

## Supplemental Tables

### Supplemental Table 1: Sequences of primers

Gene	Species	Forward	Reverse
$\alpha$ -SMA	rat	GTCCCAGACATCAGGGAGTAA	TCGGATACTTCAGCGTCAGGA
Coll1a1	rat	GAGCGGAGAGTACTGGATCGA	CTGACCTGTCTCCATGTTGCA
Col3a1	rat	TGCCATTGCTGGAGTTGGA	GAAGACATGATCTCCTCAGTGTTGA
ANP	rat	GAGCAAATCCCGTATACAGTGC	ATCTTCTACCGGCATCTTCTCC
BNP	rat	GCTGCTGGAGCTGATAAGAGAA	GTTCTTTTGTAGGGCCTTGGTC
Myh7	rat	GTGACGGTGGGAAAGGCAAAG	AAAGTGAGGATGGGTGGTCCT
AZIN1	rat	ATGAAAGGATTTATTGACGATGCAA	TTGGCATTGGGTGATTCCTC
JNK1	rat	GGCCCCACCACCAAAGA	CCTCTATTGTGTGCTCCCTTTCA
CTGF	rat	CACAGAGTGGAGCGCCTGTTC	GATGCACTTTTTGCCCTTCTTAATG
TSP-1	rat	GTGACGGAAAATCAAGTTTGCA	ACTTGGCACCAGCAAAGCA
Timp3	rat	TCTGCAACTCCGACATCG	GCGTAGTGTTTGGACTGATAGC
18s	rat	TCAAGAACGAAAAGTCGGAGG	GGACATCTAAGGGCATCAC
$\alpha$ -SMA	mouse	GTCCCAGACATCAGGGAGTAA	TCGGATACTTCAGCGTCAGGA
Coll1a1	mouse	TCTAGACATGTTTCAGCTTTGTGGAC	TCTGTACGCAGGTGATTGGTG
Col3a1	mouse	CTGTAACATGGAAACTGGGGAAA	CCATAGCTGAACTGAAAACCACC
AZIN1	mouse	ATTGACGATGCGAACTACTCCG	TTCCCAAGATCCCCACAAAA
JNK1	mouse	ATGGCTGTTCGATATTCAACCAG	CCTCTTGGGCATACCCCAC
18s	mouse	TCAAGAACGAAAAGTCGGAGG	GGACATCTAAGGGCATCAC
AZIN1	human	ATTGATGATGCAAATACTCCGT	GCCACTACATTCTGCCATTGA
JNK1	human	GGGTATGCCCAAGAGGACAGA	GTGTTGGAAAAGTGCGCTGG
18s	human	CGCTCTCTGCTCCTCCTGTTC	CGCCCAATACGACCAAATCCG

**Supplemental Table 2 Dysregulated microRNAs between ventricular tissues 21 day post-MI and sham control**

<b>MicroRNA</b>	<b>Regulation</b>	<b>FC</b>	<b>P value</b>
miR-34b-3p	Up	8.30	0.005142
miR-34c-5p	Up	7.16	4.82E-04
miR-34c-3p	Up	6.48	0.001222
miR-433-3p	Up	6.35	0.003249
miR-214-5p	Up	6.23	9.99E-04
miR-21a-5p	Up	5.79	0.004743
miR-299a-5p	Up	5.11	0.015916
miR-154-5p	Up	4.96	0.02019
miR-134-5p	Up	4.41	0.014186
miR-329-3p	Up	4.05	0.005255
miR-382-5p	Up	3.99	0.030859
miR-199a-5p	Up	3.41	0.005282
miR-431-5p	Up	3.39	0.027723
miR-146b-5p	Up	3.35	0.028579
miR-337-5p	Up	3.26	0.041026
miR-409-3p	Up	3.18	0.031695
miR-411-3p	Up	3.09	0.001084
miR-434-3p	Up	3.07	0.001056
miR-199b-5p	Up	3.06	0.016446
miR-214-3p	Up	2.88	3.50E-04
miR-127-3p	Up	2.65	0.021263
miR-7033-5p	Up	2.63	0.034635

miR-541-5p	Up	2.31	0.047772
miR-199a-3p	Up	2.31	0.020864
miR-199b-3p	Up	2.31	0.020864
miR-338-5p	down	2.15	0.04136

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Fold change (FC) >2.0 and  $P < 0.05$ .

**Supplemental Table 3. Clinical and echocardiography parameters for patients with dilated cardiomyopathy**

	Mean±SD
Age (year)	45.5±7.5
LVEF (%)	29.6±13.6
LVFS (%)	12.5±7.1
LAD (mm)	54.5±6.7
LVDd (mm)	73.4±15.5
LVDs (mm)	60.3±20.6
IVS (mm)	9.3±0.9
LVPW (mm)	8.7±1.1
RAD (mm)	50.8±8.4
RVDd (mm)	41.1±7.07

LVEF: left ventricle ejection fraction; LVFS: left ventricle fractional shortening; LAD: left atrium diameter; LVDd: left ventricular end diastolic dimension; LVDs: left ventricular end systolic dimension; IVS: interventricular septal thickness; LVPW: left ventricular posterior wall; RAD: right atrium diameter; RVDd: right ventricular end diastolic dimension.

**Supplemental Table 4: Echocardiography parameters for sham *versus* MI mice treated with miR-433 antagomir or negative control**

Group (Mean±SD)	sham+ nc antagomir (n=5)	sham+ miR-433 antagomir (n=5)	MI+ nc antagomir (n=6)	MI+ miR-433 antagomir (n=6)
LVEF (%)	56.58±1.03	60.25±2.76	41.90±2.34 ***	48.61±2.81 &
LVFS (%)	29.05±0.69	31.47±1.92	20.42±1.23 ***	24.12±1.76 &&
LVID;d (mm)	3.78±0.27	3.65±0.18	4.42±0.39 **	3.90±0.23 &
LVID;s (mm)	2.68±0.19	2.50±0.16	3.52±0.35 ***	2.96±0.15 &&
IVS;d (mm)	0.74±0.013	0.75±0.03	0.73±0.04	0.71±0.04
IVS;s (mm)	1.20±0.05	1.19±0.03	1.07±0.05	1.04±0.16
LVPW;d (mm)	0.71±0.03	0.76±0.06	0.74±0.05	0.71±0.04
LVPW;s (mm)	1.10±0.01	1.22±0.09	1.08±0.08	1.06±0.06

LVEF: left ventricle ejection fraction; LVFS: left ventricle fractional shortening; LVID;d: left ventricle internal diameter in diastole; LVID;s: left ventricle internal diameter in systole; IVS;d: interventricular septum in diastole; IVS;s: interventricular septum in systole; LVPW;d: left ventricle posterior wall in diastole; LVPW;s: left ventricle posterior wall in systole.

\*: sham+nc antagomir vs MI+nc antagomir (\*,  $P<0.05$ , \*\*,  $P<0.01$ , \*\*\*,  $P<0.001$ ).

&: MI+nc antagomir vs MI+miR-433 antagomir (&,  $P<0.05$ , &&,  $P<0.01$ , &&&,  $P<0.001$ ).

**Supplemental Table 5: Echocardiography parameters for sham *versus* MI mice treated with miR-433 sponge AAV9 or miR-scramble control**

Group (Mean±SD)	sham+ miR-scramble (n=5)	sham+ miR-433 sponge AAV9 (n=5)	MI+ miR-scramble (n=6)	MI+ miR-433 sponge AAV9 (n=6)
LVEF (%)	56.98±2.11	58.20±1.43	40.30±4.02 ***	48.91±2.17 &&&
LVFS (%)	28.30±1.05	30.40±0.90	19.56±2.22 ***	24.45±1.26 &&&
LVID;d (mm)	4.18±0.28	4.02±0.11	4.47±0.27 *	4.21±0.30 &
LVID;s (mm)	3.05±0.26	2.81±0.12	3.60±0.26 **	3.18±0.25 &&
IVS;d (mm)	0.73±0.01	0.73±0.02	0.78±0.09	0.73±0.05
IVS;s (mm)	1.20±0.03	1.19±0.03	1.07±0.11	1.05±0.06
LVPW;d (mm)	0.73±0.01	0.78±0.01	0.79±0.15	0.73±0.04
LVPW;s (mm)	1.15±0.04	1.24±0.02	1.09±0.21	1.09±0.08

LVEF: left ventricle ejection fraction; LVFS: left ventricle fractional shortening; LVID;d: left ventricle internal diameter in diastole; LVID;s: left ventricle internal diameter in systole; IVS;d: interventricular septum in diastole; IVS;s: interventricular septum in systole; LVPW;d: left ventricle posterior wall in diastole; LVPW;s: left ventricle posterior wall in systole.

\*: sham+miR-scramble vs MI+miR-scramble (\*,  $P<0.05$ , \*\*,  $P<0.01$ , \*\*\*,  $P<0.001$ ).

&: MI+miR-scramble vs MI+miR-433 sponge AAV9 (&,  $P<0.05$ , &&,  $P<0.01$ , &&&,  $P<0.001$ ).

**Supplemental Table 6: Downregulated genes between ventricular samples from miR-433 antagomir and scrambled negative control post-MI**

<b>Gene</b>	<b>FC</b>	<b>P value</b>	<b>Gene</b>	<b>FC</b>	<b>P value</b>
Sprr1a	44.53	0.015073694	Sfrp4	7.68	0.037269417
Comp	32.39	0.04126584	Frzb	7.56	0.019581094
Cthrc1	31.30	0.008341982	Colla1	7.44	0.009812925
Ltbp2	26.44	0.015757933	Thbs4	7.42	0.027873801
Sfrp2	22.63	0.007884	Pak3	7.39	0.047015797
Col8a2	21.70	0.028787106	Myh7	7.35	0.024133667
C1qtnf3	21.55	0.002769866	Cfi	7.14	0.017546257
Col12a1	20.40	0.00872916	Col14a1	7.17	0.001083992
Col11a1	19.43	0.014617499	Nppb	6.94	0.04448489
Crlf1	17.54	0.009741001	Nalcn	6.93	0.010694485
Gpr176	14.75	0.008055991	M1ap	6.87	0.0466509
Kcnma1	13.92	0.017689882	Col16a1	6.86	3.63E-05
Postn	13.48	0.006996641	Col8a1	6.77	0.018559678
Piezo2	13.33	0.031376325	Itgbl1	6.61	0.021902226
Itgbl1	12.22	0.001333599	Fbln7	6.34	0.022180125
Cilp	12.16	0.005167705	Fibin	6.31	0.03467068
Fmod	12.16	0.028673336	Fn1	6.24	0.014455058
Angptl7	11.24	0.049181934	Lox	6.05	0.012385997
Nox4	11.27	0.006278708	Zfp185	5.95	0.03060996
Mfap4	11.26	0.010031334	Pcdhb13	5.76	0.007892686
Scg2	11.16	0.027176663	Chil1	5.69	0.04528745

Col3a1	10.76	0.005615319	Lox	5.64	0.018374715
Nox4	10.76	0.015143912	Col5a2	5.59	0.024514643
Dio2	10.58	0.016902393	Pamr1	5.54	0.00665051
Scube3	10.45	0.028702611	Galr2	5.34	0.040869713
Nox4	9.68	0.005568695	Col16a1	5.33	0.037861314
Ngef	9.36	0.0409158	Zfp365	5.32	0.010182755
Cldn11	8.86	0.02503063	Cd163l1	5.29	0.033436608
Ptn	8.85	0.029836792	Adc	5.28	0.046146654
Tnmd	8.58	0.04364527	Tnc	5.19	0.018031057
Clec11a	8.14	0.001925654	Gap43	5.12	0.031155989
Wisp2	8.05	0.029018506	Col1a2	5.05	0.00692044
Kcnj15	7.87	0.04618174			

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Fold change (FC) >5 and  $P < 0.05$ .



**Supplemental Table 7: Upregulated genes between ventricular samples from miR-433 antagomir and scrambled negative control post-MI**

<b>Gene</b>	<b>FC</b>	<b><i>P</i> value</b>
Defa-ps1	34.97	5.55E-04
Cd207	14.55	0.006461942
Gngt1	11.13	0.021669813
Sfrp5	8.15	0.04697895
Armc9	8.03	0.009072512
Lef1	7.64	0.03208299
Car3	6.64	0.042693216
Catsper1	6.36	0.008788792
Pck1	6.22	0.005282127
Sarm1	5.03	2.90E-04

Fold change (FC) >5 and *P*<0.05.

## Supplemental Figures

### Supplemental Figure 1. Pharmacokinetic analysis for miR-433 antagomir *in vivo*

**A-B**, miR-433 expression levels in both plasma and heart samples were measured using qRT-PCRs at different time points after mice were administrated with a single bolus of miR-433 antagomir at the dose of 7.5 mg/kg. miR-433 was significantly downregulated in plasma and heart samples from 10 min after injection and maintained a low expression level thereafter. n=5 per group per time point. \*\*\*,  $P<0.001$  versus respective control

### Supplemental Figure 2. Fibrosis-associated gene expressions in miR-433 sponge AAV9-treated MI mice

**A-B**, downregulated pro-fibrotic genes (TGF- $\beta$ ,  $\alpha$ -SMA, CTGF, Colla1, and Col3a1) and upregulated collagen degradation (MMP2 and MMP9) in MI hearts with cardiac-specific inhibition of miR-433. n=6 for qRT-PCR, n=4 for Western blot. \*,  $P<0.05$ , \*\*,  $P<0.01$ , \*\*\*,  $P<0.001$  versus respective controls

### Supplemental Figure 3: Effect of AZIN1 siRNA and miR-433 agomir co-transfection on cardiac fibroblasts

**A-B**, AZIN1 siRNA led to knockdown of AZIN1; **C-D**, AZIN1 knockdown induced cardiac fibroblasts proliferation and differentiation into myofibroblasts, while co-transfection of AZIN1 siRNA and miR-433 agomir did not exert an additive effect. n=3 for Western blot, n=6 for qRT-PCR, n=4 for EdU and  $\alpha$ -SMA staining. Scale bar: 50  $\mu$ m. \*,  $P<0.05$ , \*\*,  $P<0.01$ , \*\*\*,  $P<0.001$  versus respective controls.

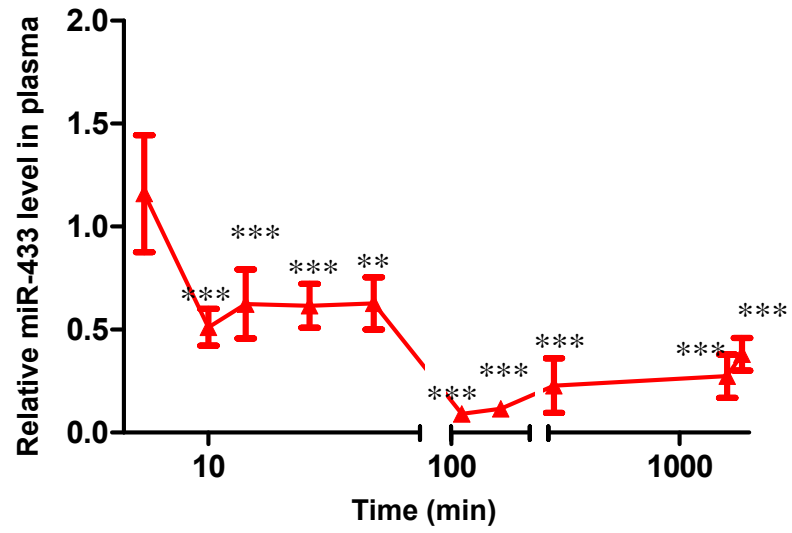
### Supplemental Figure 4: Effect of JNK1 siRNA and miR-433 agomir co-transfection on cardiac fibroblasts

**A-B**, JNK1 siRNA led to knockdown of JNK1; **C-D**, JNK1 siRNA did not further increase fibroblast proliferation, though myofibroblast differentiation was slightly

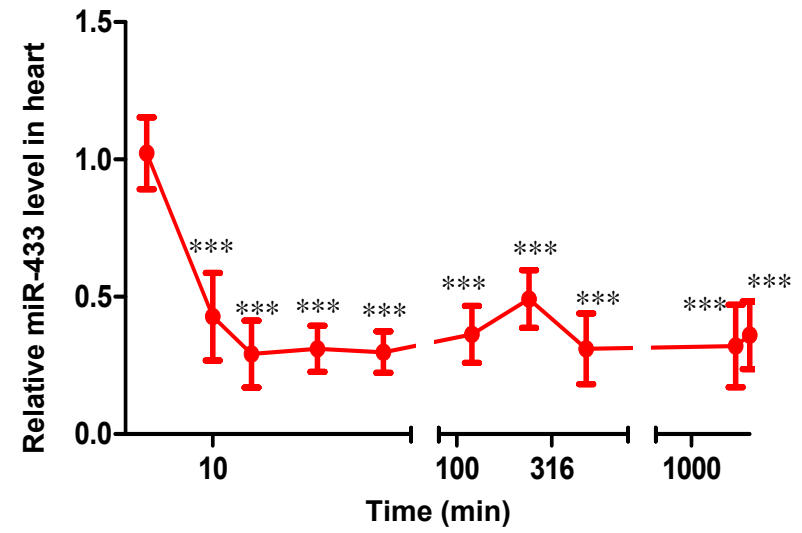
enhanced in cells co-treated with miR-433 agomir. n=3 for Western blot, n=6 for qRT-PCR, n=4 for EdU and  $\alpha$ -SMA staining. Scale bar: 50  $\mu$ m. \*,  $P < 0.05$ , \*\*,  $P < 0.01$ , \*\*\*,  $P < 0.001$  versus respective controls

# Supplemental Figure 1

**A**

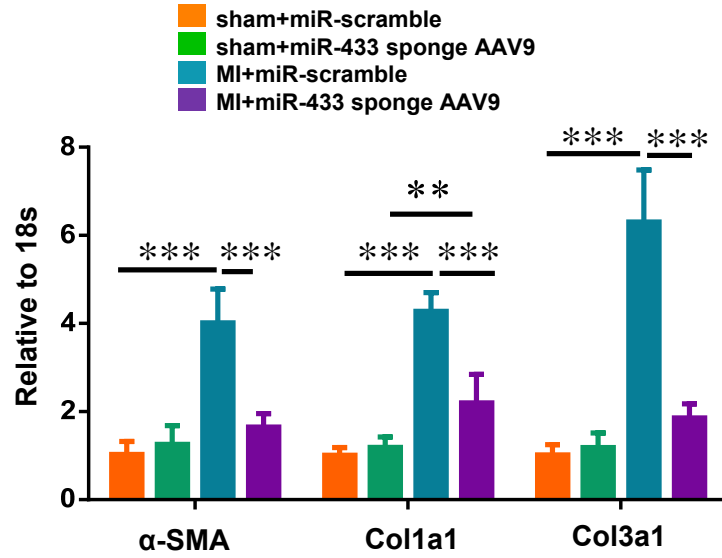


**B**

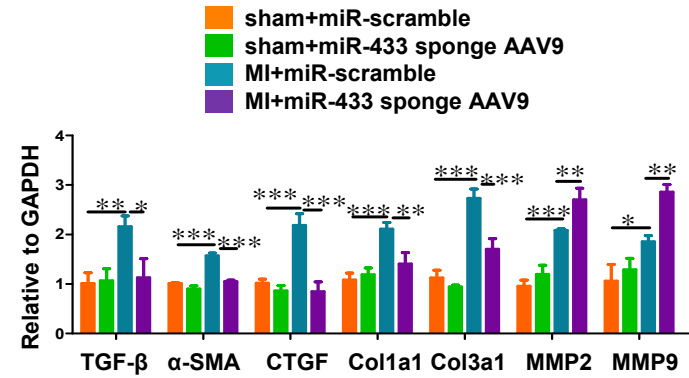
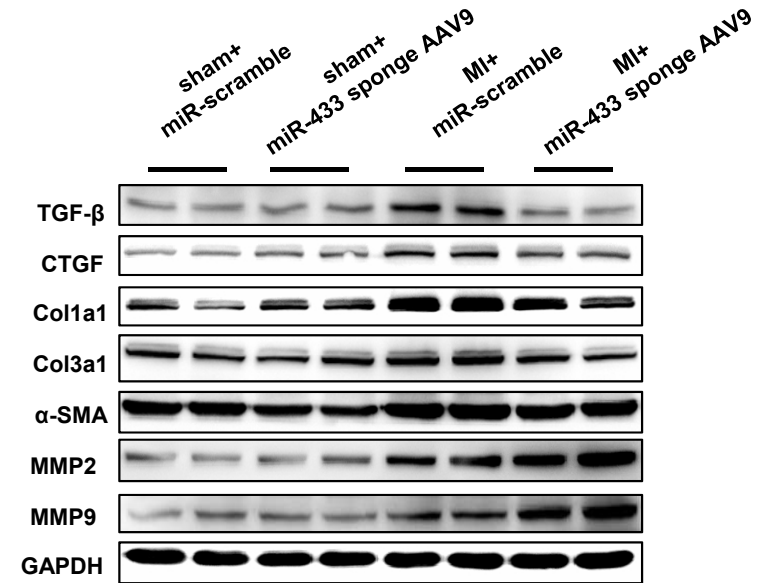


# Supplemental Figure 2

**A**

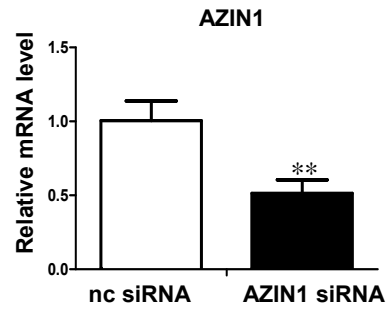


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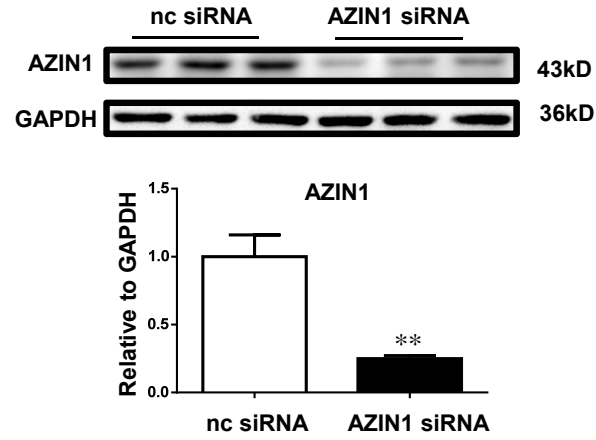


# Supplemental Figure 3

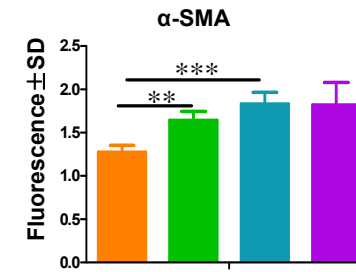
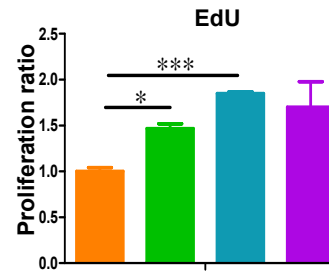
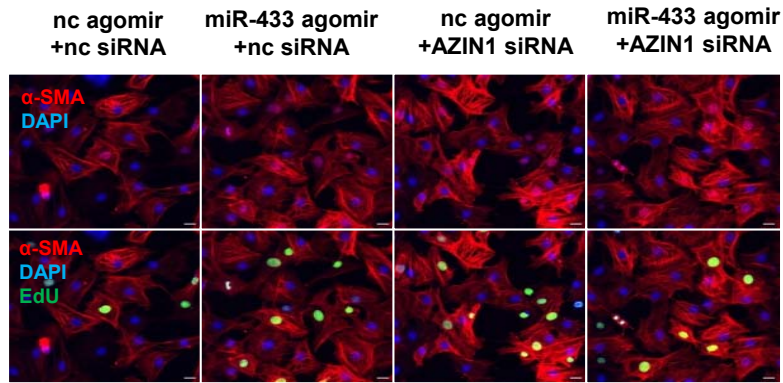
**A**



**B**

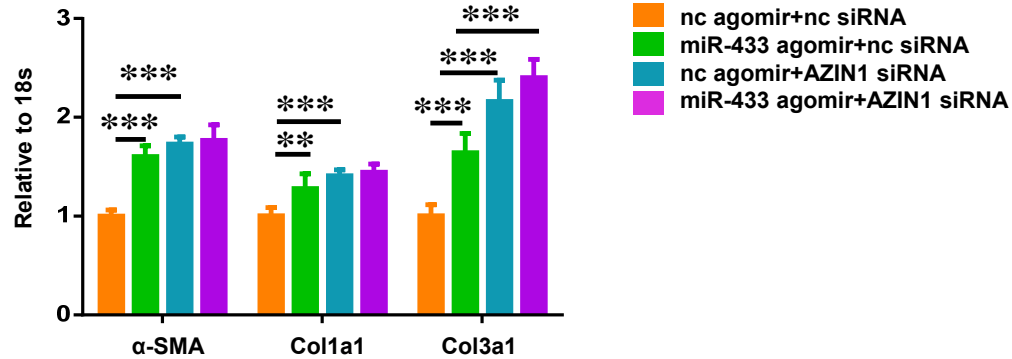


**C**



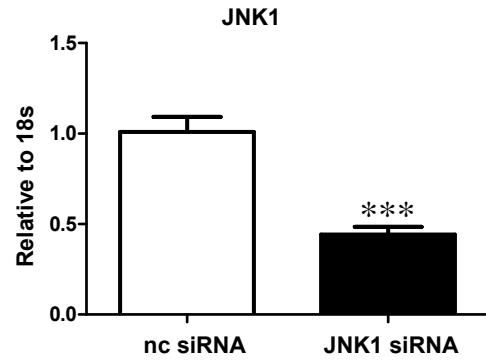
nc agomir+nc siRNA  
miR-433 agomir+nc siRNA  
nc agomir+AZIN1 siRNA  
miR-433 agomir+AZIN1 siRNA

**D**

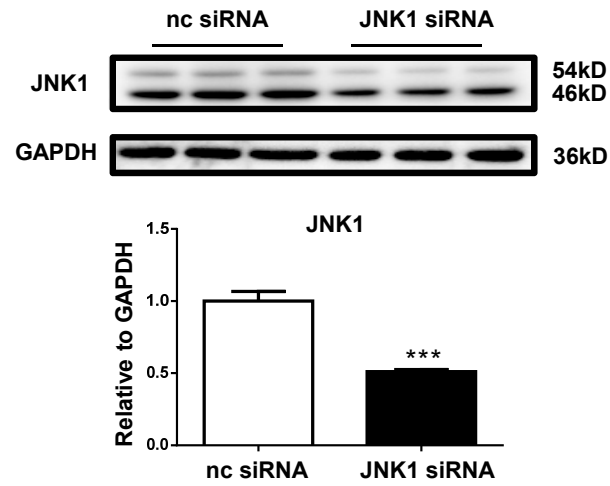


# Supplemental Figure 4

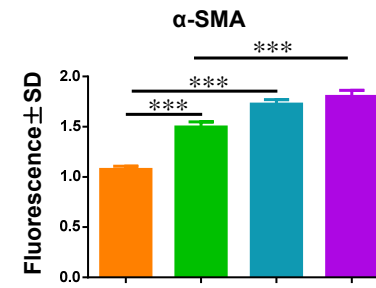
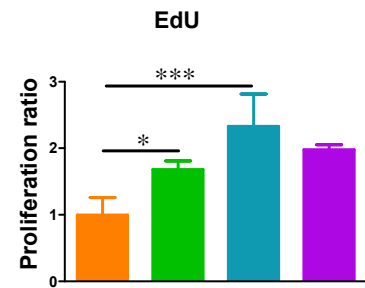
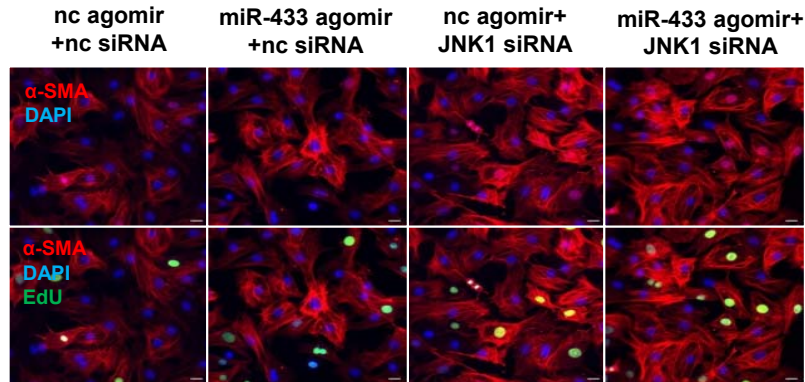
**A**



**B**

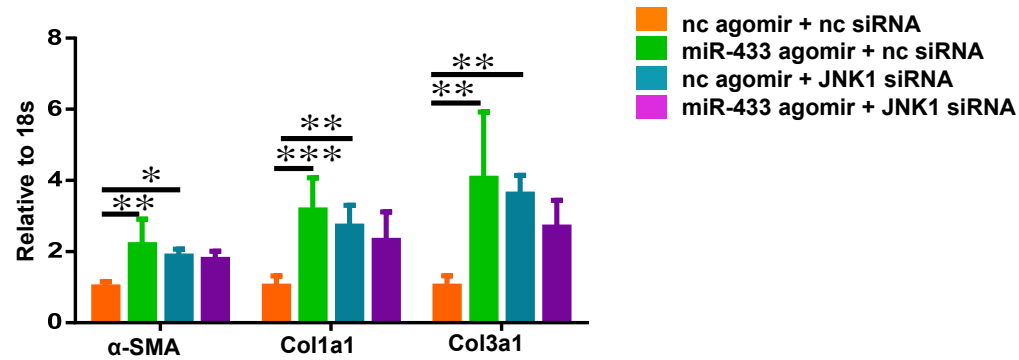


**C**



■ nc agomir + nc siRNA  
■ miR-433 agomir + nc siRNA  
■ nc agomir + JNK1 siRNA  
■ miR-433 agomir + JNK1 siRNA

**D**



■ nc agomir + nc siRNA  
■ miR-433 agomir + nc siRNA  
■ nc agomir + JNK1 siRNA  
■ miR-433 agomir + JNK1 siRNA