

Figure1A

	Sample	Blank	Standard			
0weeks-1	0.129	0.05	0.250666667			
0weeks-2	0.117					
0weeks-3	0.129					
0weeks-4	0.139					
0weeks-5	0.139			Standard concentration=5.17 mM		
0weeks-6	0.124					
0weeks-7	0.123					
0weeks-8	0.107					
0weeks-9	0.114					
0weeks-10	0.119					

	Sample	Blank	Standard			
8weeks-1	0.187	0.050333333	0.236			
8weeks-2	0.194					
8weeks-3	0.2					
8weeks-4	0.206					
8weeks-5	0.201			Standard concentration=5.17 mM		
8weeks-6	0.193					
8weeks-7	0.187					
8weeks-8	0.189					
8weeks-9	0.185					
8weeks-10	0.192					

Figure1B

	Sample	Blank	Standard			
0weeks-1	0.083	0.047	0.123			
0weeks-2	0.072					
0weeks-3	0.08					
0weeks-4	0.078					
0weeks-5	0.081					
0weeks-6	0.079			Standard concentration=2.26 mM		
0weeks-7	0.088					
0weeks-8	0.069					
0weeks-9	0.074					
0weeks-10	0.075					

	Sample	Blank	Standard			
8week-1	0.174	0.046	0.2			
8week-2	0.162					
8week-3	0.161					
8week-4	0.154					
8week-5	0.155					
8week-6	0.153			Standard concentration=2.26 mM		
8week-7	0.156					
8week-8	0.148					
8week-9	0.16					
8week-10	0.167					

Figure1C

	Sample1	Sample2	Blank1	Blank2	Standard1	Standard2	
0weeks-1	0.079	0.137	0.048	0.051	0.062	0.312333333	
0weeks-2	0.076	0.136					
0weeks-3	0.078	0.149					
0weeks-4	0.068	0.133					
0weeks-5	0.066	0.15					
0weeks-6	0.076	0.132					
0weeks-7	0.082	0.148	Standard concentration=2.55mM				
0weeks-8	0.081	0.154					
0weeks-9	0.073	0.166					
0weeks-10	0.065	0.149					

	Sample1	Sample2	Blank1	Blank2	Standard1	Standard2	
8weeks-1	0.058	0.157	0.044333333	0.056	0.065666667	0.265	
8weeks-2	0.059	0.142					
8weeks-3	0.058	0.152					
8weeks-4	0.058	0.141					
8weeks-5	0.052	0.158	Standard concentration=2.55mM				
8weeks-6	0.055	0.153					
8weeks-7	0.054	0.169					
8weeks-8	0.052	0.159					
8weeks-9	0.057	0.154					
8weeks-10	0.059	0.139					

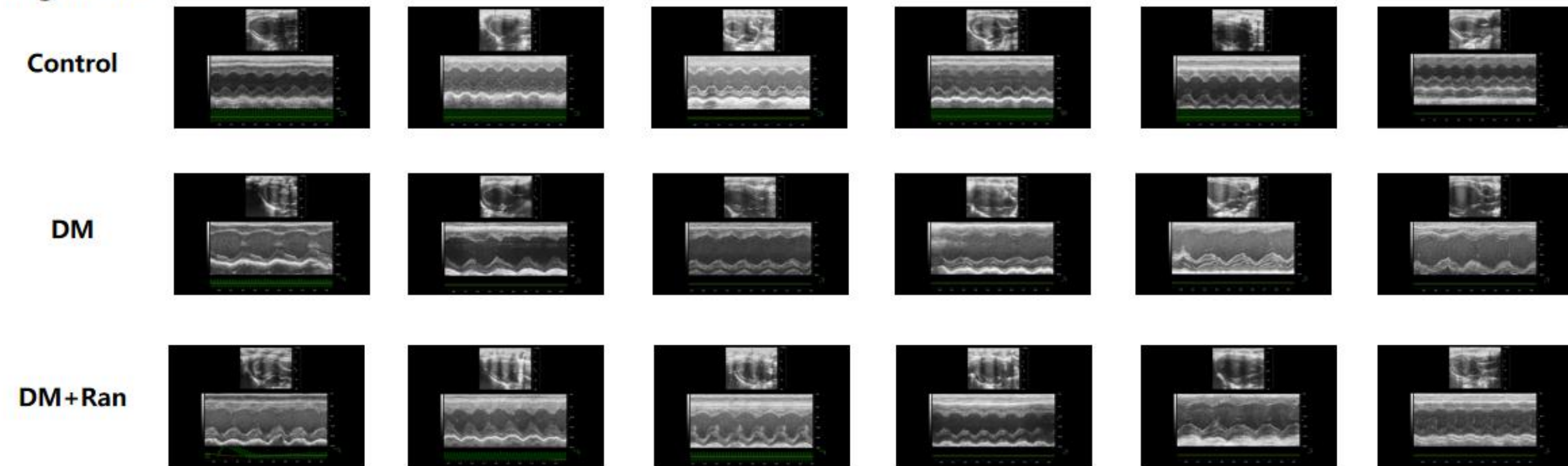
Figure1D

	Sample1	Sample2	Blank1	Blank2	Standard1	Standard2	
0week-1	0.057	0.123	0.047333333	0.052	0.057666667	0.116	
0week-2	0.062	0.125					
0week-3	0.06	0.131					
0week-4	0.055	0.122					
0week-5	0.054	0.141					
0week-6	0.062	0.14					
0week-7	0.066	0.137	Standard concentration=1.1 mM				
0week-8	0.063	0.136					
0week-9	0.066	0.143					
0week-10	0.052	0.141					

	Sample1	Sample2	Blank1	Blank2	Standard1	Standard2	
8weeks-1	0.052	0.157	0.041666667	0.049	0.062333333	0.203333333	
8weeks-2	0.05	0.158					
8weeks-3	0.055	0.161					
8weeks-4	0.053	0.172					
8weeks-5	0.059	0.149					
8weeks-6	0.058	0.162	Standard concentration=1.1 mM				
8weeks-7	0.052	0.163					
8weeks-8	0.054	0.167					
8weeks-9	0.057	0.161					
8weeks-10	0.058	0.163					

Figure1E

Fasting blood glucose data						
	0weeks	4weeks	8weeks	12weeks	16weeks	20weeks
Control	5.6	4.9	5.5	6.5	5.8	5.6
	4.7	5.2	4.9	4.7	4.7	5.8
	5.2	4.7	4.8	5.8	5.2	5.6
	4.9	5.5	4.7	4.2	4.6	4.5
	5.3	4.6	5.2	4.9	5.7	5.9
	4.6	4.8	5.1	5.6	5.5	4.7
DM	4.3	5.6	22.1	23.5	25.5	26.5
	4.8	5.8	22.3	24.7	24.6	24.9
	4.6	4.6	19.8	25.6	26.3	27.5
	5.3	5.7	25.7	24.7	25.9	28.4
	6.1	4.6	24.9	26.8	26.4	26.7
	4.9	5.7	28.6	25.7	25.6	28.4
DM+Ran 30mg/Kg	5.8	5.6	25.7	24.7	21.7	20.6
	6.3	5.9	23.6	25.8	20.5	19.8
	4.7	5.4	23.7	23.4	26.7	20.6
	4.4	5.5	18.6	19.8	19.9	21.5
	4.6	5.6	19.4	18.6	21.6	18.9
	4.5	5.1	25.4	25.4	22.8	19.9

Figure1F**Figure1G**

LVEF				LVFS			
	Control	DM	DM+Ran		Control	DM	DM+Ran
	69.146013	47.601025	52.997376		39.246116	24.999997	28.097723
	68.983898	36.753855	58.831105		38.642299	18.5079	32.028464
	73.892656	46.885832	59.308234		43.689314	24.474471	32.913174
	73.995943	42.881029	55.329503		43.595034	22.058816	29.969888
	69.83189	34.191186	59.944578		40.264649	17.282481	33.125002
	71.812096	36.572498	56.519654		42.647051	18.32061	31.301285

Figure2A

HE

Control



DM



DM+Ran



Masson

Control



DM



DM+Ran



Figure2B

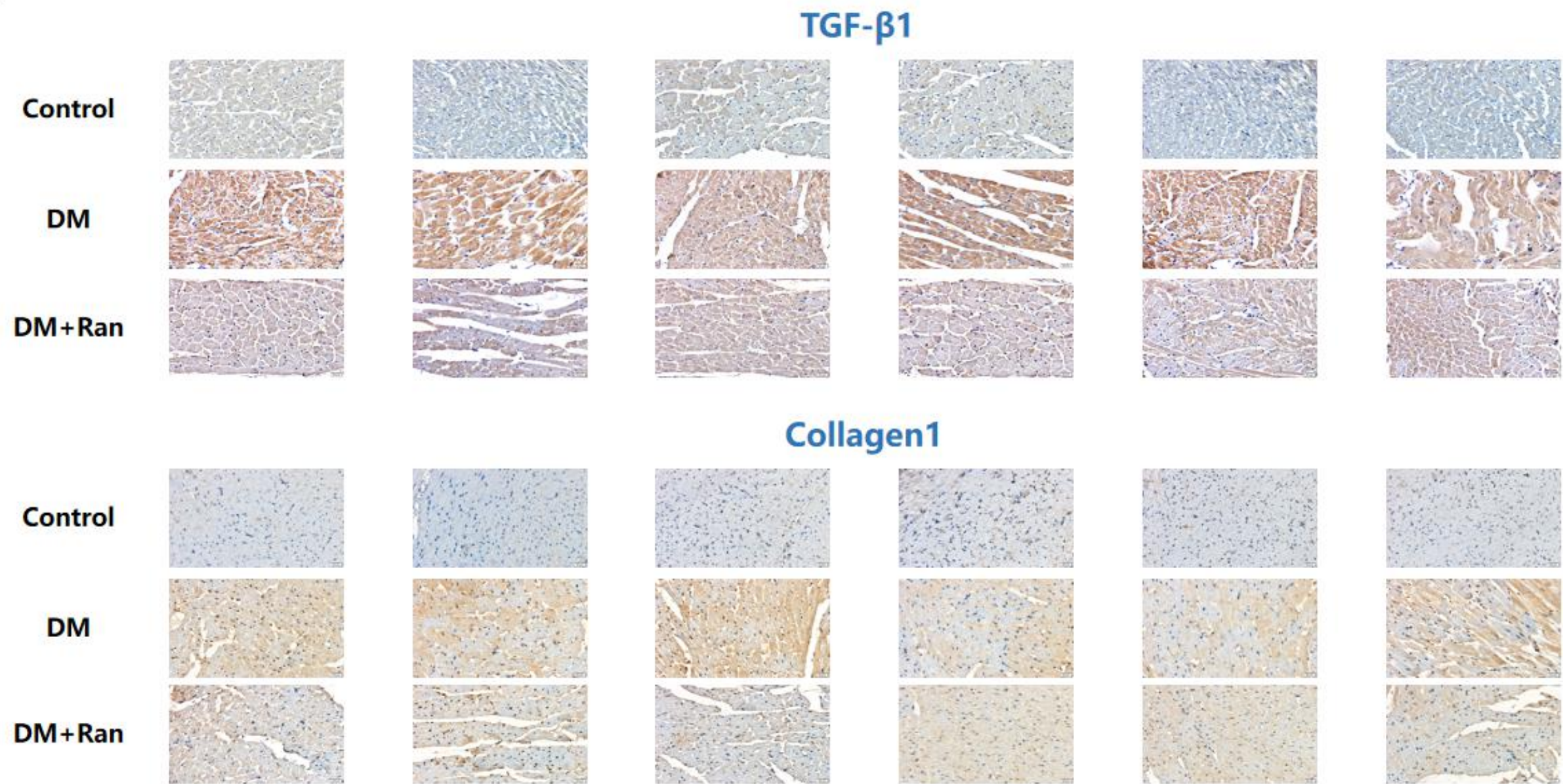
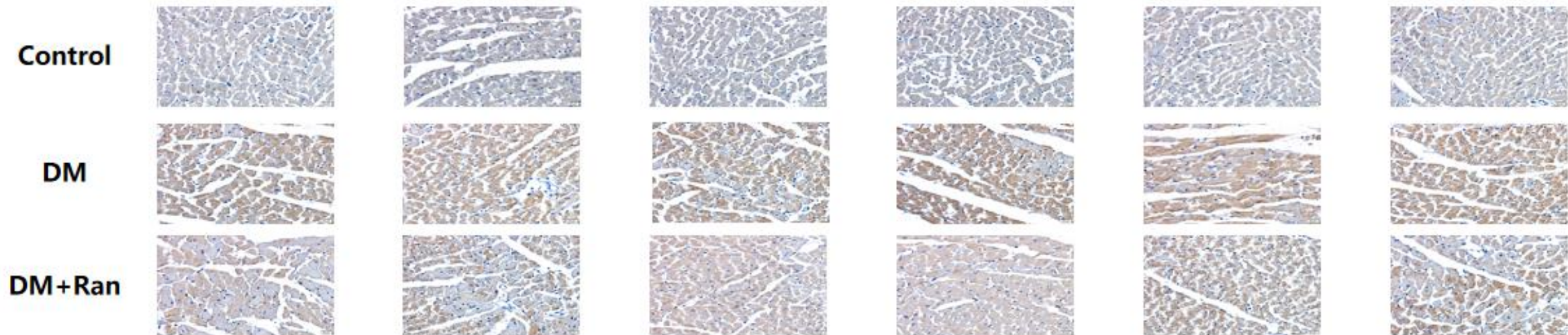


Figure2B**Collagen3****Figure2C**

	TGF-β 1	Collagen1	Collagen3
Control-1	7.71	6.05	8.59
Control-2	8.23	5.51	9.48
Control-3	6.05	4.93	14.43
Control-4	8.27	6.36	13.61
Control-5	8.96	5.39	14.22
Control-6	7.87	6.13	11.82
DM-1	37.65	24.48	34.56
DM-2	39.85	28.56	32.56
DM-3	38.43	24.94	31.99
DM-4	36.65	25.34	28.42
DM-5	36.70	23.59	28.05
DM-6	30.56	29.09	31.14
DM+Ran-1	18.25	13.57	14.29
DM+Ran-2	16.61	11.61	16.12
DM+Ran-3	17.2	15.36	21.11
DM+Ran-4	17.86	11.64	12.91
DM+Ran-5	22.28	10.60	19.97
DM+Ran-6	19.16	17.47	14.46

Figure2D

	GAPDH	TGF- β 1
Control-1	14.51	26.92
Control-2	14.69	26.95
Control-3	15.29	27.34
Control-4	15.34	27.94
Control-5	15.22	27.58
Control-6	15.74	28.18
DM-1	14.73	25.4
DM-2	15.49	25.83
DM-3	14.59	25.01
DM-4	15.73	26.29
DM-5	15.86	26.11
DM-6	14.34	24.99
DM+Ran-1	15.29	26.26
DM+Ran-2	15.64	26.63
DM+Ran-3	14.51	25.55
DM+Ran-4	14.56	25.64
DM+Ran-5	14.72	25.59
DM+Ran-6	14.83	26.45

	GAPDH	Collagen1
Control-1	15.27	26.73
Control-2	15.13	26.57
Control-3	15.29	26.49
Control-4	15.34	26.38
Control-5	14.64	25.75
Control-6	14.27	25.39
DM-1	14.73	24.84
DM-2	14.68	24.52
DM-3	15.86	25.34
DM-4	14.73	23.98
DM-5	15.86	25.61
DM-6	14.34	24.39
DM+Ran-1	15.29	25.55
DM+Ran-2	14.44	24.84
DM+Ran-3	14.51	24.91
DM+Ran-4	14.56	24.87
DM+Ran-5	14.72	24.61
DM+Ran-6	15.36	25.94

	GAPDH	Collagen3
Control-1	14.51	28.55
Control-2	15.13	29.75
Control-3	15.29	29.37
Control-4	15.34	29.28
Control-5	15.22	29.64
Control-6	14.27	28.49
DM-1	14.73	27.14
DM-2	15.49	27.88
DM-3	14.59	27.27
DM-4	15.73	28.04
DM-5	15.86	28.33
DM-6	15.47	28.23
DM+Ran-1	14.29	27.76
DM+Ran-2	14.44	27.53
DM+Ran-3	14.51	27.72
DM+Ran-4	14.56	27.36
DM+Ran-5	15.94	29.19
DM+Ran-6	15.36	28.56

Figure 2E-TGF- β 1

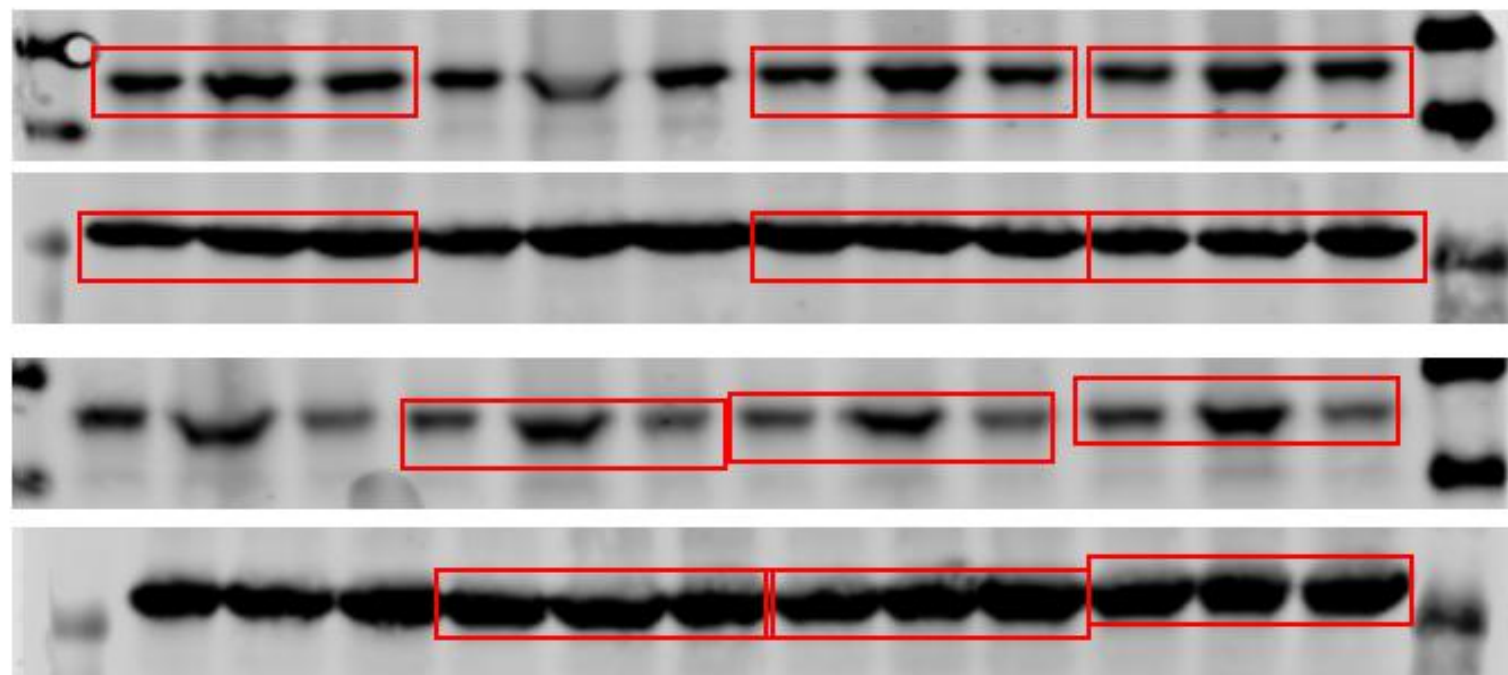


Figure 2E-Collagen1

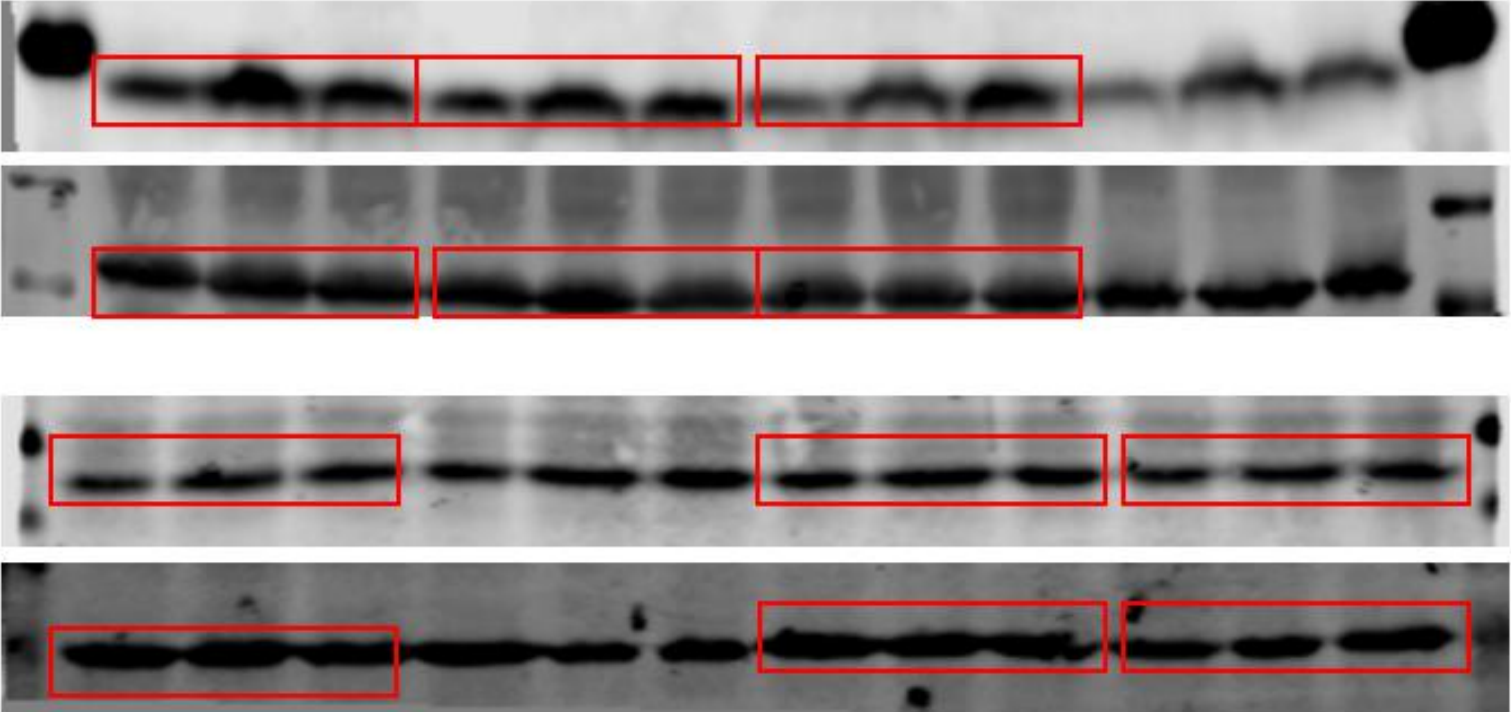


Figure 2E-Collagen3

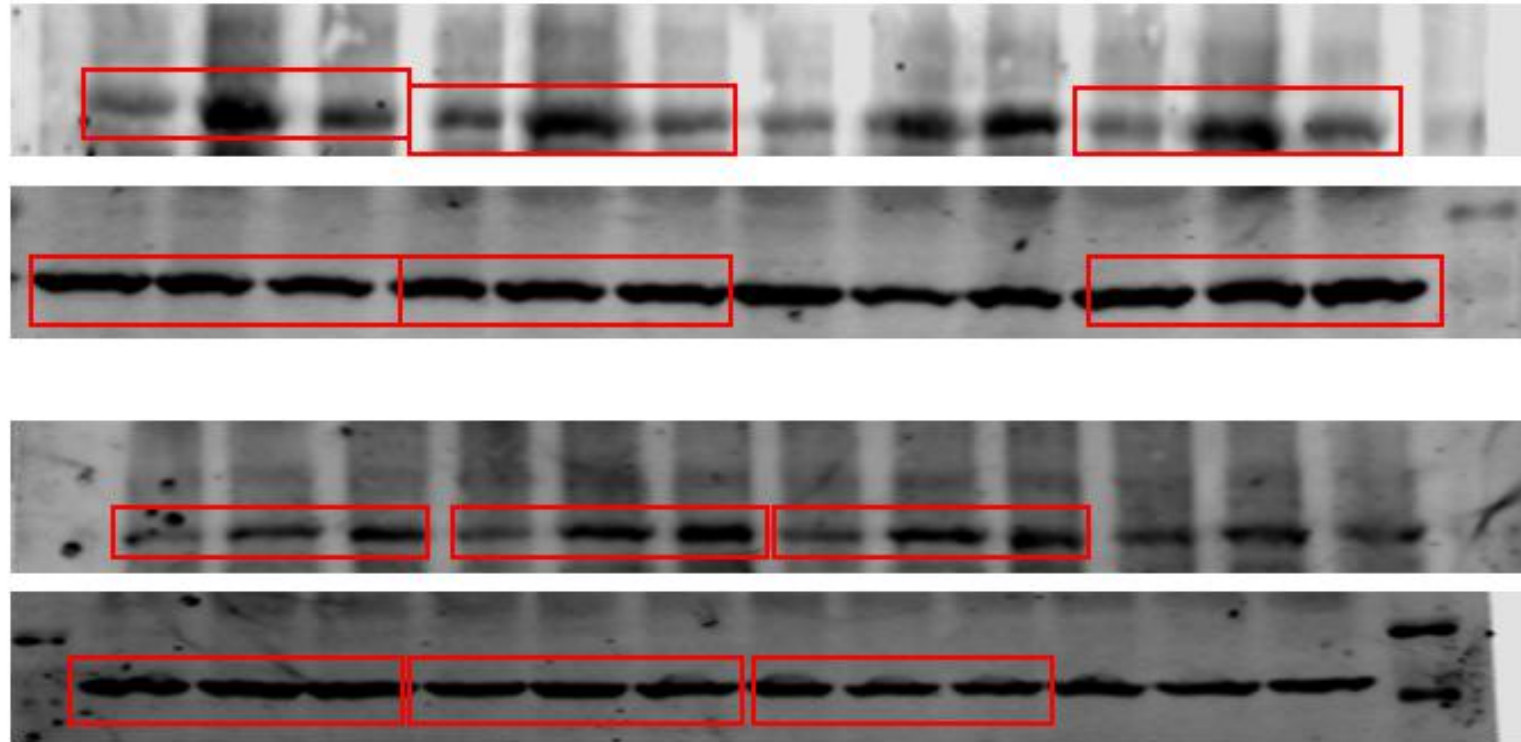
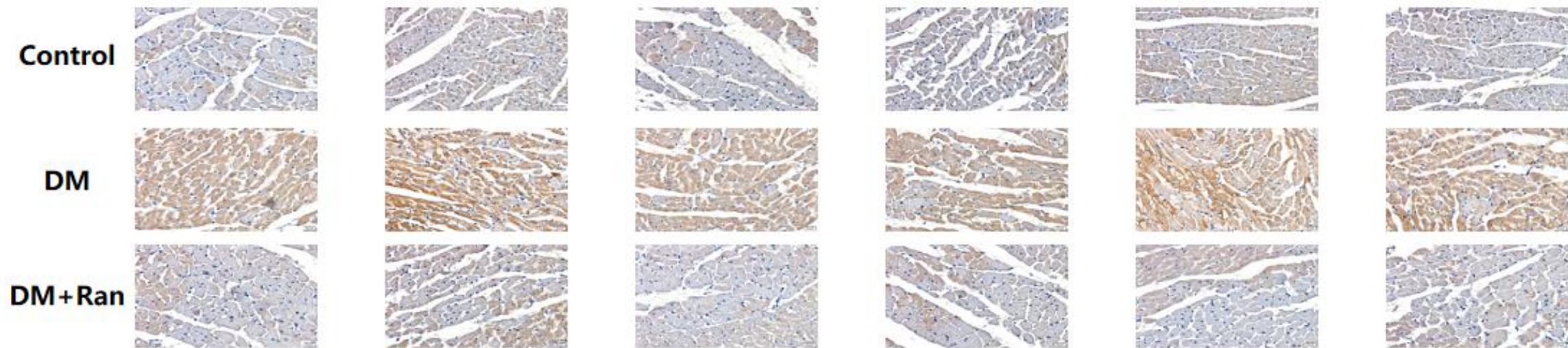


Figure 3A

Caspase-1



IL-1 β

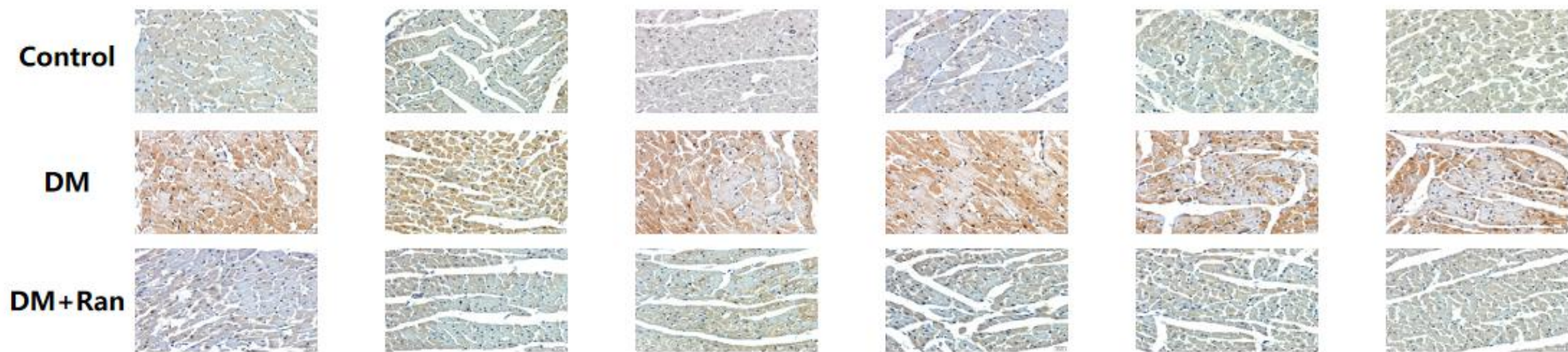
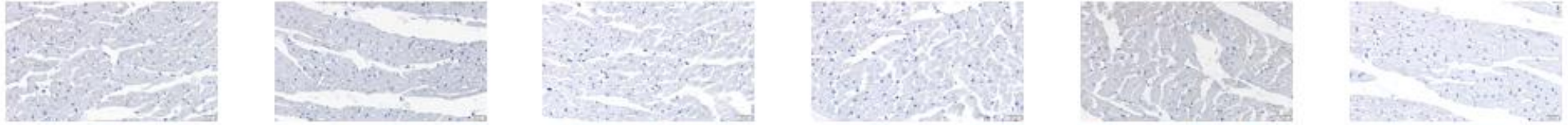
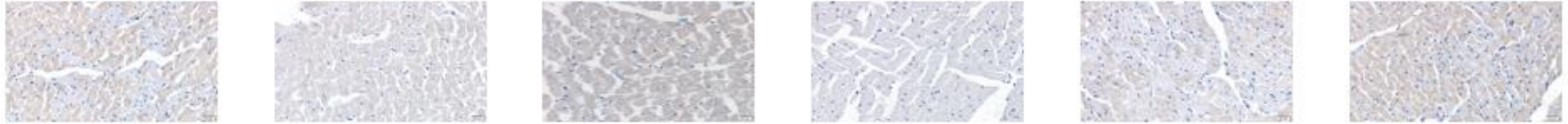


Figure3A**GSDMD****Control****DM****DM+Ran****Figure3B-D**

	Caspase-1	IL-1 β	GSDMD
Control-1	7.18	7.12	3.46
Control-2	7.86	6.79	3.94
Control-3	8.7	9.93	4.85
Control-4	8.2	11.01	2.8
Control-5	9.96	8.14	3.57
Control-6	10.29	8.91	4.36
DM-1	36.38	26.73	27.68
DM-2	39.38	30.5	24.92
DM-3	40.27	32.98	28.18
DM-4	34.85	30.27	22.74
DM-5	38.42	32.54	17.27
DM-6	34.96	28.07	22.98
DM+Ran-1	17.22	14.55	14.36
DM+Ran-2	22.87	14.46	10.6
DM+Ran-3	16.94	13.39	13.95
DM+Ran-4	17.49	15.24	14.81
DM+Ran-5	20.14	12.65	13.39
DM+Ran-6	18.3	15.35	16.81

Figure3E-F

	GAPDH	Caspase-1		GAPDH	IL-1 β
Control-1	15.27	25.73	Control-1	14.51	23.86
Control-2	15.13	25.75	Control-2	15.13	24.65
Control-3	15.29	25.67	Control-3	15.29	24.73
Control-4	15.34	25.74	Control-4	15.34	24.81
Control-5	15.22	25.69	Control-5	15.22	24.95
Control-6	14.27	24.75	Control-6	14.27	23.64
DM-1	14.73	23.42	DM-1	14.73	23.19
DM-2	14.68	23.39	DM-2	15.49	23.61
DM-3	15.86	24.55	DM-3	14.59	22.75
DM-4	15.73	24.22	DM-4	15.73	23.82
DM-5	15.86	24.65	DM-5	14.27	22.43
DM-6	15.47	24.66	DM-6	14.34	22.54
DM+Ran-1	15.29	24.76	DM+Ran-1	14.29	22.9
DM+Ran-2	15.64	24.95	DM+Ran-2	15.64	24.09
DM+Ran-3	14.51	23.75	DM+Ran-3	14.51	22.92
DM+Ran-4	15.72	25.31	DM+Ran-4	15.72	24.35
DM+Ran-5	15.94	25.14	DM+Ran-5	14.72	23.23
DM+Ran-6	15.36	25.34	DM+Ran-6	14.83	23.44

Figure 3G-Caspase-1

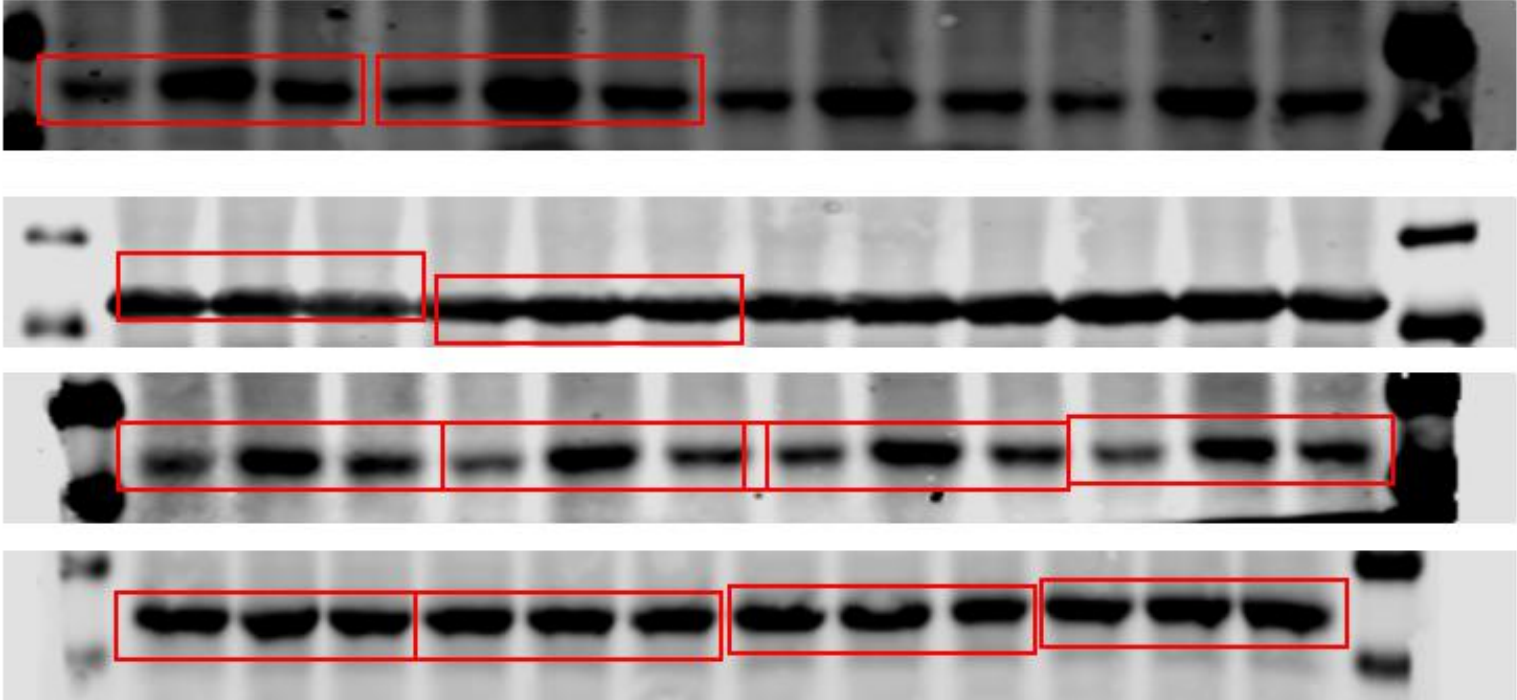


Figure 3H-IL-1 β

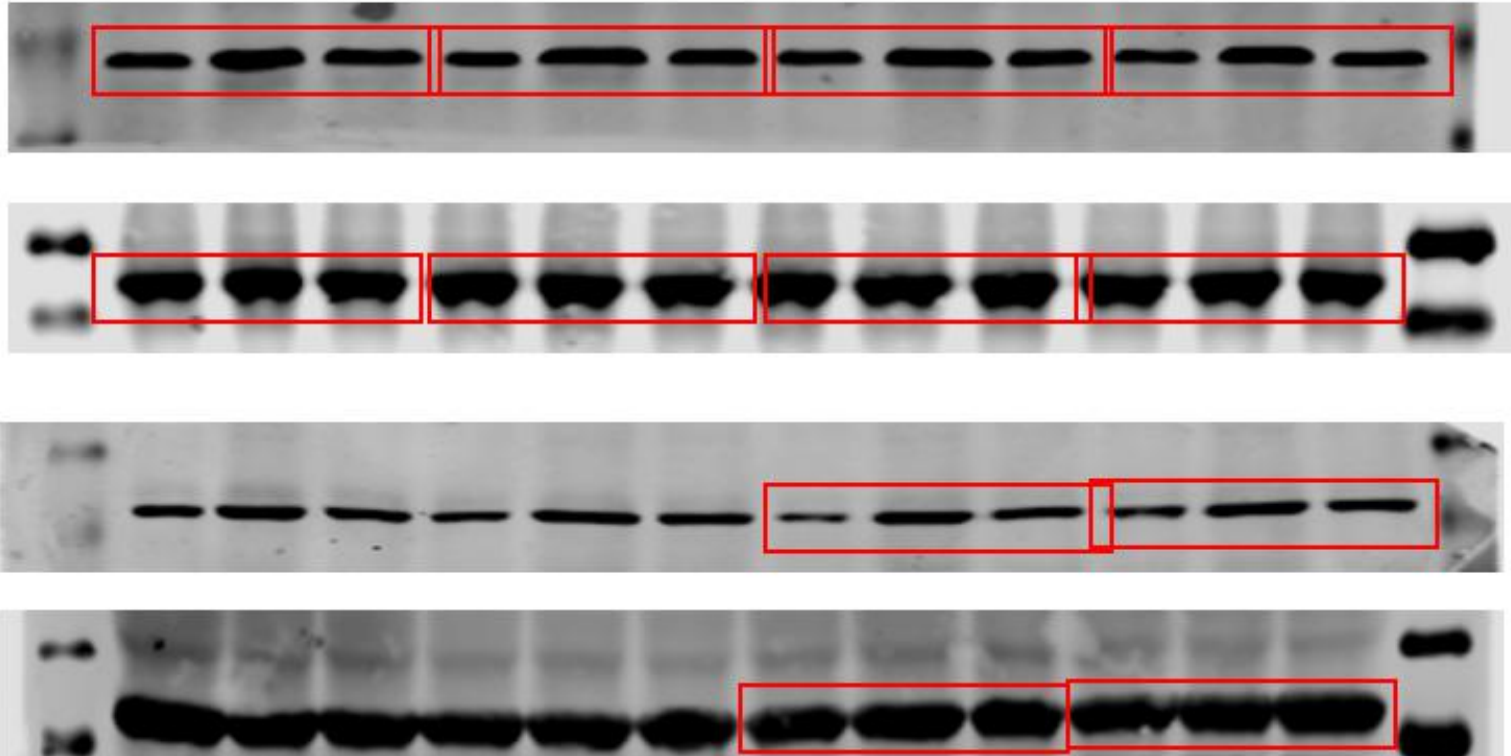


Figure3I-GSDMD

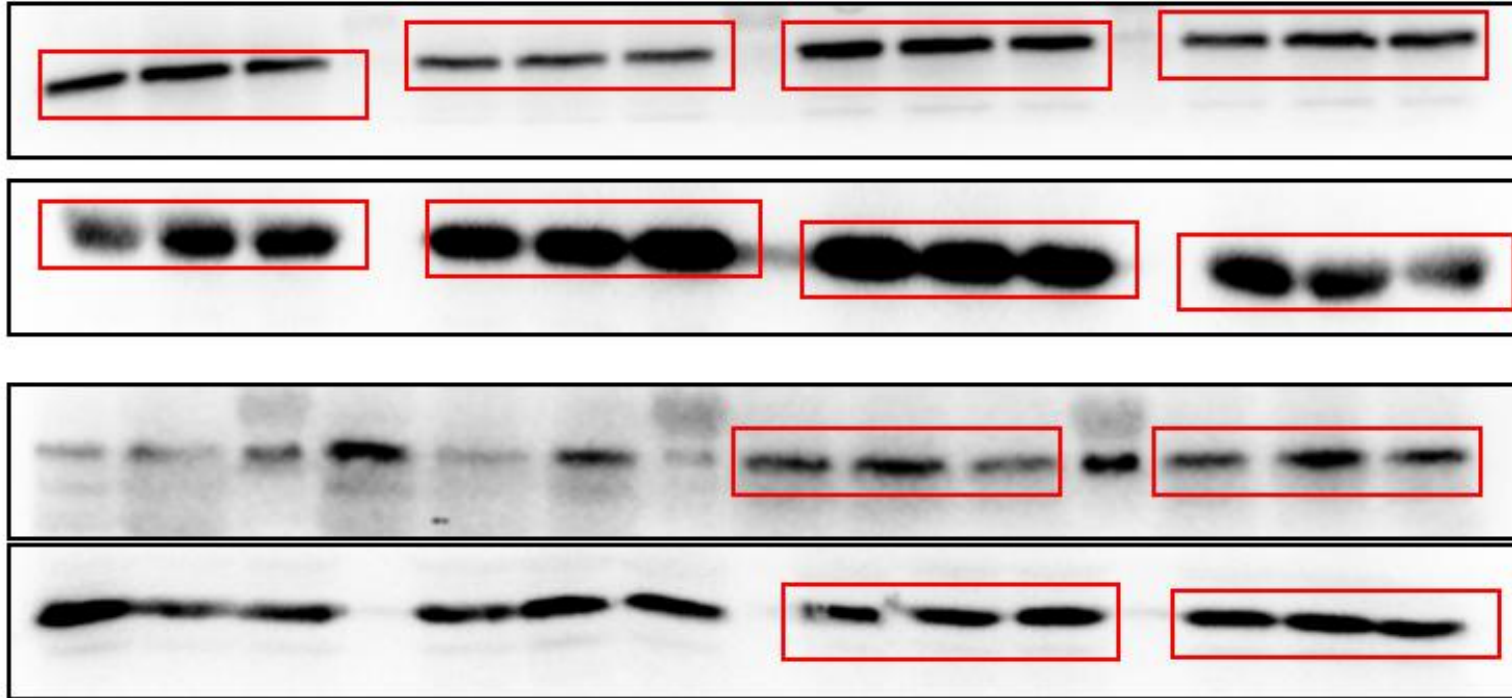


Figure4A

dataset: 1
Target: *CASP1*
 length: 1316
MiRNA: *rno-miR-135b*
 length: 23

mfe: -21.3 kcal/mol
 p-value: undefined

Position: 181

```

target 5' G   UAAAAA   CCCC G  GC   G   3'
          UCAC     AGGA     G   AAGCCA
          AGUG     UCCU     C   UUCGGU
miRNA  3'   UA       UA    UU    AU  5'
  
```

```

Caspase-1-WT 5'-- AAAAGGACCCCGGGCAAGCCAGA --3'
Rno-miR-135b 3'-- AGUGUAUCCUACUUUUCGGUAU --5'
Caspase-1-Mut 5'-- AAAAGGACCCCGGGCGAATGGGA --3'
  
```

	miRNA	Background	Firefly	Renilla	R/F
CDS+CDS+3' UTR CASP1	NC1	70	1337104	15952665	11.931
	NC2	73	1442564	16763688	11.621
	NC3	79	1438264	17726661	12.325
	rno-miR-135b 1	80	1219363	7153338	5.866
	rno-miR-135b 2	71	1567536	8919137	5.69
	rno-miR-135b 3	68	1388713	8431935	6.072
CDS+CDS+3' UTR mut CASP1	NC1	81	659318	5109513	7.75
	NC2	86	483149	4014036	8.308
	NC3	92	497855	4063386	8.162
	rno-miR-135b 1	77	692401	5654557	8.167
	rno-miR-135b 2	78	612271	5132015	8.382
	rno-miR-135b 3	73	616980	4948909	8.021

Figure4B-D

	U6	miR-135b
NG+AMO-NC-1	11.21	27.42
NG+AMO-NC-2	11.28	27.45
NG+AMO-NC-3	11.82	27.93
HG+AMO-NC-1	11.9	28.82
HG+AMO-NC-2	11.87	28.92
HG+AMO-NC-3	11.64	28.73
HG+Ran+AMO-NC-1	11.46	27.79
HG+Ran+AMO-NC-2	11.2	27.51
HG+Ran+AMO-NC-3	11.11	27.75
HG+Ran+AMO-135b-1	11.12	29.58
HG+Ran+AMO-135b-2	11.33	29.91
HG+Ran+AMO-135b-3	11.41	29.92

	GAPDH	Caspase-1
NG+AMO-NC-1	17.9	30.03
NG+AMO-NC-2	17.89	30.04
NG+AMO-NC-3	16.21	28.3
HG+AMO-NC-1	17.44	28.08
HG+AMO-NC-2	15.84	26.29
HG+AMO-NC-3	15.86	26.28
HG+Ran+AMO-NC-1	17.33	29.01
HG+Ran+AMO-NC-2	15.82	27.51
HG+Ran+AMO-NC-3	15.76	27.54
HG+Ran+AMO-135b-1	16.22	27.2
HG+Ran+AMO-135b-2	16.23	27.34
HG+Ran+AMO-135b-3	16.26	27.35

	GAPDH	IL-1 β
NG+AMO-NC-1	17.9	26.71
NG+AMO-NC-2	17.89	26.66
NG+AMO-NC-3	17.94	26.71
HG+AMO-NC-1	17.44	25.35
HG+AMO-NC-2	15.86	24.02
HG+AMO-NC-3	15.91	24.01
HG+Ran+AMO-NC-1	17.78	26.34
HG+Ran+AMO-NC-2	15.81	24.4
HG+Ran+AMO-NC-3	15.76	24.36
HG+Ran+AMO-135b-1	17.75	25.92
HG+Ran+AMO-135b-2	16.23	24.49
HG+Ran+AMO-135b-3	16.26	24.5

Figure 4D-F

caspase-1



IL-1 β



GSDMD

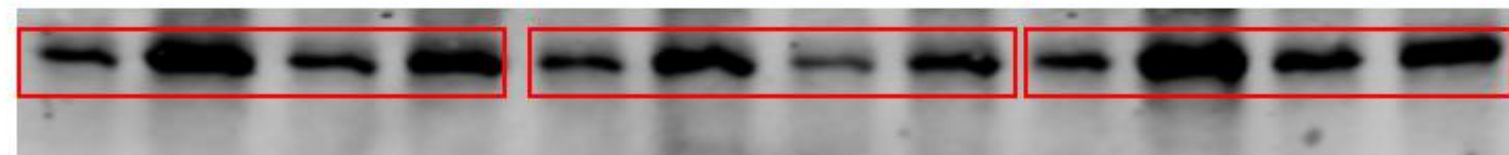
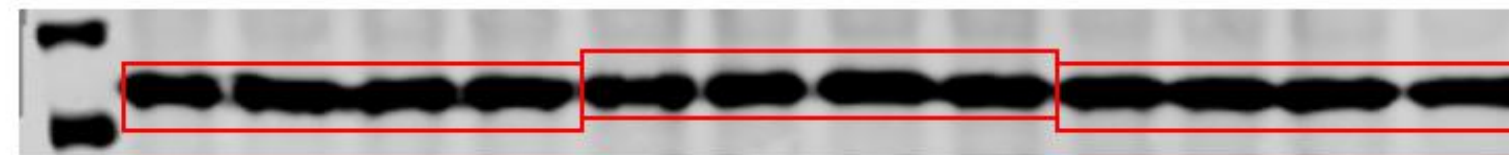
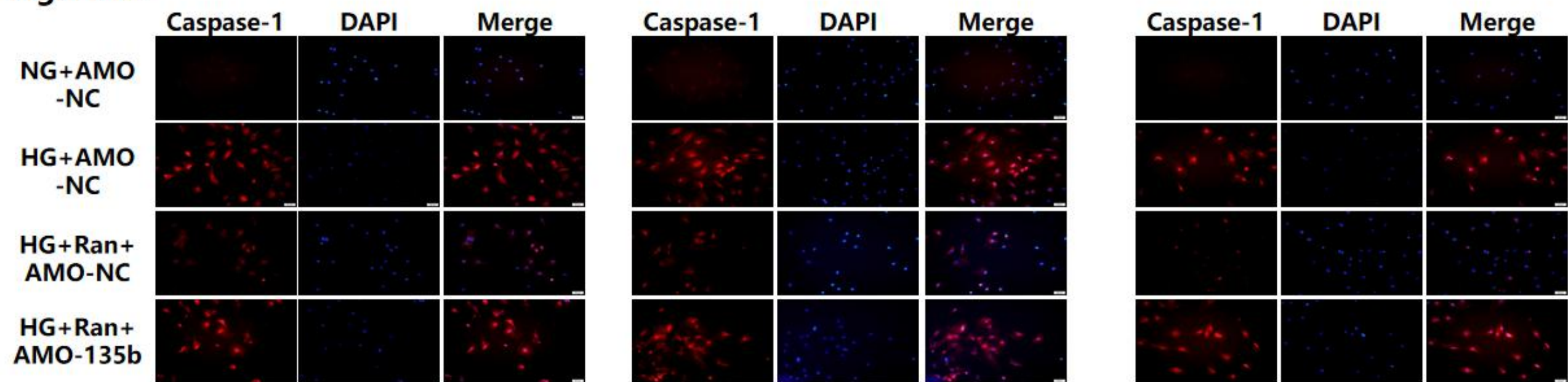


Figure4G



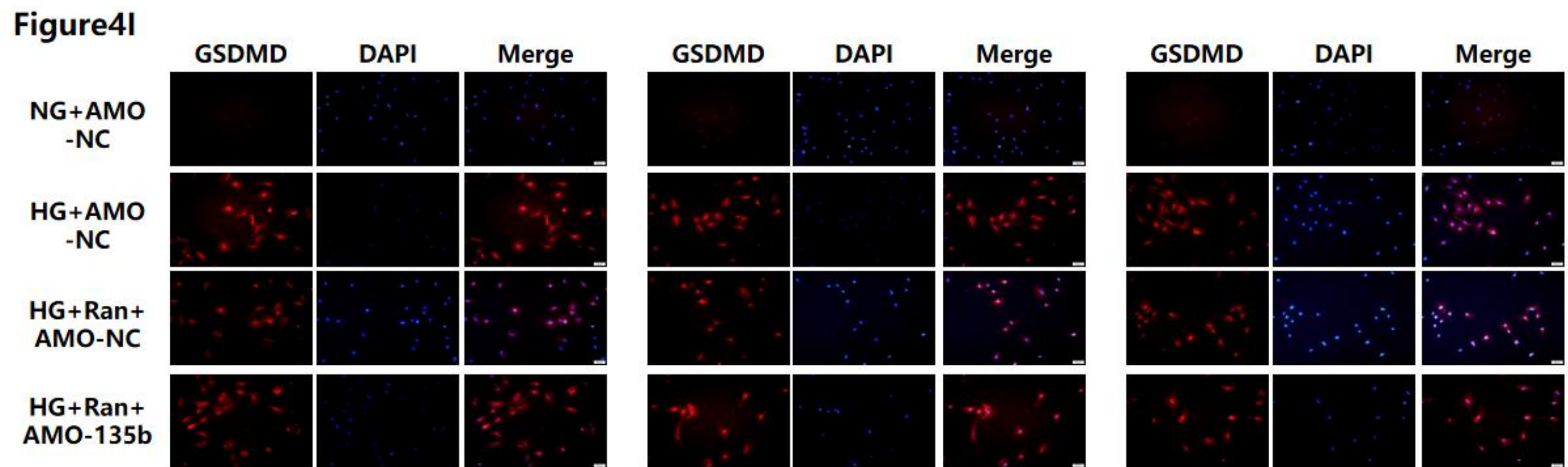
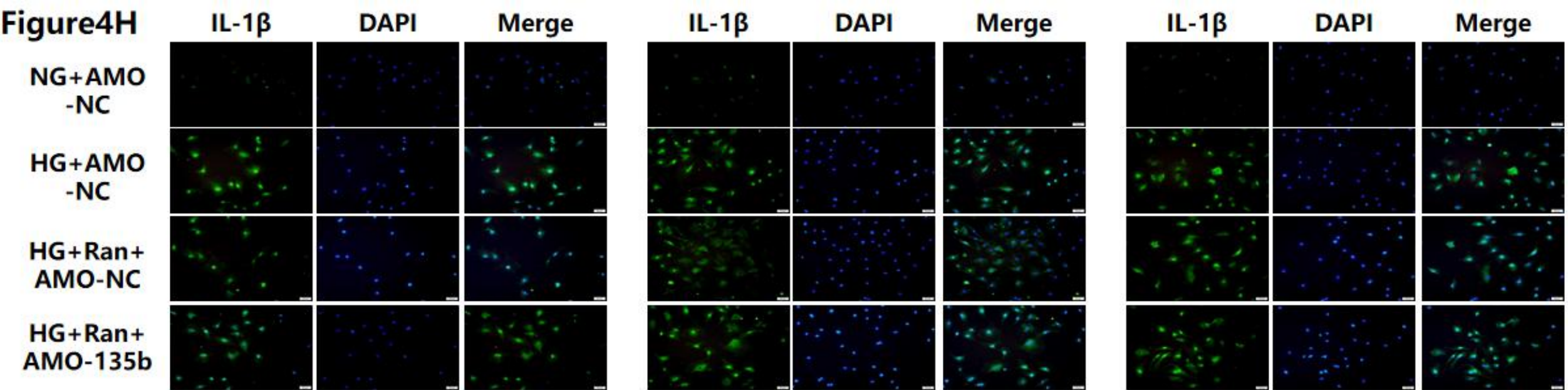
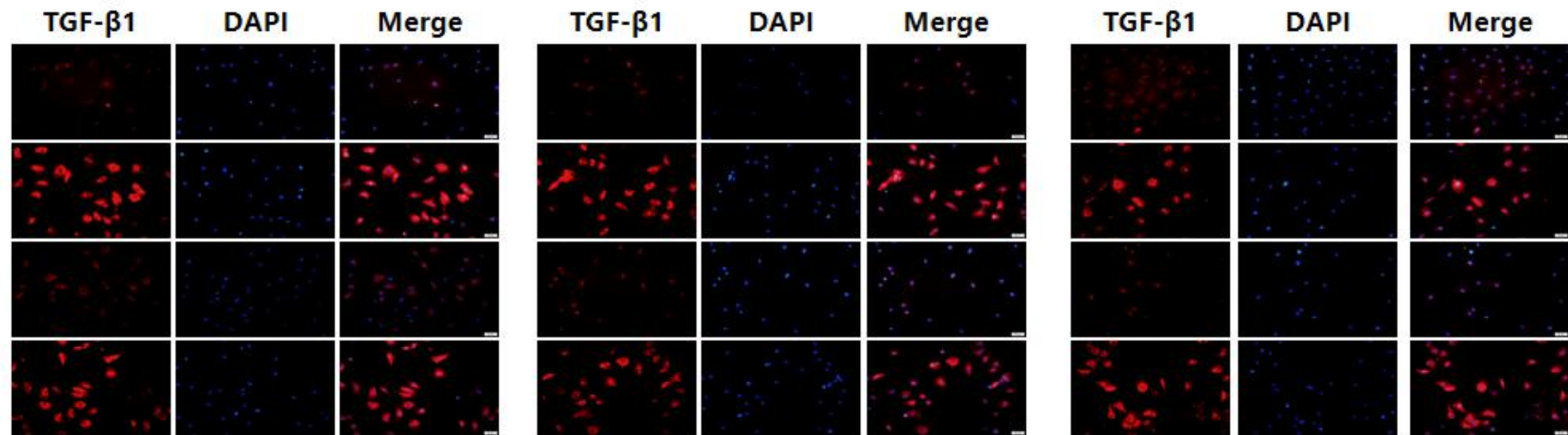
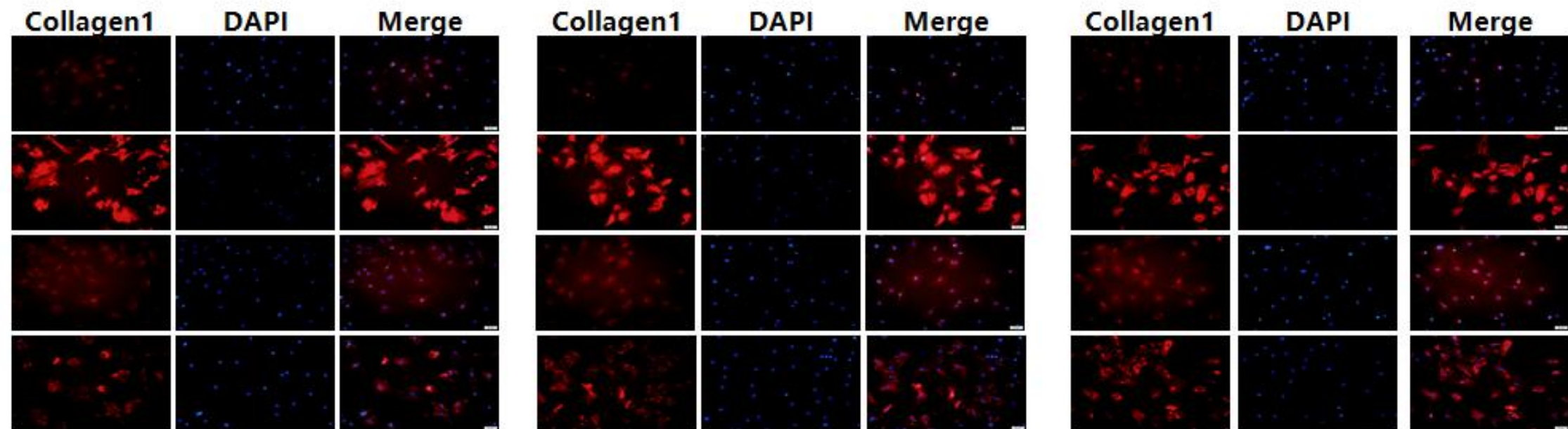


Figure 5A**Figure 5B**

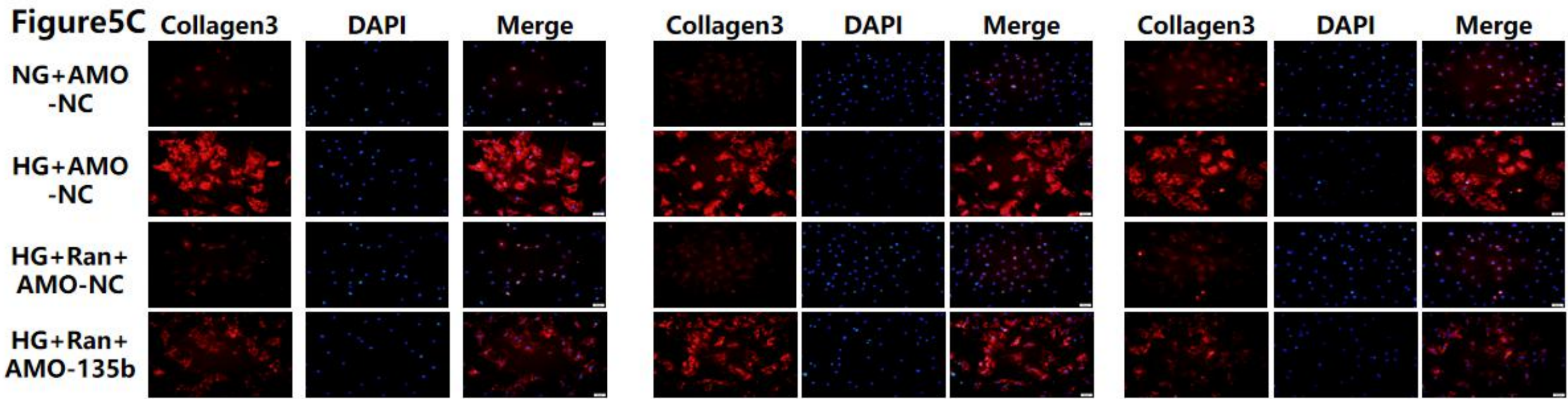


Figure 5D-F

	GAPDH	TGF- β 1
NG+AMO-NC-1	17.89	29.52
NG+AMO-NC-2	17.94	29.26
NG+AMO-NC-3	16.21	27.56
HG+AMO-NC-1	15.86	26.27
HG+AMO-NC-2	17.44	27.69
HG+AMO-NC-3	15.91	26.22
HG+Ran+AMO-NC-1	18.21	29.08
HG+Ran+AMO-NC-2	17.78	28.73
HG+Ran+AMO-NC-3	15.82	26.55
HG+Ran+AMO-135b-1	17.75	28.34
HG+Ran+AMO-135b-2	16.22	26.88
HG+Ran+AMO-135b-3	16.23	26.75

	GAPDH	Collagen1
NG+AMO-NC-1	17.94	25.92
NG+AMO-NC-2	16.3	24.27
NG+AMO-NC-3	16.25	24.18
HG+AMO-NC-1	17.44	23.51
HG+AMO-NC-2	15.86	22.03
HG+AMO-NC-3	15.91	22.12
HG+Ran+AMO-NC-1	18.21	25.22
HG+Ran+AMO-NC-2	17.78	25.2
HG+Ran+AMO-NC-3	15.76	23.07
HG+Ran+AMO-135b-1	17.75	24.55
HG+Ran+AMO-135b-2	17.79	24.7
HG+Ran+AMO-135b-3	16.26	22.97

	GAPDH	Collagen3
NG+AMO-NC-1	17.9	24.25
NG+AMO-NC-2	17.89	24.34
NG+AMO-NC-3	17.94	24.17
HG+AMO-NC-1	17.44	22.61
HG+AMO-NC-2	15.86	20.91
HG+AMO-NC-3	15.91	20.94
HG+Ran+AMO-NC-1	18.21	23.77
HG+Ran+AMO-NC-2	15.82	21.47
HG+Ran+AMO-NC-3	15.76	21.59
HG+Ran+AMO-135b-1	17.79	23.23
HG+Ran+AMO-135b-2	16.23	21.58
HG+Ran+AMO-135b-3	16.26	21.66

Figure 5G-TGF- β 1

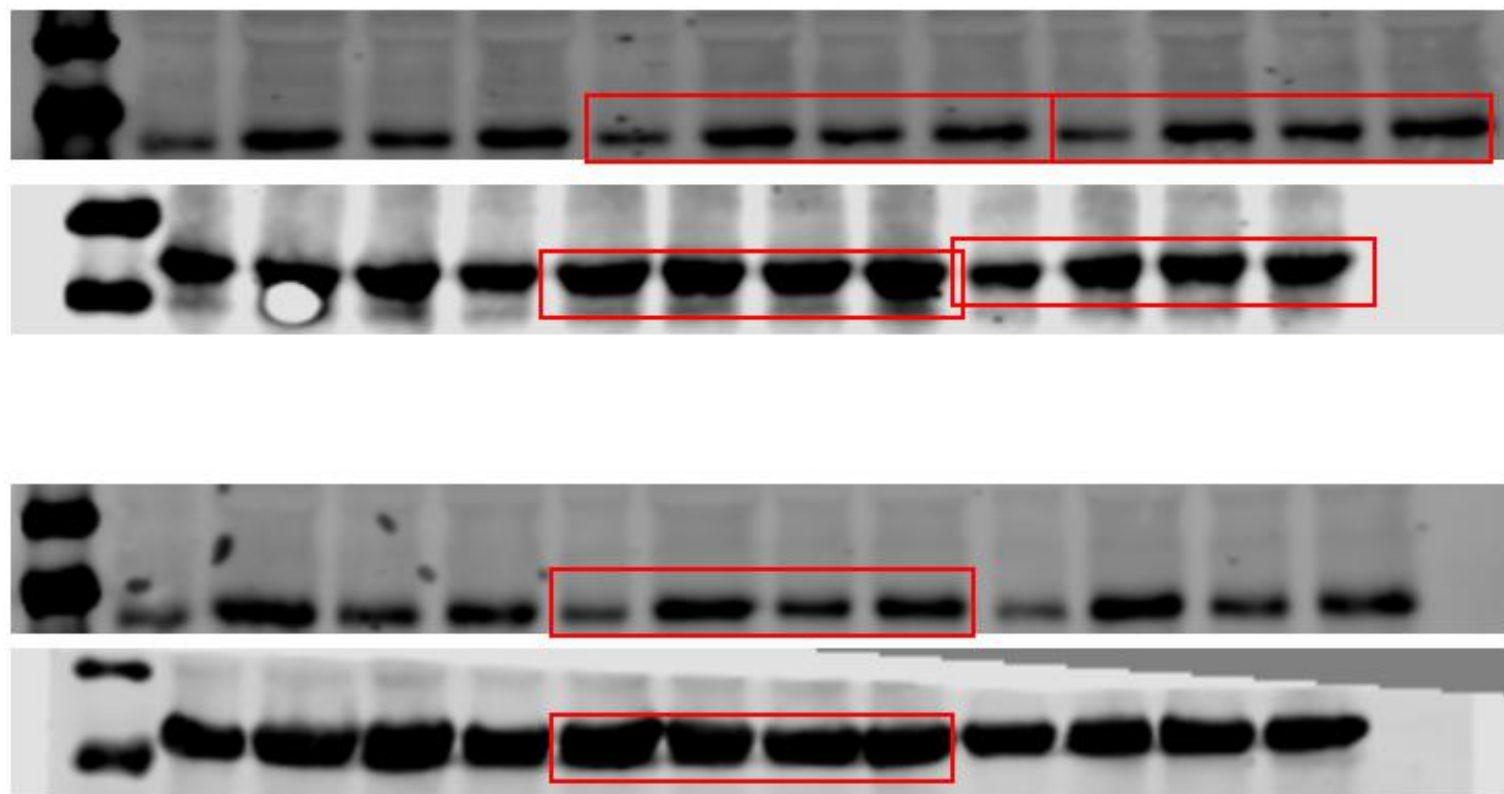


Figure 5H-Collagen1

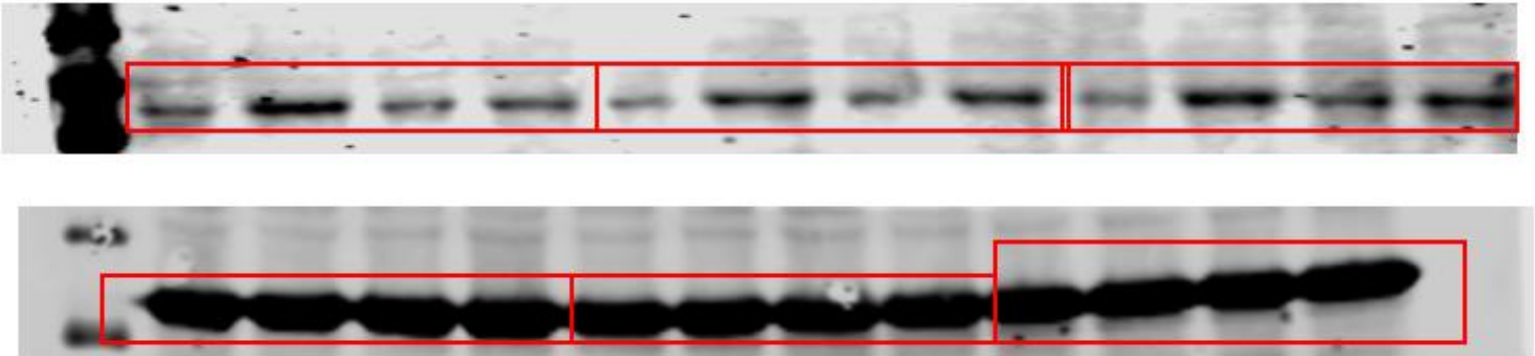


Figure 5I-Collagen3

