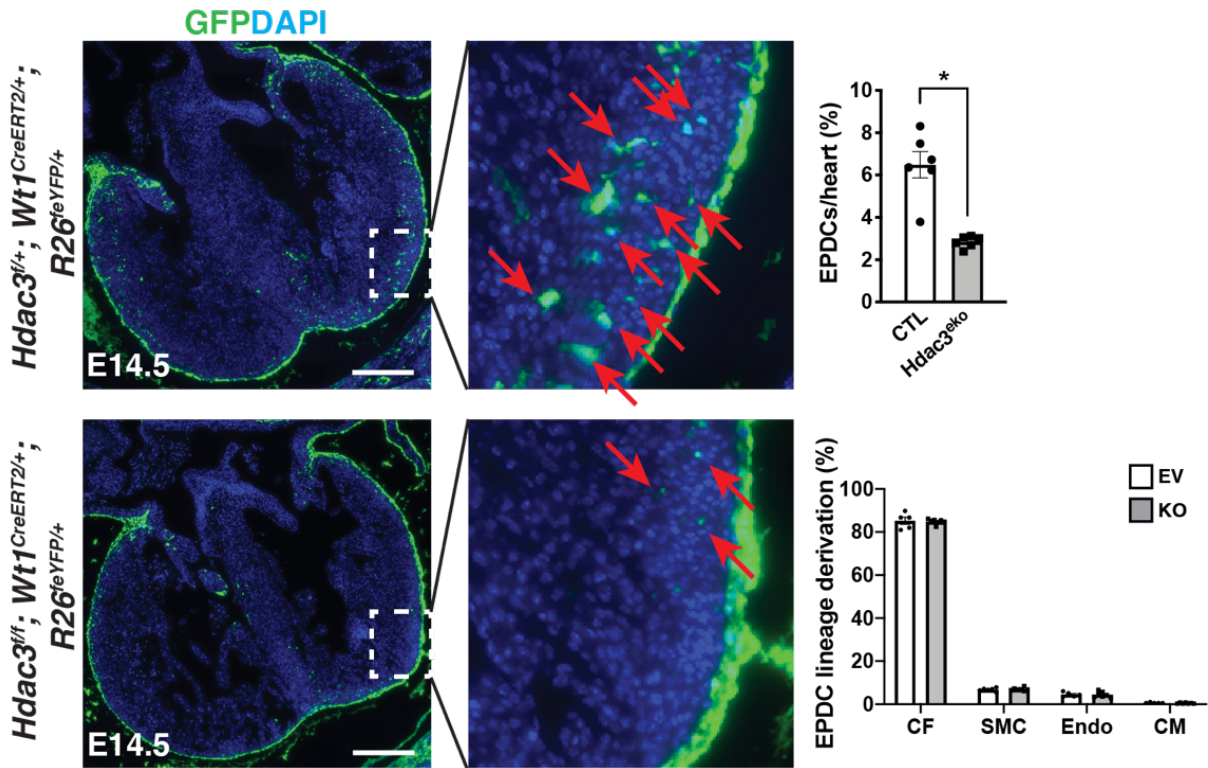


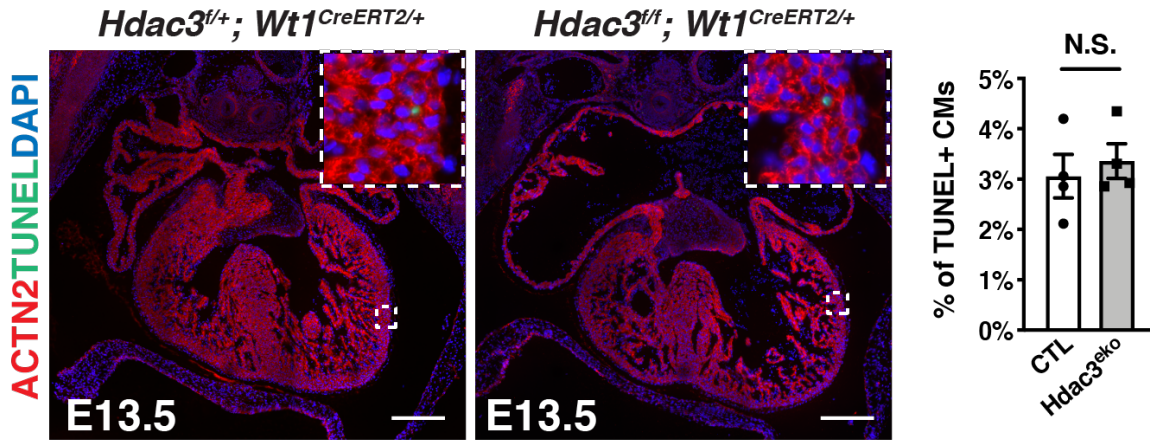
Supplemental Figure 1. No leakage of *Wt1^{CreERT2/+}*.

Representative micrographs of HDAC3 and GFP immunofluorescence staining of E12.5 *Hdac3^{f/+}; Wt1^{CreERT2/+}; R26^{eYFP/+}* and *Hdac3^{f/f}; Wt1^{CreERT2/+}; R26^{eYFP/+}* hearts. Corn oil was given to dams intraperitoneally (150 mg/kg body weight) at E8.5 (scale bars: 25 μ m). eYFP immunosignal was detected by GFP antibody. In the absence of tamoxifen administration, there was neither *Hdac3* deletion nor eYFP reporter activity in the epicardium.



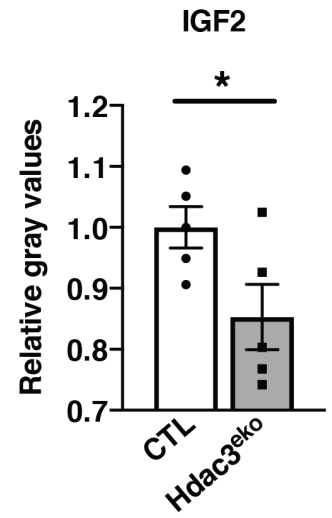
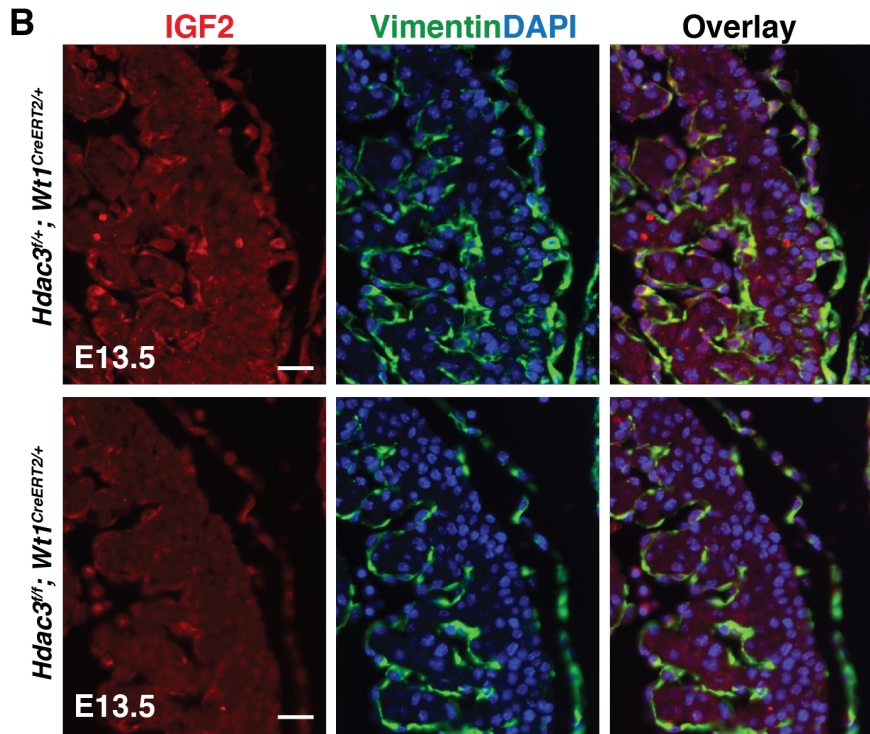
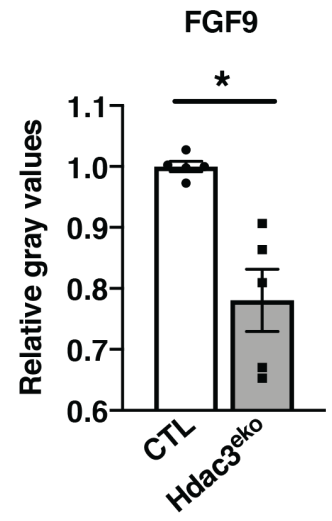
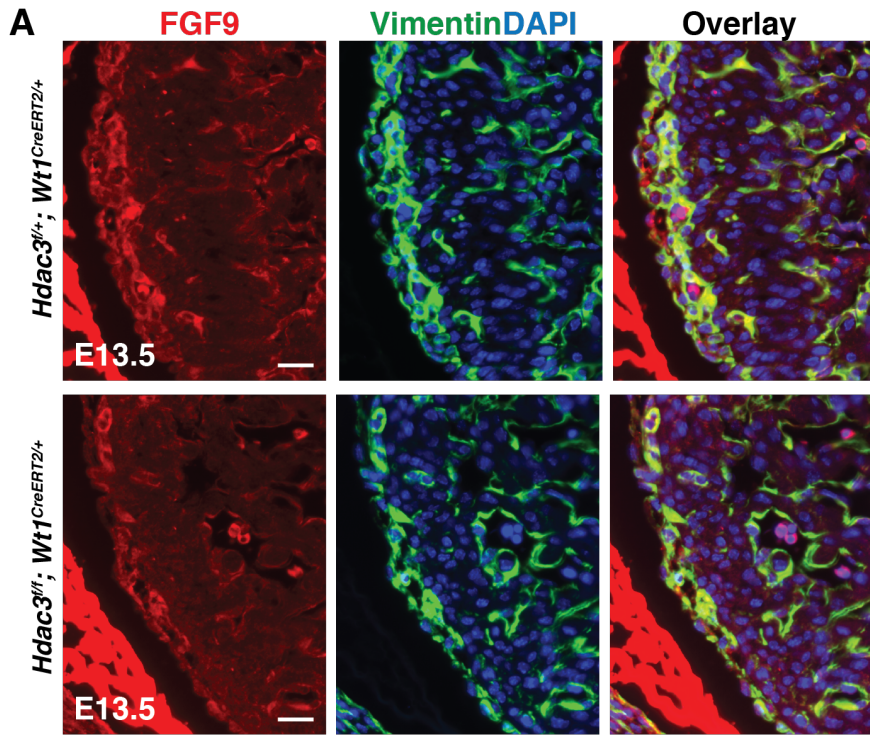
Supplemental Figure 2. Reduction of EPDCs in *Hdac3^{eko}* hearts.

Representative micrographs of GFP immunofluorescence staining of E14.5 *Hdac3^{fl/+}; Wt1^{CreERT2/+}; R26^{eYFP/+}* (control [CTL]) and *Hdac3^{fl/fl}; Wt1^{CreERT2/+}; R26^{eYFP/+}* (*Hdac3^{eko}*) hearts. Quantifications of percentage of EPDCs/heart and derivation percentage of each cell type are shown on the right (* $P < 0.05$ by Student's *t*-test; CF, cardiac fibroblast (Vimentin+); SMC, smooth muscle cells (smMHC11+); Endo, endothelial cells (CD31+); CM, cardiomyocyte (ACTC1+); scale bar, 250 μ m). EPDCs (GFP+, denoted by red arrows) were significantly fewer in *Hdac3^{eko}* hearts as compared to CTL hearts, whereas the contribution to each lineage by EPDCs was not significantly different between *Hdac3^{eko}* and CTL hearts.



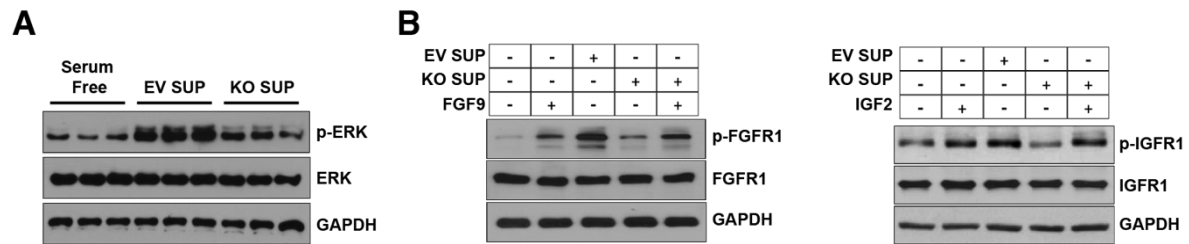
Supplemental Figure 3. No significant change for cell death in *Hdac3^{eko}* hearts.

Representative micrographs of TUNEL staining of E13.5 *Hdac3^{f/f}; Wt1^{CreERT2/+}* (*Hdac3^{eko}*) and *Hdac3^{f/+}; Wt1^{CreERT2/+}* (CTL) and hearts. TUNEL+ signals are in green. Quantification of TUNEL+ cardiomyocytes (CMs) is shown on the right (N.S., not significant; scale bars: 250 μ m).



Supplemental Figure 4. Reduced expression of FGF9 and IGF2 in *Hdac3^{eko}* hearts.

Representative immunofluorescence staining of FGF9 (A) and IGF2 (B) on E13.5 *Hdac3^{ff}*; *Wt1^{CreERT2/+}*; *R26R^{eYFP/+}* and (*Hdac3^{eko}*) *Hdac3^{f/+}*; *Wt1^{CreERT2/+}*; *R26R^{eYFP/+}* (CTL) hearts. Vimentin was used to mark cardiac fibroblasts, cardiac endothelial cells and the epicardium. Quantifications of immunofluorescence intensity of FGF9 and IGF2 are shown on the right (scale bars: 25 μ m).



Supplemental Figure 5. The downstream signaling of FGF9 or iGF2 in cultured cardiomyocytes. Representative western blots of p-ERK, p-FGFR1, or p-IGF1R in serum-starved cultured E13.5 cardiomyocytes after treatment of MEC supernatants and/or mouse recombinant FGF9 or IGF2 proteins (final concentration: 100 ng/ml).

Full unedited gels for

Figure 2A

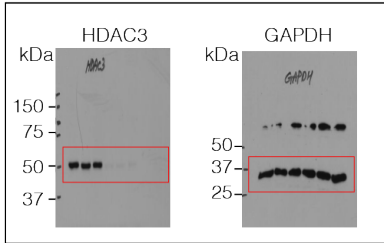


Figure 2E

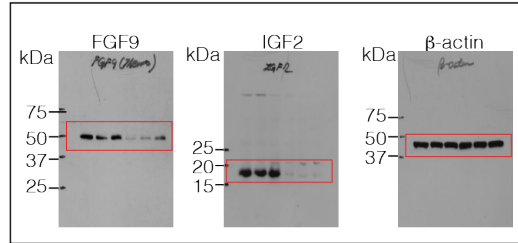


Figure 4B

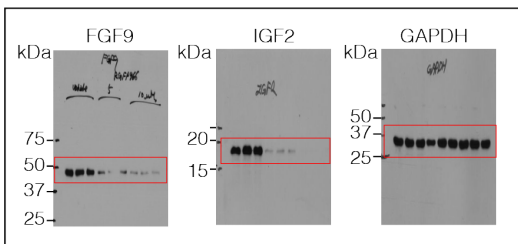


Figure 5D

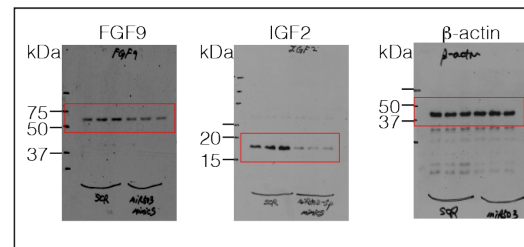
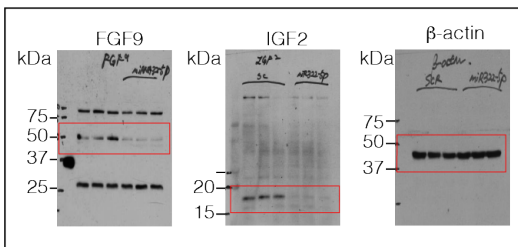


Figure 6B

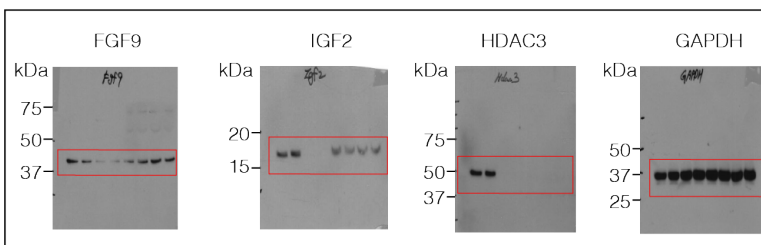
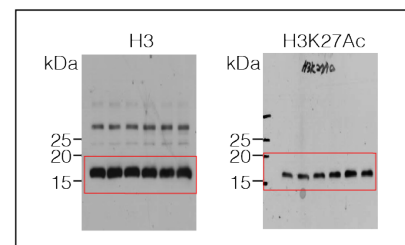


Figure 7A



Supplemental Figure 6. Documentation of full scans of Western blots.

Supplemental Table 1. qRT-PCR primers

	Forward	Reverse
<i>Fgf9</i>	5'-GGGGAGCTGTATGGATCAGA-3'	5'-TCCCGTCCTTATTTAATGCAA-3'
<i>Igf2</i>	5'-CGCTTCAGTTTGTCTGTTCG-3'	5'-GCAGCACTCTTCCACGATG-3'
<i>Gapdh</i>	5'-TCCTGGTATGACAATGAATACGGC- 3'	5'-TCTTGCTCAGTGTCCCTTGCTGG-3'

Supplemental Table 2. ChIP qRT-PCR primers

	Forward	Reverse
Primer 1	5'-GGATGGTTTTTTGTGCTTTCC-3'	5'-TAAGCCACGCCA CTGAAAAT-3'
Primer 2	5'-CAACTTAAGGAGTGGGGCTGT-3'	5'-CAATGAATGCTGGGTCCTTT-3'
Primer 3	5'-GCATGGCATCTGCAACATTA-3'	5'-CTCACTCCCTGGGTTTGTGT-3'
Gene Desert	5'-CAGCATGAAAATGGAGGTCA-3'	5'-TGAGGGTAAAGGTGCTTGCT-3'

Supplemental Table 3. Antibody used for immunofluorescence or western blot

Antibody	Species	Vendor	Catalog #
BrdU	Mouse	eBioscience	14-5071-80
p-H3	Rabbit	Cell Signaling	9701S
ACTC1	mouse	ARP	03-61075
ACTC1	Rabbit	Abcam	Ab46805
WT1	Mouse	Santa Cruz	sc-7385
GFP	Goat	Abcam	ab6673
HDAC3	Rabbit	Abcam	ab7030
HDAC3	Rabbit	Santa Cruz	Sc-11417
CD31	Rat	Dianova	Dia-310
smMHC11	Mouse	Abcam	Ab683
Vimentin	Rabbit	Cell Signaling	5741
IGF2	Goat	Thermo Fisher	PA5-47946
FGF9	Rabbit	Abcam	ab206408
FGF9	Mouse	Santa Cruz	Sc-8413
FGFR1	Rabbit	Cell Signaling	9740S
p-FGFR1 (Tyr653/654)	Rabbit	Cell Signaling	52598S
IGFR1	Rabbit	Cell Signaling	3027S
p-IGFR1	Rabbit	Sigma	SAB4300069
ERK	Mouse	BD Biosciences	610123
p-ERK	Rabbit	Cell Signaling	9101
H3K27Ac	Rabbit	Abcam	ab4729
H3	Rabbit	Abcam	ab176842
β-actin	Rabbit	Cell Signaling	4970
GAPDH	Mouse	Proteintech	HRP-60004