

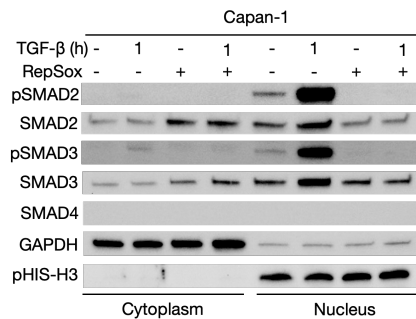
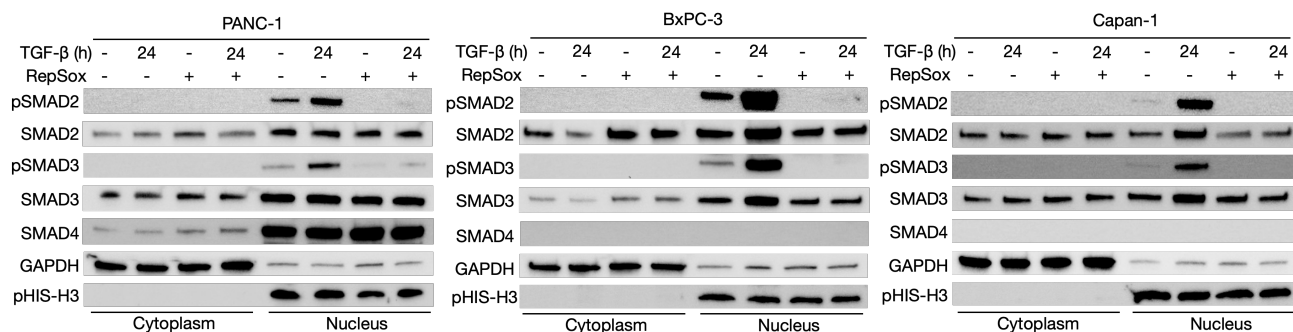
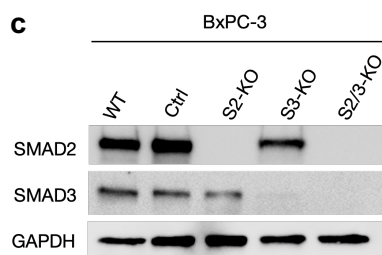
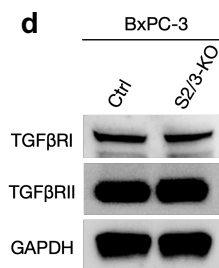
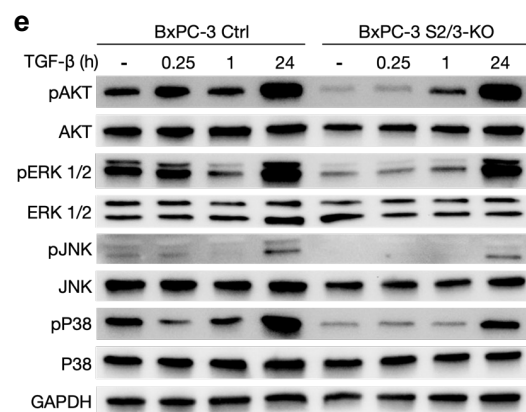
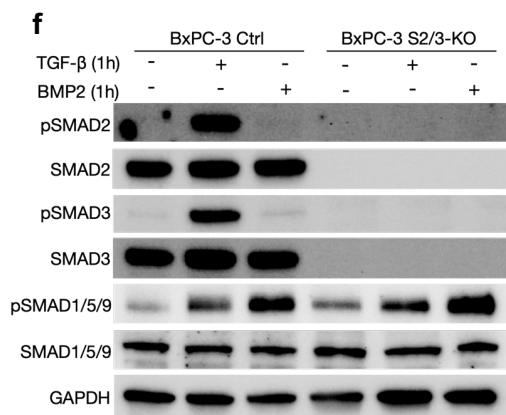
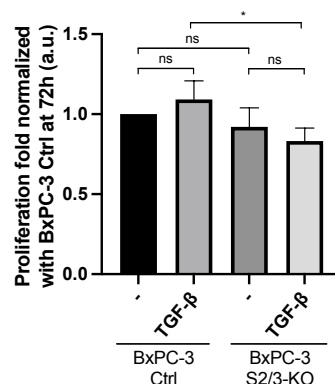
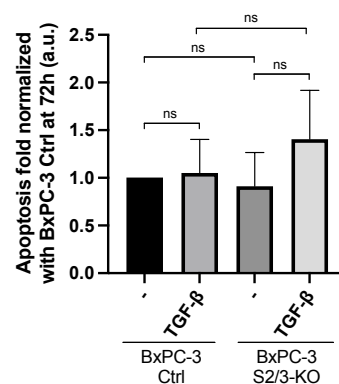
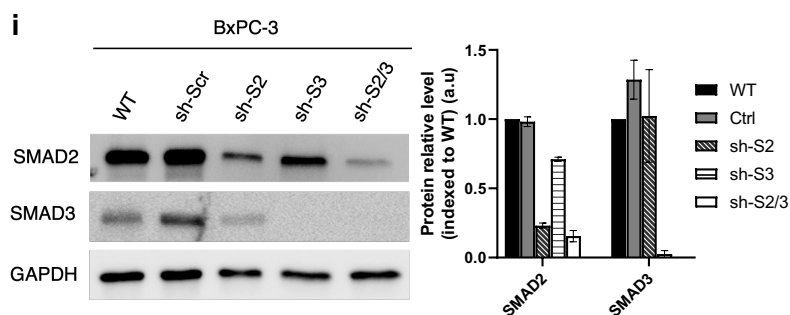
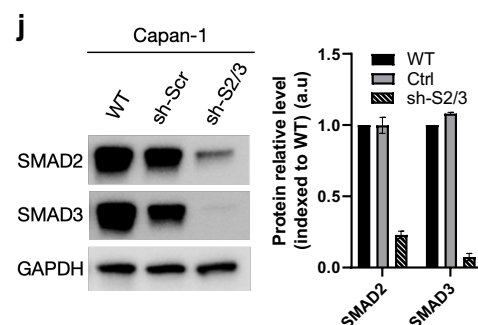
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Figure S1 – Generation of a double SMAD2/SMAD3 knockout/knockdown in BxPC-3 and Capan-1 (SMAD4-negative) pancreatic cancer cell lines. **a.** Immunoblot of phospho-SMAD2 (pSMAD2), SMAD2, phospho-SMAD3 (pSMAD3), SMAD3 and SMAD4 after treatment with TGF- β and/or TGF- β R1 kinase activity inhibitor (RepSox) for 1 h on cytoplasmic (GAPDH as control) and nuclear fractions (phospho-histone H3 (pHIS-H3) as control) prepared from SMAD4-negative Capan-1 cells. One representative image out of three is shown. **b.** Immunoblot of phospho-SMAD2 (pSMAD2), SMAD2, phospho-SMAD3 (pSMAD3), SMAD3 and SMAD4 after treatment with TGF- β and/or TGF β R1 kinase activity inhibitor (RepSox) for 24 h on cytoplasmic (GAPDH as control) and nuclear fractions (phospho-histone H3 (pHIS-H3) as control) prepared from SMAD4-positive PANC-1 cells and SMAD4-negative BxPC-3 and Capan-1 cells. One representative image out of three is shown. **c.** Immunoblot of SMAD2, SMAD3 and GAPDH on WT, control, S2-KO, S3-KO and S2/3-KO BxPC-3 cells, genetically engineered by CRISPR-Cas9. One representative image out of three is shown. **d.** Immunoblot of TGF- β receptors I (TGF- β RI) and II (TGF- β RII) and GAPDH on control and S2/3-KO BxPC-3 cells (one representative blot out of 3 independent repeats). **e.** Immunoblot of pAKT, AKT, pERK1/2, ERK1/2, pJNK, JNK, pP38, p38 and GAPDH on control and S2/3-KO BxPC-3 cells treated with TGF- β for 15 min, 1 h or 24 h. One representative image out of three is shown. **f.** Immunoblot of pSMAD2, SMAD2, pSMAD3, SMAD3, pSMAD1/5/9 and SMAD1/5/9 and GAPDH on control and S2/3-KO BxPC-3 cells treated or not with TGF- β or BMP2 for 1 h. One representative image out of three is shown. **g.** Proliferation analysis of control and S2/3-KO BxPC-3 cells treated or not with TGF- β for 72 h. Means $\pm$ SEM are shown (n=3). One-tailed Wilcoxon/Mann-Whitney test; *, p-value < 0.05; ns, not significant. **h.** Apoptosis rate analysis of BxPC-3 control and S2/3-KO BxPC-3 cells treated or not with TGF- β for 72 h. Means $\pm$ SEM are shown (n=3). One-tailed Wilcoxon/Mann-Whitney test; ns, not significant. **i.** Immunoblot of SMAD2, SMAD3 and GAPDH on WT, control (sh-Scr), S2-KD (sh-S2), S3-KD (sh-S3) and S2/3-KD (sh-S2/3) BxPC-3 cells, transfected with specific shRNA targeting SMAD2 or SMAD3. One representative image out of three is shown. SMAD2 and SMAD3 were quantified from three independent experiments and represented as graphs of mean values $\pm$ SD. **j.** Immunoblot of SMAD2, SMAD3 and GAPDH on WT, control (sh-Scr), and S2/3-KD (sh-S2/3) Capan-1 cells. One representative image out of three is shown. SMAD2 and SMAD3 were quantified from three independent experiments and represented as graphs of mean values $\pm$ SD.

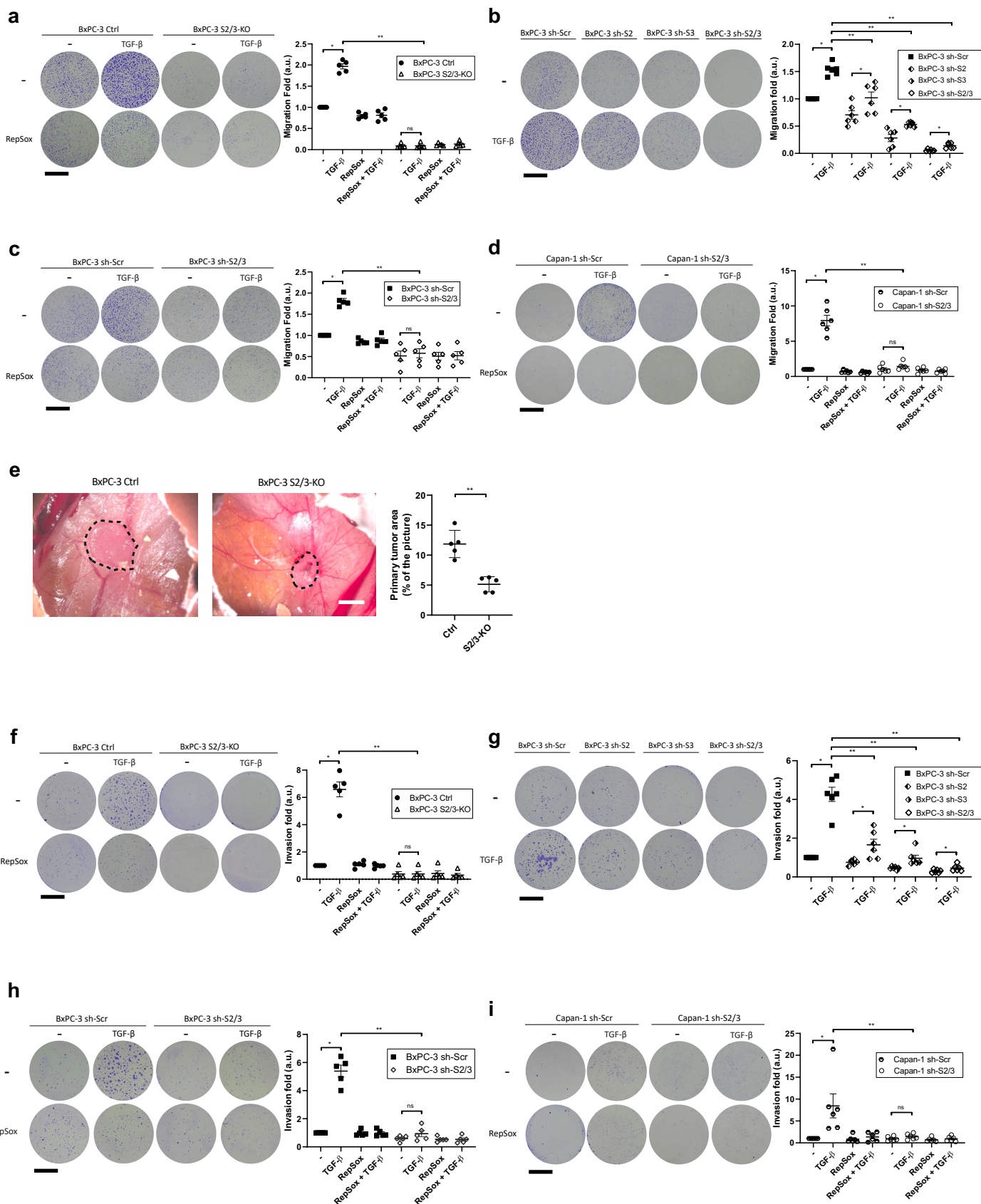


Figure S2 – SMAD2 and SMAD3 are crucial in the migratory and invasive potential of BxPC-3 and Capan-1 (SMAD4-negative) cells in response to TGF- β . **a.** Images of a transwell migration assay with control and S2/3-KO BxPC-3 cells cultured for 24 h in the presence or absence of TGF- β and/or RepSox, the TGF- β R1 kinase activity inhibitor. Scale bar = 3mm. Means $\pm$ SEM are shown (n=5). One-tailed Wilcoxon/Mann-Whitney test; **, p-value <0.01; *, p-value <0.05; *ns*, not significant. **b.** Images of a transwell migration assay with control (sh-Scr), S2-KD (sh-S2), S3-KD (sh-S3) and S2/3-KD (sh-S2/3) BxPC-3 cells cultured for 24 h in the presence or absence of TGF- β . Scale bar = 3mm. Means $\pm$ SEM are shown (n=6). One-tailed Wilcoxon/Mann-Whitney test; **, p-value <0.01; *, p-value <0.05. **c.** Images of a transwell migration assay with control (sh-Scr) and S2/3-KD (sh-S2/3) BxPC-3 cells cultured for 24 h in the presence or absence of TGF- β and/or RepSox, the TGF- β R1 kinase activity inhibitor. Scale bar = 3mm. Means $\pm$ SEM are shown (n=5). One-tailed Wilcoxon/Mann-Whitney test; **, p-value <0.01; *, p-value <0.05; *ns*, not significant. **d.** Images of a transwell migration assay with control (sh-Scr) and S2/3-KD (sh-S2/3) Capan-1 cells cultured for 72 h in the presence or absence of TGF- β and/or RepSox, the TGF- β R1 kinase activity inhibitor. Scale bar = 3mm. Means $\pm$ SEM are shown (n=6). One-tailed Wilcoxon/Mann-Whitney test; **, p-value <0.01; *, p-value <0.05; *ns*, not significant. **e.** Images of control or S2/3-KO tumors, 7 days after engraftment on chicken embryo chorioallantoic membranes. Scale bar = 5mm. Tumor mean area (horizontal bar) $\pm$ SD is represented. One-tailed Wilcoxon/Mann-Whitney; **, p-value < 0.01. **f.** Images of transwell invasion assay in matrigel with control and S2/3-KO BxPC-3 cells cultured for 72 h in the presence or absence of TGF- β and/or RepSox. Scale bar = 3mm. Graphs represent mean values (horizontal bar) $\pm$ SEM (n=5). One-tailed Wilcoxon/Mann-Whitney test; **, p-value <0.01; *, p-value <0.05; *ns*, not significant. **g.** Images of a transwell invasion assay with control (sh-Scr), S2-KD (sh-S2), S3-KD (sh-S3) and S2/3-KD (sh-S2/3) BxPC-3 cells cultured for 72 h in the presence or absence of TGF- β . Scale bar = 3mm. Graphs represent mean values (horizontal bar) $\pm$ SEM (n=6). One-tailed Wilcoxon/Mann-Whitney test; **, p-value <0.01; *, p-value <0.05. **h.** Images of a transwell invasion assay with control (sh-Scr) and S2/3-KD (sh-S2/3) BxPC-3 cells cultured for 72 h in the presence or absence of TGF- β and/or RepSox, the TGF- β R1 kinase activity inhibitor. Scale bar = 3mm. Graphs represent mean values (horizontal bar) $\pm$ SEM (n=5). One-tailed Wilcoxon/Mann-Whitney test; **, p-value <0.01; *, p-value <0.05; *ns*, not significant. **i.** Images of a transwell invasion assay with control (sh-Scr) and S2/3-KD (sh-S2/3) Capan-1 cells cultured for 96 h in the presence or absence of TGF- β and/or RepSox, the TGF- β R1 kinase activity inhibitor. Scale bar = 3mm. Graphs represent mean values (horizontal bar) $\pm$ SEM (n=6). One-tailed Wilcoxon/Mann-Whitney test; **, p-value <0.01; *, p-value <0.05; *ns*, not significant. Figure S2

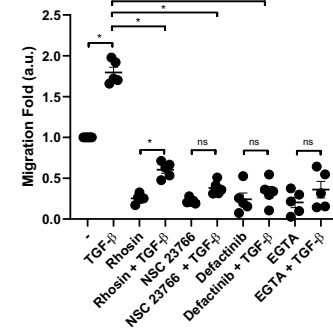
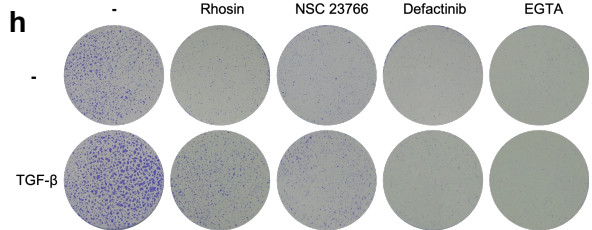
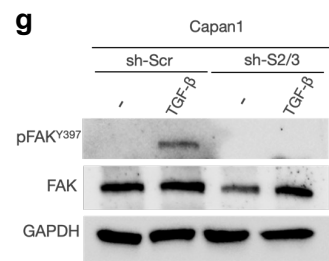
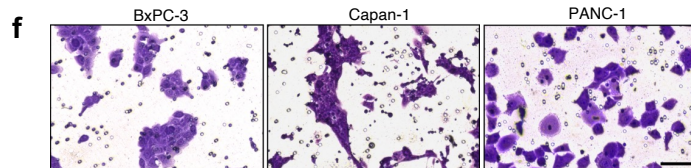
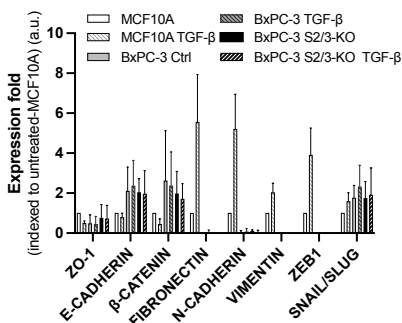
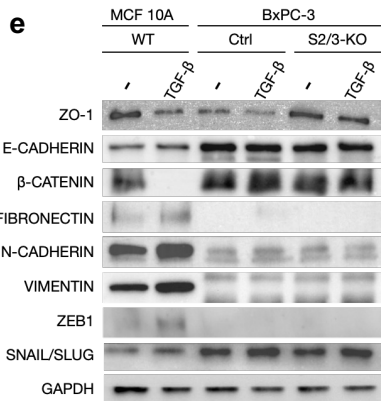
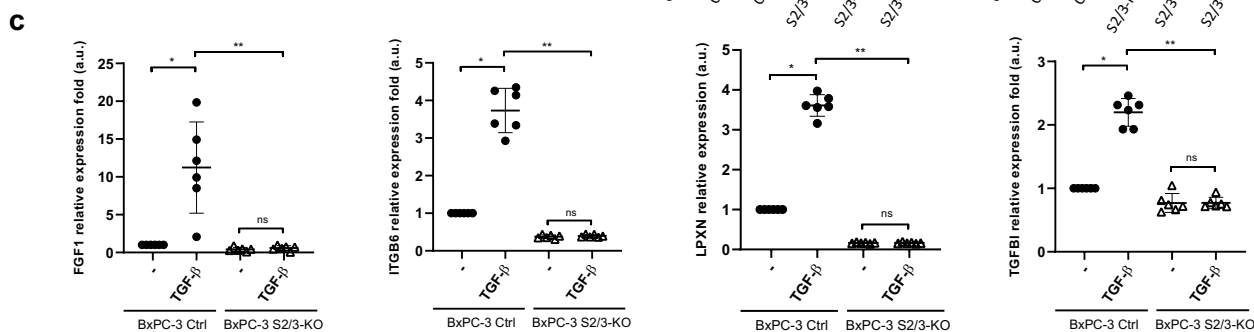
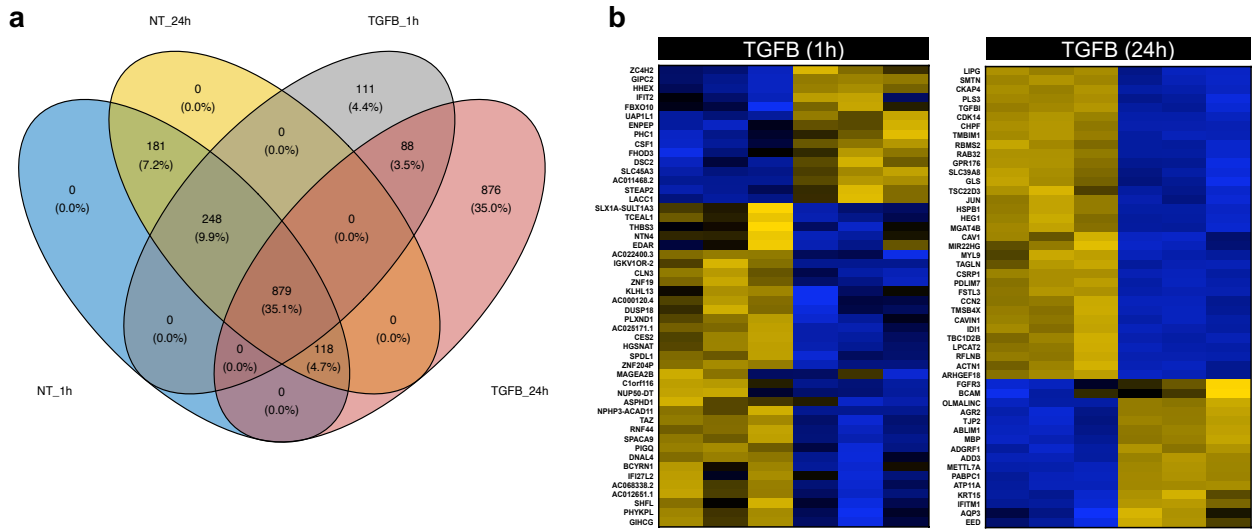


Figure S3 – SMAD2/3 initiate a collective migration transcriptional program in response of TGF- β in a SMAD4-null PDAC context. **a.** Venn diagram showing the intersection of genes with significant differential expression levels (absolute log2 fold change > 1 and adjusted p-value < 0.05) between conditions (control vs S2/3-KO) in four sets of experimental design: BxPC-3 cells untreated (after 1 h or 24 h) or treated with TGF- β (after 1 h or 24 h). **b.** Heatmaps showing the top 50 differentially expressed genes, ranked according to their adjusted p-value, between control and S2/3-KO BxPC-3 cells after 1 h or 24 h of TGF- β treatment. Clustering method: Complete; distance: Euclidean. **c.** RT-qPCR of FGF1, ITGB6, LPXN and TGFBI gene expression in control and S2/3-KO BxPC-3 cells, treated or not with TGF- β for 24 h. Graphs represent mean values (horizontal bar) $\pm$ SEM (n=6). One-tailed Wilcoxon/Mann-Whitney test; **, p-value <0.01; *, p-value <0.05; *ns*, not significant. **d.** RT-qPCR of FGF1, ITGB6, LPXN and TGFBI genes expression in S2/3-KO and S2/3-Rescue cells, treated or not with TGF- β for 24 h. Graphs represent mean values (horizontal bar) $\pm$ SEM (n=6). One-tailed Wilcoxon/Mann-Whitney test; **, p-value <0.01; *, p-value <0.05. **e.** Immunoblot of Zonula-occludens-1 (ZO-1), E-CADHERIN, β -CATENIN, FIBRONECTIN, N-CADHERIN, VIMENTIN, ZEB1, SNAIL/SLUG, and GAPDH on MCF 10A (SMAD4⁺ breast cancer cell line), control and S2/3-KO BxPC-3 (SMAD4⁻) cell lines treated or not with TGF- β for 5 days. Quantification was done on three independent experiment and results are presented as mean index $\pm$ SEM to untreated-MCF10A cells. **f.** High magnification of transwell migration assay after TGF- β treatment (24h), showing collective migration of BxPC-3 and Capan-1 but not PANC-1 cells. Black scale bar = 50 μ m. **g.** Immunoblot of phospho-Focal Adhesion Kinase (pFAK^{Y397}), Focal Adhesion Kinase (FAK) and GAPDH on control (sh-Scr) and S2/3-KD (sh-S2/3) Capan-1 cells treated or not with TGF- β for 24 hours. Immunoblot was repeated three times, one representative image is shown. **h.** Images of a transwell migration assay with control BxPC-3 cells cultured for 24 h in the presence or absence of RhoA inhibitor (Rhosin), Rac-1 inhibitor (NSC 23766), phospho-FAK inhibitor (Defactinib), the calcium-chelator (EGTA) and TGF- β . Scale bar = 3mm. Graphs represent mean values $\pm$ SEM (n=5). One-tailed Wilcoxon/Mann-Whitney test; *, p-value <0.05; *ns*, not significant.

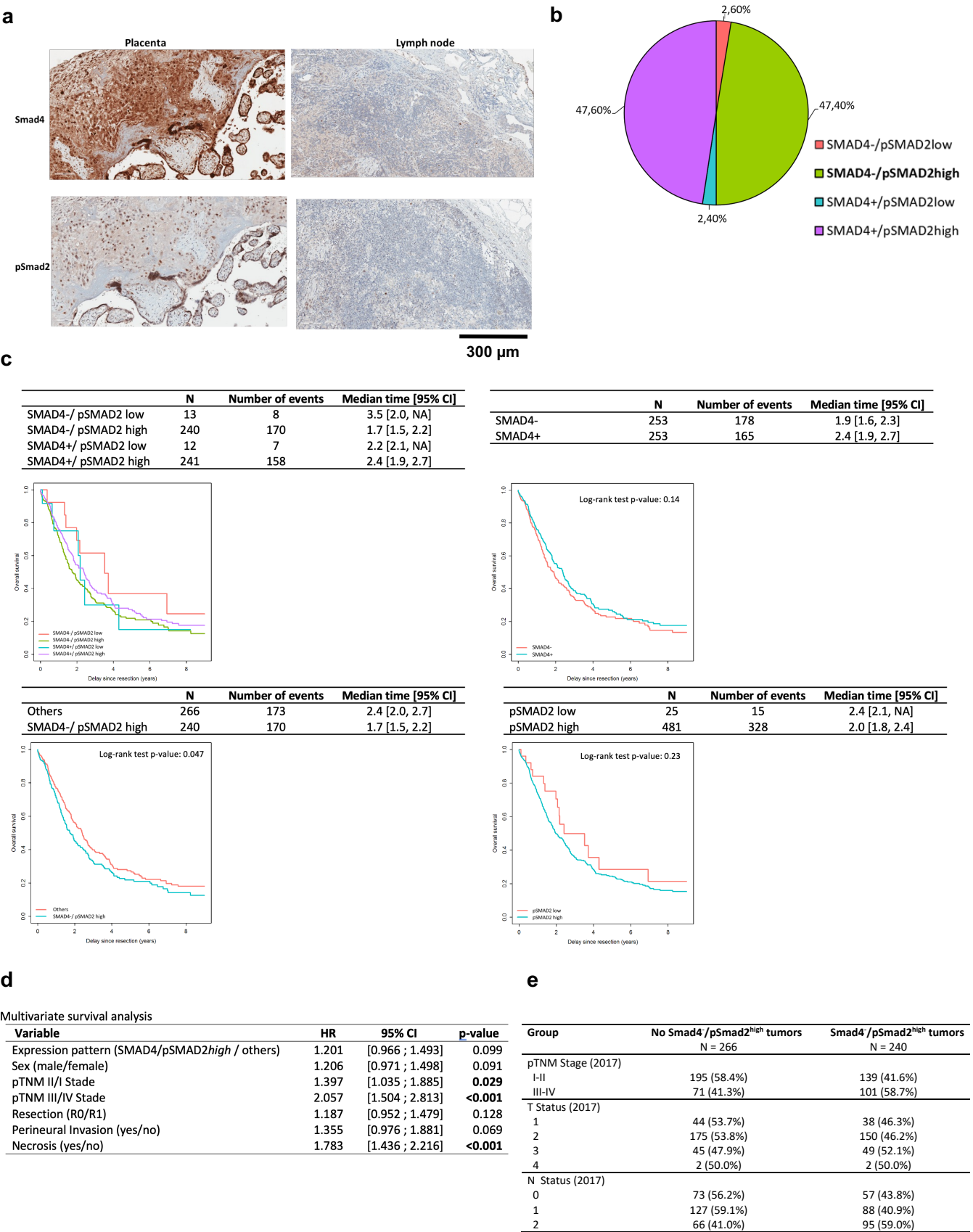


Figure S4 – Distribution and multivariate analyses of clinical data from 506 PDAC patients

a. Immunohistochemistry for SMAD4 and pSMAD2 in Negative (lymphocytes in the lymph node) and positive (trophoblastic cells of the placenta) control tissues. Representative images are shown.

b. Graphic representation of the percentage of each group of human PDAC according to SMAD4 and pSMAD2 status.

c. Survival curves of patient cohort considering each group of human PDAC according to SMAD4 and pSMAD2 status or only SMAD4 expression, or only pSMAD2 level, or the SMAD4-/pSMAD2^{high} tumors *versus* the other group.

d. Multivariate survival analysis including the model of pTNM staging.

e. Tumor distribution according to the pTNM stage, the T status and the N status are correlated with the SMAD4-/pSMAD2^{high}.

Differentially expressed genes between control and S2/3-KO BxPC3 cells after TGF-β1 treatment.

TGFB_1h (111)		TGFB_24h (876)															
AC011468.2	AL109976.1	RCSD1	COBL	TMPS55	ZNF165	PHLDA1	FLT3	CXKC5	SULT1A3	NAALAD2	CYP3A5	GPR160	PPARGC1B	GCSHP5	MAP1LC3B	GOLGA6L5P	LGAL57B
PAGE1	DNAL4	AC020915.5	AL590708.1	SECL	FGD3	PXDC1	GDPD1	SLC31A2	CHRNA8	H56ST2	UNC5B-AS1	HCP5	PRKG2	RIPOR1	MIR193BHG	ZNF710-AS1	ROS1
CCR5AS	PLXND1	CABP4	AC100860.1	TMEM255A	AC008014.1	GABARAPL1	ELK3	DISP2	DIQ2	AC110619.1	C9orf152	GFGR3	LINC01089	RARS1	IFFO2	HIC1	LPXN
EBI3	CARF	AL162151.2	LYZ	PPM1H	PABPC1	TRABD2A	UBLCF1	FAM166C	GJB2	ELF5	KLRC2	B4GALNT3	ADIRF	EPPK1	MYX3B	COL1A1	ZNF365
LINC02015	TENT5B	FAM96AP2	METTL7A	EV2B	MZF1	C1orf122	CRIP2	TSPAN5	FGF1	DMD	SNAI3	CCDC80	ILDR1	TRBC2	ENL6	KPNA7	CFAP57
OXC72	IFI27L2	AC136475.3	CCL22	MAP3K5	MMS1	PHL2	SLC224A	CYP26B1	KIAA1755	RAB34	RALGPS1	TKK	ABLIM1	TMEM98	KLHL25	STAT4	NDP
AZGP1	RNF44	AL138885.4	SOX21-AS1	RAB3A	LRTOMT	SLC36A1	MYADM	SLC1A4	NDRG4	RAB34	RN7SL2	ARHGAP30	AKR1C3	ADCY7	RNF130	GLUPR2	AC114501.2
AL596214.1	LRRC37A3	SLC6A20	LINC02635	SASH1	SYOE2	ZFP1	ITPR2	ESAM	FAM20A	LINC02377	GDGF6	H2AC19	CXADR	PLAAT1	SLCSA12	MIR22HG	PDLIM3
AC104083.1	ZNF19	AC016682.1	MMRN2	PHEX	SYTL5	CLTB	LRRRC8C	ACTN1	TFEB	STR6A	CYP4B1	TMEM63C	RAD9A	RAB11FIP3	AP000769.1	AC090994.1	NID1
AGAP5	THAP7-AS1	CCL17	ERP27	LCCA4	CEMP1	TCF7L1	ZNF561-AS1	MFS2D2A	AC012645.1	SLC26A11	KCNJ2-AS1	LINC01186	GA56-AS1	TMBIM1	SNAI2	RABGAP1L-DT	HTR1D
BEST1	HNF4G	FMO3	KRT15	MALAT1	DDX12P	DNAJB5	SIPA1	FSTL3	CRYBA2	LINC02257	AC027020.2	ITGA9-AS1	PER2	GNG2	STARD9	FILIP1L	MAF
AC091390.5	SHFL	PRR15L	MCPIH1-AS1	PTPRZ1	NUTM2D	KLK7	AC008687.7	CCDC74A	PLPP4	PFRC1	AC188616.1	KCNH3	CTSC	AP3B2	LAMC2	LPAR5	IL2RB
CXCL2	SPACA9	AC097709.1	EPHA7	HOOK1	DNAAF3	PRDM8	NDRG1	PIK3P1	CREB5	LINC02863	MWH7B	POF1B	ADD3	INTS12	SMTN	MFAP3L	NKX6-1
FBXO2	SRCAP	BX470111.1	CAPN8	GDPL1	LLGL2	GLA	LIPG	PRSS27	AQP1	AC021733.4	AC140479.7	EXOC6	ANK1	RBM52	RAB32	SHISA4	MYCT1
RAET1K	PHYKPL	LACC1	SLX1A-SULT1A3	AC021733.4	AC140479.7	EXOC6	ANK1	RBM52	RAB32	BMP5	CA9	PRODH	AC005083.1	VGLL3	NHCP1	LACTB	CSDC2
STX19	THB53	PHC1	ALS12274.1	BMP5	CA9	PRODH	AC005083.1	VGLL3	NHCP1	FAM183A	C15orf62	NEAT1	CHEK2	TPM4	CDC92	PLEKHG1	NOG
ARHGEF37	EDAR	HHEX	AC104695.2	F5	OLMALINC	AC008771.1	AC009005.1	RAB24	EMP3	DSC2	AC022826.2	BCAS1	ARRB2	RDH13	PDPN	TNFAIP1	PTGS2
GIPC2	AC008443.1	CSF1	HLA-F-AS1	FUT9	PLAC8	SLC25A21	RCCD1	FAM177A1	STAT5A	MAP6D1	LCN2	AP001273.1	LRRCE1	UBE2D3	ANTXR2	MIR181A2HG	NK01
IL131RA	ZNF204P	ASPHD1	LINC02009	FMO6P	LCN2	AP001273.1	LRRCE1	UBE2D3	ANTXR2	PIGQ	SH3BGR	LYNX1-SLURP2	TGFB3	C11orf54	EZR	FBLN5	MOST2P
ENPEP	MAGEA2B	SPDL1	AC074141.1	FHOD3	FAM229A	MYO16	COL5A3	CCL2	AC068896.3	NTN4	IGKV1OR-2	SCG5	IFIT2	AC000120.4	ASPHD1	LINC02009	PIGQ
FBXO10	INPP51	LBDH1	AC093010.3	IL17RE	SCS5	TMEM44-AS1	AC012651.1	SLCSA5	ALDH1A1	PLD6	IKZF2	PLK3	MGLL	AC011462.5	TMEM44-AS1	AC012651.1	HGSNAT
SLC45A3	TGM1	BX284668.5	AC123768.2	IFI27	AC000120.4	ASPHD1	LINC02009	AC092811.1	STEAP4	KRT13	PLEKH1	TPCN1	RRA5	FES	AL590004.3	CLN3	AL137060.6
STEAP2	MAST1	LBHD1	AC093010.3	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313	TCEAL1	IGKV1OR-2
CDYL2	AC068338.2	SPDL1	AC074141.1	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313	TAZ	NHPH3-ACAD11
UAP1L1	AC008267.5	BX284668.5	AC123768.2	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313	NUP50-DT	
LACC1	SLX1A-SULT1A3	LBHD1	AC093010.3	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		
ZC4H2	AC092720.3	SPDL1	AC074141.1	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		
PHC1	ALS12274.1	LBHD1	AC093010.3	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		
HHEX	AC104695.2	SPDL1	AC074141.1	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		
DSC2	AC022826.2	BX284668.5	AC123768.2	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		
CSF1	HLA-F-AS1	LBHD1	AC093010.3	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		
MAP6D1	WHAMMP3	SPDL1	AC074141.1	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		
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DUSP18	LMF1	LBHD1	AC093010.3	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		
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CE2	GPR1	LBHD1	AC093010.3	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		
AC025171.1	MTTP	SPDL1	AC074141.1	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		
BCYRN1	AC022400.3	LBHD1	AC093010.3	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		
KLHL13	GHCG	SPDL1	AC074141.1	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		
C1orf116	OR2A20P	LBHD1	AC093010.3	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		
AL132712.2	ADORA2A	SPDL1	AC074141.1	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		
BX284668.5	AC123768.2	LBHD1	AC093010.3	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		
LBHD1	AC093010.3	SPDL1	AC074141.1	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		
SPDL1	AC074141.1	LBHD1	AC093010.3	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		
NTN4	AC114267.1	SPDL1	AC074141.1	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		
TMEM44-AS1	AC012651.1	LBHD1	AC093010.3	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		
HGSNAT	AC079594.2	SPDL1	AC074141.1	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		
CLN3	AL137060.6	LBHD1	AC093010.3	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		
TCEAL1	IGKV1OR-2	SPDL1	AC074141.1	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		
TAZ	NHPH3-ACAD11	LBHD1	AC093010.3	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		
NUP50-DT		SPDL1	AC074141.1	IFIT2	AC000120.4	ASPHD1	LINC02009	LINC00615	FGFBP3	AC007342.5	HDAC9	CSR1	SLC46A3	TNFRSF19	LINC00313		

TGFB_1hTGFB_24h (88)		TGFB_24h (876)															
ZNF816-ZNF321P	NUAK1	RCSD1	COBL	TMPS55	ZNF165	PHLDA1	FLT3	CXKC5	SULT1A3	NAALAD2	CYP3A5	GPR160	PPARGC1B	GCSHP5	MAP1LC3B	GOLGA6L5P	LGAL57B
MGAM2	CNCJ15	AC020915.5	AL590708.1	SECL	FGD3	PXDC1	GDPD1	SLC31A2	CHRNA8	H56ST2	UNC5B-AS1	HCP5	PRKG2	RIPOR1	MIR193BHG	ZNF710-AS1	ROS1
COLEC11	F3	CABP4	AC100860.1	TMEM255A	AC008014.1	GABARAPL1	ELK3	DISP2	DIQ2	AC110619.1	C9orf152	GFGR3	LINC01089	RARS1	IFFO2	HIC1	LPXN
CH25H	AMIG02	AL162151.2	LYZ	PPM1H	PABPC1	TRABD2A	UBLCF1	FAM166C	GJB2	ELF5	KLRC2	B4GALNT3	ADIRF	EPPK1	MYX3B	COL1A1	ZNF365
MUC5B	ZSWIM4	FAM96AP2	METTL7A	EV2B	MZF1	C1orf122	CRIP2	TSPAN5	FGF1	DMD	SNAI3	CCDC80	ILDR1	TRBC2	ENL6	KPNA7	CFAP57
CLPSL1	ROBO1	AC136475.3	CCL22	MAP3K5	MMS1	PHL2	SLC224A	CYP26B1	KIAA1755	RAB34	RALGPS1	TKK	ABLIM1	TMEM98	KLHL25	STAT4	NDP
FAM184B	TMEM92	AL138885.4	SOX21-AS1	RAB3A	LRTOMT	SLC36A1	MYADM	SLC1A4	NDRG4	RAB34	RN7SL2	ARHGAP30	AKR1C3	ADCY7	RNF130	GLUPR2	AC114501.2
CP2	PPP1R14B-AS1	SLC6A20	LINC02635	SASH1	SYOE2	ZFP1	ITPR2	ESAM	FAM20A	LINC02377	GDGF6	H2AC19	CXADR	PLAAT1	SLCSA12	MIR22HG	PDLIM3
LAMB4	MSX2	AC016682.1	MMRN2	PHEX	SYTL5	CLTB	LRRRC8C	ACTN1	TFEB	STR6A	CYP4B1	TMEM63C	RAD9A	RAB11FIP3	AP000769.1	AC090994.1	NID1
N4BP2L1	CAMK2N1	CCL17	ERP27	LCCA4	CEMP1	TCF7L1	ZNF561-AS1	MFS2D2A	AC012645.1	SLC26A11	KCNJ2-AS1	LINC01186	GA56-AS1	TMBIM1	SNAI2	RABGAP1L-DT	HTR1D
LINC00342	LHX5	FMO3	KRT15	MALAT1	DDX12P	DNAJB5	SIPA1	FSTL3	CRYBA2	LINC02257	AC027020.2	ITGA9-AS1	PER2	GNG2	STARD9	FILIP1L	MAF
SLC16A6	STXBP1	PRR15L	MCPIH1-AS1	PTPRZ1	NUTM2D	KLK7	AC008687.7	CCDC74A	PLPP4	PFRC1	AC188616.1	KCNH3	CTSC	AP3B2	LAMC2	LPAR5	IL2RB
AC016588.2	CAMK2N2	AC097709.1	EPHA7	HOOK1	DNAAF3	PRDM8	NDRG1	PIK3P1	CREB5	LINC02863	MWH7B	POF1B	ADD3	INTS12	SMTN	MFAP3L	NKX6-1
AC090517.5	SLCA43	BX470111.1	CAPN8	GDPL1	LLGL2	GLA	LIPG	PRSS27	AQP1	AC021733.4	AC140479.7	EXOC6	ANK1	RBM52	RAB32	SHISA4	MYCT1
AC006504.5	KIAA1191	AC021733.4	AC140479.7	EXOC6	ANK1	RBM52	RAB32	SHISA4	MYCT1	FAM183A	C15orf62	NEAT					

Table S1. Differentially expressed genes between control and S2/3-KO BxPc-3 cells after TGF-β1 treatment

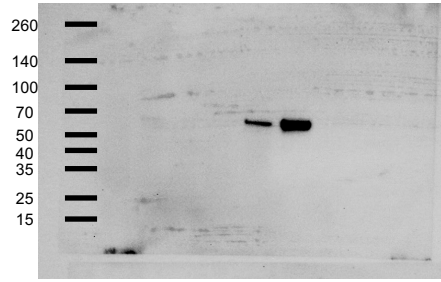
SMAD2/3 putative targets in response to TGF-β1, in the absence of SMAD4.

SMAD2/3 targets after TGF-β1 treatment, in the absence of SMAD4 (144)		
AC020915.5	FILIP1L	NLRP1
ABLM2	FLG	NOG
AC004870.2	FN1	ODF3L1
AC008687.4	FOXL1	PCDHGC5
AC010343.3	GCNT3	PDLIM7
AC011294.1	GDPD5	PIK3IP1
AC037198.1	GFPT2	PLEKHG1
AC090994.1	GJB2	PODXL
AC114501.2	GOLGA8G	POU2F2
ACKR3	GPR132	PROC
ADAM19	GPR157	PRODH
ADAMTS6	H19	PTGS2
ADH7	HAPLN3	PTPRB
AGR2	HIC1	PTPRE
AKAP12	HOXC13	PTPRK
AKR1B10	HOXC13-AS	RHOV
AL358334.2	IL20RA	RNASE7
AL451123.1	ITGB6	RRAD
AMTN	KCNJ15	SEMA3C
ANKRD33B	KCNJ2	SERPINE1
APCDD1L-DT	KLF7	SERPINE2
AQP1	KLHL25	SH2D3C
ATP6V1B1	KPNA7	SIAH3
C5AR1	KRT13	SLC26A2
C5AR2	KRT15	SLC46A3
CASZ1	LAMC2	SOX9
CCDC74A	LARGE1	SPHK1
CCDC80	LARGE2	SPOCD1
CDKN1A	LGALS7B	STAT4
CGB5	LINC00313	STEAP4
CGB7	LINC00589	SYNPO
CGB8	LINC00862	TAGLN
CHST11	LINC02551	TFEB
CLCA4	LIPG	TGFBI
CLIC3	LNCOG	TGM2
COL1A1	LOXL2	TLR6
CORO1A	LPAR5	TMEM45A
CRIP2	LPCAT2	TMEM92
CSPG4	LPXN	TNFRSF19
CYP26B1	MAF	TUBA1A
DAZL	MATN3	TXK
DEFB1	MICAL1	VGLL1
DISP2	MIR100HG	VGLL3
DYSF	MIR22HG	WNT4
EFNA2	MUC1	
ELFN1	MYADM	
ESAM	MYH16	
FAM214B	MYL9	
FBXO39	NDRG4	
FGF1	NKILA	

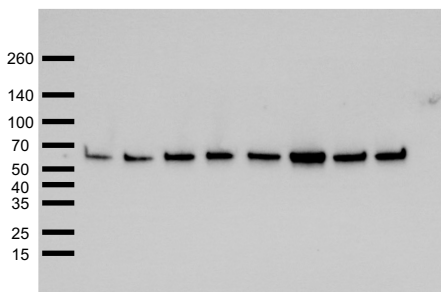
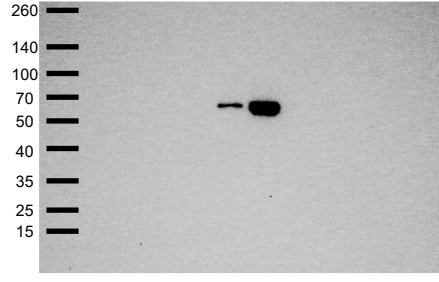
Table S2. SMAD2/3 putative targets in response to TGF-β1 in the absence of SMAD4

Gene target (human)	Primer sequence (5'-3')
FGF1	F:TACTCTGAGAAGAAGACACC
	R:GCGCTTTCAAGACTAAAGAG
ITGB6	F:TGATCCTTAAGTTGAGACCAG
	R:CTCCTTTATTGTGTGAGGTC
LPXN	F:GTTAGATGCCTTATTGGAGG
	R:GGA CTGTGTTATCCTGAATAG
TGFB1	F:GGATTGTAAGTGTGAAGTGTG
	R:CAATGATCTGCTGGATGTTG
GAPDH	F:CGGAGTCAACGGATTGGTCGTAT
	R:AGCCTTCTCCATGGTGGTGAAGAC

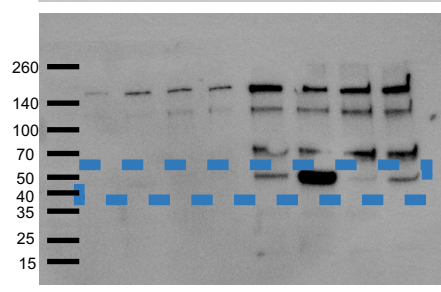
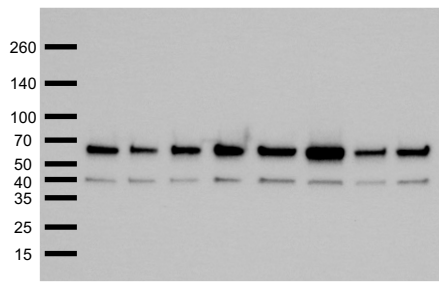
Table S3. Primers sequences used in RT-qPCR



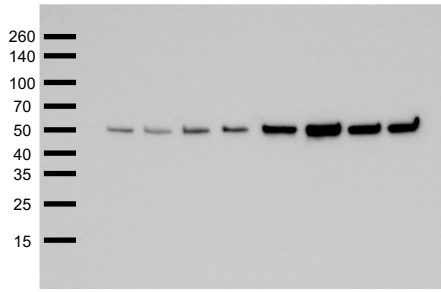
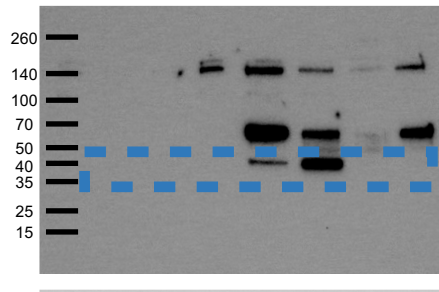
pSMAD2



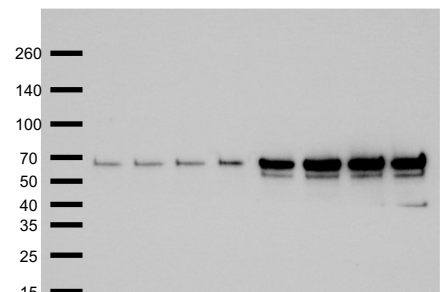
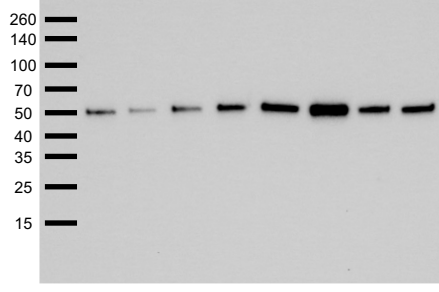
SMAD2



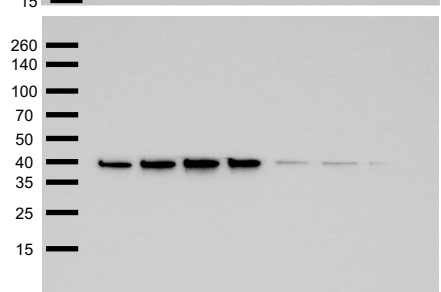
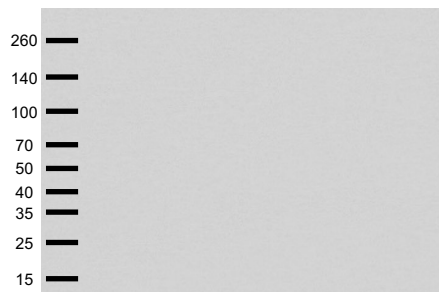
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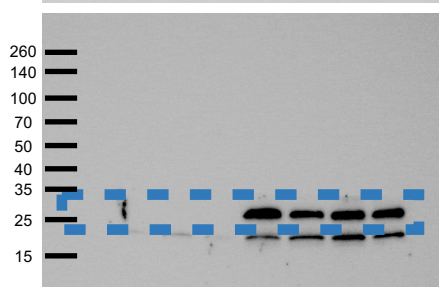
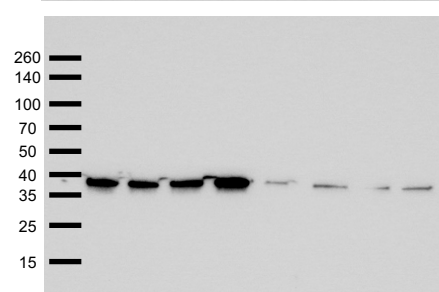
SMAD3



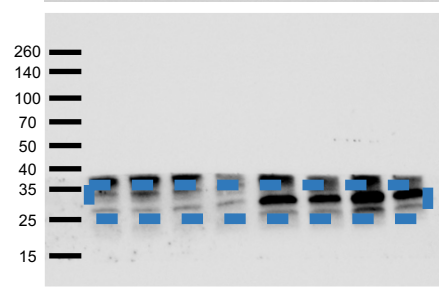
SMAD4

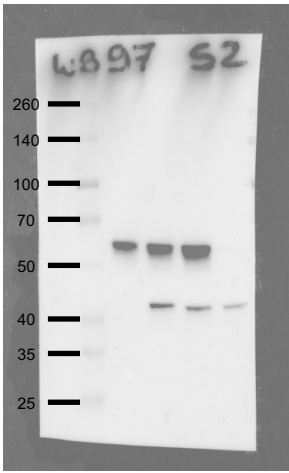


GAPDH

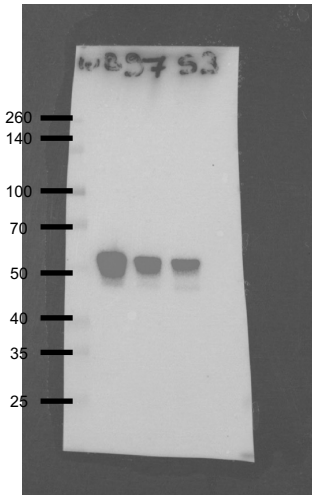


pHIS-H3

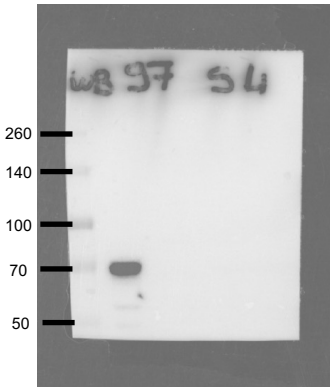




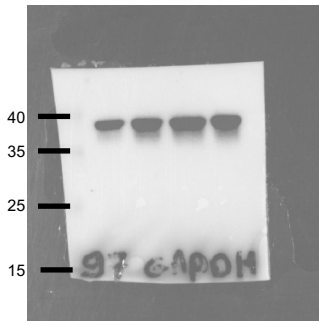
SMAD2



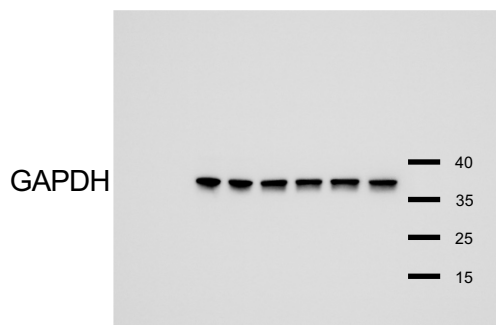
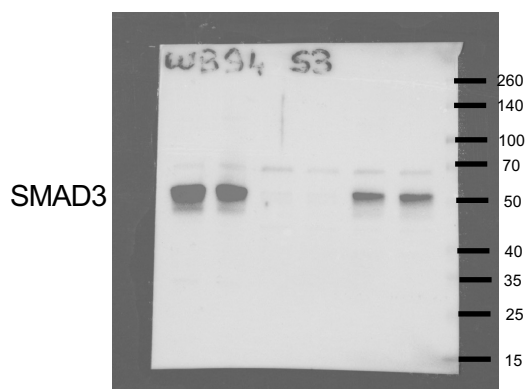
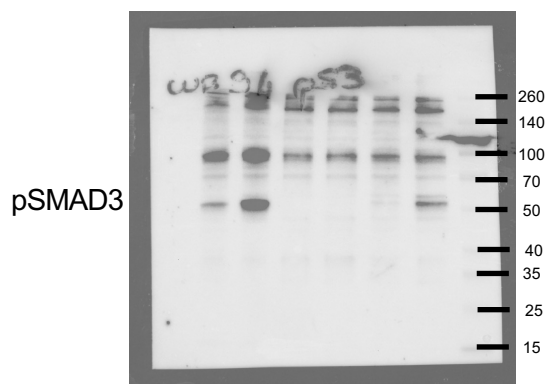
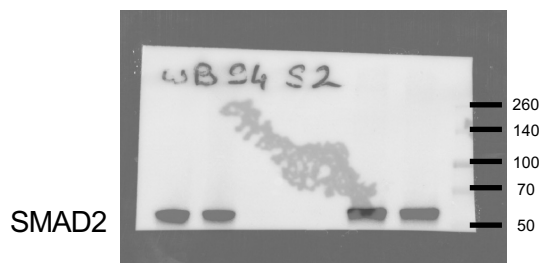
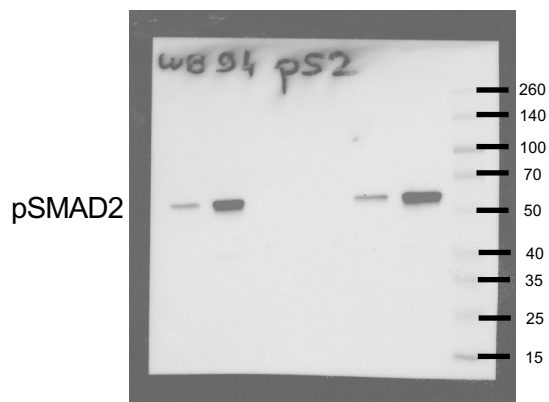
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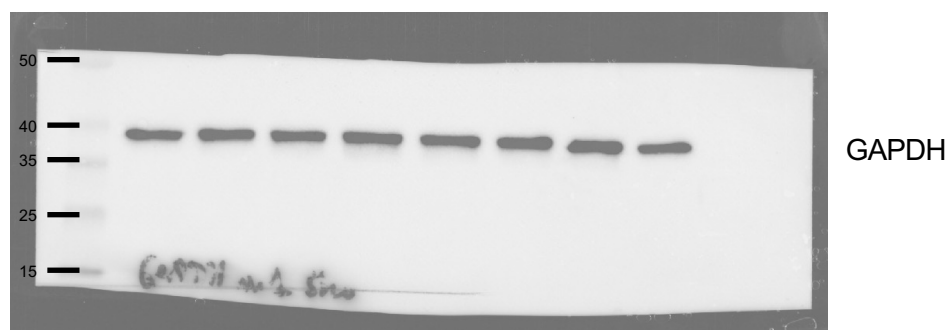
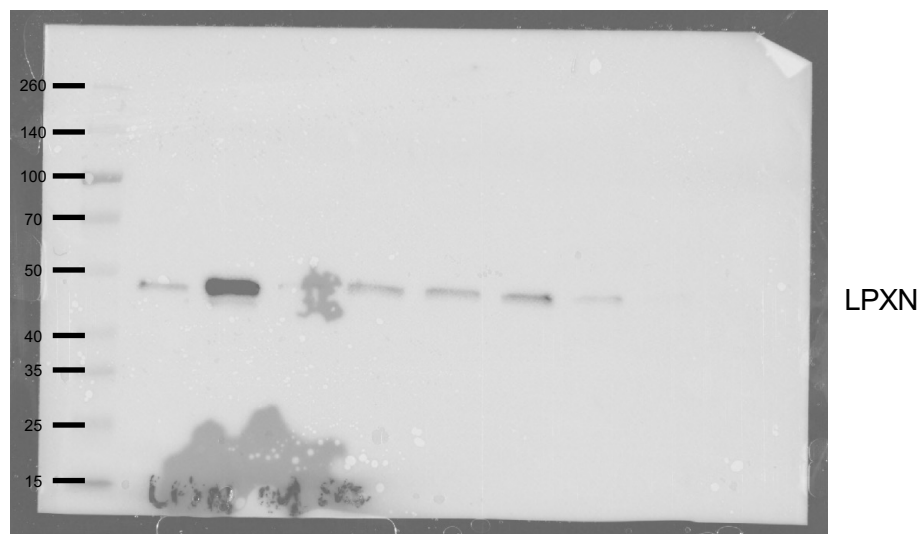
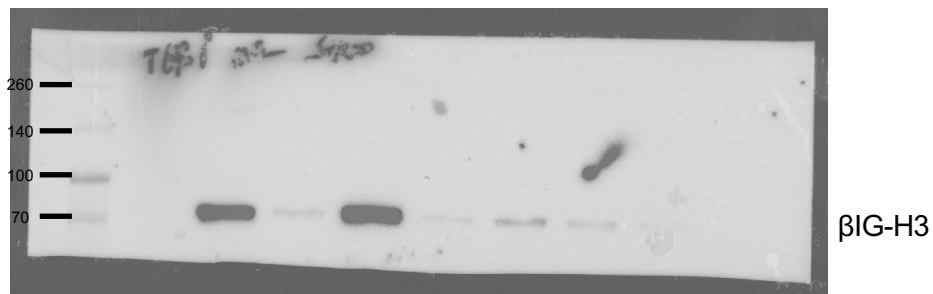


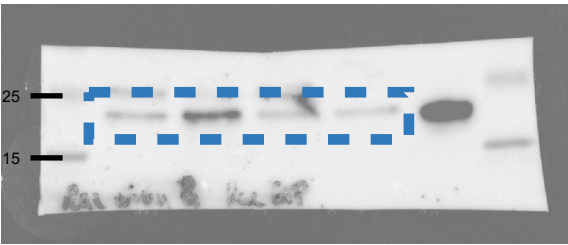
SMAD4



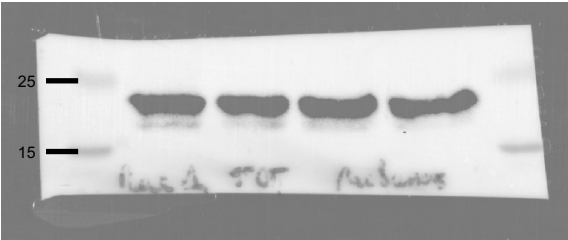
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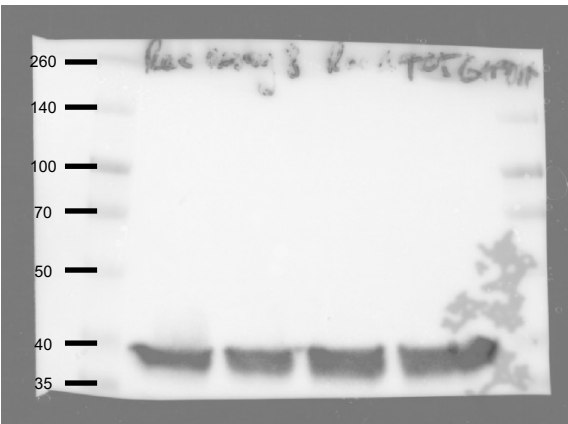




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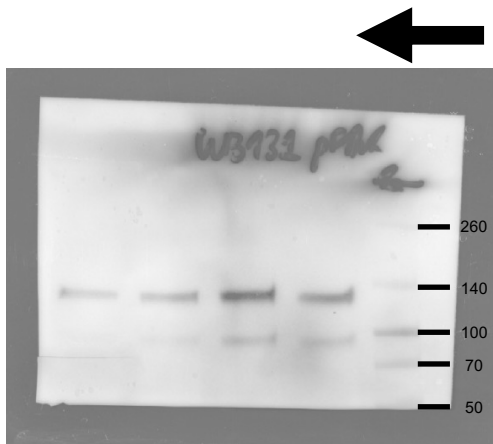


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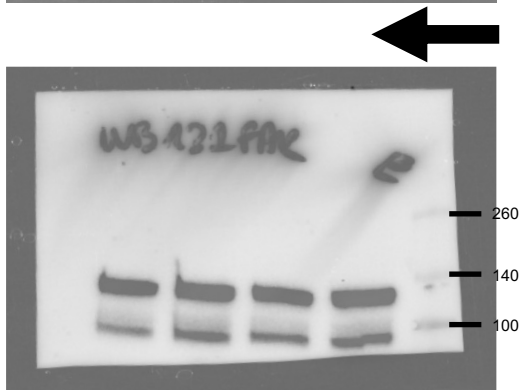


GAPDH

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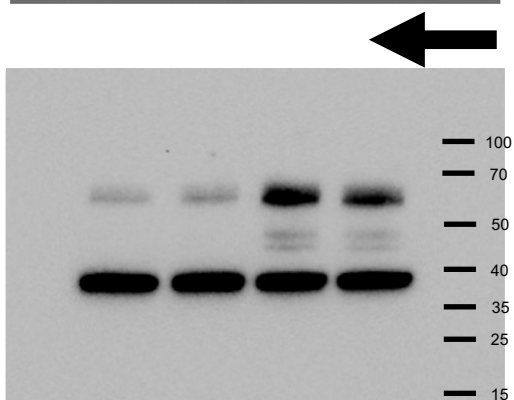


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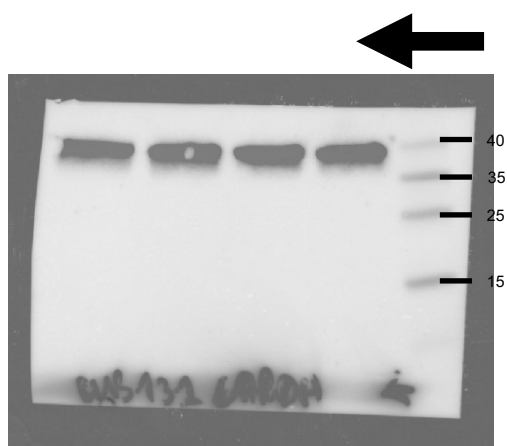


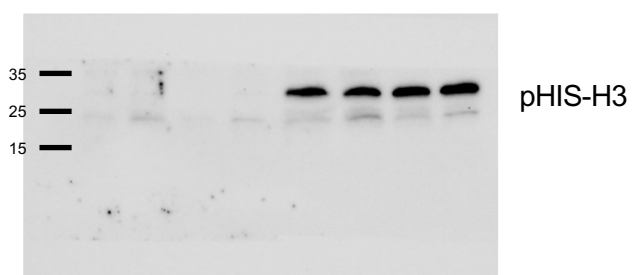
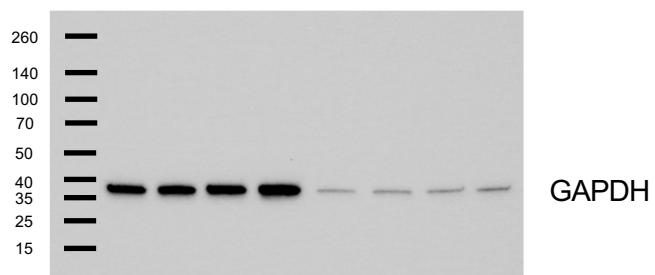
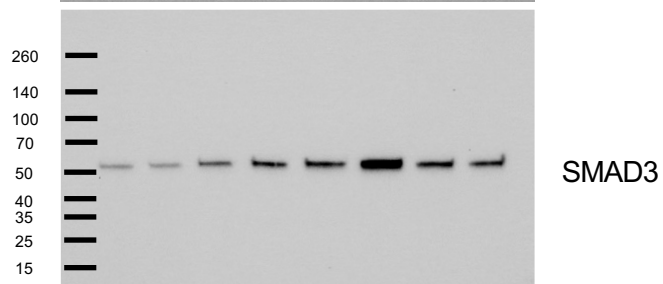
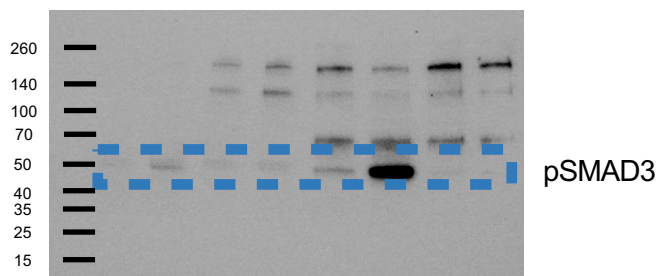
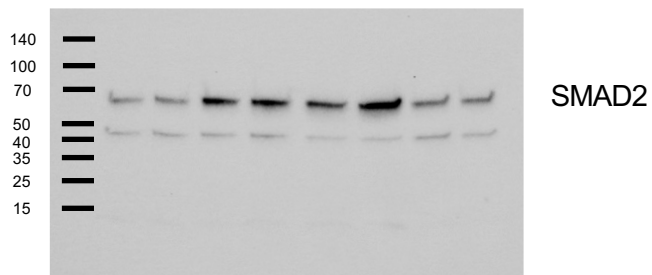
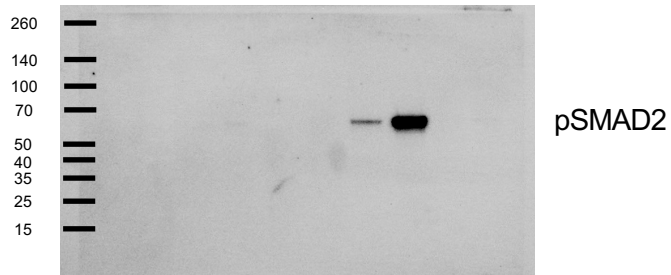
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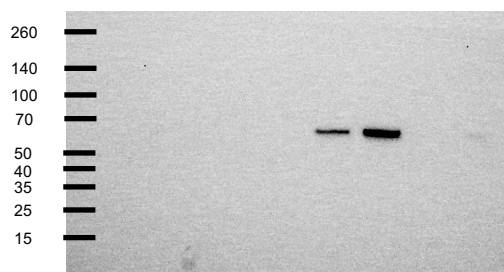
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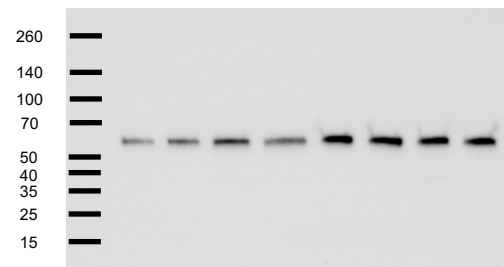
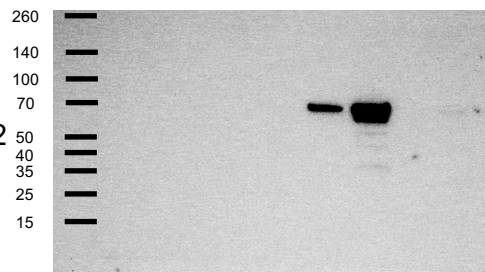
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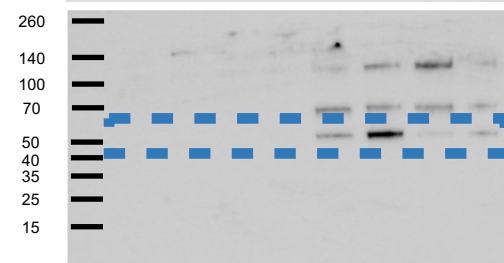
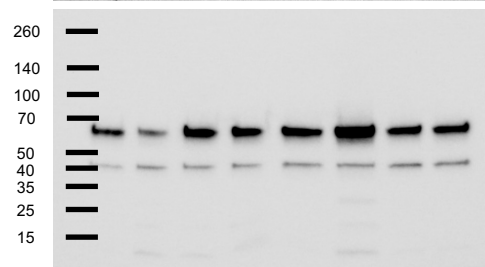




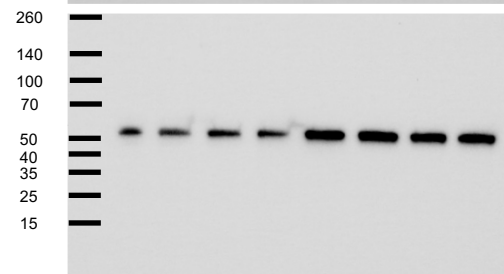
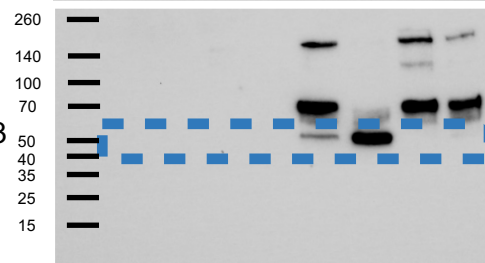
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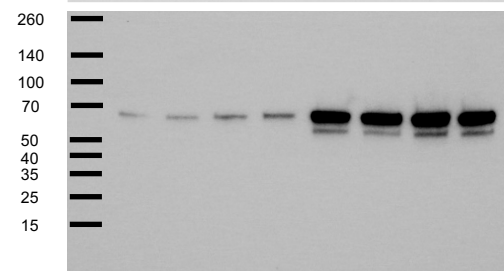
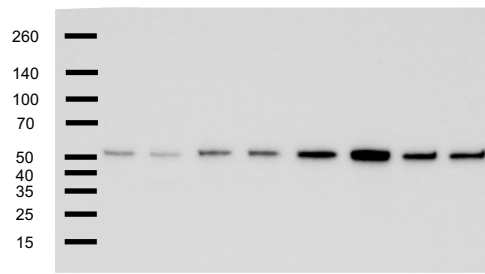
SMAD2



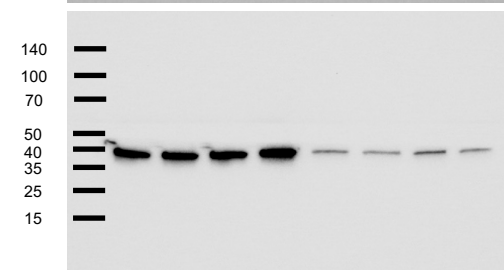
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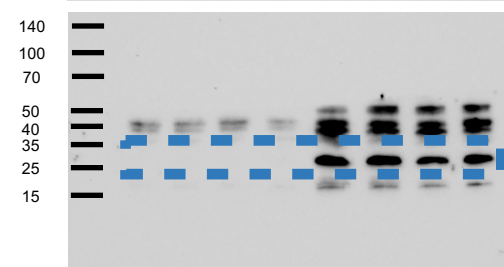
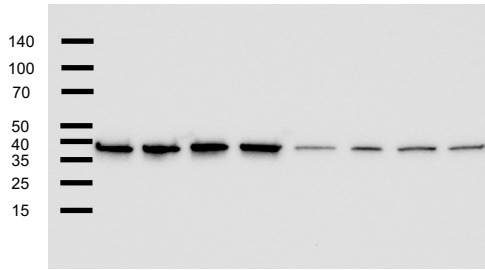
SMAD3



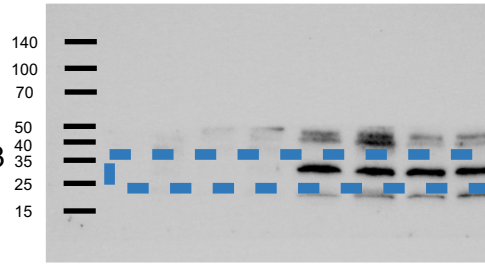
SMAD4

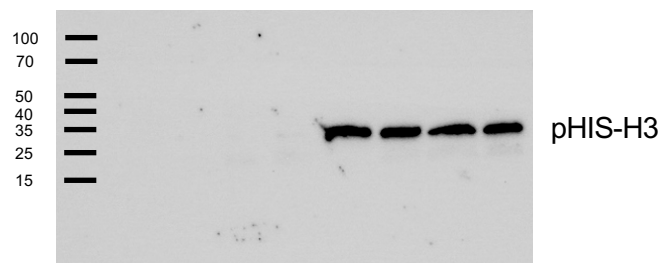
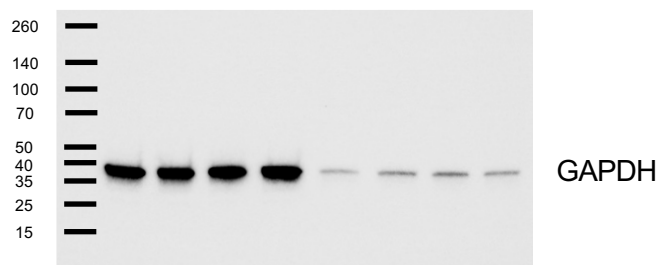
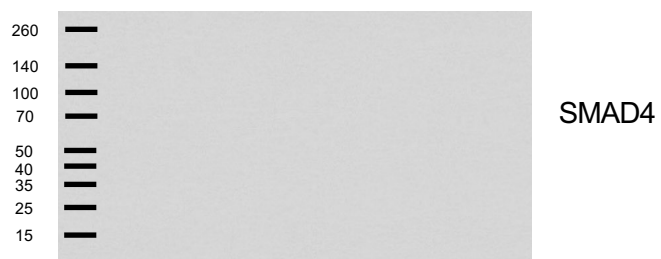
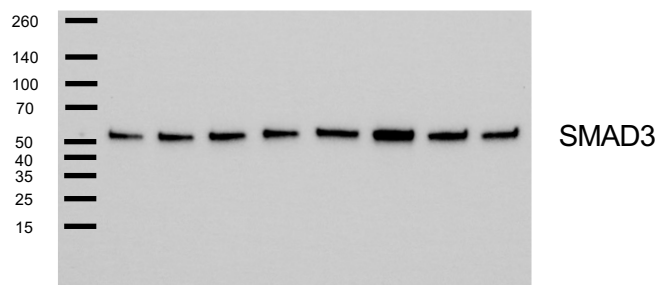
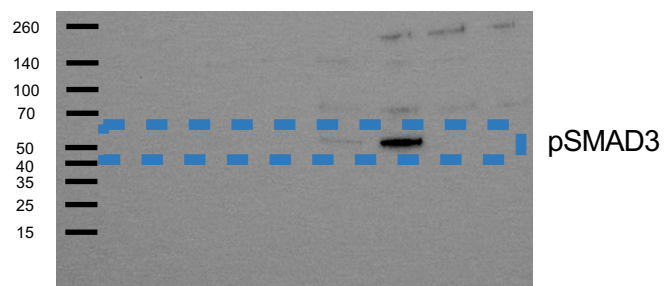
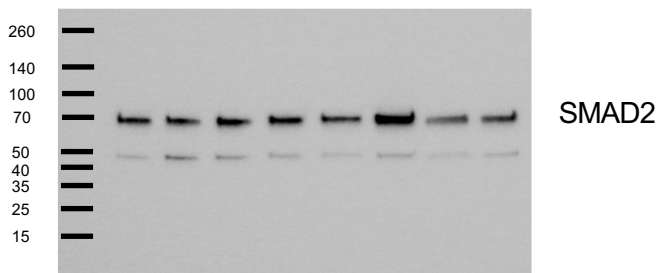
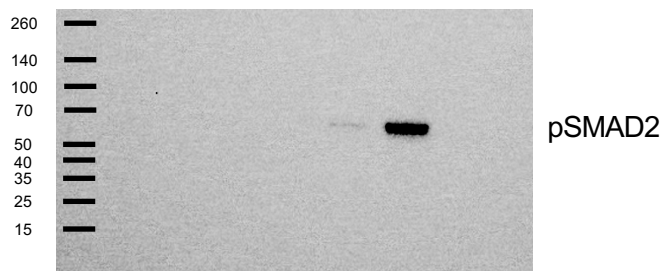


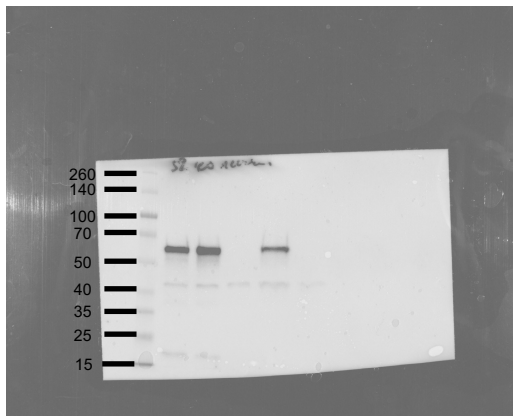
GAPDH



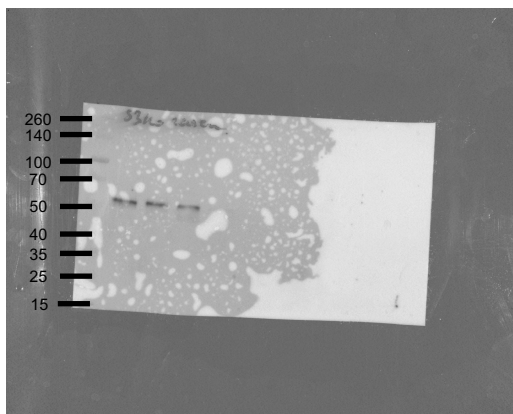
pHIS-H3



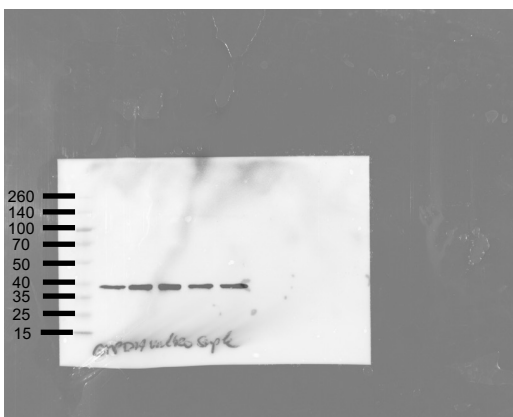




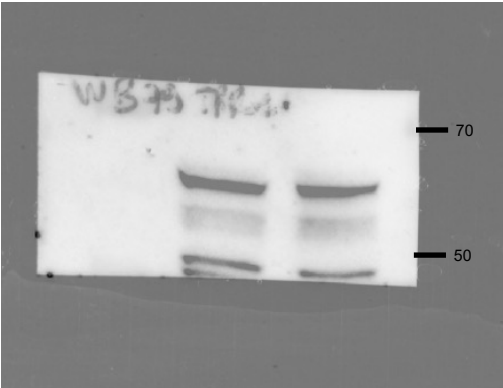
SMAD2



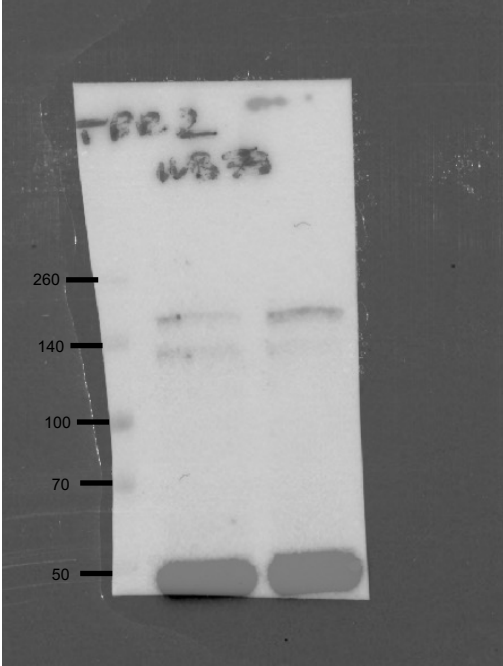
SMAD3



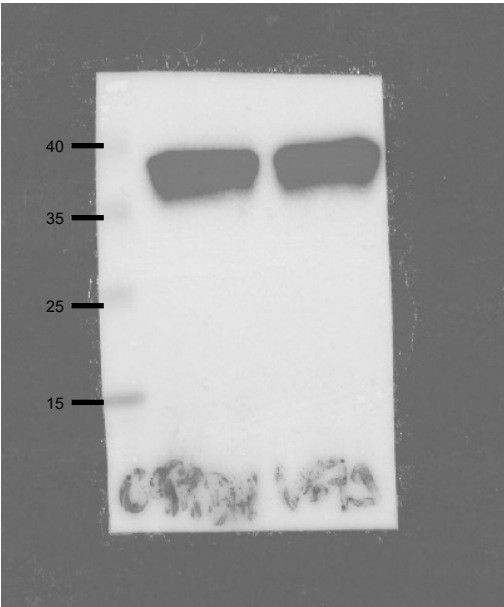
GAPDH



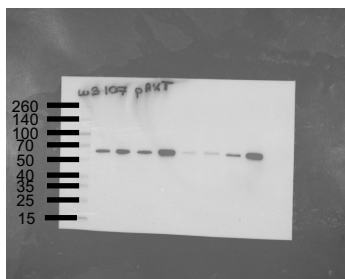
TGFβRI



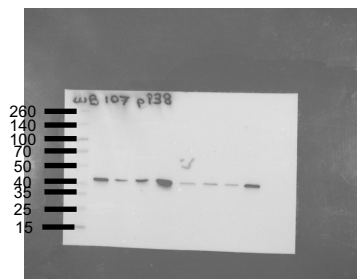
TGFβRII



GAPDH



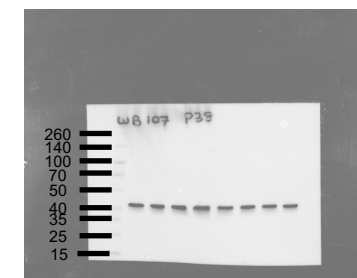
pAKT



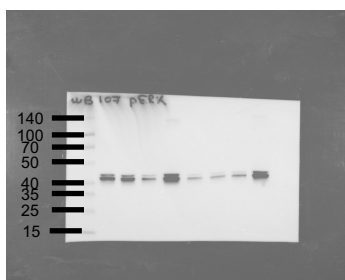
pP38



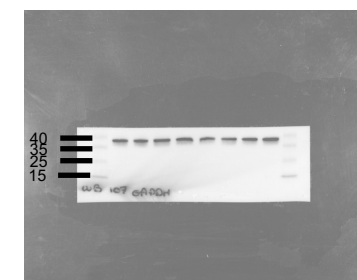
AKT



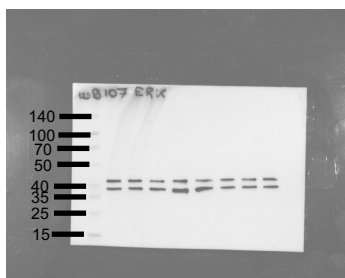
P38



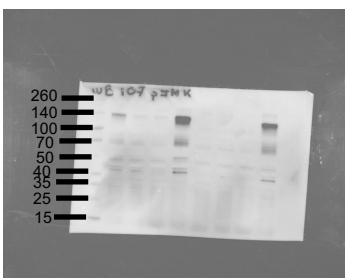
pERK1/2



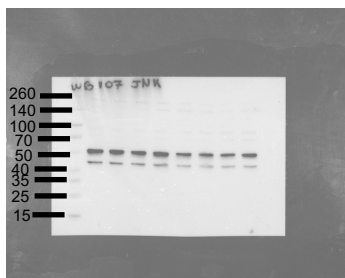
GAPDH



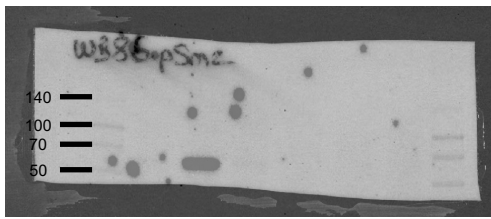
ERK1/2



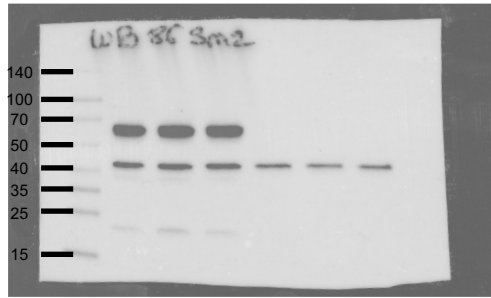
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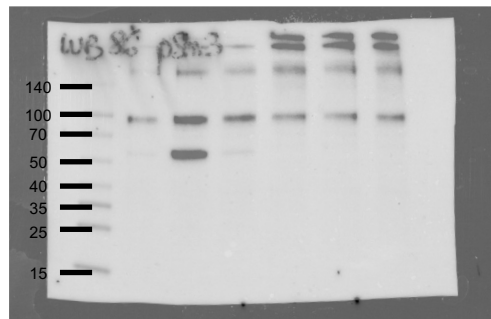
JNK



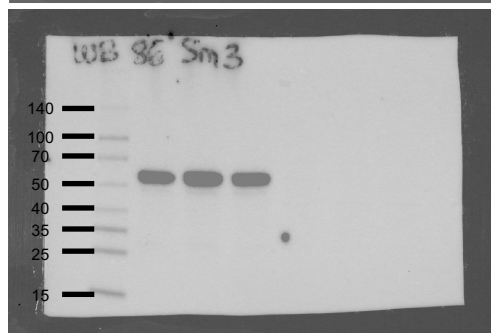
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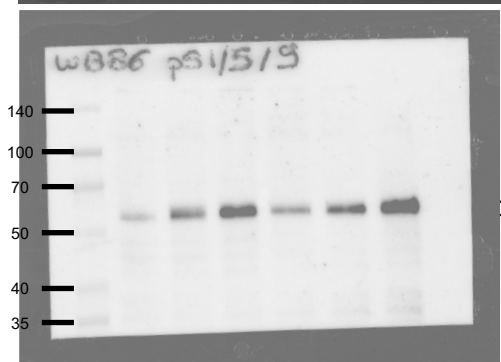
SMAD2



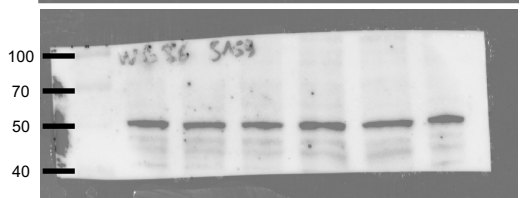
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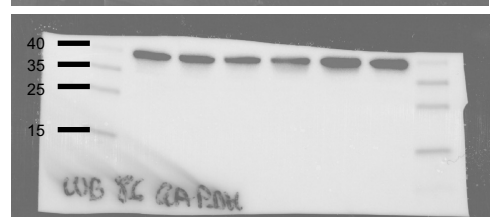
SMAD3



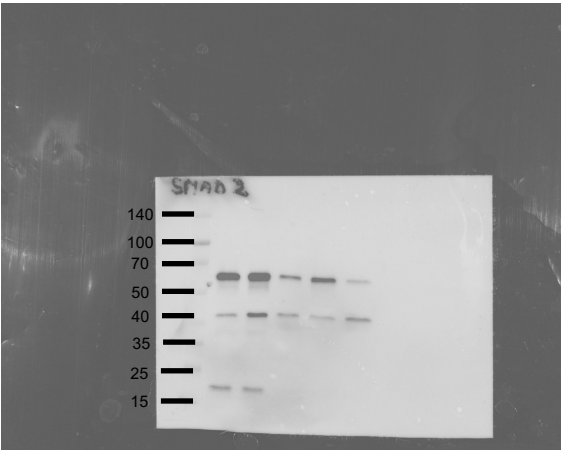
pSMAD1/5/9



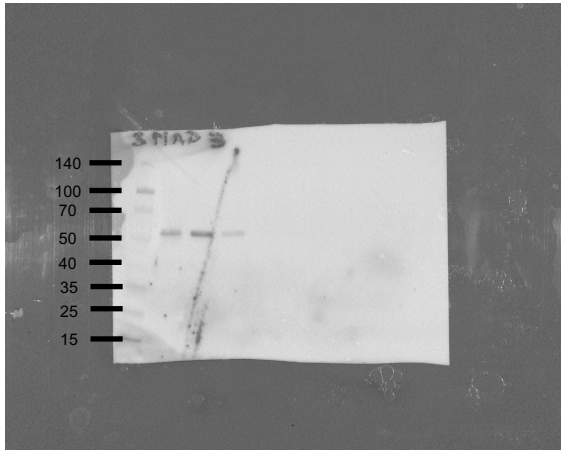
SMAD1/5/9



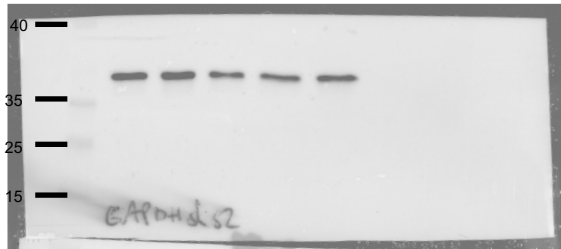
GAPDH



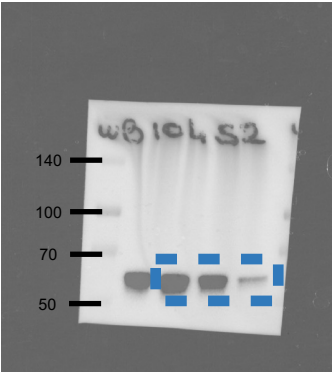
SMAD2



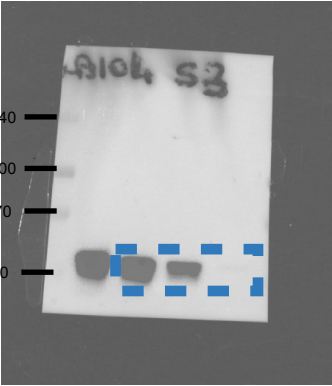
SMAD3



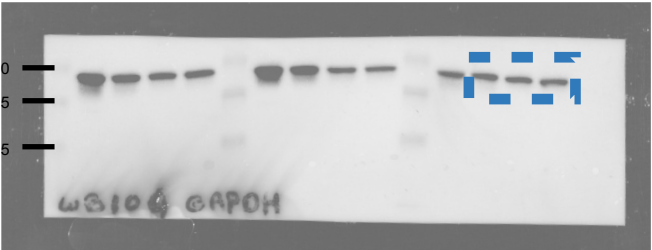
GAPDH



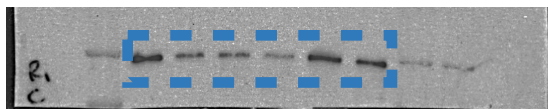
SMAD2



SMAD3



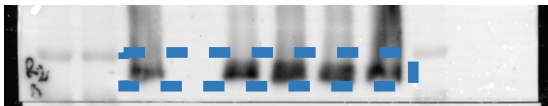
GAPDH



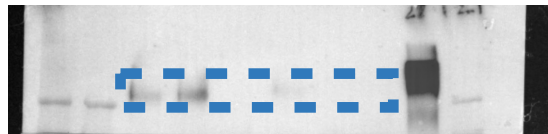
ZO-1



E-CADHERIN



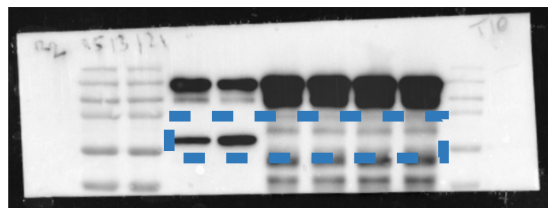
β-CATENIN



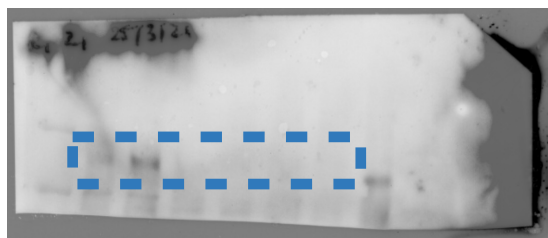
FIBRONECTIN



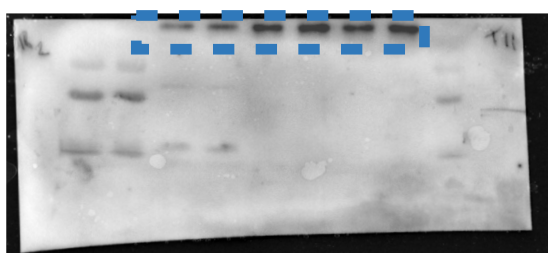
N-CADHERIN



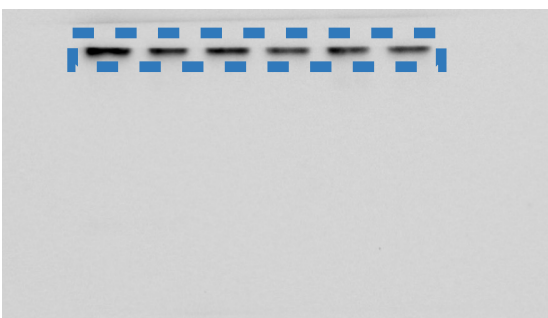
VIMENTIN



ZEB1



SNAIL/SLUG



GAPDH

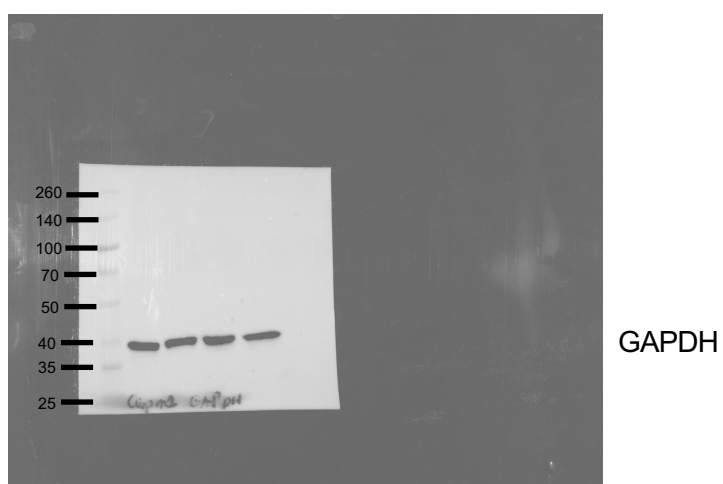
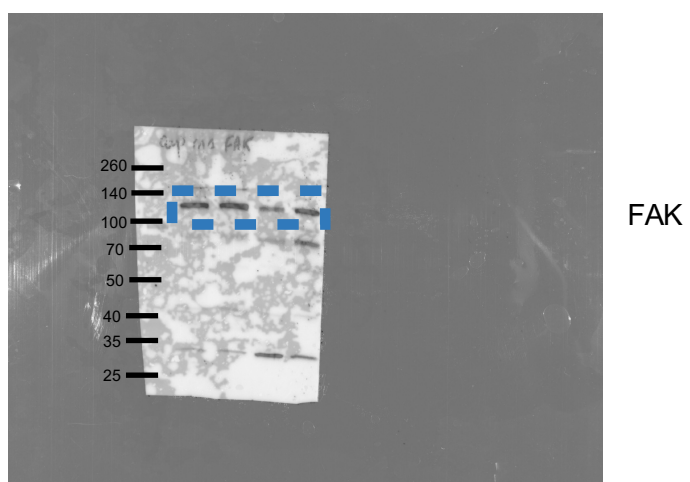
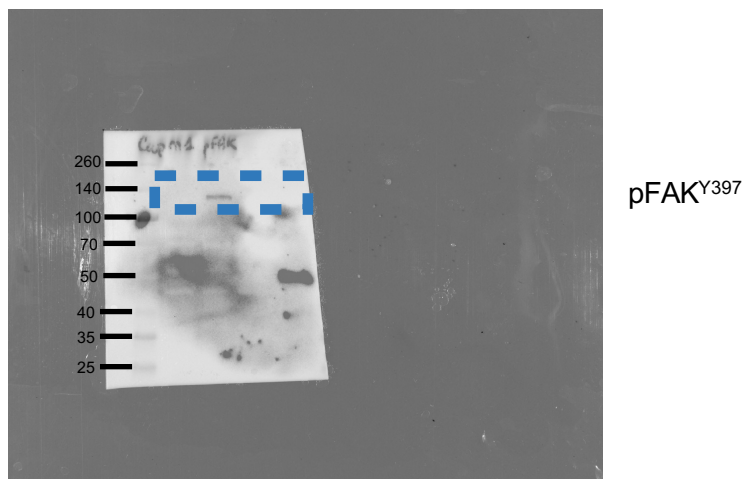


Figure S5 – Unprocessed blots