Supplemental Information

Synergistic action of master transcription factors controls epithelial-to-mesenchymal transition

Hongyuan Chang[1,4*], Yuwei Liu[1*], Mengzhu Xue[1*], Haiyue Liu[2,4], Shaowei Du[1], Liwen Zhang[1,3,4,5], Peng Wang[1,4,5‡]

1. Laboratory of Systems Biology, Shanghai Advanced Research Institute, Chinese Academy of Sciences

2. Shanghai Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences

3. Shanghai Institute of Materia Medica, Chinese Academy of Sciences

4. University of Chinese Academy of Sciences

5. School of Life Science and Technology, ShanghaiTech University

[‡]To whom correspondence should be addressed. Tel: 86-21-20350913;

Fax: 86-21-20350912; E-mail: wangpeng@sari.ac.cn

Table S1. Lists of genes differentially expressed during TGF-β-induced EMT.

| Epithelial-high genes | ABCB6, ABCC1, ABCC2, ABCC3, ABCC4, ABCD3, ABCG2, ABHD3, ABHD4, ACAA2, ACAD9, ACADSB, ACAT2, ACOT13, ACSM3, ACY1, ADAM15, ADCY3, ADI1, ADK, ADM, ADORA2B, AFG3L2, AGFG1, AGPAT5, AGPAT9, AGR2, AHCYL1, AIFM1, AIMP1, AJUBA, AKR1B1, AKR1B10, AKR1C1, AKR1C2, AKR1C3, ALCAM, ALDH3A1, ALDH3A2, ALDH3B1, ALDH9A1, ALDOA, ALYREF, ANAPC13, ANKEF1, ANKRD18A, ANKRD18B, ANKRD54, ANLN, ANP32E, ANXA3, ANXA4, AP1M1, AP2B1, APITD1, APOC1, AR, AREG, ARHGAP11A, ARHGAP26, ARRB2, ASB9, ASF1B, ASPH, ATAD2, ATAD5, ATG10, ATP2A2, ATP2B1, ATP5G1, ATP6V1E2, ATP8B1, ATPAF1, ATXN10, AURKA, AVPI1, B4GALNT1, B4GALT4, B9D1, BACE2, BAG1, BAG2, BARD1, BIN1, BIRC5, BLM, BNIP3, BRCA1, BRCC3, BRI3BP, BRIP1, BRIX1, BSG, BUB1B, C10orf54, C11orf24, C12orf4, C14orf80, C1QBP, C1R, C1S, C1orf112, C2CD5, C3, C3orf14, C5, C7orf50, CA12, CACYBP, CAMK2D, CAV1, CBR1, CCDC34, CCDC85C, CCNA2, CCNB1, CCND3, CCNE1, CCNF, CD109, CD320, CD99L2, CDC20, CDC25B, CDC42EP4, CDC45, CDC6, CDCA2, CDCA3, CDCA4, CDCA5, CDCA7, CDCA7L, CDCA8, CDH1, CDK1, CDK2, CDK5RAP2, CDKN3, CEACAM6, CELSR1, CENPE, CENPH, CENPI, CENPK, CENPM, CENPN, CENPO, CENPU, CENPW, CEP250, CEP55, CEP78, CEP85, CFD, CFL2, CHAF1A, CHEK2, CHKA, CHML, CHP1, CHRAC1, CKAP2, CKB, CLASP2, CLIP1, CLMN, CLN6, CLSPN, CLTC, CNOT1, CNTNAP3, COASY, COMTD1, COPG2, COPS7A, COQ2, COQ7, COQ9, COTL1, COX15, CP, CPEB2, CPNE7, CPS1, CPT1A, CRIP1, CSE1L, CSGALNACT1, CSTF2, CTD-2600O9.1, CTNNAL1, CTNND1, CTSC, CTSD, CTSS, CUL4B, CUTC, CWF19L1, CXCL1, CXCL5, CYB5A, CYB5B, CYCS, CYP1B1, CYP4F3, CYTH3, DAK, DARS2, DBF4, DCAF7, DCDC2, DCLRE1A, DCTPP1, DCXR, DDA1, DDX1, DDX11, DDX18, DDX24, DDX39A, DDX46, DEPDC1, DEPDC1B, DESI1, DHFR, DHRS4L2, DHX57, DHX9, DIAPH3, DIO2, DKK1, DLAT, DNA2, DNM2, DOCK5, DONSON, DPH6, DPY19L3, DSN1, DST, DSTNP2, DTL, DTYMK, DUSP4, DUSP5, DZIP3, E2F1, EARS2, EBP, ECH1, ECT2, EDN1, EED, EFCAB11, EFHD2, EFTUD2, EIF2AK1, EIF3B, EIF4A3, EIF5A, ELF3, ELOVL6, EMC9, EME1, EML4, EMP2, ENO1, ENTPD6, EPDR1, EPHX1, EPT1, ERCC6L, EREG, ERMP1, ESCO2, EXO1, EXOC6, EXOSC2, EXOSC9, EZH2, EZR, FADS3, FAM107B, FAM111B, FAM20B, FAM20C, FAM216A, FAM83D, FANCA, FANCD2, FANCG, FANCI, FARP2, FARSB, FDXR, FECH, FEN1, FGA, FGB, FGL1, FH, FIGNL1, FLOT1, FLVCR1, FOPNL, FOXRED1, FTH1, FTL, G6PD, GALM, GAMT, GAPDH, GART, GATS, GATSL2, GBE1, GCLC, GCLM, GCNT2, GDF15, GEMIN4, GGA2, GGT1, GINS1, GINS2, GINS4, GLA, GLIS3, GLP2R, GLYR1, GMNN, GMPPB, GMPS, GNE, GOT2, GPC1, GPCPD1, GPD2, GPI, GPRC5A, GPX2, GSE1, GSR, GTSE1, H2AFX, H2AFY, HACL1, HADH, HAT1, HAUS6, HDHD1, HEATR5A, HELLS, HFE, HHEX, HIF1A, HILPDA, HIP1, HIST1H1D, HIST1H1E, HIST1H2AI, HIST1H2BI, HIST1H4A, HIST1H4I, HIST3H2A, HIST3H2BB, HKDC1, HMBS, HMCES, HMGA1, HMGB2, HMGB3, HMGCS1, HMGN2, HMGN3, HMMR, HNRNPA2B1, HNRNPR, HP1BP3, HPS3, HSD17B8, HSDL2, HSP90AA1, HSPA14, HSPA1A, HSPA1B, HSPA4, HSPA4L, HSPE1, HYLS1, ICT1, IDH2, IFI35, IFRD2, IFT122, IFT81, IFT88, IGFBP6, IL6ST, ILF3, IMMP2L, IMPA2, INCENP, INHBB, INSL4, IPO11, IRF2BP2, ISYNA1, ITGB3BP, ITGB5, JAK1, JUND, KAT5, KCTD1, KCTD3, KIAA0101, KIAA0391, KIAA1524, KIAA1598, KIF11, KIF14, KIF20B, KIF22, KIF23, KITLG, KLF5, KLHDC4, KNSTRN, KNTC1, KPNA2, KPNB1, KRT18, KRT19, KRT8, KYNU, LACTB2, LAPTM4B, LAS1L, LASP1, LBR, LCN2, LDHB, LETM1, LIG1, LIG3, LIMD1, LINC00467, LITAF, LLGL2, LMNA, LMO7, LPAR1, LPCAT1, LPIN1, LRP5, LRP8, LRPPRC, LRR1, LRRC16A, LRRC23, LRRC58, LRRC8D, LSM4, LSMD1, LUC7L2, LXN, LY6E, LYN, MAD2L1, MAGOHB, MALL, MAP2K6, MAP3K14, MAP4K3, MAPKAPK3, MASTL, MCCC2, MCM10, MCM2, MCM3, MCM4, MCM5, MCM6, MCM7, MCM8, MCM9, MCU, MDH2, ME1, MEIS2, |

|	
	MELK, MEPCE, METRN, MFF, MFI2, MGLL, MID1, MIS18BP1, MITF, MLF2, MLH1, MLK4, MLTK, MMAB, MMP24, MMP24-AS1, MMP7, MND1, MOK, MPDU1, MPHOSPH6, MPHOSPH9, MPP3, MRPL54, MRPS35, MRTO4, MSH2, MSH5, MSH6, MTHFD1, MTSS1L, MVD, MYBL2, MYCBP, MYLK, MYO15B, MYO18A, MYO1B, MYO5C, MYOF, MZT1, NAA15, NAGLU, NAMPT, NAT10, NCAPD2, NCAPD3, NCAPG, NCAPG2, NCAPH, NCAPH2, NCBP1, NCL, NCOA7, NDC1, NDC80, NEDD4L, NEIL3, NEK2, NEK6, NELFCD, NEO1, NFX1, NLN, NME1, NOC2L, NOL12, NOLC1, NOP56, NOP58, NQO1, NR0B1, NR2F6, NR3C1, NSF, NSUN2, NT5C2, NTHL1, NTN4, NUDT1, NUDT15, NUP153, NUP155, NUP160, NUP205, NUP210, NUP35, NUP50, NUP98, NUPL1, NUSAP1, NXN, OAS3, OIP5, OLFML2A, OMA1, ORC1, ORC5, OSGIN1, PA2G4, PAAF1, PAGR1, PAICS, PAPSS2, PARD6B, PARN, PARP2, PARPBP, PARVB, PAXIP1, PBK, PBX1, PCBD1, PCCB, PCGF5, PCNA, PCSK6, PDLIM1, PDLIM5, PEG10, PFAS, PFKFB3, PGAM1, PGD, PHACTR2, PHF19, PHKB, PHTF2, PIGW, PIR, PKD2, PKDCC, PKMYT1, PKP3, PLA2G16, PLA2G4A, PLK1, PLK2, PLK4, PLS1, PM20D2, PMM2, PNKD, POF1B, POLA1, POLA2, POLD2, POLDIP2, POLE, POLE2, POLQ, POLR2D, POLR2E, POLR2L, POLR3K, POR, PPCDC, PPFIBP2, PPIF, PPP2R1B, PPP2R2C, PPP2R5D, PRC1, PRDX3, PRIM1, PRIM2, PRKAG2, PRMT5, PROCR, PRR13, PRSS23, PSIP1, PSMC5, PSMD1, PSMD11, PSMD5, PSME2, PTBP1, PTGES3, PTGR1, PTGR2, PTGS2, PTP4A1, PTPN2, PTPRG, PTPRJ, QDPR, QTRTD1, RAB10, RAB11FIP1, RAB15, RAB27B, RACGAP1, RAD18, RAD51AP1, RAD51C, RAD54B, RANBP1, RBBP8, RBL1, RBPMS, RCCD1, RDH10, RFC2, RFC3, RFC4, RFC5, RFFL, RFWD3, RFX5, RHNO1, RHOBTB3, RHOQ, RHPN2, RITA1, RMI2, RN7SL3, RNASEH2A, RNF115, ROCK2, RP1-60O19.1, RP11-396K3.1, RP11-443P15.2, RP11-674N23.1, RPA1, RPA2, RPA3, RPGRIP1L, RPL13P5, RPL39L, RPS6KA3, RRM1, RRM2, RUVBL1, RUVBL2, S100A4, S1PR3, SARS2, SCARA3, SCARB1, SDPR, SEC23B, SEC23IP, SEMA4B, SEPHS2, SETD7, SF3B2, SGK223, SGOL1, SGOL2, SH2D4A, SH3BP4, SHCBP1, SHMT1, SIVA1, SKA1, SKA2, SLBP, SLC12A2, SLC16A5, SLC23A2, SLC25A10, SLC25A11, SLC27A2, SLC2A4RG, SLC35A4, SLC45A4, SLC47A1, SLC48A1, SLC6A6, SLC9A3R1, SLC9A3R2, SLPI, SMAD3, SMAD6, SMC1A, SMC2, SMC3, SMCHD1, SMPD4, SNORD3B-2, SNRNP200, SNRNP25, SNRPA1, SNRPD1, SNX8, SOGA2, SORD, SPAG5, SPATA5, SPC24, SPC25, SQSTM1, SRBD1, SRC, SREBF1, SRRT, SRSF2, SRXN1, SSBP4, SSRP1, STAT1, STAT6, STIL, STIP1, STOM, STRA13, SUCLG2, SULT1A4, SUV39H2, SUZ12, SVIL, SWAP70, SYNGR2, SYNJ2, SYNM, TACC1, TACC2, TACC3, TACO1, TANGO6, TARS2, TBC1D31, TBC1D5, TBCE, TBL1X, TCERG1, TEAD4, TESC, TEX10, TFDP1, TFRC, TGFBR2, THEM4, THOC3, THOP1, THRAP3, TIMELESS, TIMM23, TIPIN, TK1, TKT, TLCD1, TLE4, TM4SF18, TM4SF20, TM4SF4, TM7SF2, TMEM106B, TMEM14B, TMEM199, TMEM56, TMEM97, TMOD3, TMPO, TMX4, TNFAIP2, TNS3, TOB1, TOMM40, TOMM70A, TOP2A, TOPBP1, TOR3A, TPCN1, TPM3P9, TPP2, TPX2, TRAF2, TRAM1, TRAP1, TRIM16, TRIM16L, TRIML2, TRIOBP, TRIP13, TRIP6, TRMT2B, TRMT6, TRNP1, TSEN54, TSPAN4, TSR1, TTF2, TTI1, TUBA1B, TUBB4B, TUBG1, TXN, TXN2, TXNRD1, TXNRD2, TYMS, U2AF2, UBAP2L, UBE2S, UBE2T, UBR7, UGCG, UGDH, UGP2, UHRF1, UHRF1BP1L, UNG, UNKL, UPK1B, UPP1, USP1, USP10, USP5, USP53, UTP11L, VCP, VPRBP, VRK1, WBP11, WBSCR16, WDHD1, WDR34, WDR62, WDR76, WDR77, WEE1, WISP2, WNT7B, WRAP53, WWP2, XPO7, XRCC2, XRCC3, YTHDC2, ZBED5, ZFAND5, ZFX, ZNF587B, ZNF789, ZWILCH, ZWINT
Mesenchymal-high genes	AADAC, ABHD2, ABLIM3, AC007362.1, AC098614.2, ACP6, ACSF2, ADAM19, ADAMTS6, ADAMTS9, ADD3, AFAP1L2, AKR1E2, AKT3, AL132709.5, AL132709.8, AL589743.1, ALPK2, AMIGO2, ANKRD50, ANXA8L2, AP1S2, APBB2, APPL2, ARHGEF40, ARL15, ARL4C, ARL4D, ARNTL2, ASL, ATP13A2, ATXN1, B4GALNT4, BAZ2B, BBX, BCAS3, BDNF, BHLHE40, BICD1, BMP1, BMP6, BPGM, BTG1, C11orf80, C12orf76, C3orf52, C8orf4, CACNB3, CALCOCO1, CAMK2G, CAPRIN2, CASC10, CASC15, CBLB, CCDC80, CCDC92, CCNG2, CD151, CD44, CD58, CD59, CD70, CDH11, CDH2, CDH4, CDH6, CEACAM19,

	CEP170, CGB8, CHD9, CHST11, CITED4, CLDN2, CLIC4, CLIP2, CMTM3, CNPY4, COL22A1, COL4A1, COL4A2, COL4A3, COL4A4, COL5A2, COL7A1, CORO2B, CRLF1, CSNK1G3, CSRNP1, CSRP2BP, CTD-2066L21.3, CTD-2314B22.3, CTD-2576D5.4, CTTNBP2NL, CYBRD1, DBN1, DCBLD1, DCDC1, DDIT4, DEPDC7, DFNA5, DGKA, DGKD, DHRS2, DIRC2, DIXDC1, DLG1, DNAJB2, DNAJB4, DNMBP, DOCK2, DOCK4, DPYD, DPYSL3, DSE, DSG2, DSP, DUSP1, DUSP10, DUSP6, DYRK1B, DYRK2, DZIP1, E2F5, EDEM3, EFEMP1, ELK3, ELL2, ELP4, EMB, ENDOD1, ENO3, ETV4, ETV5, EVA1A, EVA1B, F2R, F2RL1, FAM114A1, FAM168A, FAM214B, FAM43A, FAM89B, FAT3, FBN1, FBXO32, FER, FERMT1, FGD6, FHL1, FHOD3, FIBCD1, FKBP7, FLRT2, FN1, FNDC3A, FNDC3B, FOXP1, FOXS1, FP15737, FRMD6, FST, FSTL1, FUT8, FXYD5, GABARAPL1, GABRA5, GABRB3, GAL, GALNT1, GLIPR1, GLIPR2, GNG4, GOLGA8A, GOLGA8B, GPAM, GPC6, GPR137B, GRAMD1B, GREM1, GSN, HAS2, HBP1, HDAC5, HES1, HGSNAT, HLA-C, HMGA2, HRH1, HTR1D, HTRA1, IER3, IFNA1, IFNE, IFNWP19, IGFBP7, IGFL1, IGFL2, IGFL3, IGFL4, IL11, IL15, IL32, IL8, INHBA, INPP4B, INPPL1, ITGA1, ITGA11, ITGA2, ITGA3, ITGA5, ITGAV, ITGB6, IVNS1ABP, JAG1, JARID2, JMJD1C, KCNG1, KCNJ6, KCNMA1, KCNN4, KDM5B, KDSR, KIAA0556, KIAA1109, KIAA1549L, KIFC2, KIRREL3, KLF6, KLHL24, LAMB1, LAMC2, LARP6, LCE3D, LDLRAD4, LGMN, LHX8, LINC-PINT, LINC00152, LINC00941, LIX1L, LPCAT2, LPCAT4, LPHN2, LRP11, LRRC8C, LTBP1, LTBP2, LTBP3, LYPD1, MAML3, MAN2B1, MAP1LC3A, MAPK8IP3, MAPRE3, MARCH4, MBOAT2, MCL1, MEG3, MEG8, MEIS3, MEX3B, MFAP3L, MICAL1, MICAL2, MIR22HG, MIR31HG, MIR4435-1HG, MLLT11, MMP2, MORC4, MORF4L2, MRC2, MSC, MSN, MT1X, MT2A, MTAP, NAGK, NAP1L1, NBEA, NBPF20, NEBL, NFKBIZ, NGEF, NHS, NID1, NIPAL4, NKAIN4, NNMT, NOD1, NPC2, NPR3, NPTX1, NR1D2, NREP, NRG1, NRP2, NT5E, NUAK1, OBSL1, OCIAD2, P4HA2, P4HA3, PAN3, PBXIP1, PCMTD1, PCMTD2, PDE4B, PDE4D, PDGFC, PDLIM7, PDP1, PDZK1, PEA15, PGM2L1, PHC1, PHC2, PHF20, PHLDA1, PICALM, PIGCP1, PIK3AP1, PIP4K2A, PITPNC1, PLAU, PLAUR, PLCB4, PLCXD2, PLEK2, PMAIP1, PMEPA1, PNRC1, PODXL, PPFIBP1, PPP1R18, PPP1R3C, PRR5L, PSD3, PSMD2, PTGFRN, PTHLH, PTK7, PTPRE, PTPRK, PYGL, QPCT, R3HDML, RAB3B, RAB8B, RAET1G, RAI14, RALB, RARB, RASAL2, RASGRF2, RASGRP3, RASSF10, RASSF8, RBP1, RELL1, RGL2, RGS2, RHOU, RND1, RNF182, RNF2, ROBO1, RP11-1002K11.1, RP11-145E5.5, RP11-166D19.1, RP11-180P8.1, RP11-244K5.8, RP11-420A23.1, RP11-479G22.8, RP11-572C15.6, RP11-65J21.3, RP11-706O15.5, RP11-709B3.2, RP11-757F18.5, RP11-81H3.2, RTKN, S100A13, S100A16, SACS, SAT1, SCARNA5, SCARNA7, SCG5, SCN9A, SDC4, SEC14L2, SEMA3C, SENP7, SERPINE2, SFRP1, SFXN3, SGCD, SGK1, SGSM2, SH3KBP1, SH3YL1, SIRPA, SLC16A4, SLC22A3, SLC25A29, SLC25A36, SLC25A37, SLC29A1, SLC2A3, SLC30A1, SLC35E2B, SLC35F2, SLC38A2, SLC39A10, SLC4A7, SLCO1B3, SLFN5, SLIT3, SLN, SMAD2, SMARCA1, SMOC1, SMYD3, SNHG14, SNORA53, SNORD116-20, SNORD3D, SOCS2, SOCS5, SOCS6, SOX4, SPARC, SPHK1, SPOCK1, SPRY2, SPSB1, SPTLC2, SRPX, STARD4, STAT2, STC1, STK38L, STRA6, STXBP5, SULF2, SYT1, SYT13, TAGLN, TCEAL1, TCEAL3, TCF4, TCP11L1, TCP11L2, TENM3, TGFB1, TGFB1I1, TGFBI, TGFBR1, THBD, THBS1, THBS3, TIMP2, TIMP4, TIPARP, TLN2, TMEM156, TNFAIP6, TNFRSF10D, TNFRSF12A, TNKS, TNKS1BP1, TNS1, TOM1, TP53I3, TPM1, TPM2, TPST1, TSC22D1, TSC22D3, TSPAN2, TSPAN5, UBA6, UBTD1, USP11, VCAN, VEGFA, VGLL3, VIM, VPS8, WLS, WNT5B, XYLT1, ZBED6, ZBTB38, ZEB1, ZFP36, ZFP36L1, ZFP90, ZKSCAN1, ZNF124, ZNF185, ZNF581
Partial-EMT-high genes	ABLIM1, AC009403.2, AC034220.3, ACAT1, ACLY, ACOX3, ADA, ADAM9, ADCY7, AGPAT2, AGPS, ALDH1A3, ANKLE2, AP1M2, ARCN1, ARFGAP1, ARHGEF18, ASCC2, ASS1, ATP13A3, BAIAP2L1, BLOC1S2, BTBD11, C15orf48, C2orf82, CAPN2, CARD10, CDC42EP3, CDC42SE1, CDR2, CDR2L, CERCAM, CLDN4, CLPTM1L, COL1A1, COL27A1, CPLX2, CTD-2377D24.6, CTIF, CTPS1, CXXC5, DAAM1, DDAH1, DDB2, DMPK, DNMT3B, DVL1, DZIP1L,

ECE1, EFR3B, EHD4, EIF1AD, EIF5B, EML1, EPB41, EPS8L2, ETS2, F3, FAM101B, FAM129B, FAM177A1, FAM83G, FAM98A, FGF2, FGFR1, FITM2, FKBP11, FRYL, FSTL3, FURIN, GALNT14, GALNT18, GIPC1, GNB4, GOLGA4, GPR56, GRK5, GXYLT1, GXYLT2, HAPLN3, HINFP, HN1L, HNF4A, HPCAL1, HR, HSPB1, INO80C, ITPR3, JMJD6, JUNB, JUP, KANK2, KIAA0930, KIF16B, KIF21A, KIF3C, KRT7, KRT80, LAMB3, LBH, LFNG, LIMK2, LINC00842, LMNB2, LRRC59, LRRC8A, LTBP4, MAFK, MANF, MDGA1, METAP1, MFGE8, MFSD12, MICALL2, MYEOV, MYO1C, NCF2, NF2, NR1H3, NT5DC2, NUMBL, P2RY2, PACSIN3, PDCD6IP, PDGFB, PDXK, PFKP, PGRMC2, PHLDB1, PLCB3, PLS3, POLD4, POMT2, PPP1R13L, PPP1R14A, PRDX1, PRKAR2A, PRPS1, PTGES, PTPLB, PTRF, PVR, RASGRP1, RBMS3, RDX, RHOD, RHOF, RP11-509E16.1, RP3-416H24.1, RRAS, RSU1, S100A3, S1PR5, SAMD11, SELM, SEMA6B, SEPT9, SERINC2, SERPINE1, SFN, SGMS1, SIM2, SLC12A4, SLC22A5, SLC2A1, SLC2A8, SLC39A7, SLC41A2, SLC7A6, SLFNL1, SORL1, SPATS2, SPDL1, SULT2B1, SYNE1, TAPT1, TARSL2, TAX1BP3, TGFB2, TMC7, TMEM184A, TMEM256-PLSCR3, TNFAIP8, TOP3B, TPD52, TRAPPC10, TRIM47, TSPAN15, TTC7A, TUBA4A, TUBB6, TUFT1, UACA, UAP1, UBASH3B, UNC13D, USP31, VPS54, WDR1, WWC2

Table S2. Lists of transcription factors with a motif enrichment p-value < 0.05 in proximal enhancers, distal enhancers and enhancers within gene body.

	Epithelial-high gene enhancers	Partial-EMT-high gene enhancers	Mesenchymal-high gene enhancers
Proximal enhancers (<= 10 kb from TSS)	ARNTL2, E2F1, ELF3, ETS2, ETV4, FOXP1, HMGA1, HNF4A, JUNB, JUND, KLF5, KLF6, MAFK, MSC, NR1D2, PBX1, STAT1, STAT2, STAT6, TEAD4, TFDP1, ZFX	E2F1, E2F5, ELK3, ETS2, ETV4, ETV5, FOXP1, HMGA1, HNF4A, JUNB, JUND, KLF5, KLF6, MAFK, NR2F6, NR3C1, SMAD3, SOX4, STAT1, STAT2, STAT6, TEAD4, ZFX	E2F1, ELF3, ETS2, ETV4, ETV5, FOXP1, HNF4A, JUNB, JUND, KLF5, KLF6, MAFK, MSC, NR3C1, RFX5, STAT1, STAT2, STAT6
Distal enhancers (> 10 kb from TSS)	ARNTL2, BRCA1, E2F1, E2F5, ELF3, ETS2, ETV4, FOXP1, HNF4A, JUNB, JUND, MAFK, NR1D2, NR3C1, RFX5, STAT1, STAT2, STAT6, TEAD4	AR, ARNTL2, E2F1, ELF3, ETS2, ETV4, FOXP1, GLIS3, HHEX, HIF1A, JUNB, JUND, KLF6, MAFK, NR2F6, NR3C1, SMAD3, SOX4, STAT1, STAT2, STAT6, ZFX, ZKSCAN1	E2F1, ELF3, ELK3, ETS2, ETV4, ETV5, JUNB, JUND, MAFK, NR1D2, NR3C1, RFX5, SMAD3, SOX4, STAT1, STAT2, STAT6, TEAD4, ZEB1
Enhancers within gene body	ARNTL2, E2F1, ELF3, ELK3, ETS2, ETV4, ETV5, FOXP1, HNF4A, JUNB, JUND, KLF5, KLF6, MAFK, MSC, NR1D2, NR1H3, SOX4, SREBF1, STAT1, STAT2, STAT6, TEAD4, ZFX	AR, E2F1, ETV4, FOXP1, HNF4A, JUNB, JUND, KLF5, MAFK, NR2F6, NR3C1, SMAD3, SOX4, STAT1, STAT2, TEAD4, ZFX	ELF3, ELK3, ETS2, ETV4, ETV5, FOXP1, HNF4A, JUNB, JUND, KLF5, KLF6, MAFK, MSC, NR3C1, RFX5, SMAD2, SMAD3, SOX4, STAT1, STAT2, STAT6, TEAD4, ZEB1

A

0 h   24 h   48 h

72 h   96 h

B
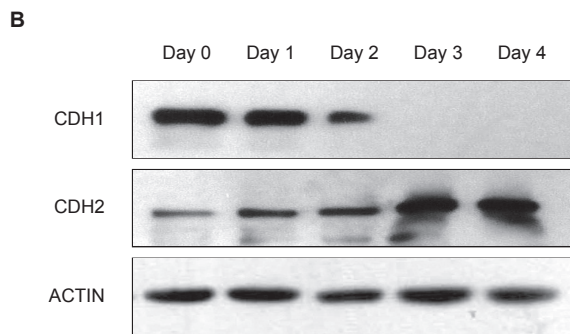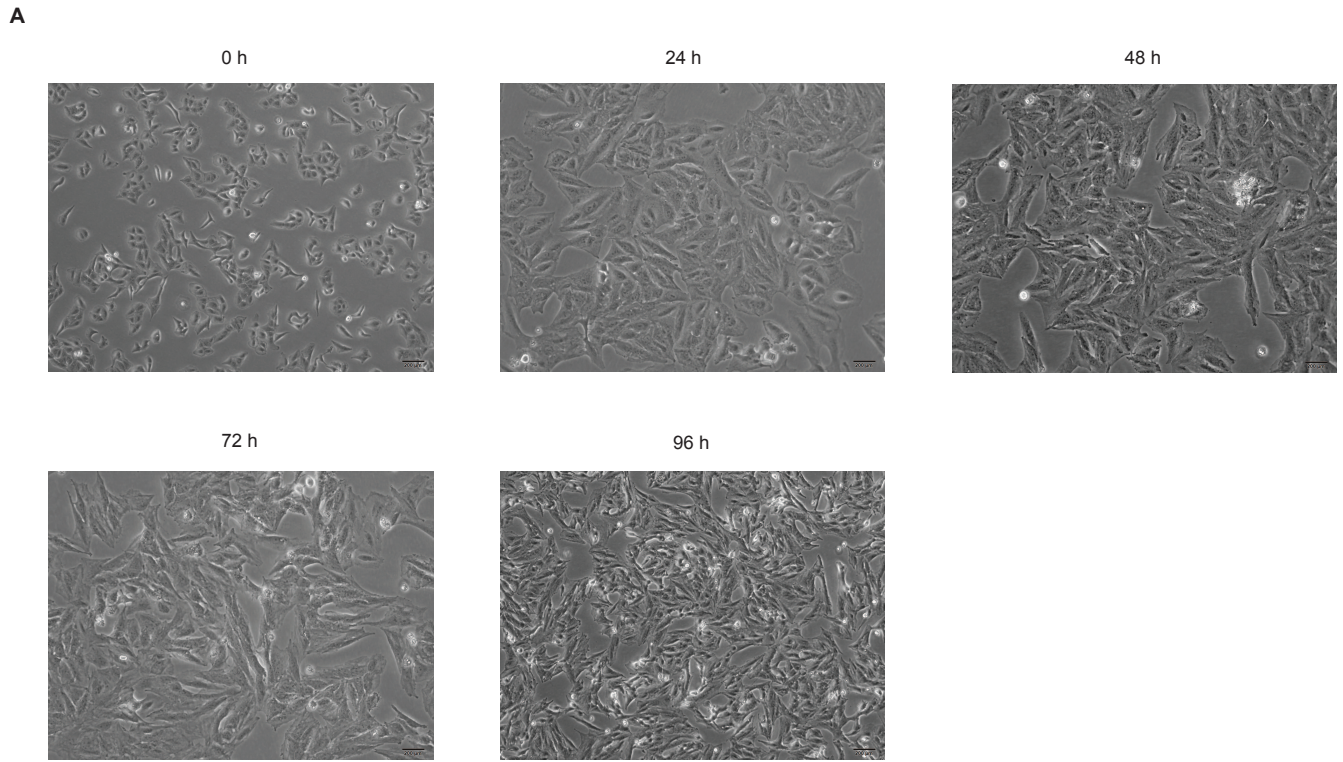
Figure S1. TGF-β induces EMT in A549 cells.
(A) Morphology of A549 cells treated with TGF-β for 5 days. (B) Protein abundance of EMT markers analyzed by Immunoblotting.
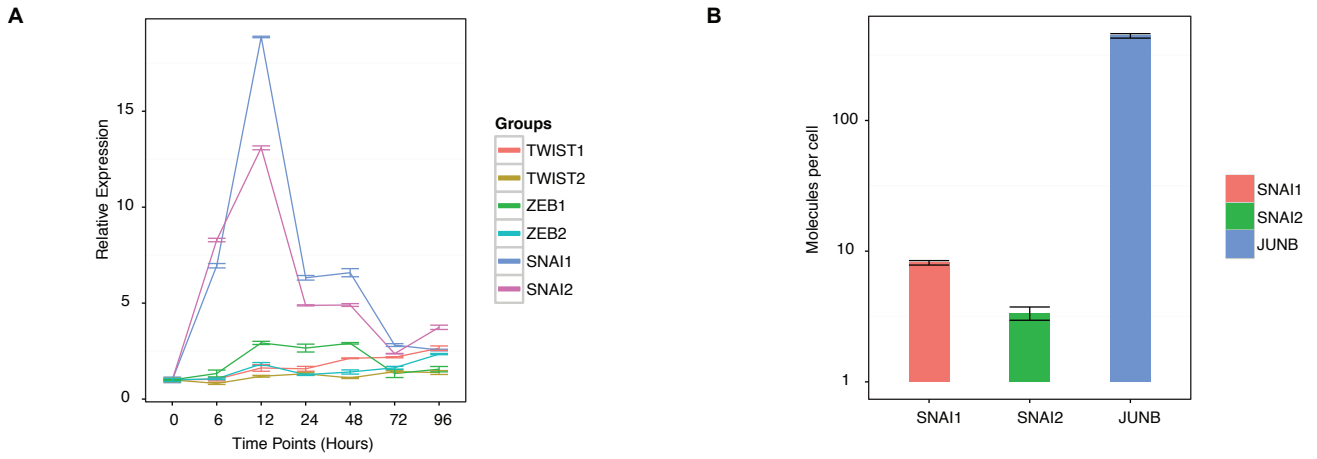
A
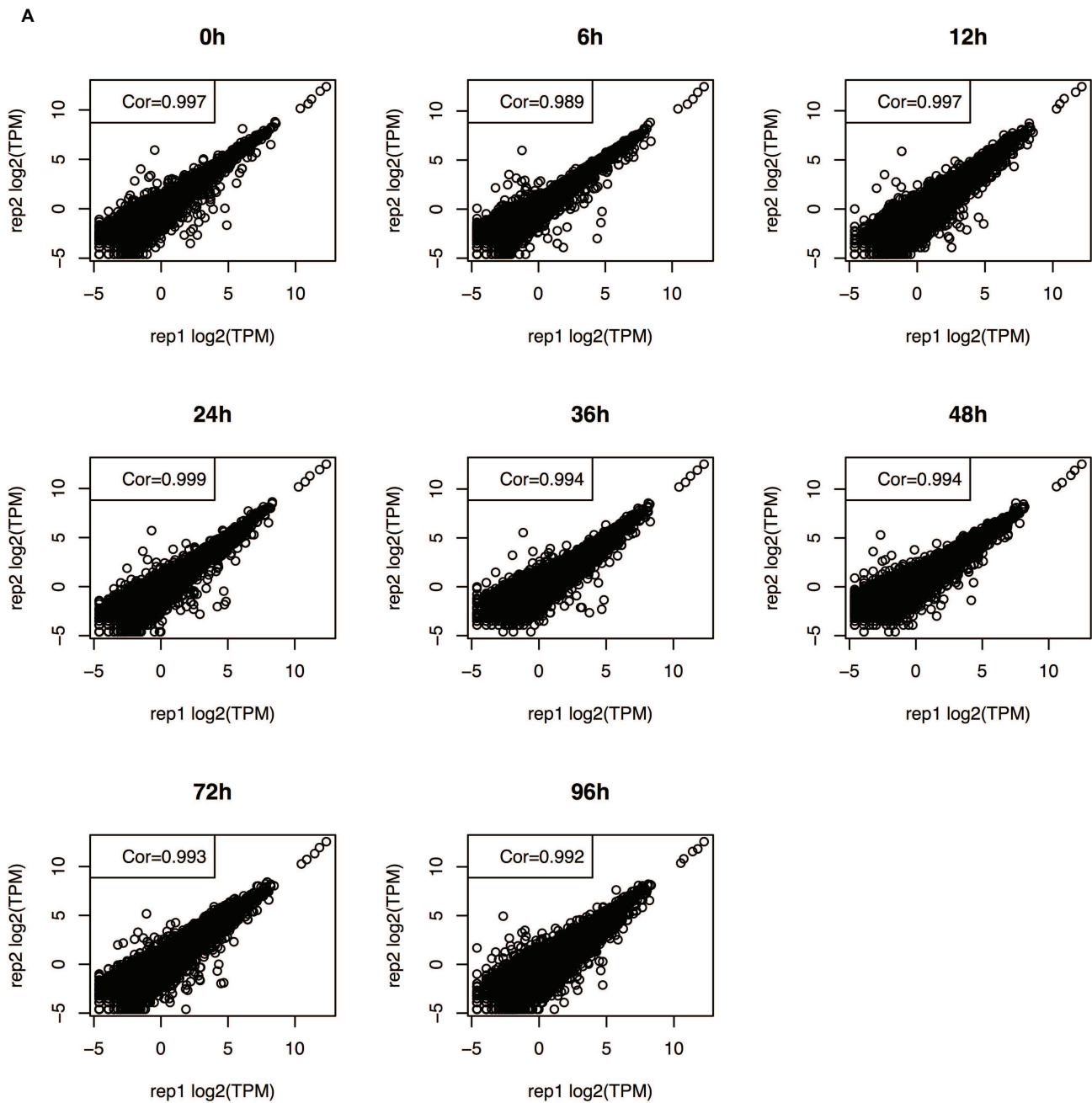
B

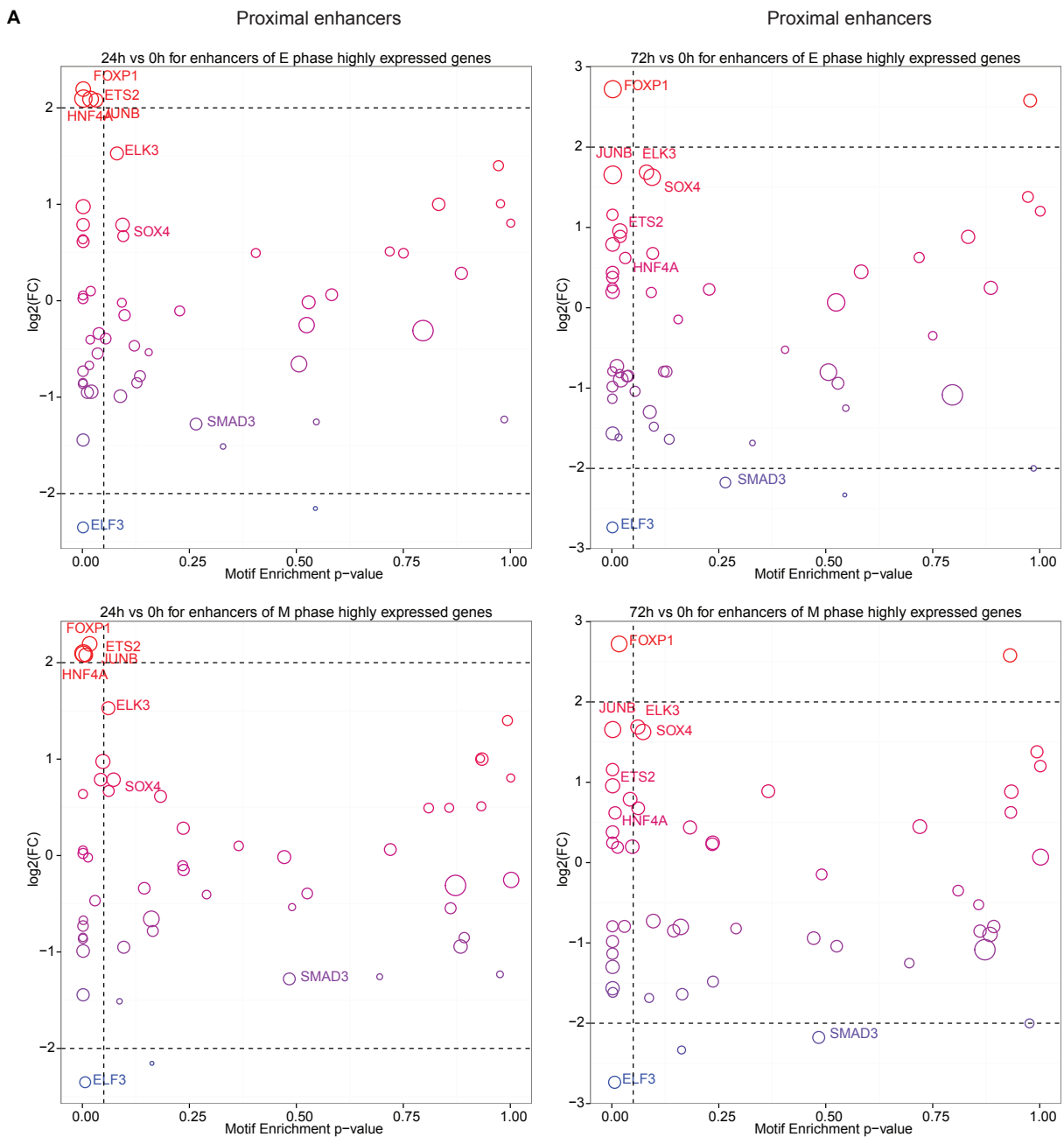| Time course	0h	6h	12h	24h	36h	48h	72h	96h
Rep1 Library Size (Million)	37.3	43.5	41.5	36.7	44.3	45.4	37.2	39.0
Rep2 Library Size (Million)	36.6	39.4	40.1	36.1	39.0	40.2	39.5	37.5

Figure S2. RNA-seq statistics.
(A) Scatter plots of TPM (transition per million) showing robust correlation between biological replicates of RNA-seq. **(B)** Table summarizing number of reads per sample.

A

B

Figure S3. PCR analyses of known Transcriptional drivers of EMT.
(A) Time-course qPCR analyses showing the relative expression changes of SNAI1/2, TWIST1/2 and ZEB1/2 during TGF-β-induced EMT. **(B)** Absolute qPCR analyses showing the molecules per cell for SNAI1, SNAI2 and JUNB at 12 h into TGF-β-induced EMT.

A

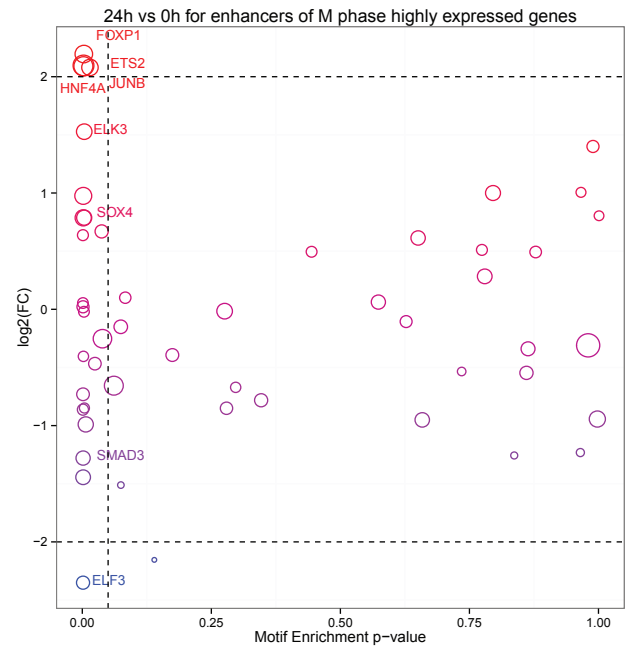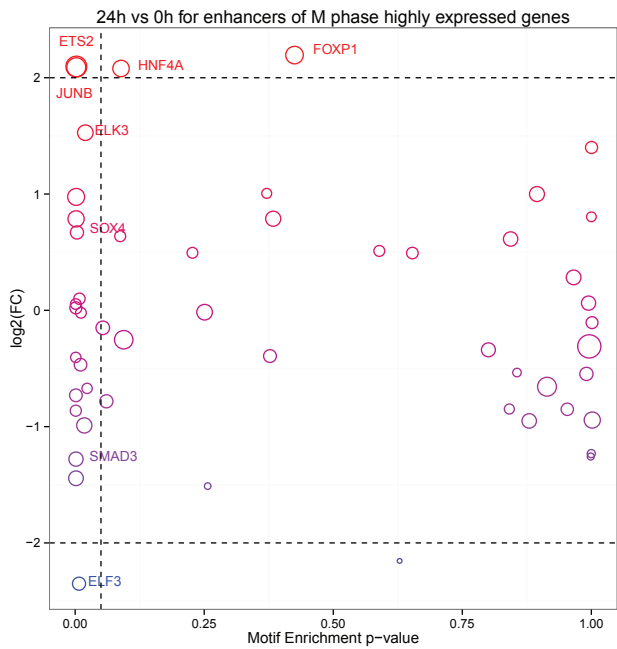Proximal enhancers

Proximal enhancers

B Distal enhancers

24h vs 0h for enhancers of E phase highly expressed genes

24h vs 0h for enhancers of M phase highly expressed genes

24h vs 0h for enhancers of P phase highly expressed genes

C Gene body enhancers

24h vs 0h for enhancers of E phase highly expressed genes

24h vs 0h for enhancers of M phase highly expressed genes
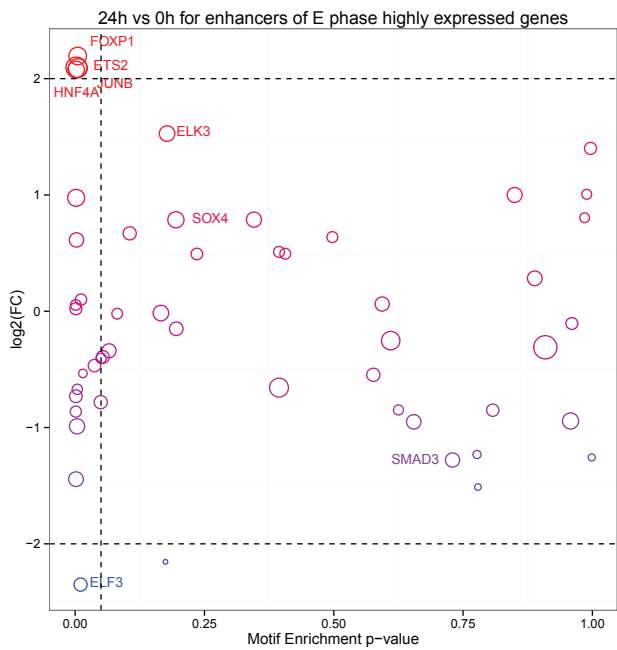
24h vs 0h for enhancers of P phase highly expressed genes
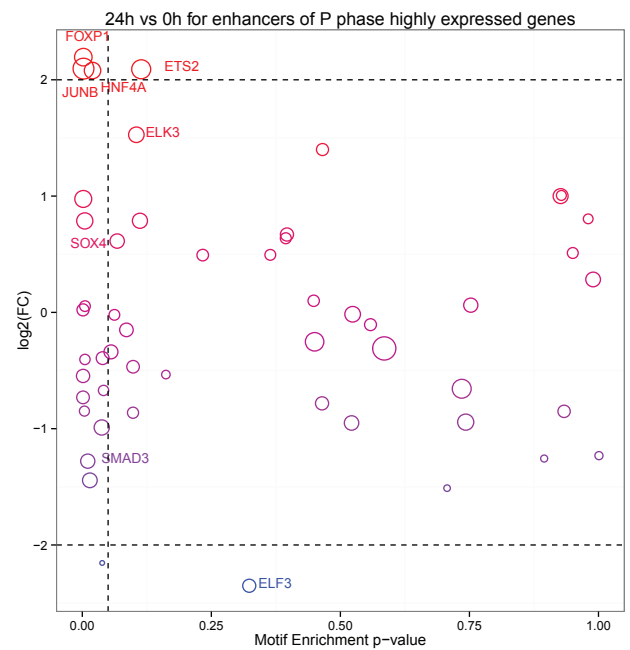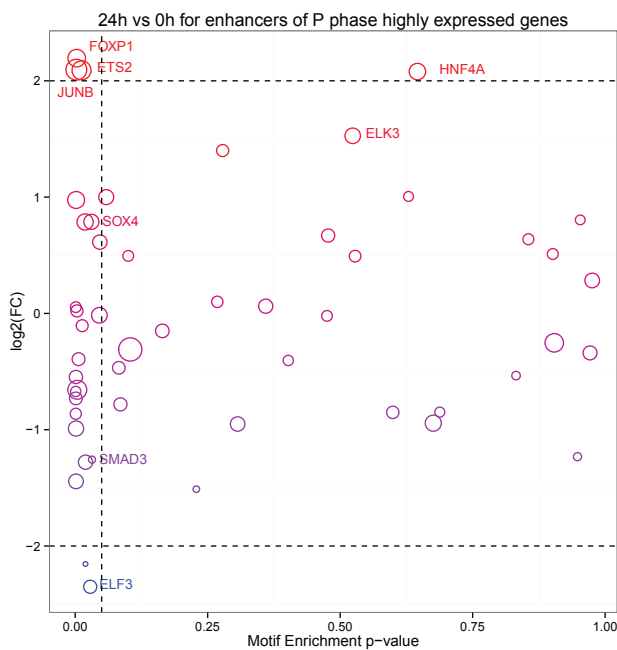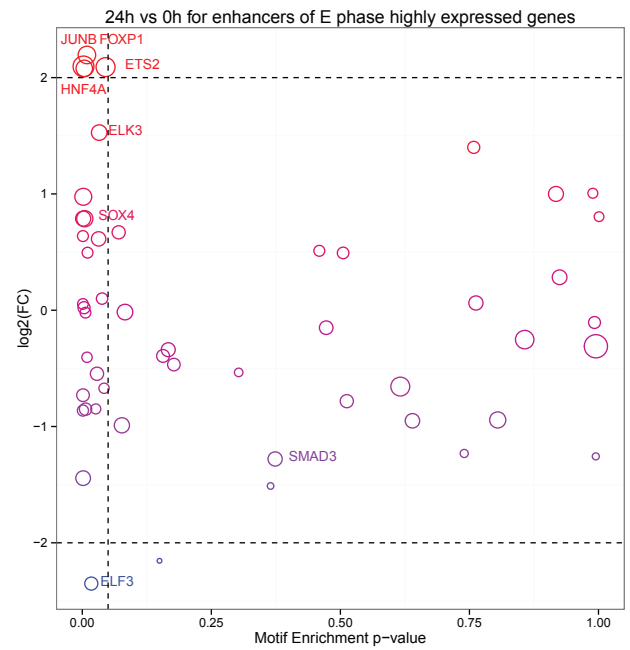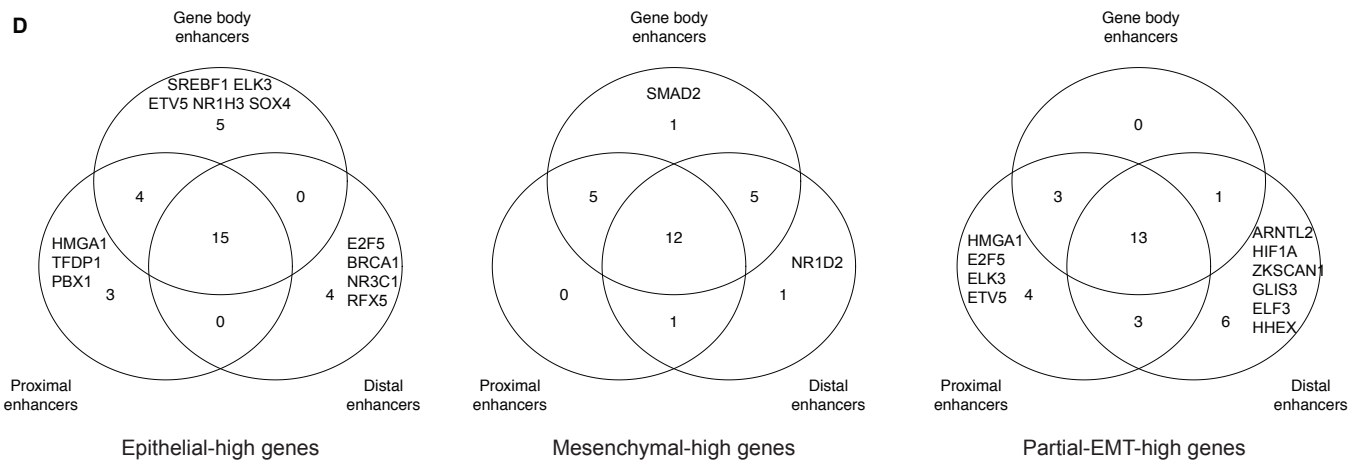
Figure S4. ETS2, HNF4A, JUNB and FOXP1 are putative master TFs for EMT.
(A) Enrichment p-values of TF binding motifs in the proximal enhancers of epithelial high genes (x-axis) are plotted against expression changes during EMT (y-axis; 24 h vs. 0 h, right panel; 72 h vs. 0 h, left panel). Each circle represents a TF. Dotted lines represent the cutoff for enrichment (p-value < 0.05) and differential expression (absolute fold change >=2). **(B)** Same as (A) but with Enrichment p-values calculated from distal enhancers. **(C)** Same as (A) but with Enrichment p-values calculated from gene body enhancers. **(D)** Venn diagrams showing the overlap of TFs enriched in proximal enhancers, distal enhancers and gene body enhancers for epithelial-high, partial-EMT-high and mesenchymal-high genes.
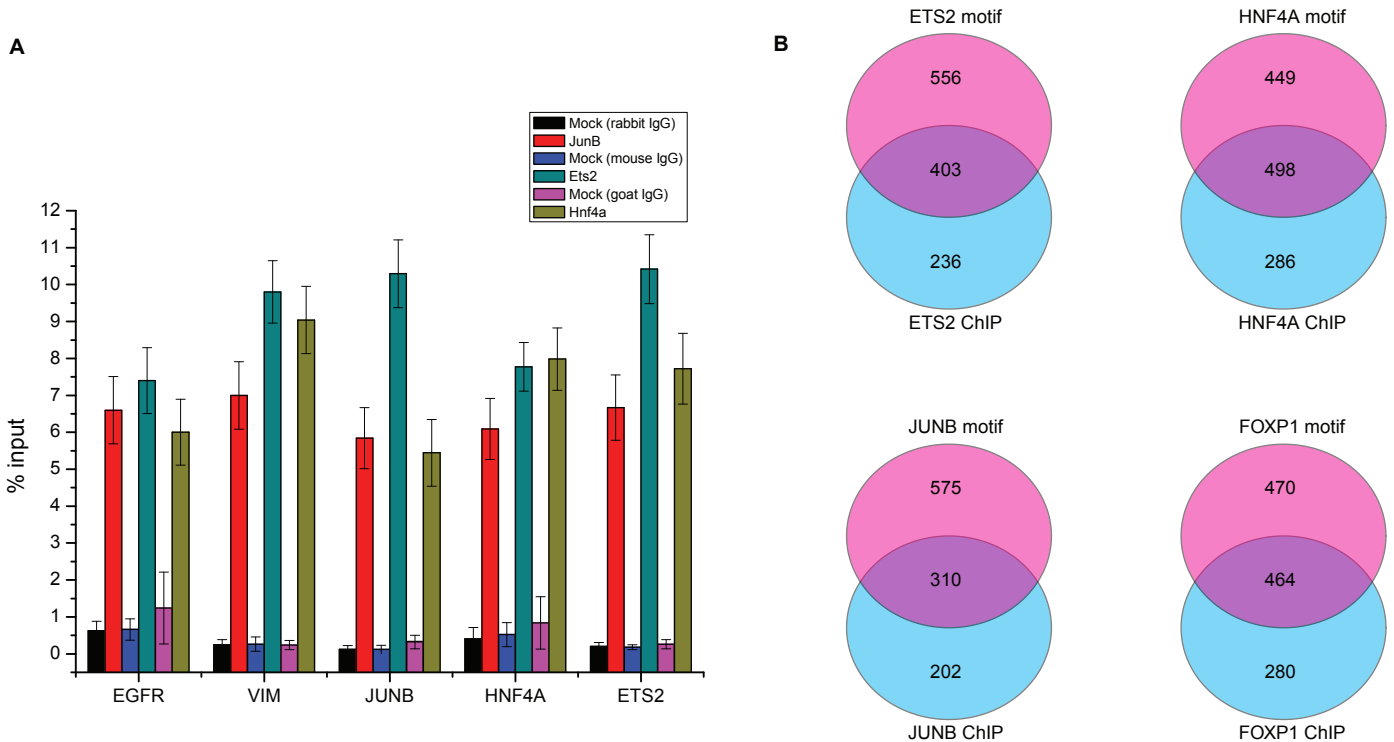

Figure S5. ChIP data supports that ETS2, HNF4A and JUNB are master TFs for EMT.
**(A)** ChIP-qPCR analyses showing the binding of ETS2, HNF4A and JUNB to selected EMT gene enhancers.
(B) Venn diagrams depicting the overlap between target EMT genes predicted by presence of binding motif in enhancers (upper circle) or ChIP-seq peak in enhancers (lower circle).
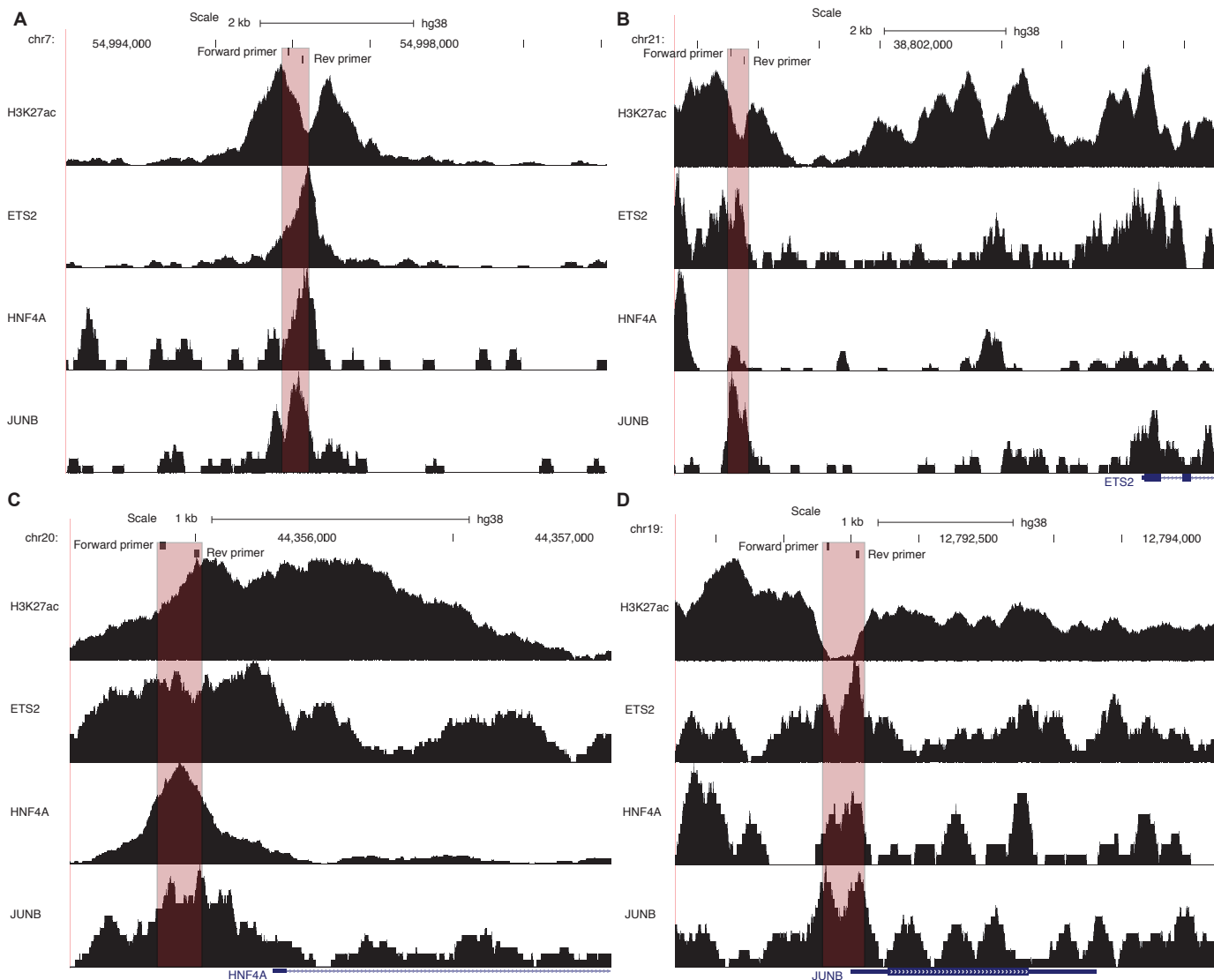
Figure S6. Cumulative binding of ETS2, HNF4A and JUNB at EMT-associated enhancers.
(A-D) Genome browser tracks showing the cumulative binding of ETS2, HNF4A and JUNB at enhancers near EGFR (A), ETS2 (B), HNF4A (C) and JUNB (D). The pink rectangles highlight the regions targeted by ChIP-qPCR primers.
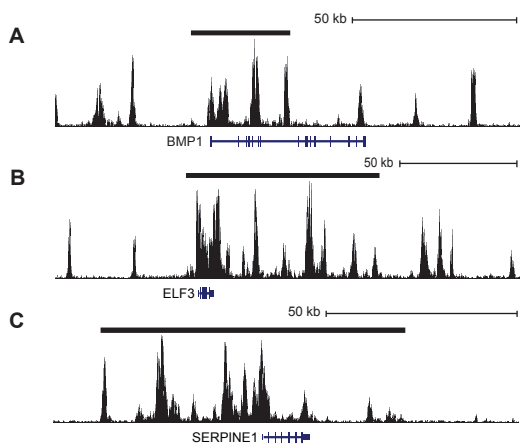
Figure S7. Key EMT genes are associated with super-enhancers.
**(A-C)** Genome browser representation of super-enhancers associated with BMP1, ELF3 and SERPINE1.
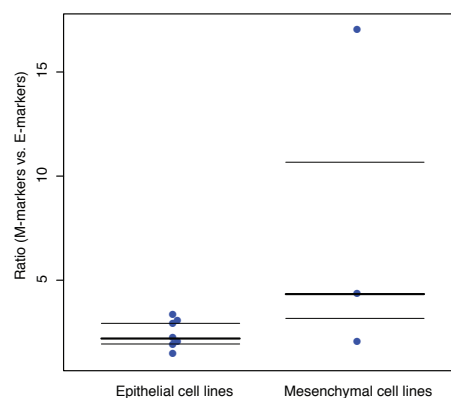
Figure S8. The distribution of E-markers associated with super-enhancers vs. M-markers associated with super-enhancers.
Scatter plots dowing the distribution of the ratios between M-markers associated with super-enhancers vs. E-markers associated with super-enhancers.
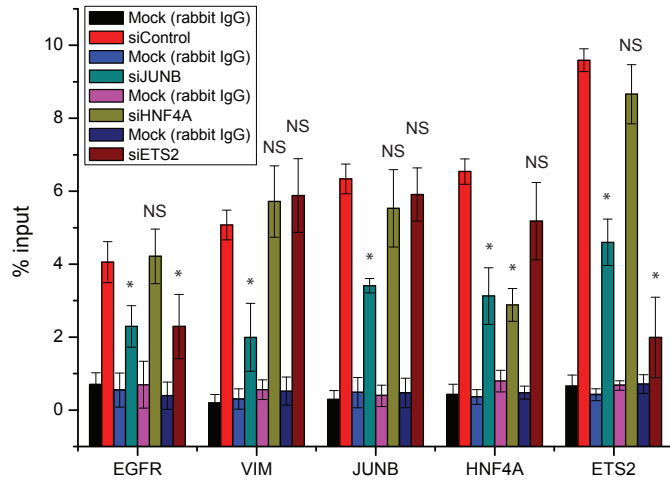
Figure S9. BRD4 bound to sites occupied by ETS2, HNF4A and JUNB.
ChIP-qPCR analyses showing the binding of BRD4 to sites co-bound by ETS2 HNF4A and JUNB and the effects of siETS2, siHNF4A and siJUNB on BRD4 binding. NS = not significant; * = p < 0.01.
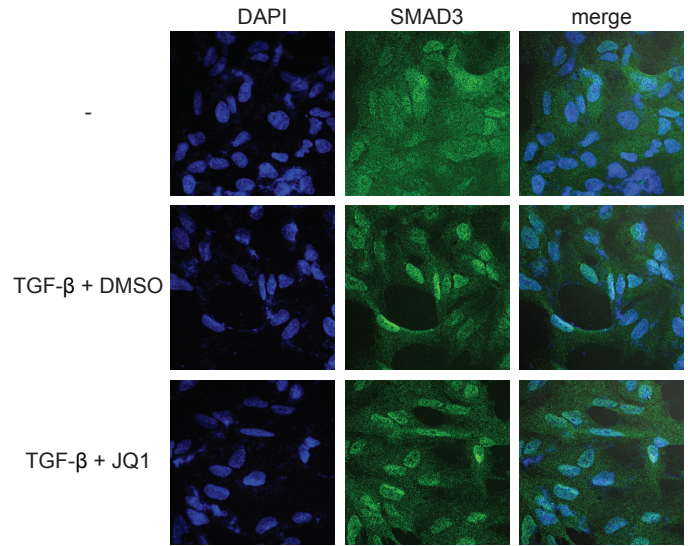
Figure S10. JQ1 didn't disrupt SMAD3 functionality.
Immunofluorescence staining for SMAD3 in A549 cells stimulated with TGF-β for 24 h in the presence of JQ1 or DMSO.