

SUPPLEMENTAL MATERIAL

Table S1. Information of primary antibodies.

Antibody	Cat no.	Company	Source	Application	Dilution	Molecular weight
EDIL3	SC-293337	Santa Cruz	Mouse	WB,IF	1:500	54kDa
CD31	SC-376764	Santa Cruz	Mouse	WB,IF	1:500	130kDa
α SMA	ab5694	Abcam	Rabbit	WB,IF	1:1000	42kDa
VE-Cadherin	YT4869	Immunoway	Rabbit	WB	1:1000	120kDa
Vimentin	10366-1-AP	Proteintech	Rabbit	WB	1:1000	54kDa
CoraLite® Plus 488-conjugated Vimentin	CL488-10366	Proteintech	Rabbit	FC	1:100	-
USP10	8501S	Cell Signaling Technology	Rabbit	WB	1:1000	110kDa
Ubiquitin	A19686	ABclonal	Rabbit	WB	1:1000	-
Smad4	46535	Cell Signaling Technology	Rabbit	WB	1:1000	70kDa
Tgf- β 1	SC-130348	Santa Cruz	Mouse	WB	1:500	25kDa
Bmp2	100875	GeenTex	Rabbit	WB	1:1000	47kDa
Bmp4	129156	GeenTex	Rabbit	WB	1:1000	49kDa
Bmp7	ab214821	Abcam	Rabbit	WB	1:1000	44kDa
P-Smad2/3	3108	Cell Signaling Technology	Rabbit	WB	1:1000	37/50kDa
T-Smad2/3	8685	Cell Signaling Technology	Rabbit	WB	1:1000	37/50kDa
Smad7	SC-101152	Santa Cruz	Mouse	WB	1:500	46kDa
Snail1	340942	Zenbio	Rabbit	WB	1:1000	29kDa
Twist1	YN2923	Immunoway	Rabbit	WB	1:1000	22kDa
ITGB3	A19073	ABclonal	Rabbit	WB	1:1000	110kDa
GAPDH	GTX100118	GeenTex	Rabbit	WB	1:5000	37kDa
P-Erk	4370S	Cell Signaling Technology	Rabbit	WB	1:1000	42/44kDa
T-Erk	4695S	Cell Signaling Technology	Rabbit	WB	1:1000	42/44kDa
P-Akt	4060S	Cell Signaling Technology	Rabbit	WB	1:1000	60kDa
T-Akt	9272S	Cell Signaling Technology	Rabbit	WB	1:1000	60kDa

P-P65	3033S	Cell Signaling Technology	Rabbit	WB	1:1000	65kDa
T-P65	8242S	Cell Signaling Technology	Rabbit	WB	1:1000	65kDa

Table S2. Primers for quantitative real-time PCR.

Genes	Forward (5' to 3')	Reverse (5' to 3')
MOUSE		
Smad4	CATTCCAGCGTGCCATTTC	TTCAAAGTAAGCAATGGAGCAC
GAPDH	ACTCCACTCACGGCAAATTC	TCTCCATGGTGGTGAAGACA
HUMAN		
USP4	CCCTACCGAGGCGTGGAATA	CGACTTTGCAGTGCTTGACA
USP10	AATAAAGGGGAAGTGGTGC	CTATCATGGGTGTTGACGT
USP14	ATGCCGCTCTACTCCGTTACT	GCCTTGAATACCATTGGAGGTTTC
Smad4	CAGGATCAGTAGGTGGAATAGC	TCTTTGATGCTCTGTCTTGGG
GAPDH	CCATGGAGAAGGCTGGGG	CAAAGTTGTCATGGATGACC

Table S3. Body Characteristics and Echocardiography Measurements for WT and KO Mice Treated With DOX or saline at 3 weeks following completion of DOX challenge (2.5mg/kg/week, six weeks).

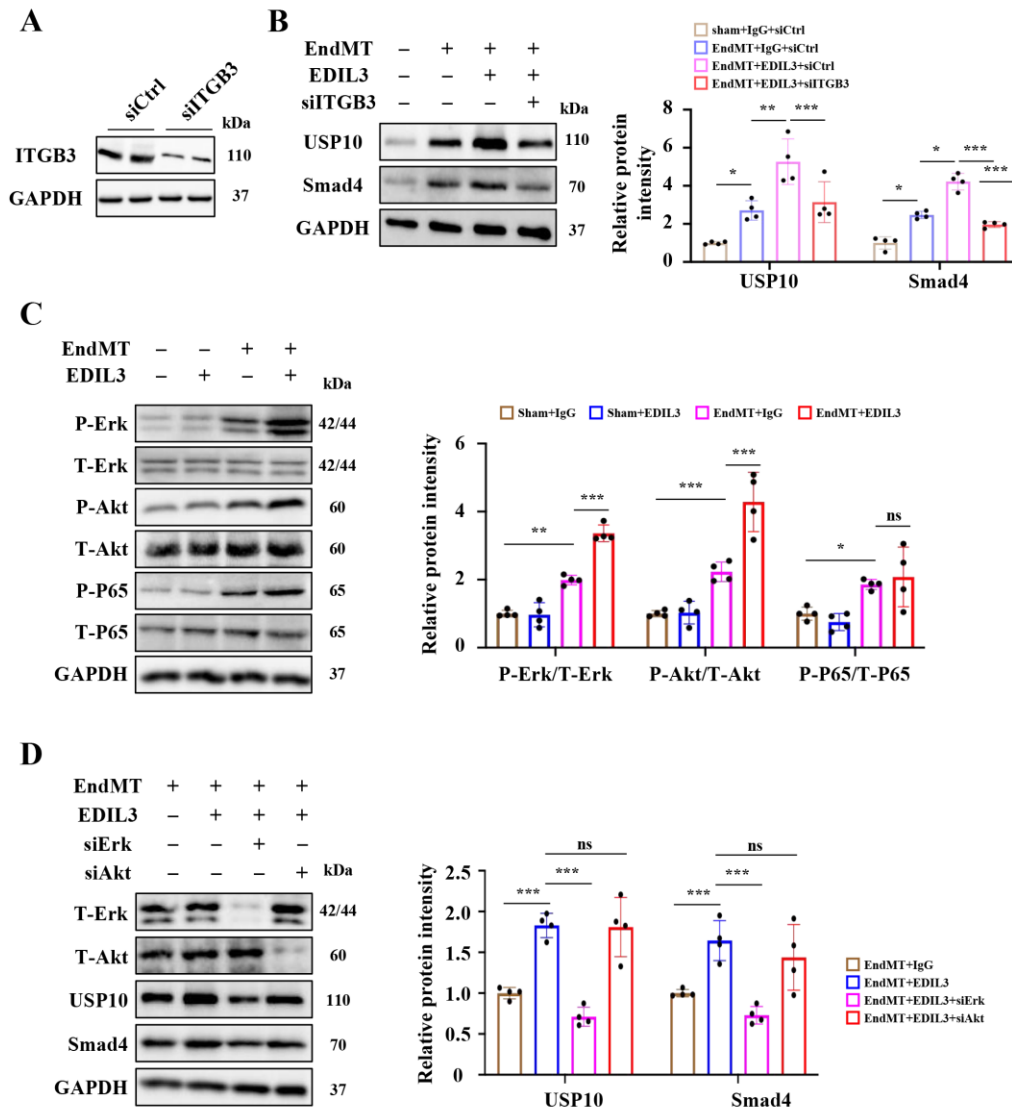
Group	Sham-WT	Sham-KO	DCM-WT	DCM-KO
Number of animals	n=10	n=10	n=10	n=10
Body characteristics				
HW(mg)	140.0±3.4	136.9±4.4	91.3±2.4*	102.2±6.3#
BW(g)	31.4±0.7	31.4±0.9	22.1±0.6*	24.4±0.8
HW/BW(mg/g)	4.45±0.11	4.35±0.19	4.12±0.07*	4.17±0.24
HW/TL(mg/mm)	6.25±0.21	6.09±0.22	4.48±0.17*	4.98±0.33#
Cardiac structure				
IVSd(mm)	0.87±0.10	0.90±0.23	0.78±0.09*	0.75±0.10
LVIDd(mm)	3.65±0.39	3.55±0.26	3.95±0.37*	3.72±0.33
LVPWd(mm)	0.88±0.15	0.92±0.15	0.57±0.10*	0.80±0.08#
IVSs(mm)	1.50±0.13	1.45±0.15	1.08±0.16*	1.20±0.06
LVIDs(mm)	1.83±0.23	1.87±0.16	3.01±0.20*	2.55±0.27#
LVPWs(mm)	1.37±0.24	1.37±0.05	0.78±0.08*	0.87±0.19
Cardiac function				
LVEDV(ml)	0.13±0.04	0.12±0.03	0.16±0.04	0.13±0.03
LVESV(ml)	0.02±0.01	0.02±0.01	0.07±0.01*	0.04±0.01#
SV(ml)	0.11±0.04	0.10±0.02	0.08±0.03*	0.09±0.02
EF(%)	85.8±2.0	85.7±2.3	53.5±6.9*	65.9±4.9#
FS(%)	49.8±2.4	47.4±3.1	23.4±3.7*	31.4±3.7#

HW, heart weight; BW, body weight; TL, tibia length; DCM, , dilated cardiomyopathy; IVS, intraventricular septum; LVID, left ventricular internal dimension; LVPW, left ventricular posterior wall thickness; LVEDV, left ventricular end-diastolic volume; EF, ejection fraction; FS, fractional shortening. * indicated P < 0.05 vs. Sham-WT group. # indicated P < 0.05 vs. DCM-WT group.

Figure S1. Scheme of DOX challenge in mice and time points of functional assessments.



Figure S2. Inhibiting $\beta 3$ intergrin/ERK signal blocked USP10 expression promoted by EDIL3.



(A) Representative immunoblots for ITGB3 in HUVECs (n=2). (B) Representative immunoblots and corresponding quantification showing USP10 and Smad4 (n=4). (C) Representative immunoblots and corresponding quantification showing P-Erk, T-Erk, P-Akt, T-Akt, P-P65 and T-P65 (n=4). (D) Representative immunoblots and corresponding quantification showing T-Erk, T-Akt, USP10 and Smad4 (n=4). Data are presented as mean \pm SD and were analyzed using two-way ANOVA followed by Tukey test. ns indicated $P > 0.05$, * indicated $P < 0.05$, ** indicated $P < 0.01$, *** indicated $P < 0.001$. EDIL3, epidermal growth factor-like repeats and discoidin I-like domains 3; EndMT, endothelial to mesenchymal transition; HUVEC, human umbilical vein endothelial cell; USP, ubiquitin specific peptidase; ITGB3, integrin $\beta 3$; Erk, extracellular signal-regulated kinases; Akt, protein kinase B.