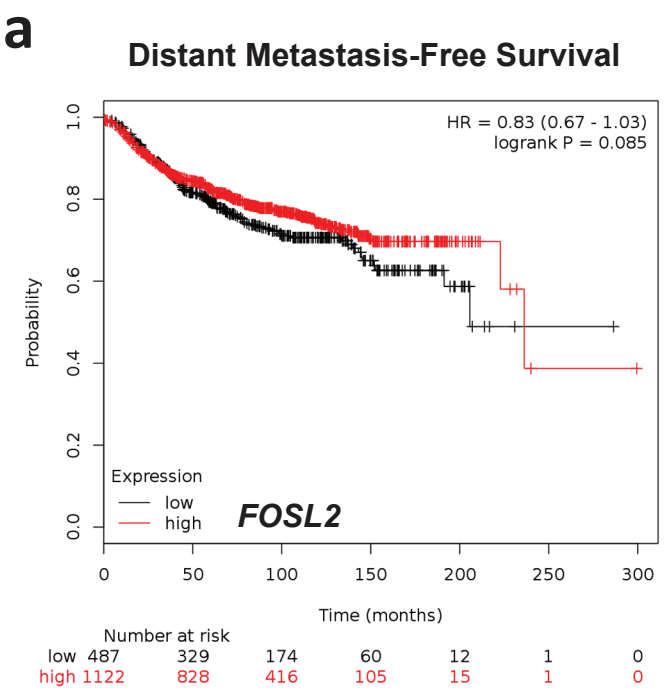
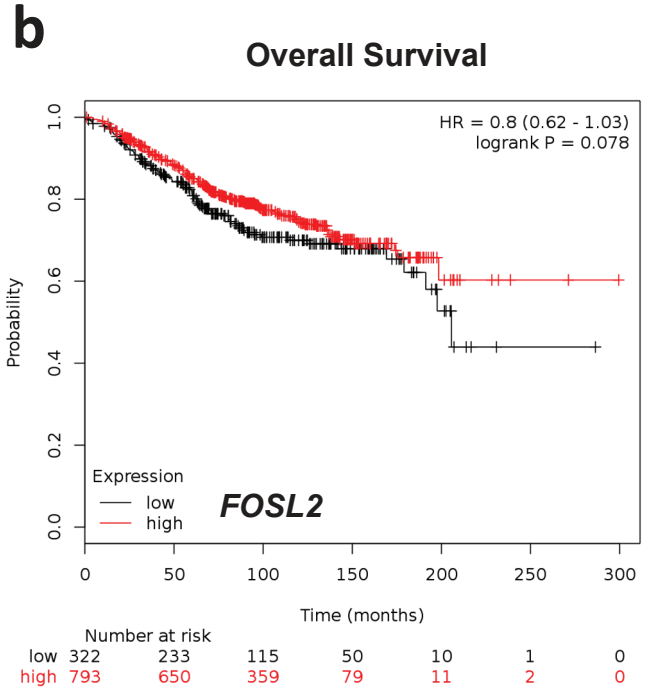
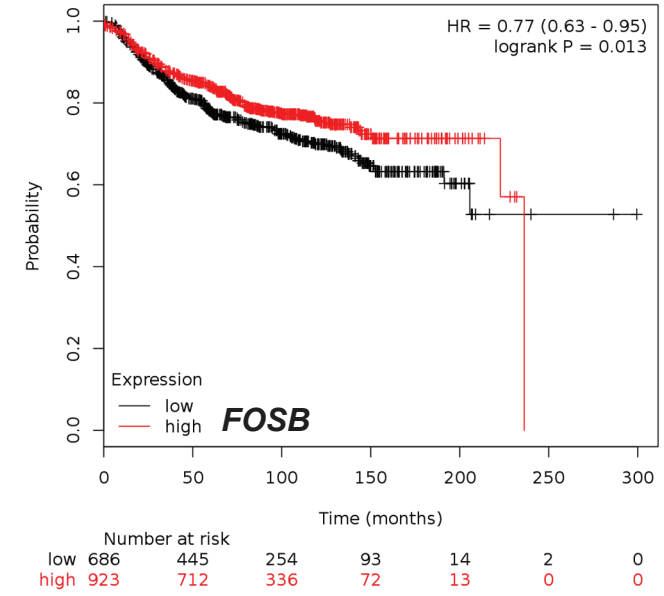
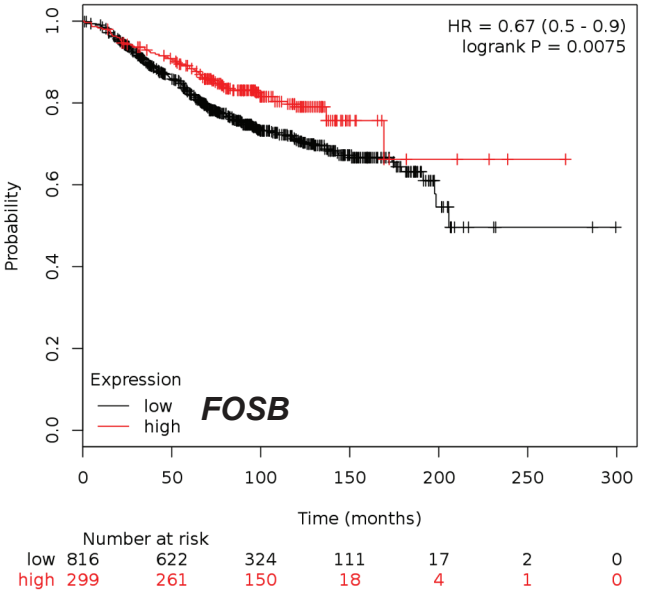
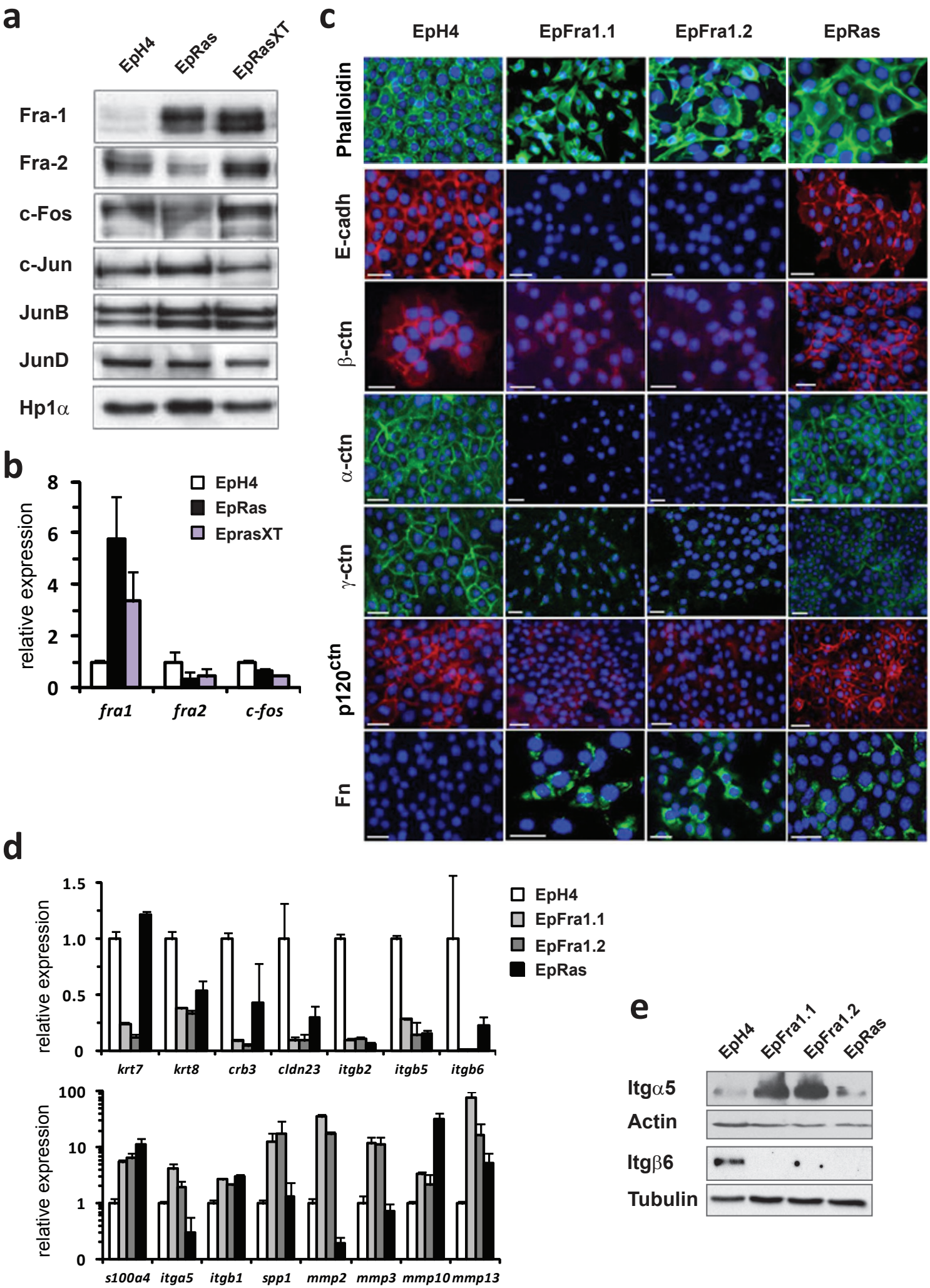

a
Distant Metastasis-Free Survival
HR = 0.83 (0.67 - 1.03)
logrank P = 0.085
Probability
Expression
low
high
FOSL2
Time (months)
Number at risk
low 487 329 174 60 12 1 0
high 1122 828 416 105 15 1 0


b
Overall Survival
HR = 0.8 (0.62 - 1.03)
logrank P = 0.078
Probability
Expression
low
high
FOSL2
Time (months)
Number at risk
low 322 233 115 50 10 1 0
high 793 650 359 79 11 2 0

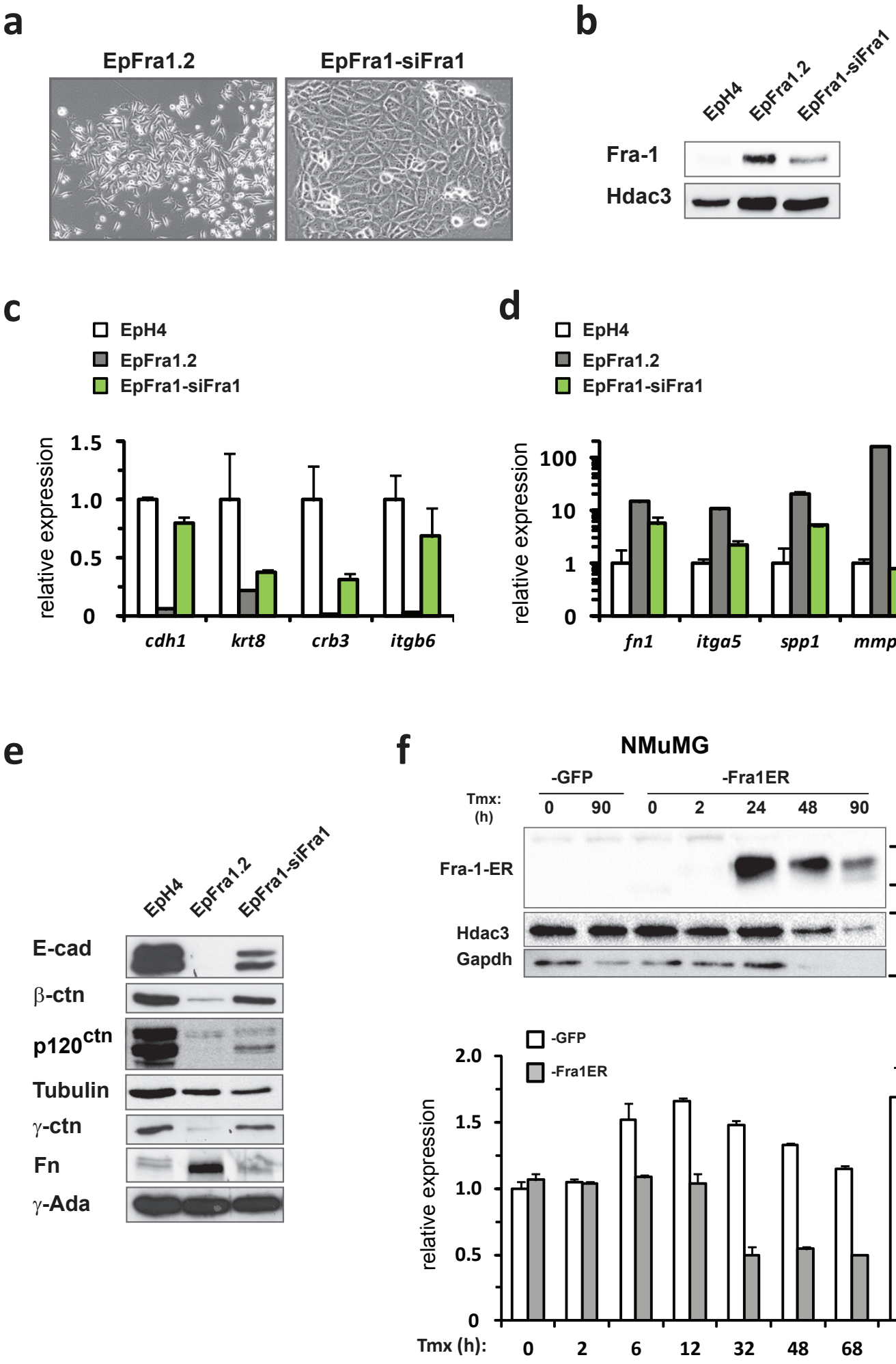

c
Distant Metastasis-Free Survival
HR = 0.77 (0.63 - 0.95)
logrank P = 0.013
Probability
Expression
low
high
FOSB
Time (months)
Number at risk
low 686 445 254 93 14 2 0
high 923 712 336 72 13 0 0


d
Overall Survival
HR = 0.67 (0.5 - 0.9)
logrank P = 0.0075
Probability
Expression
low
high
FOSB
Time (months)
Number at risk
low 816 622 324 111 17 2 0
high 299 261 150 18 4 1 0

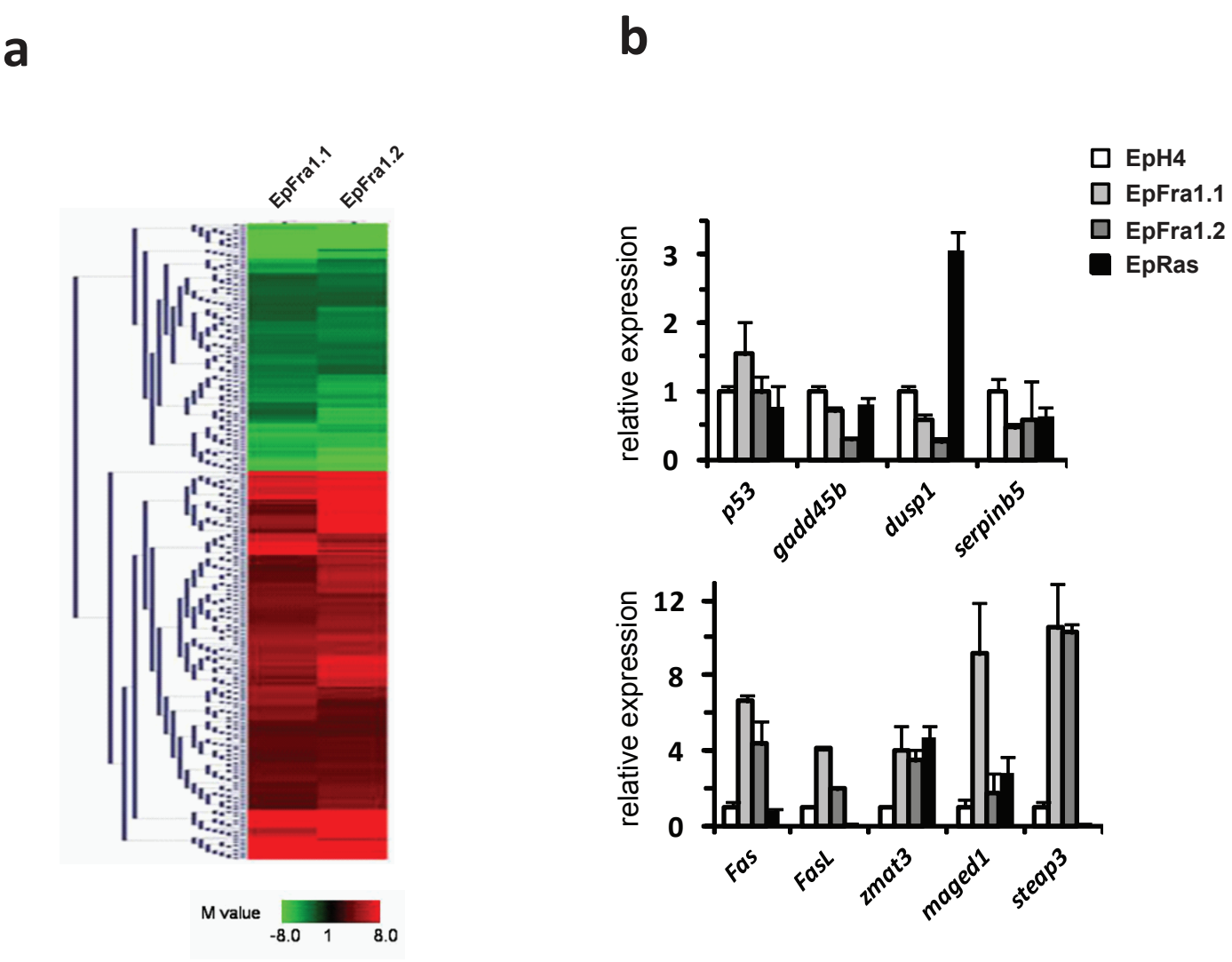
Sup Figure 1


a
EpH4
EpRas
EpRasXT
Fra-1
Fra-2
c-Fos
c-Jun
JunB
JunD
Hp1α
b
relative expression
EpH4
EpRas
EprasXT
fra1
fra2
c-fos
c
EpH4
EpFra1.1
EpFra1.2
EpRas
Phalloidin
E-cadh
β-ctn
α-ctn
γ-ctn
p120ctn
Fn
d
relative expression
EpH4
EpFra1.1
EpFra1.2
EpRas
krt7
krt8
crb3
cldn23
itgb2
itgb5
itgb6
s100a4
itga5
itgb1
spp1
mmp2
mmp3
mmp10
mmp13
e
EpH4
EpFra1.1
EpFra1.2
EpRas
Itgα5
Actin
Itgβ6
Tubulin

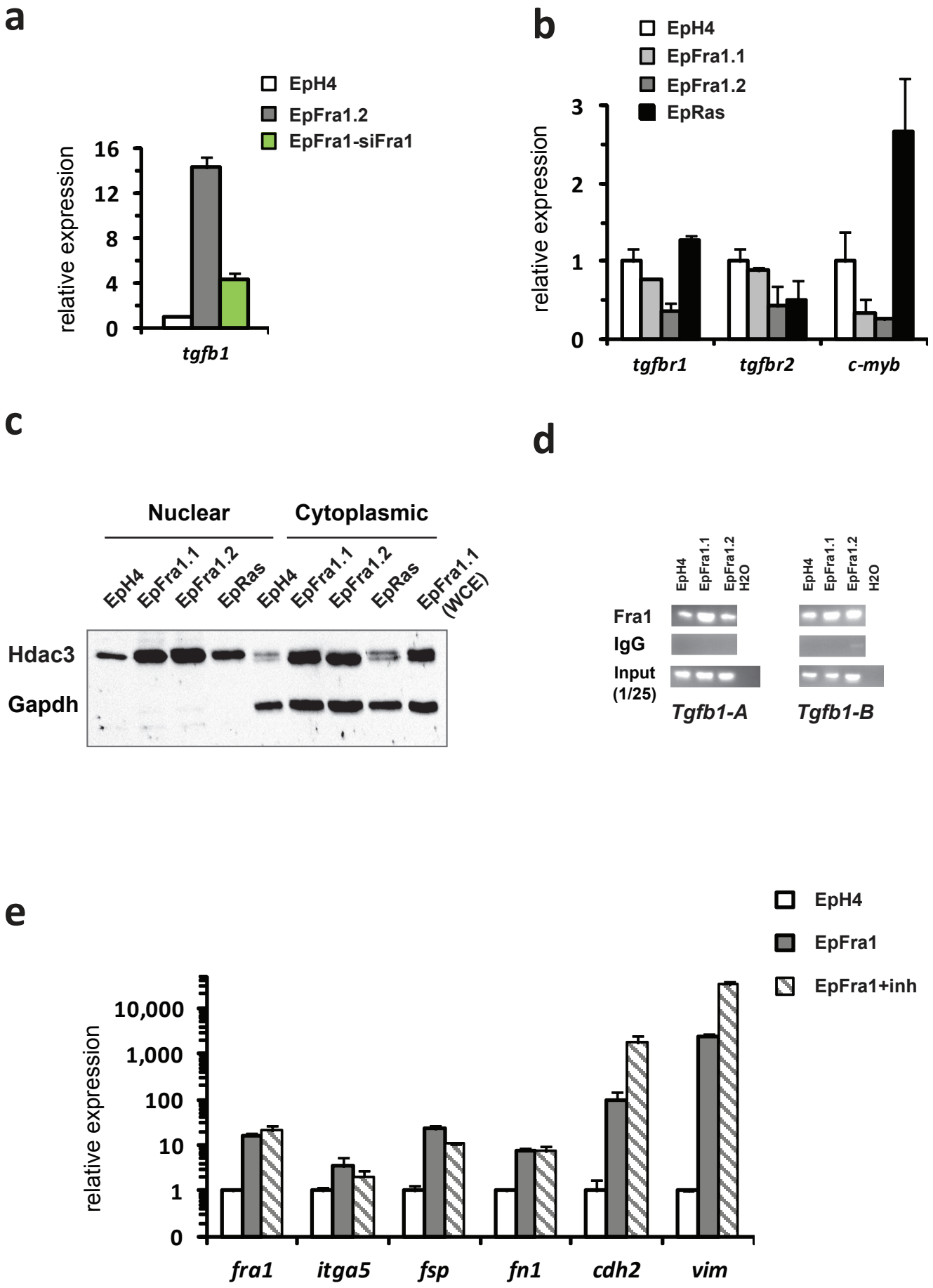
Sup Figure 2


a
EpFra1.2
EpFra1-siFra1
b
EpH4
EpFra1.2
EpFra1-siFra1
Fra-1
Hdac3
c
EpH4
EpFra1.2
EpFra1-siFra1
relative expression
1.5
1.0
0.5
0
cdh1
krt8
crb3
itgb6
d
EpH4
EpFra1.2
EpFra1-siFra1
relative expression
100
10
1
0
fn1
itga5
spp1
mmp2
e
EpH4
EpFra1.2
EpFra1-siFra1
E-cad
β-ctn
p120ctn
Tubulin
γ-ctn
Fn
γ-Ada
f
NMuMG
-GFP
-Fra1ER
Tmx: (h)
0
90
0
2
24
48
90
Fra-1-ER
Hdac3
Gapdh
100
70
55
35
-GFP
-Fra1ER
relative expression
2.0
1.5
1.0
0.5
0
Tmx (h):
0
2
6
12
32
48
68
72

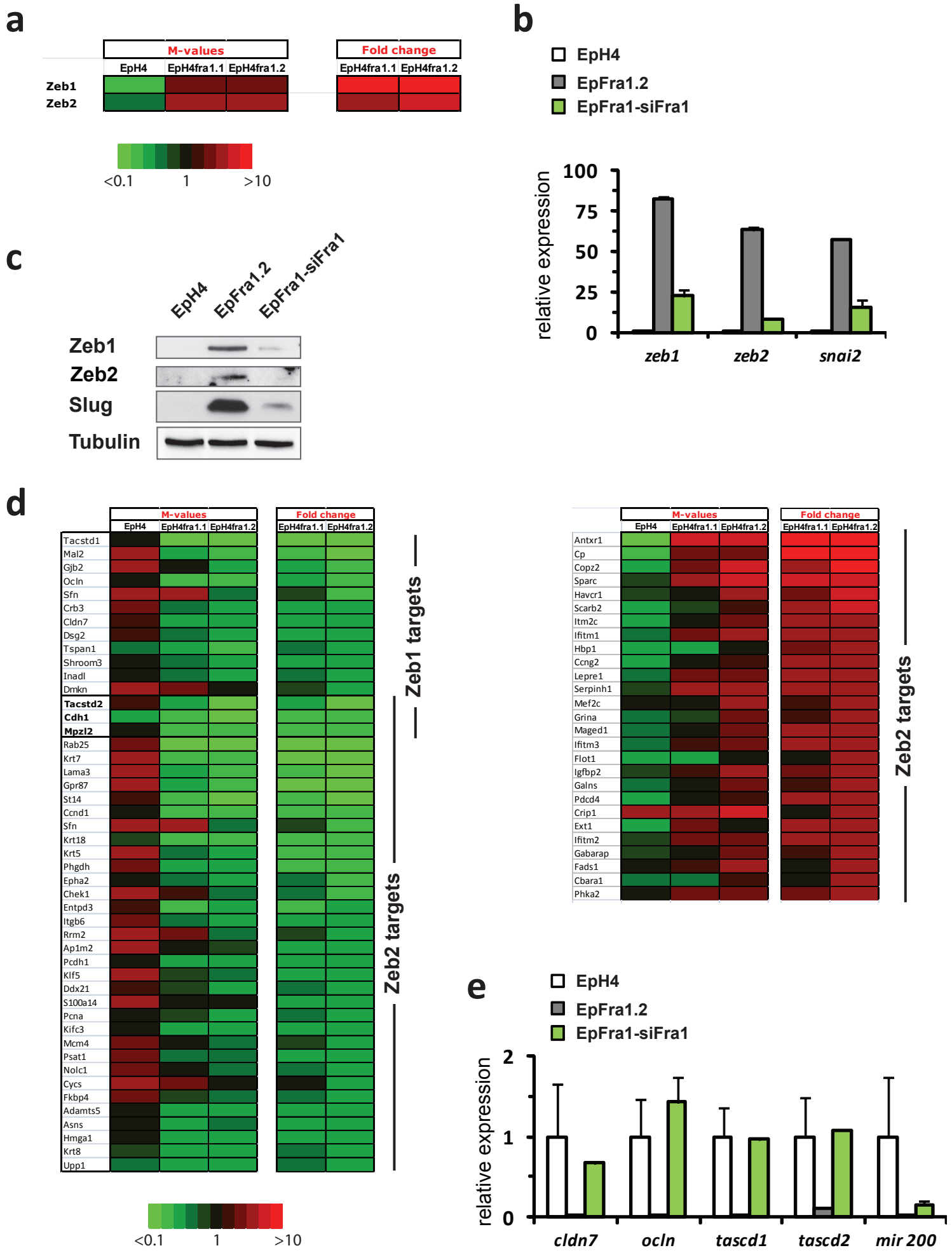
Sup Figure 3


a
EpFra1.1
EpFra1.2
M value
-8.0
1
8.0
b
EpH4
EpFra1.1
EpFra1.2
EpRas
relative expression
0
1
2
3
p53
gadd45b
dusp1
serpinb5
relative expression
0
4
8
12
Fas
FasL
zmat3
maged1
steap3

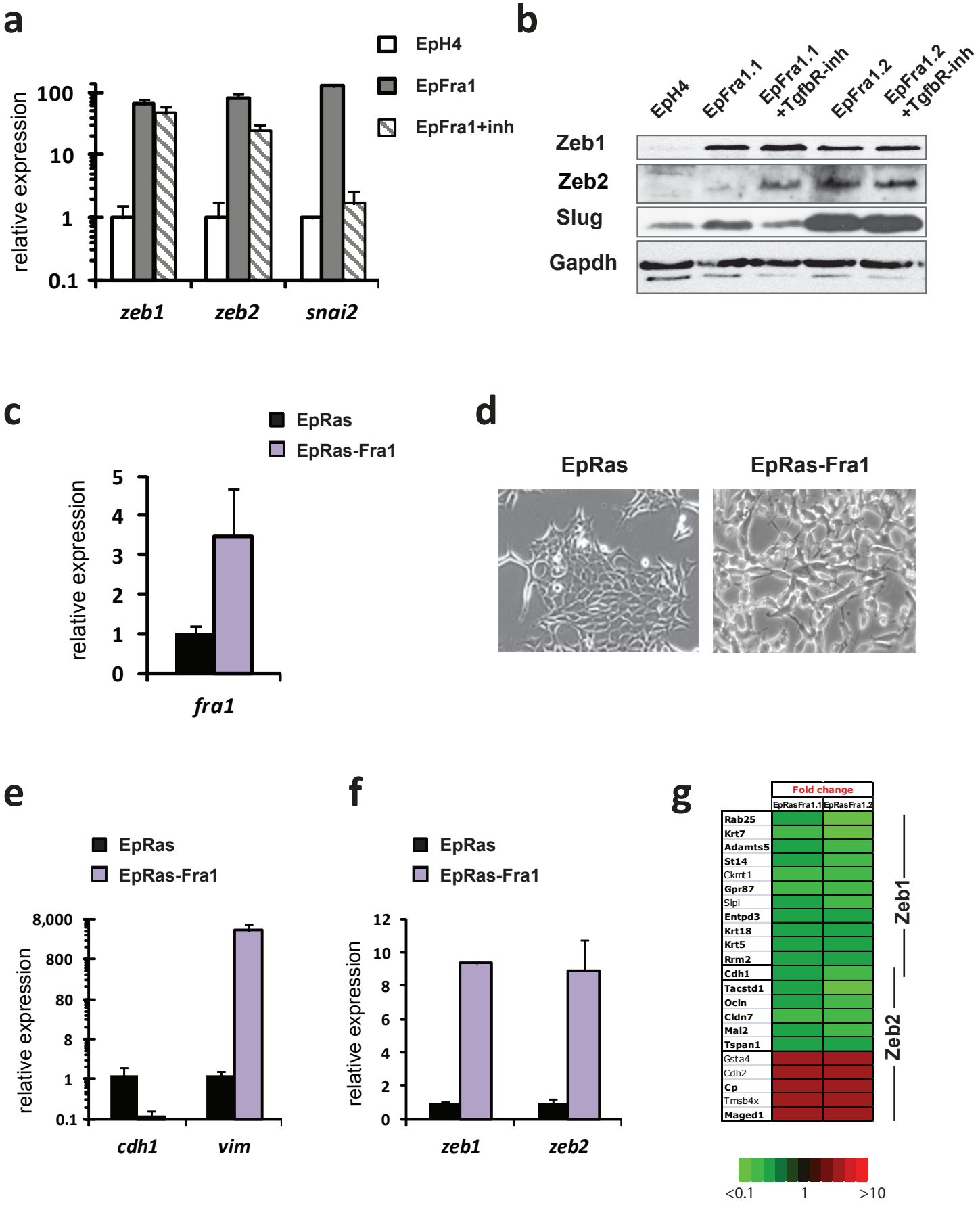
Sup Figure 4


a
EpH4
EpFra1.2
EpFra1-siFra1
relative expression
16
12
8
4
0
tgfb1
b
EpH4
EpFra1.1
EpFra1.2
EpRas
relative expression
3
2
1
0
tgfbr1
tgfbr2
c-myb
c
Nuclear
Cytoplasmic
EpH4
EpFra1.1
EpFra1.2
EpRas
EpH4
EpFra1.1
EpFra1.2
EpRas
EpFra1.1 (WCE)
Hdac3
Gapdh
d
EpH4
EpFra1.1
EpFra1.2
H2O
EpH4
EpFra1.1
EpFra1.2
H2O
Fra1
IgG
Input (1/25)
Tgfb1-A
Tgfb1-B
e
EpH4
EpFra1
EpFra1+inh
relative expression
10,000
1,000
100
10
1
0
fra1
itga5
fsp
fn1
cdh2
vim

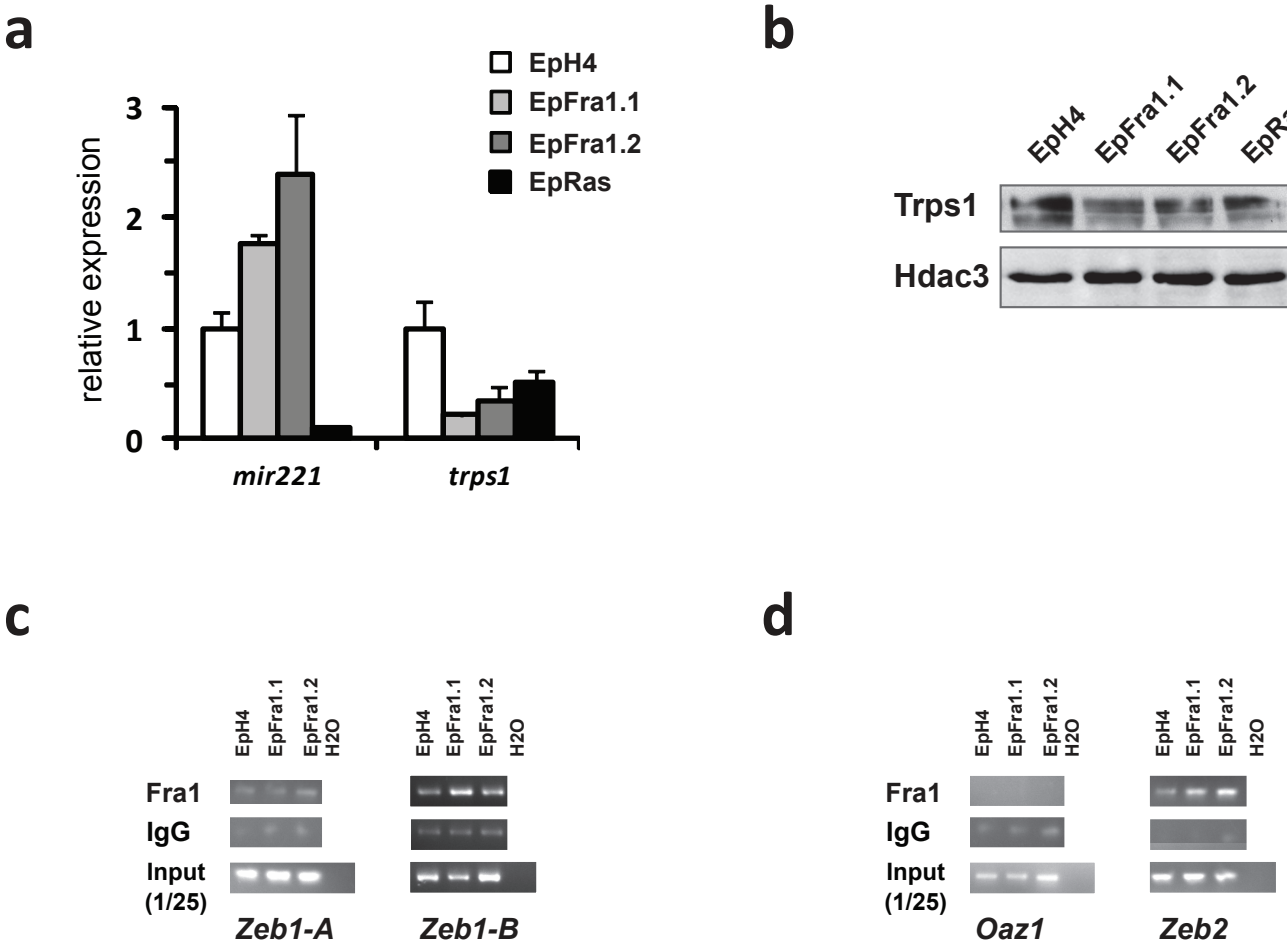
Sup Figure 5


a
M-values
Fold change
EpH4
EpH4fra1.1
EpH4fra1.2
EpH4fra1.1
EpH4fra1.2
Zeb1
Zeb2
<0.1
1
>10
b
EpH4
EpFra1.2
EpFra1-siFra1
relative expression
100
75
50
25
0
zeb1
zeb2
snai2
c
EpH4
EpFra1.2
EpFra1-siFra1
Zeb1
Zeb2
Slug
Tubulin
d
M-values
Fold change
Tacstd2
Mal2
Gjb2
Ocln
Sfn
Crb3
Cldn7
Dsg2
Tspan1
Shroom3
Inadl
Dmkn
Tacstd2
Cdh1
Mpzl2
Rab25
Krt7
Lama3
Gpr87
St14
Ccnd1
Sfn
Krt18
Krt5
Phgdh
Epha2
Chek1
Entpd3
Itgb6
Rrm2
Ap1m2
Pcdh1
Klf5
Ddx21
S100a14
Pcna
Kifc3
Mcm4
Psat1
Nolc1
Cycs
Fkbp4
Adamts5
Asns
Hmga1
Krt8
Upp1
Zeb1 targets
Zeb2 targets
Antxr1
Cp
Copz2
Sparc
Havcr1
Scarb2
Itm2c
Ifitm1
Hbp1
Ccng2
Lepre1
Serpinh1
Mef2c
Grina
Maged1
Ifitm3
Flot1
Igfbp2
Galns
Pdcd4
Crip1
Ext1
Ifitm2
Gabarap
Fads1
Cbara1
Phka2
Zeb2 targets
<0.1
1
>10
e
EpH4
EpFra1.2
EpFra1-siFra1
relative expression
2
1
0
cldn7
ocln
tascd1
tascd2
mir 200

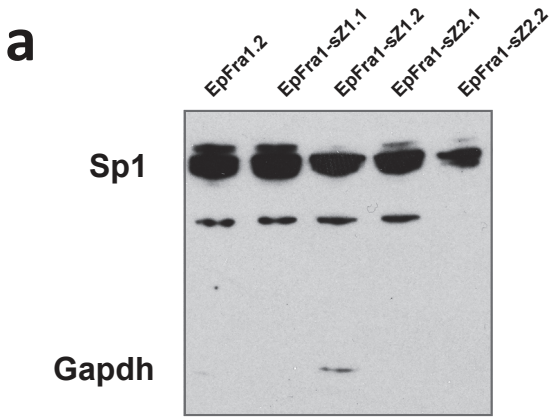
Sup Figure 6

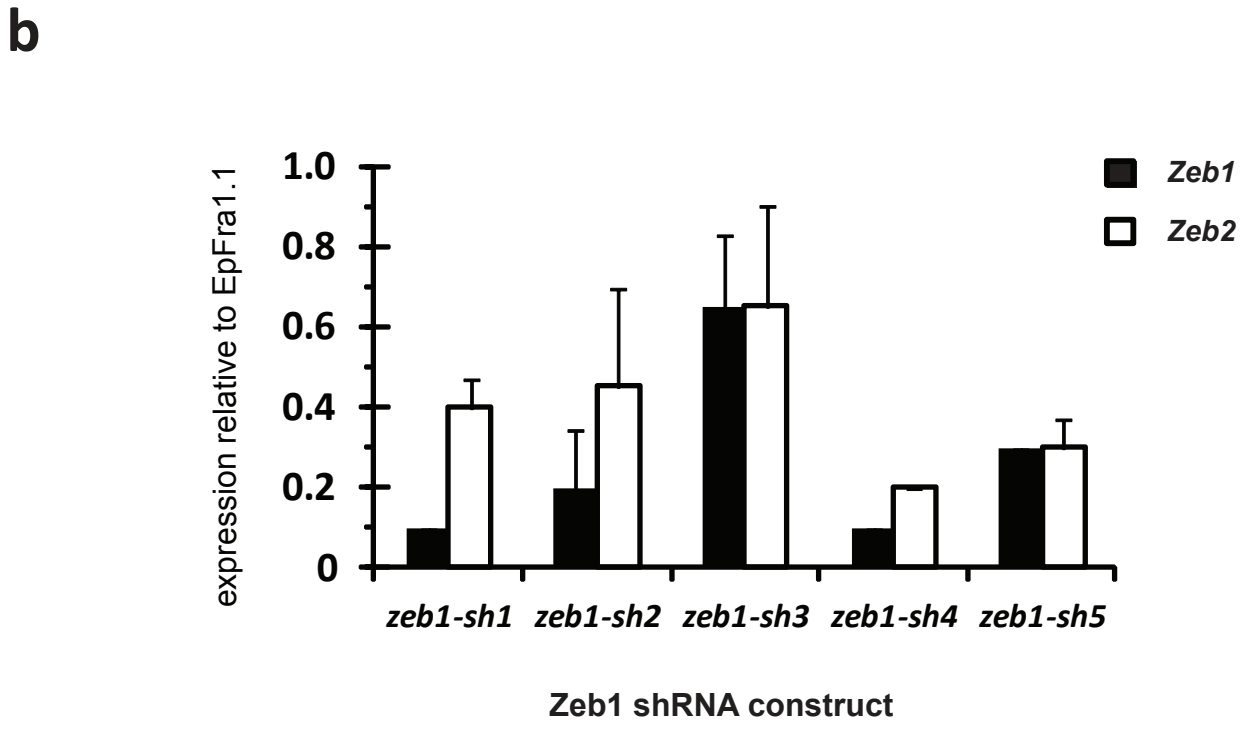

a
EpH4
EpFra1
EpFra1+inh
relative expression
100
10
1
0.1
zeb1
zeb2
snai2
b
EpH4
EpFra1.1
EpFra1.1 +TgfbR-inh
EpFra1.2
EpFra1.2 +TgfbR-inh
Zeb1
Zeb2
Slug
Gapdh
c
EpRas
EpRas-Fra1
relative expression
5
4
3
2
1
0
fra1
d
EpRas
EpRas-Fra1
e
EpRas
EpRas-Fra1
relative expression
8,000
800
80
8
1
0.1
cdh1
vim
f
EpRas
EpRas-Fra1
relative expression
12
10
8
6
4
2
0
zeb1
zeb2
g
Fold change
EpRasFra1.1
EpRasFra1.2
Rab25
Krt7
Adamts5
St14
Ckmt1
Gpr87
Slpi
Entpd3
Krt18
Krt5
Rrm2
Cdh1
Tacstd1
Ocln
Cldn7
Mal2
Tspan1
Gsta4
Cdh2
Cp
Tmsb4x
Maged1
Zeb1
Zeb2
<0.1
1
>10

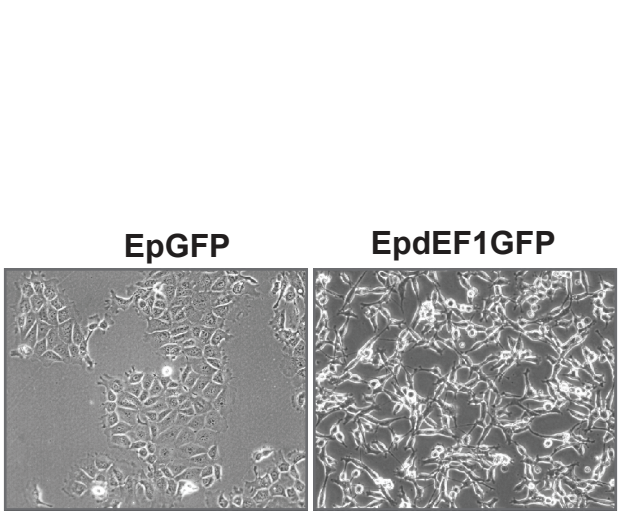
Sup Figure 7

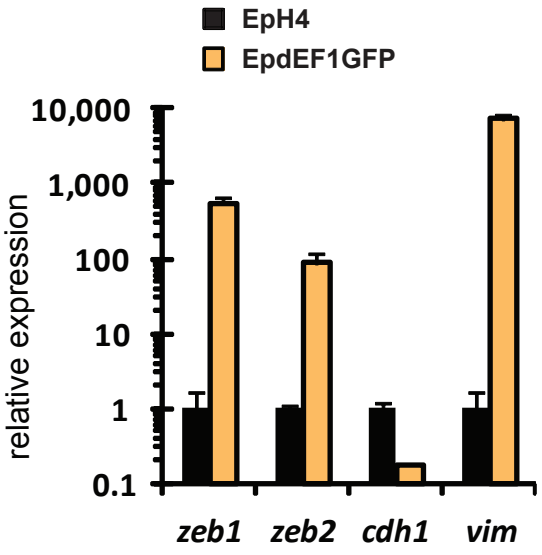

a
EpH4
EpFra1.1
EpFra1.2
EpRas
relative expression
3
2
1
0
mir221
trps1
b
EpH4
EpFra1.1
EpFra1.2
EpRas
Trps1
Hdac3
c
EpH4
EpFra1.1
EpFra1.2
H2O
Fra1
IgG
Input (1/25)
Zeb1-A
Zeb1-B
d
Oaz1
Zeb2

Sup Figure 8

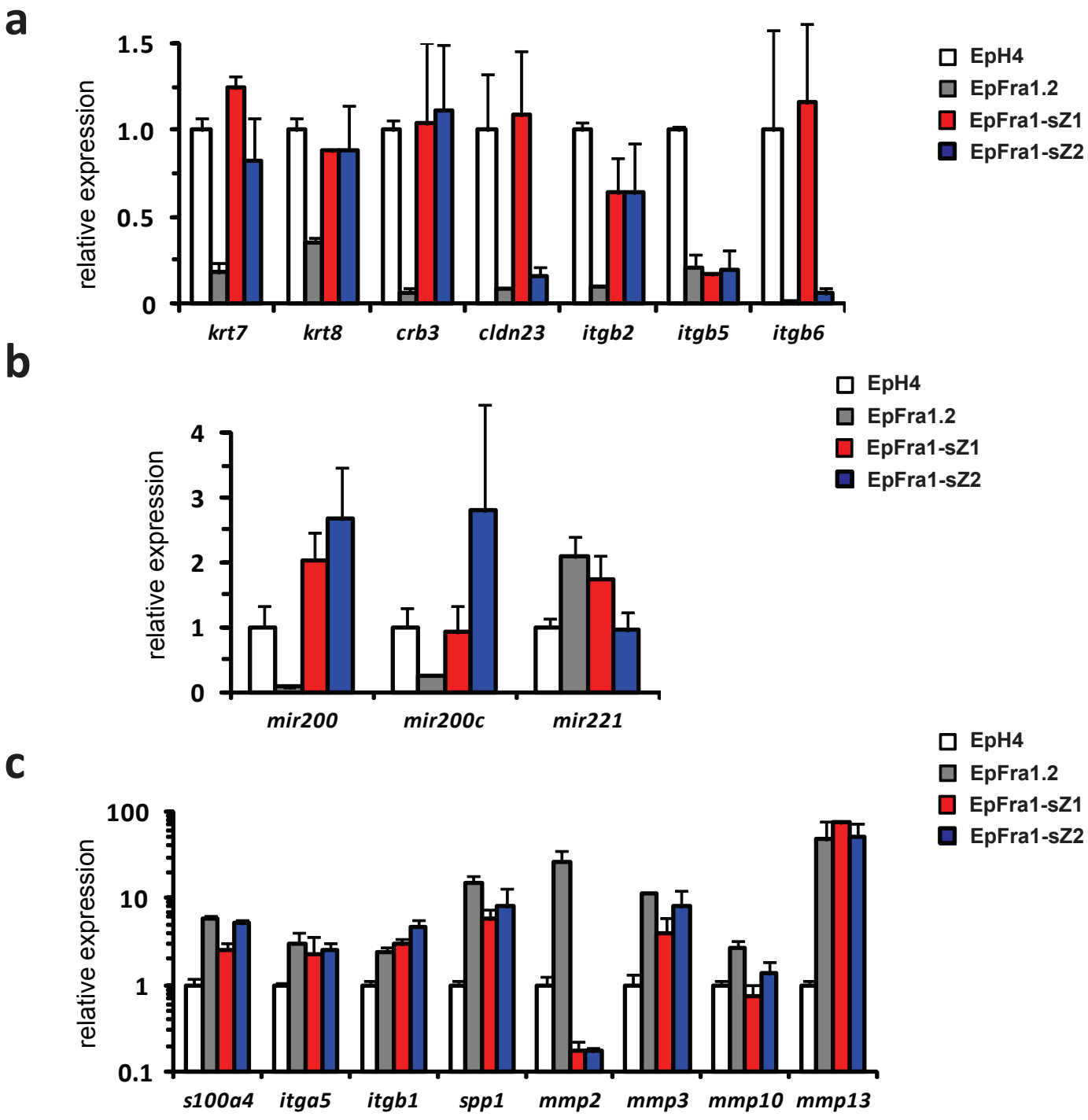

a
EpFra1.2
EpFra1-sZ1.1
EpFra1-sZ1.2
EpFra1-sZ2.1
EpFra1-sZ2.2
Sp1
Gapdh


b
expression relative to EpFra1.1
1.0
0.8
0.6
0.4
0.2
0
Zeb1
Zeb2
zeb1-sh1
zeb1-sh2
zeb1-sh3
zeb1-sh4
zeb1-sh5
Zeb1 shRNA construct

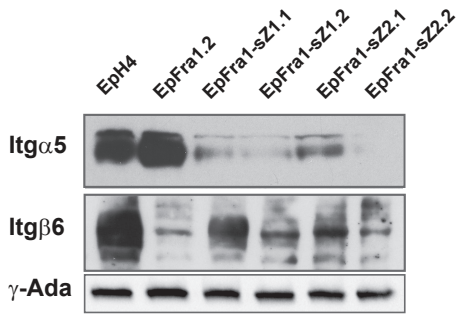

c
EpGFP
EpdEF1GFP


d
EpH4
EpdEF1GFP
relative expression
10,000
1,000
100
10
1
0.1
zeb1
zeb2
cdh1
vim

Sup Figure 9



d



Sup Figure 10

TF motifs: Genes with promoter regions [-2kb,2kb] around transcription start site containing the motif:

Up regulated set

 # genes in comparison (n): 381

Motif	Description	p value	annotated TF:
CArG box	ATGCCCATATATGGWNNT	6.57 e^{-4}	SRF
CArG box	DCCWTATATGGNCWN	1.67 e^{-3}	SRF
	NKNTTGCNYAAYNN	1.91 e^{-3}	C/EBPbeta
	NNAACATCTGGA	3.7 e^{-3}	ZNF238
	NNNNNNCNNTNTGTNCTNN	3.38 e^{-3}	GR
	NCTATAAAAR	1.09 e^{-2}	TAF TATA
	NNANNGTAAACAANNN	1.14 e^{-2}	FOXF2
CArG box	CCAWATAWGGMNMNG	1.48 e^{-2}	SRF
	GRGAAAMBBWCAGS	1.48 e^{-2}	PTF1A
CArG box	SCCAWATAWGGMNMNNNN	1.53 e^{-2}	SRF
	RTAAACA	1.61 e^{-2}	FOXF2
	GGGAGGRR	1.84 e^{-2}	MAZ
CRE	VGTGACGTMACN	2.03 e^{-2}	ATF-2

Down regulated set

 # genes in comparison (n): 246

Motif	Description	p value	annotated TF:
E-box	VSNGCAGGTGKNCNN	3.68 e^{-3}	TCF3
TRE	TGANTCA	5.27 e^{-3}	JUN
TRE	TGACTCANNSKN	7.08 e^{-3}	JUN
E-box	CAGGTG	1.02 e^{-2}	TCF3
TRE	TGAGTCAN	1.24 e^{-2}	JUN
TRE	NNNTGAGTCAKCN	1.45 e^{-2}	JUN
E-box	WNWCACCTGWNN	2.54 e^{-2}	TCF8
CRE	VGTGACGTMACN	2.54 e^{-2}	ATF-2
MYOG/E-box	RGCAGSTG	2.60 e^{-2}	
TRE	NNTGACTCANN	2.86 e^{-2}	JUN
E-box	RRCAGGTGNCV	3.06 e^{-2}	TCF3
E-box	NNYNYACCTGWVT	3.72 e^{-2}	TCF8
TRE	SRTGAGTCANC	3.72 e^{-2}	

Sup Table 1

Antibodies

antigen	supplier	cat#
a-Catenin	BD Transduction Labs	610193
Actin	Sigma	A 2066
b-Catenin	BD Transduction Labs	610154
c-Jun	Santa Cruz	sc-44
c-Myb	Millipore	05-175
E-Cadherin	BD Transduction Labs	610404
E-Cadherin	R&D	AF748
Fibronectin	Sigma	F3648
Fra-1	Santa Cruz	sc-183
Fra-2	Santa Cruz	sc-171
g-Adaptin	BD Transduction Labs	610385
Gapdh	Sigma	G8795
g-catenin	BD Transduction Labs	610253
Hdac3	Santa Cruz	sc-11417
HP1 a	Euromedex	2HP-2G9-AS
Integrin a5	Santa Cruz	sc-10729
Integrin b6	R&D	AF2389
JunB	Santa Cruz	sc-73
JunD	Santa Cruz	sc-74
Ki67	DAKO	M7249
p120ctn	BD Transduction Labs	612536
rabbit IgG	Abcam	ab46540
Slug	Cell Signaling	9585
SP1	Santa Cruz	sc-059
Trps1	Abcam	ab125197
Tubulin	Sigma	T 9026
Vimentin	Cell Signaling	3932
Zeb1	Sigma	SAB3500514
Zeb2	Santa Cruz	sc-48789

shRNA (pLKO.1 MISSION™, Sigma)

target	clones:	cat#
Fra-1	TRCN0000042683 to 42687	SHCLND-NM_010235
Zeb1	TRCN00000235850 to 235854	SHCLNV-NM_011546.2
Zeb2	TRCN00000070883 to 70887	SHCLNV-NM_015753
Control	nontarget	SHC002

Sup Table 2

gene	forward primer	reverse primer	application/notes
cdh1	AGCCATTGCCAAGTACATCC	AAAGACCGGCTGGGTAAACT	qRT-PCR
cdh2	GGGACAGGAACACTGCAAAT	CGGTTGATGGTCCAGTTTCT	qRT-PCR
cdh3	CCACAGACAGTGGAAACCCT	GATGTTCAGCACTTGAGGCA	qRT-PCR
c-fos	GGGACAGCCTTTCCTACTACCAT	GATCTGCGCAAAAGTCCTGTG	qRT-PCR
cldn23	CCAGCAGCTTTAATGGCTTT	TTGGAAGACAAGCTCAACCT	qRT-PCR
cldn7	GAGCTGCAAAATGTACGACT	AACATGGCTAAGAAGCCCAA	qRT-PCR
c-myb	CTCCCTACCTGAAGAAAGTGC	AGATCACACCACGAAGAATC	qRT-PCR
crb3	CAACTCAACCCCCAGGTGAT	AGGAGGACTCCCAGAATGGA	qRT-PCR
ctnna1	ACTTCAAATGGGACCCCAAA	TTGGTGTTTACCAGGGTTGT	qRT-PCR
ctnnb1	GTGCAATTCCTGAGCTGACA	CTTAAAGATGGCCAGCAAGC	qRT-PCR
ctnnd1	CCAATCAATTACGGGCCTTC	GTCCATGAAGGTAAGGGGAG	qRT-PCR
fn1	AGGCGGAAATTCCAATGGTG	CCCAATGCGATACATGACCC	qRT-PCR
fra-1	AGAGCTGCAGAAGCAGAAGG	CAAGTACGGGTCCTGGAGAA	qRT-PCR
fra-2	ATCCACGCTCACATCCCTAC	GTTTCTCTCCCTCCGGATTC	qRT-PCR
gapdh	AACTTTGGCATTGTGGAAGG	ACACATTGGGGGTAGGAACA	qRT-PCR
hprt	CTGGTGAAAAGGACCTCTCG	CACAGGACTAGAACACCTGC	qRT-PCR
itga5	AGCCATTTAGCCTTCAGTGT	GATGATGATCCACAACGGGA	qRT-PCR
itgb1	CAAGTGCCATGAGGGAAATG	CTGTGCTACATTCACAGTGC	qRT-PCR
itgb2	GGTGCAGCTCATCAAGAATG	TTGCCTATACTCGATGCTCC	qRT-PCR
itgb5	AGTTTGCCAAGTTCCAAAGTGAG	TTTCTGTACAGGGGGTTTGAG	qRT-PCR
itgb6	AATGGCACTTCTGCCAAAGA	GAAGGTATGTTTCCAGGCAAG	qRT-PCR
jup	GTCCCTTTGCCTTTTGTTCG	GGCTGCTCAATAAGGTTCATC	qRT-PCR
krt7	CTGGACATTGAGATCGCCAC	GAGCATTGCTTCCCATGGTT	qRT-PCR
krt8	CTGGCTTCAGCTACGGAATG	TCAGAAGACTCGGACACCAG	qRT-PCR
mir200	TATCATCAGCCTGTCTTCGG	GACAGTGCTGGATTTCTTGG	qRT-PCR: mir200-429 polycistron
mir200c	GGGTTGCTGCCAGATAAAAG	ATACTGCCGGGTAATGATGG	qRT-PCR: mir200c-141 polycistron
mir221	GCATGAACCTGGCATACAAT	CTGAAACCCAGCAGACAATG	qRT-PCR: mir 221-222 polycistron
mmp10	TGGACACTTGCACCCTCAGG	ATCTTCTTCACGGTGGGAGG	qRT-PCR
mmp13	CAGTTGACAGGCTCCGAGAA	CGTGTGCCAGAAGACCAGAA	qRT-PCR
mmp2	GGTTTCCCTAAGCTCATCGC	GCTTCCAAACTTCACGCTCT	qRT-PCR
mmp3	GTTGTGTGCTCATCCTACCC	TCATCTCCAACCCGAGGAAC	qRT-PCR
ocln	GAATGGCAAGCGATCATACC	CATCCACACTCAAGGTCAGA	qRT-PCR
rpl4	CTACTGCACTGGCAACCAAA	TCTTGGCAACCACCTTTTTC	qRT-PCR
rps29	ATGGGTCACCAGCAGCTCTA	GCCTATGTCCTTCGCGTACT	qRT-PCR
s100a4	TGAGCAACTTGGACAGCAACA	TTCCGGGGTTCCTTATCTGGG	qRT-PCR
snai1	CATGTCTGGACCTGGTTCCT	AAGGGTCCTTGAGGGAGGTA	qRT-PCR
snai2	AAAGCCTTTCTCTTGCCCTC	AGCAGCCAGACTCCTCATGT	qRT-PCR
spp1	TGGCTGAATTCTGAGGGACT	CTATAGGATCTGGGTGCAGG	qRT-PCR
tascd1	CGATCCAGAACAACGATGGG	GTGTCCTTGTCGGTTCTTCG	qRT-PCR
tascd2	AGATGAGAAGCGAACCTAGC	AGAATTAACAGGCCAACCCA	qRT-PCR
tgfb1	GTCCTTGCCCTCTACAACCA	GTTGGACAACTGCTCCACCT	qRT-PCR
tgfb2	CCCACATCTCCTGCTAATGT	CGAAGGCAGCAATTATCCTG	qRT-PCR
tgfb3	TCAGCCCAATGGAGACATAC	GGGTTGTGGTGATCCTTTTG	qRT-PCR
tgfbr-1	ACCGTGTGCCAAATGAAGAG	TTCTCCAAACCGACCTTTGC	qRT-PCR
tgfbr-2	GGACCCTACTCTGTCTGTGG	TGGAGTAGACATCCGTCTGC	qRT-PCR
trps1	AGAGAGCAAGACCAAGGATG	ATTCTTTCGCCAGAGAGAGG	qRT-PCR
vim	GTGCGCCAGCAGTATGAAAG	GCATCGTTGTTCCGGTTGG	qRT-PCR
zeb1	GCATCCAAAGAGCAAGAAGC	ACTGGGCTGCTCAAGACTGT	qRT-PCR
zeb2	CTATTCCCCTGCATCAGCAT	GGCTTGTCAGTCCTTTCTCG	qRT-PCR
Tgfb1-A	GAGGCCACTAGAAACCTAAC	CTTTGTGGTCTCTTCACTCT	ChIP qPCR: genomic
Tgfb1-B	GCTGGTTGAGAGAAGAGGAA	CAAGAAGTCCCCACGTCTC	ChIP qPCR: genomic
Zeb1 -A	CAAAGTGCGCAACTCGTCT	GGACGCTGCAGAGTTTGAAT	ChIP qPCR: genomic
Zeb1 -B	AACAGATGACTTAACGGGGG	CTGCAGCGATCAAGAATCTC	ChIP qPCR: genomic
Zeb2	CGGCTGAGGACTTTTCTGAG	CGAGGGGATCAGAGACAAGA	ChIP qPCR: genomic
Oaz1	AGTCAGCGGGATCACAGTCT	CTGGGAGCTCGATGTAGAGG	ChIP qPCR: genomic

Sup Table 3