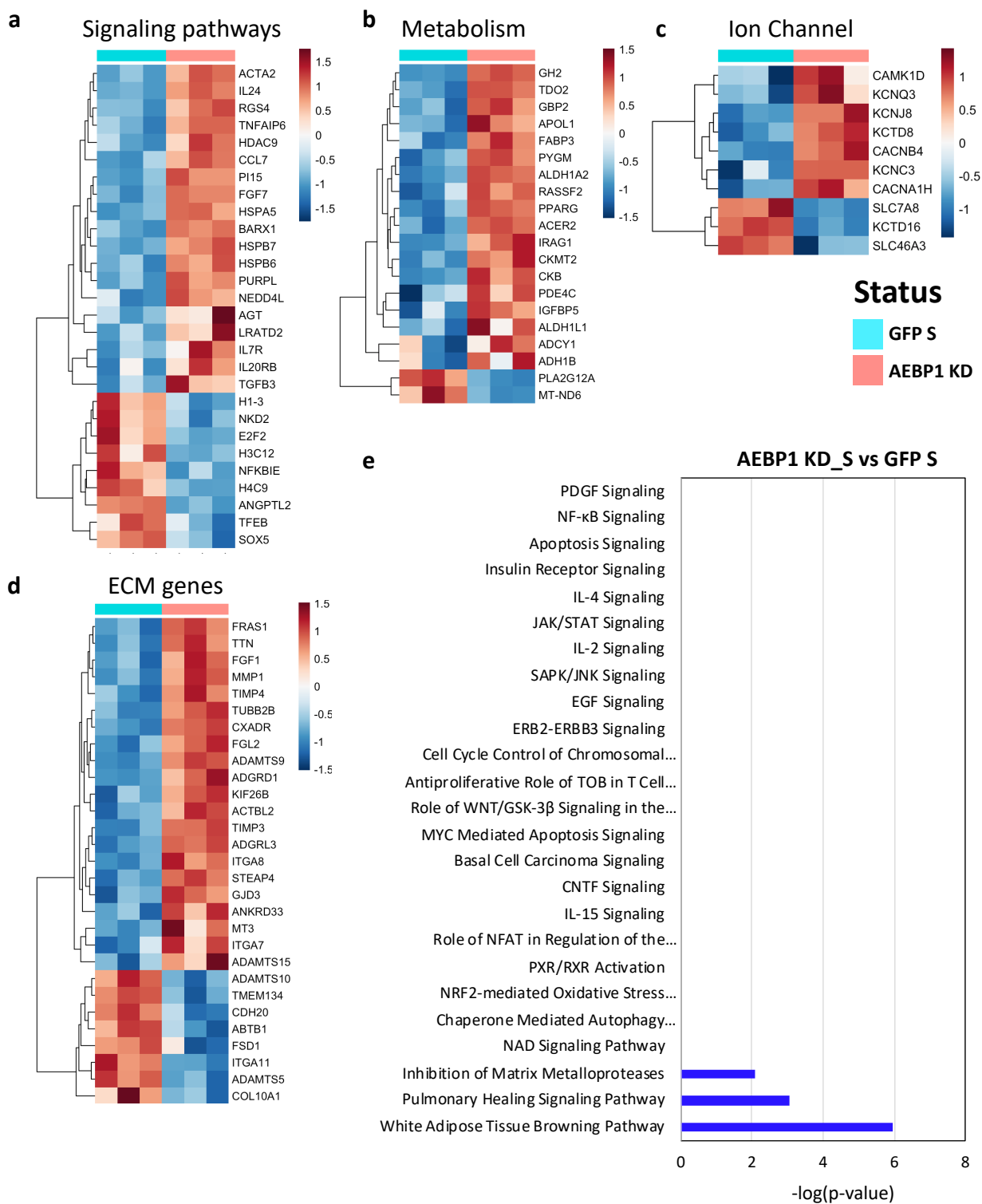
Supplemental Fig. 1



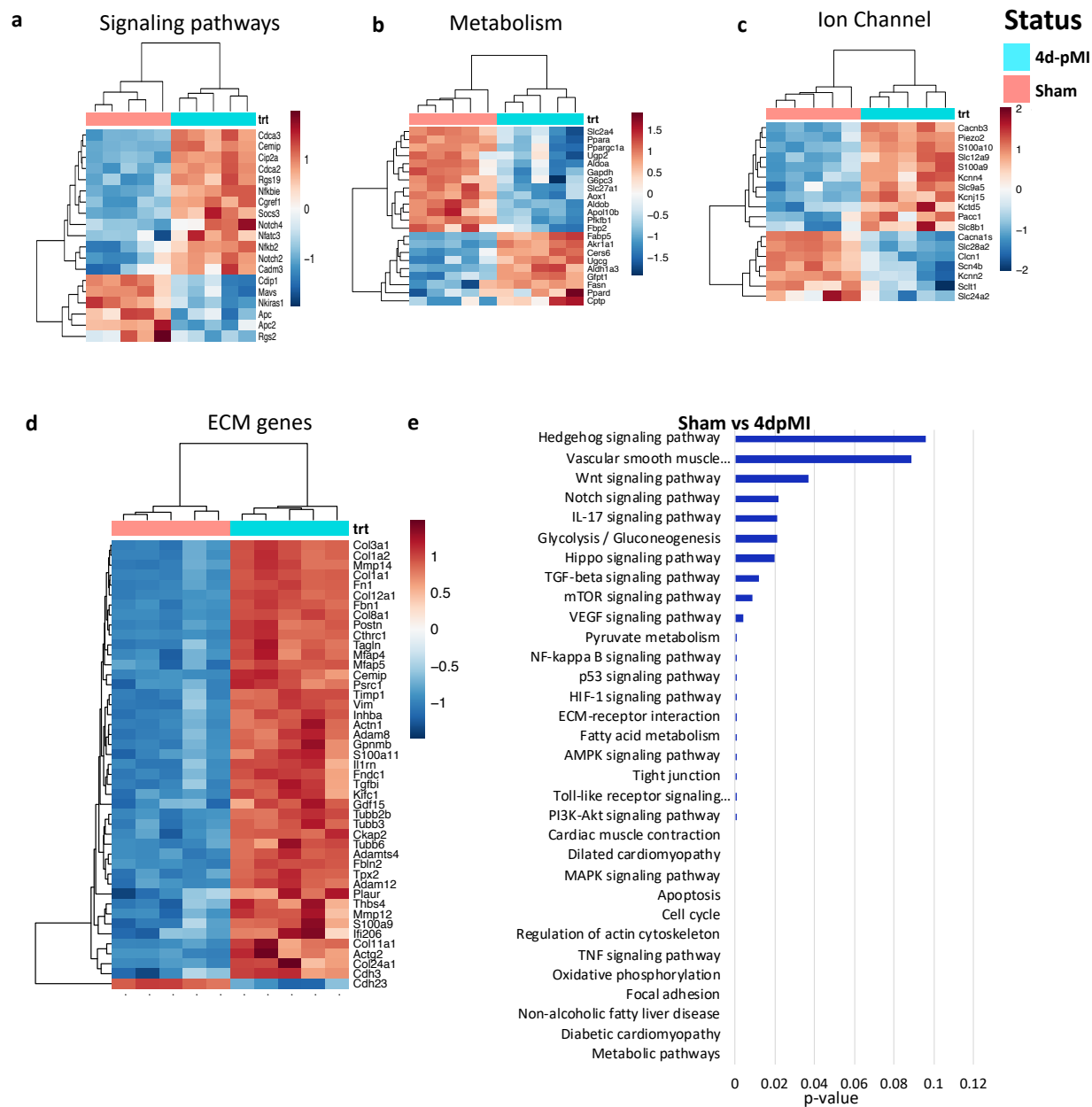
Supplemental Fig. 2



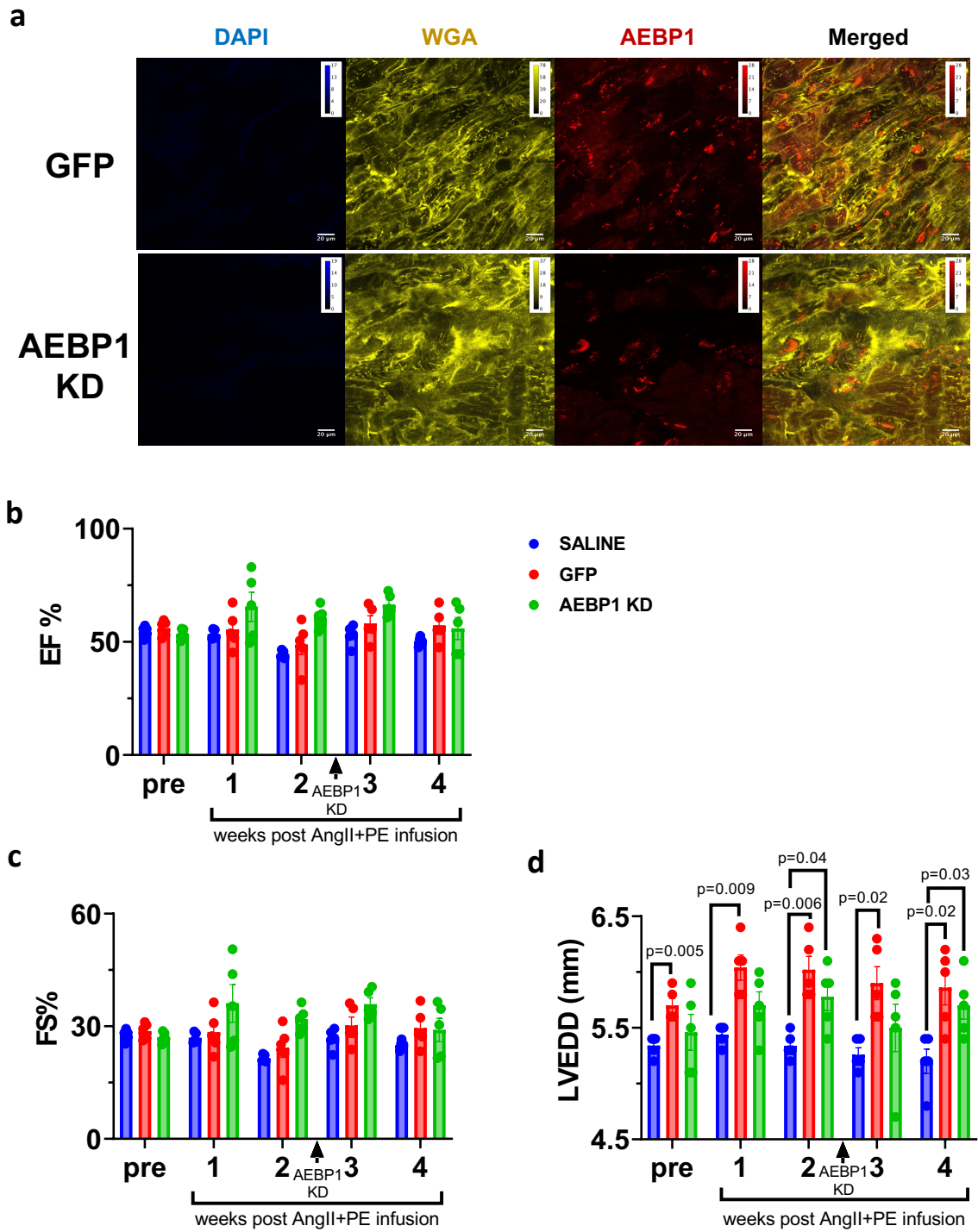
Supplemental Fig. 3



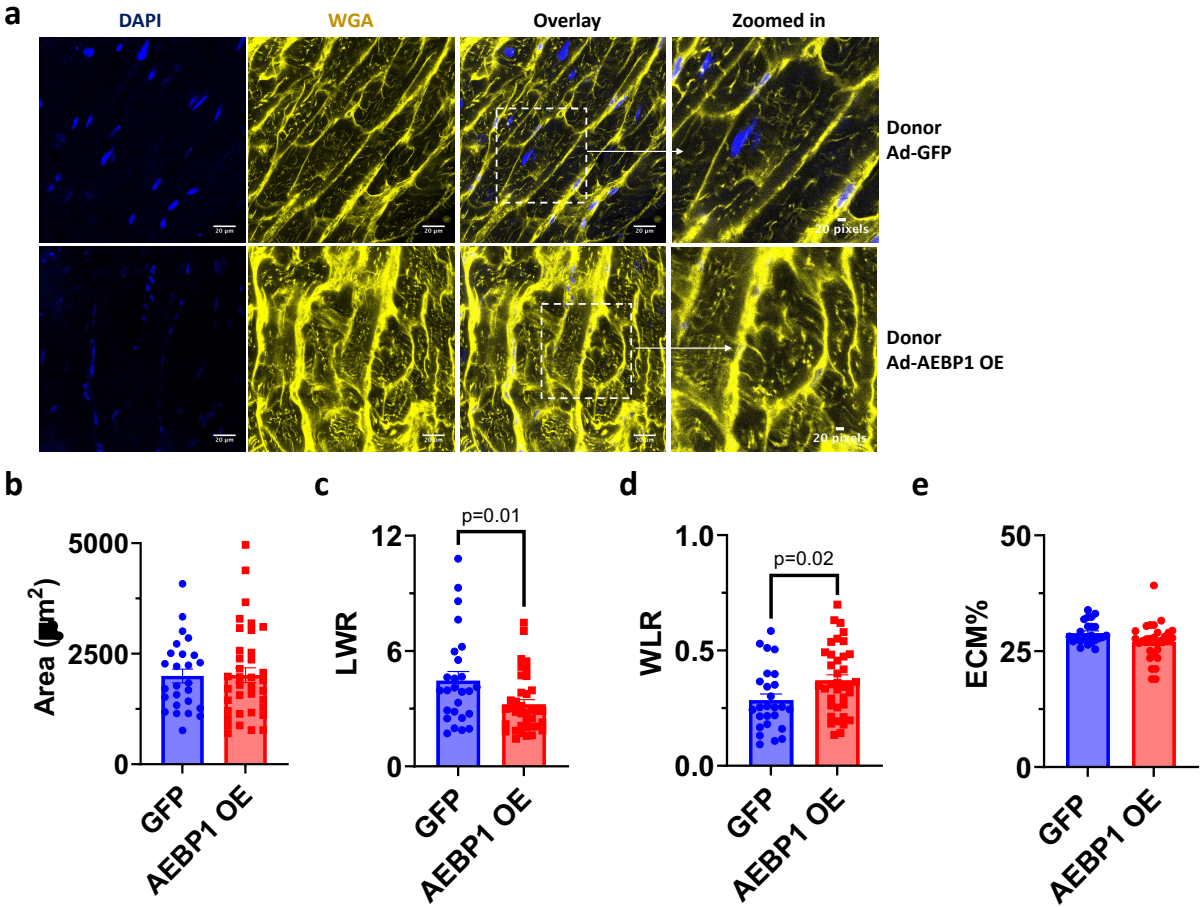
Supplemental Fig. 4



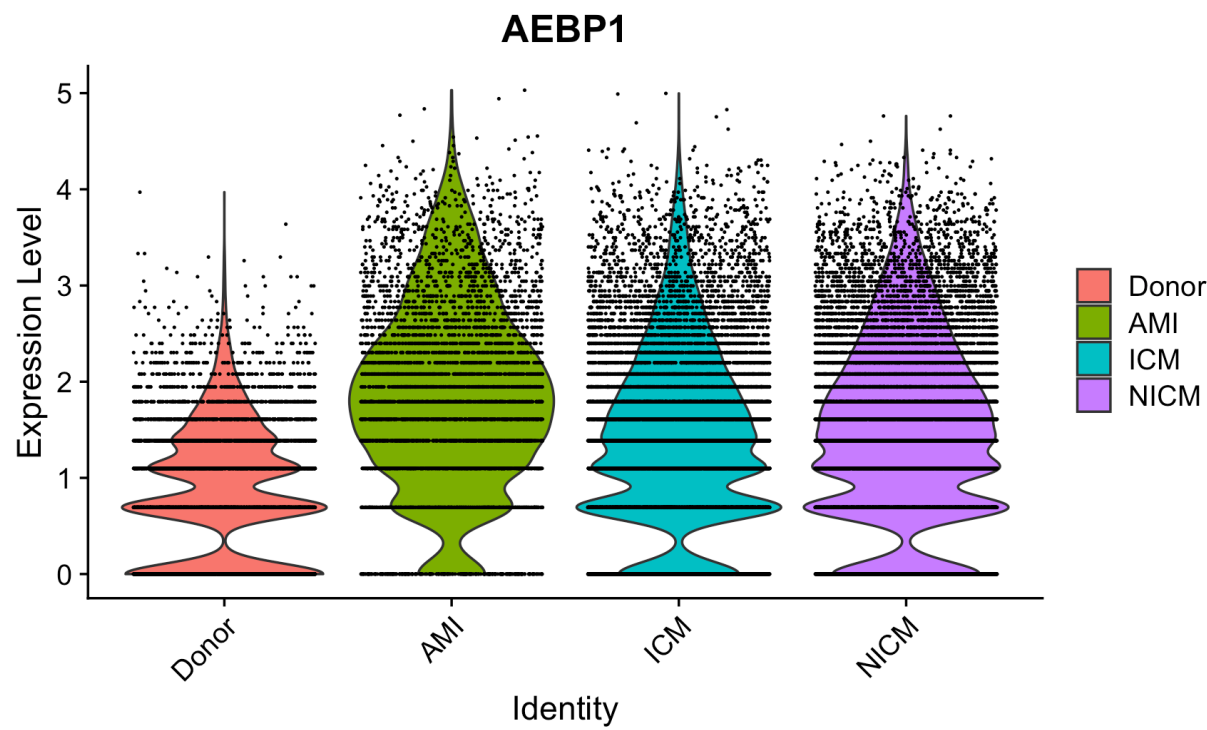
Supplemental Fig. 5



Supplemental Fig. 6



Supplemental Fig. 7



Supplemental Fig. 8

