

Table 1. Small GTPase screening for YAP/TAZ localization regulators
(related to Fig. 1a)

ID	GTPase	Mutant	Family	Tag	High Stiffness	Low Stiffness
1	ARF1	WT	ARF	Myc	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
2	ARF3	WT	ARF	Myc	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
3	ARF6	WT	ARF	Myc	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
4	ARF6	QL	ARF	Myc	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
5	RAB1A	WT	RAB	HA	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
6	RAB1A	QL	RAB	HA	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
7	RAB5	WT	RAB	HA	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
8	RAB5	QL	RAB	HA	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
9	RAB7	QL	RAB	Myc	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
10	RAB8	WT	RAB	GFP	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
11	RAB8	QL	RAB	GFP	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
12	RAB10	WT	RAB	HA	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
13	RAB10	QL	RAB	HA	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
14	RAB11	WT	RAB	HA	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
15	RAB11	QL	RAB	HA	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
16	RAB22	WT	RAB	Myc	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
17	RAB22	QL	RAB	Myc	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
18	RHOA	L63	RHO	Myc	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
19	RAC1	L61	RHO	Myc	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
20	CDC42	L61	RHO	Myc	Nuclear and cytoplasmic	Cytoplasmic; similar with Ctrl
21	RAN	WT	RAN	HA	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
22	RAN	QL	RAN	HA	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
24	RAGA-RAGC	QL-SN	RAS	HA	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
25	RHEB	QL	RAS	Myc	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
26	RALA	WT	RAS	GFP	Nuclear and cytoplasmic	Cytoplasmic; similar with Ctrl
27	RALB	WT	RAS	RFP	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
28	RALB	QL	RAS	RFP	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
29	HRAS	V12	RAS	HA	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
30	KRAS	V12	RAS	HA	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
31	NRAS	V12	RAS	HA	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
32	RAP1B	V12	RAS	Flag	Nuclear; similar with Ctrl	Cytoplasmic; similar with Ctrl
33	RAP2A	V12	RAS	HA	Cytosolic	More cytoplasmic than Ctrl

Table 2. Gene ontology analysis of gene regulated by ECM stiffness (related to Fig. 4i)

Term	Count	Percentage	P-value	Fold Enrichment	Benjamini
regulation of gene expression	121	26.48	2.81E-06	1.45	1.08E-02
regulation of nitrogen compound metabolic process	122	26.70	3.25E-06	1.45	6.29E-03
cell projection organization	50	10.94	3.43E-06	2.01	4.43E-03
regulation of nucleobase-containing compound metabolic process	115	25.16	4.51E-06	1.46	4.37E-03
regulation of cellular macromolecule biosynthetic process	111	24.29	1.08E-05	1.45	8.37E-03
regulation of RNA metabolic process	105	22.98	1.92E-05	1.46	1.24E-02
regulation of nucleic acid-templated transcription	102	22.32	1.95E-05	1.47	1.08E-02
regulation of macromolecule biosynthetic process	112	24.51	2.40E-05	1.42	1.16E-02
regulation of RNA biosynthetic process	102	22.32	2.44E-05	1.46	1.05E-02
regulation of transcription, DNA-templated	101	22.10	2.59E-05	1.46	1.00E-02
transcription, DNA-templated	100	21.88	4.51E-05	1.45	1.58E-02
nucleic acid-templated transcription	102	22.32	1.01E-04	1.41	3.22E-02
myelination	10	2.19	1.16E-04	5.27	3.40E-02
ensheathment of neurons	10	2.19	1.46E-04	5.12	3.97E-02
axon ensheathment	10	2.19	1.46E-04	5.12	3.97E-02
muscle structure development	26	5.69	1.71E-04	2.30	4.34E-02
RNA biosynthetic process	103	22.54	2.48E-04	1.38	5.84E-02
gene expression	132	28.88	2.55E-04	1.30	5.65E-02
cell projection morphogenesis	31	6.78	3.20E-04	2.03	6.66E-02
nervous system development	64	14.00	3.99E-04	1.54	7.84E-02
neurogenesis	47	10.28	4.15E-04	1.70	7.74E-02
regulation of transcription from RNA polymerase II promoter	56	12.25	4.66E-04	1.59	8.25E-02
cell part morphogenesis	31	6.78	4.85E-04	1.98	8.21E-02
nucleobase-containing compound biosynthetic process	111	24.29	4.86E-04	1.33	7.88E-02
heterocycle biosynthetic process	112	24.51	5.12E-04	1.33	7.96E-02
aromatic compound biosynthetic process	112	24.51	5.75E-04	1.32	8.55E-02

Table 3. Gene ontology analysis of genes regulated by ECM, Hippo pathway and RAP2 (related to Extended Data Fig. 10g,h)

Term	Count	Percentage	P-value	Fold Enrichment	Benjamini
cell adhesion	44	24.58	4.91E-10	2.78	1.63E-06
biological adhesion	44	24.58	5.48E-10	2.77	9.12E-07
circulatory system development	26	14.53	1.85E-06	2.96	2.05E-03
cardiovascular system development	26	14.53	1.85E-06	2.96	2.05E-03
cell-cell adhesion	29	16.20	2.64E-06	2.68	2.19E-03
vasculature development	20	11.17	3.66E-06	3.52	2.44E-03
growth	25	13.97	4.85E-06	2.88	2.69E-03
blood vessel development	19	10.61	6.43E-06	3.54	3.06E-03
anatomical structure formation involved in morphogenesis	28	15.64	6.52E-06	2.61	2.71E-03
hippo signaling	6	3.35	1.22E-05	19.53	4.51E-03
actin cytoskeleton organization	18	10.06	1.46E-05	3.50	4.86E-03
cell development	38	21.23	1.69E-05	2.07	5.10E-03
tissue morphogenesis	19	10.61	1.82E-05	3.28	5.03E-03
cell morphogenesis involved in differentiation	21	11.73	2.10E-05	3.00	5.35E-03
cell-substrate adhesion	13	7.26	2.80E-05	4.56	6.64E-03
angiogenesis	15	8.38	3.01E-05	3.90	6.66E-03

Table 4. Antibodies used in the study

Gene	Usage	Vendor	Catalog	Dilution
ARHGAP29	WB	Santa Cruz Biotechnology	sc-365554	1:400
β -catenin	IF	BD Biosciences	610154	1:250
pERK1/2	WB	Cell Signaling Biotechnology	4370	1:2000
GFP	IF	Cell Signaling Biotechnology	2956	1:100
GM130	IHC	BD Biosciences	610823	1:500
HLA class 1	IHC	Abcam	ab70328	1:100
Laminin V	IHC	EMD Millipore	MAB19562X	1:1000
PDZGEF2	WB	Santa Cruz Biotechnology	sc-398642	1:400
RhoA	WB	Cell Signaling Biotechnology	2117	1:1000
Ras	WB	Cell Signaling Biotechnology	3339	1:2000
Ras (G12V)	WB	Cell Signaling Biotechnology	14412	1:2000
PLCy1	WB	Cell Signaling Biotechnology	5690	1:1000
PLD1	WB	R&D systems	F5615-SP	1:1000
PLD2	WB	Cell Signaling Biotechnology	13904	1:1000
RAP2	WB	BD Biosciences	610215	1:1000
TWIST	IF	Santa Cruz Biotechnology	sc-81417	1:100
YAP/TAZ	IHC	Cell Signaling Biotechnology	8418	1:100

Other antibodies used in this study were described elsewhere (ref 17).