

Fig. S1. The non-coding transcriptome is a key component of the TGF- β response of lung fibroblasts. Circos plot showing the genome-wide transcriptional profiling of TGF- β -regulated mRNAs and ncRNAs in lung fibroblasts (Datasets 1 and 2). (b,d,f) Log₂ FoldChange of differentially expressed lincRNAs (d), protein-coding genes near to lincRNA candidate loci (<500kb) (b), and miRNAs (f). Upregulated and downregulated genes are shown in red and green respectively. (a,c,e) Associated protein-coding gene names (a), lincRNA names (c) colored according to their biotype: lincRNAs (orange), pri-miRNAs (green), antisense RNAs (turquoise), pseudogenes (blue), and mature miRNA names (e). (g,h) Inner links representing local lincRNAs-protein-coding genes (black) and lincRNAs-miRNAs (blue) co-regulation associations.

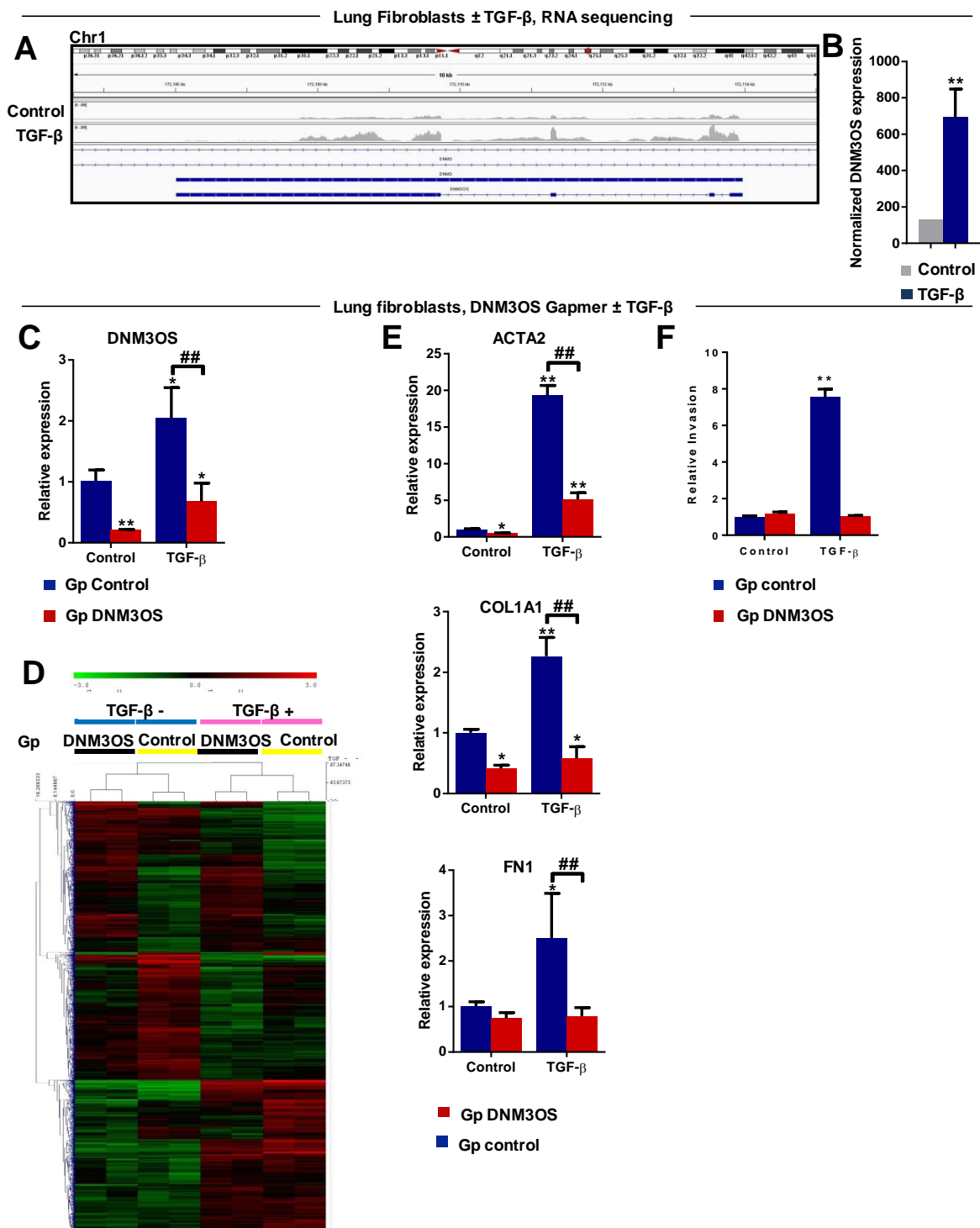


Fig. S2. Identification of DNM3OS as a key effector of TGF-β signaling. (A) Screenshot from Integrative Genomic Viewer displaying representative RNA-Seq data of the DNM3OS locus (Dataset 1). An increase of total reads associated with the unprocessed transcript (variant 1, long non-coding RNA, 7,957 bp lncRNA, NR_038397.2) and the spliced transcript (variant 2, 4,051 bp linear ncRNA, lncRNA, NR_103486.1) following TGF-β treatment is shown. (B) Bar charts showing the normalized expression of DNM3OS in control or TGF-β stimulated cells. Data from high-throughput sequencing are expressed as normalized counts ± SEM for three independent experiments. ** P<0.01. (C-E) Functional impact of DNM3OS silencing on TGF-β signaling in pulmonary fibroblasts. MRC5 cells were transfected with either a control or a DNM3OS-specific gapmer (Gp) and then incubated with or without TGF-β (C) Bar charts showing the relative expression of DNM3OS in the indicated conditions. Data are expressed as mean ± SEM. (n=3) * P<0.05 ** P<0.01 ## P<0.01. (D) Heatmap comparing the normalized log2 expression of significantly modulated transcripts obtained by microarray analysis (n=2 per group, Dataset 3). (E) Bar charts showing the relative expression of ACTA2 (α-SMA) COL1A1 and FN1 compared to PPIA in the indicated conditions. Data are expressed as mean ± SEM. (n=3) * P<0.05 ** P<0.01 ## P<0.01. (F) Bar charts showing the relative quantification of invasion in the indicated conditions. Data are expressed as mean ± SEM (n=3). ** P<0.01.

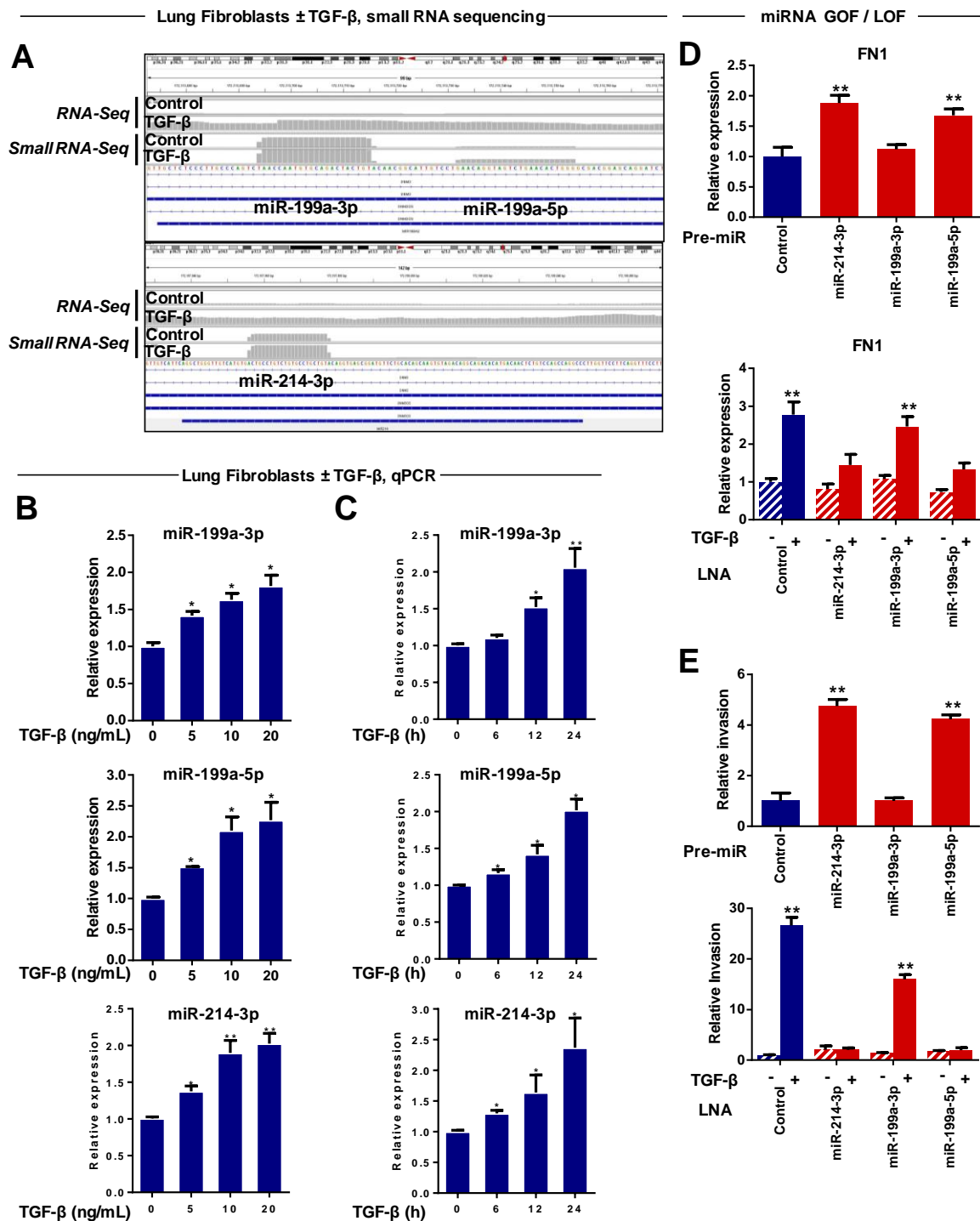


Fig. S3. DNMT3OS is processed into three profibrotic miRNAs in lung fibroblasts. (A) Screenshot from IGV browser displaying representative small RNA-Seq data of the DNMT3OS locus in TGF-β-exposed human pulmonary fibroblasts or control conditions (Dataset 2). Zoomed in view of the regions corresponding to miR-199a2 and miR-214, which shows, in response to TGF-β, an increase number of reads associated with the following mature miRNAs: miR-199a-3, miR-199a-5p and miR-214-3p. As the expression of miR-214-5p represents only 5% of the total reads of miR-214, this miRNA was not considered relevant. (B,C) Bar charts showing dose- (B) and time-dependent (C) expression of DNMT3OS-associated miRNAs in MRC5 cells exposed or not to TGF-β. RNU44 was used as reference. Data are expressed as mean ± SEM (n=3). * P<0.05 ** P<0.01. (D) Bar charts showing the relative expression of FN1 compared to PPIA in the indicated condition. Data are expressed as mean ± SEM. (n=3) ** P<0.01. (E) Bar charts showing the relative quantification of invasion in the indicated conditions. Data are expressed as mean ± SEM (n=3). ** P<0.01.

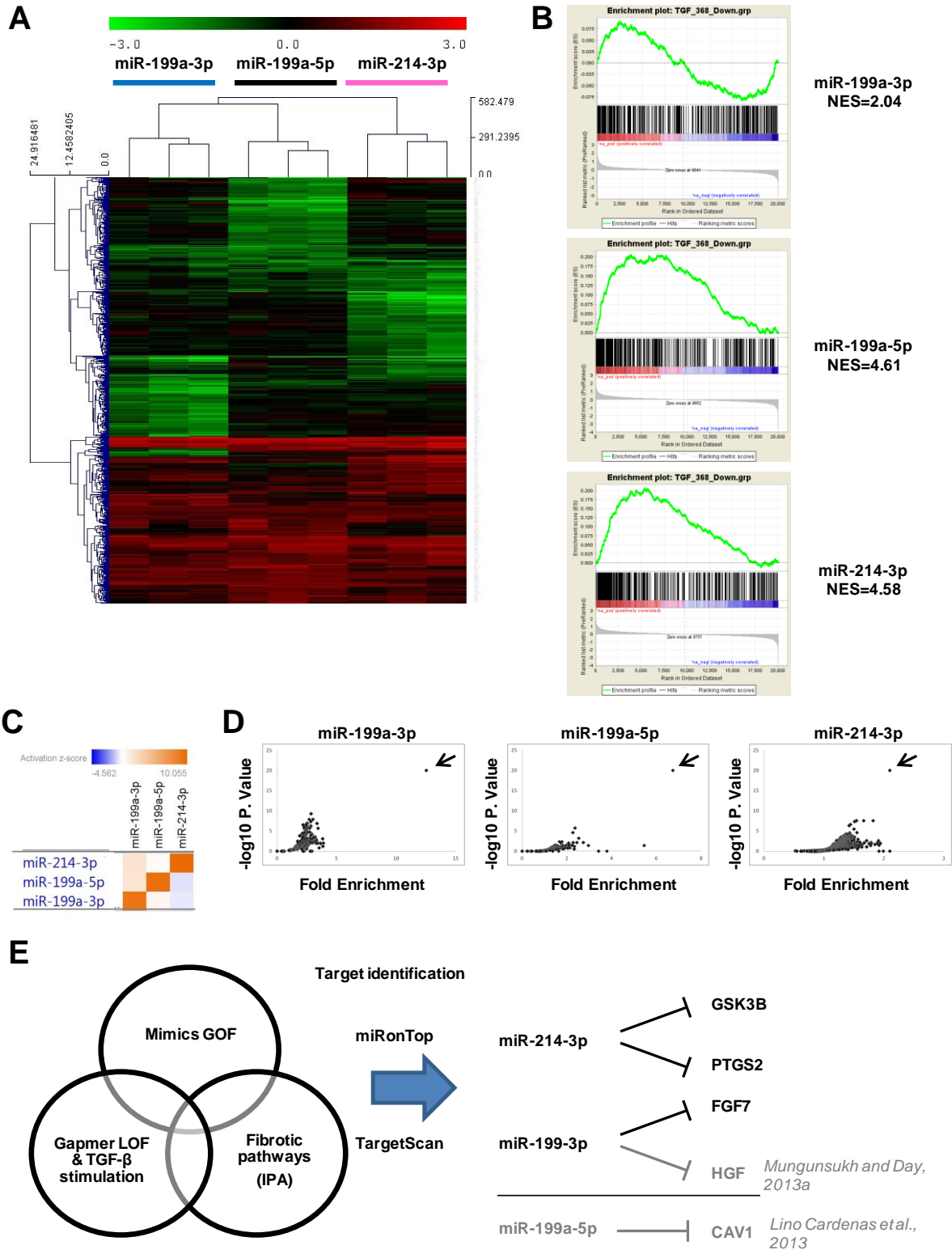


Fig. S4. Identification of the cellular pathways and gene targets associated with the miR-199a~214 cluster in human lung fibroblasts. (A) Heatmap showing the genes differentially expressed after individual miRNA mimics overexpression in lung fibroblasts (dataset 4). **(B)** GSEA plots of an experimental TGF- β -signature (Dataset 5) showing a significant enrichment of miR-199a-5p and miR-214-3p down-regulated transcripts. Genes whose expression is downregulated after miRNA mimics overexpression were compared to an experimental TGF- β signature obtained in the same cells (MRC5 cells). TGF- β signature consists of 368 transcripts downregulated in response to TGF- β (\log_2 ratio < -1 , adj.p value < 0.01). In each case, graphs show the enrichment plot, the score at the peak corresponding to the ES and the position of the TGF- β gene set in the ranked list of genes (each transcript is indicated by a vertical bar). **(C,D)** Overrepresentation of miRNA predicted targets in the set of downregulated transcripts following miR-199a-5p/3p and miR-214-3p transfection using **(C)** Ingenuity Pathway Analysis and **(D)** the webtool miRonTop. Each arrow indicates the corresponding overexpressed miRNA **(E)** Global strategy combining genomics data and bioinformatics tools to identify miR-199a-3p and miR-214-3p target genes (GOF: gain of function, LOF: loss of function).

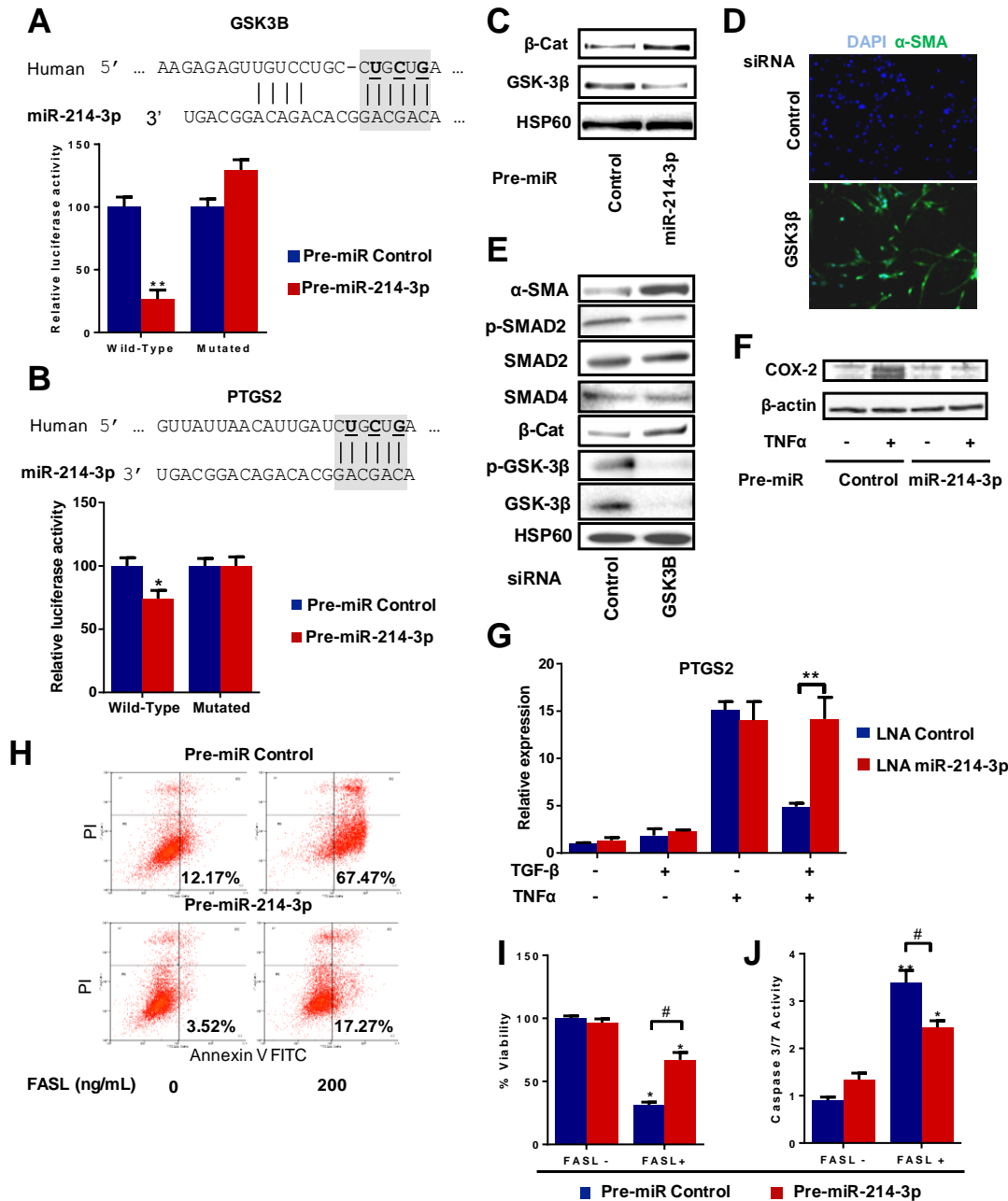


Fig. S5. miR-214-3p mediates TGF- β -induced lung fibroblast activation by targeting two distinct targets: GSK-3 β and COX-2. (A,B) GSK3B and PTGS2 are direct targets of miR-214-3p. Position of miR-214-3p functional target site in hGSK3B and hPTGS2 3' UTR and validation of the functional interaction between miR-214-3p and its targets using luciferase reporter assay. The "seed" region of the miRNA is highlighted in grey. Bases that have been mutated in the psiCHECK-2 construct are underlined. Pre-miR-214-3p or control and hGSK3B or hPTGS2 3'UTR-derived psiCHECK-2 constructs were transfected in HEK293 cells. All renilla luciferase activities were normalized with firefly luciferase activity. (n=3) ** P<0.01. (C) Western Blot showing the impact of miR-214-3p overexpression in lung fibroblasts on β -catenin and GSK-3 β protein expression. HSP60 was used as a loading control. One representative experiment out of two is shown. (D,E) Effects of siRNA-mediated depletion of GSK-3 β in lung fibroblasts on myofibroblast differentiation, SMAD signaling and GSK-3 β / β -catenin axis. MRC5 cells were transfected with validated siRNA against GSK-3 β or control. (D) Immunofluorescence analysis using antibodies against α -SMA (green) and DAPI (blue). Representative images out of 2 experiments are shown at $\times 10$ magnification (E) Western Blot showing α -SMA expression, SMAD signaling (p-SMAD2 and SMAD2 and SMAD4) and the GSK-3 β / β -catenin axis (p-GSK-3 β , GSK-3 β and β -catenin). HSP60 was used as a loading control. One representative experiment out of two is shown. (F,G) Gain and loss of function experiments showing that miR-214-3p suppresses COX-2 expression. (F) Western blot showing COX-2 level. β -actin was used as a loading control. One representative experiment out of two is shown. (G) Bar chart showing PTGS2 relative expression compare to PPIA in the indicated conditions. Data are expressed as mean \pm SEM. (n=3) ** P<0.01. (H-J) miR-214-3p overexpression protects lung fibroblasts from FASL-induced cell death. Cell viability was quantified using (H) annexin V / Propidium iodide by flow cytometry (one representative experiment out of 3 is shown), (I) ATP-based assay (n=3, * P<0.05, # P<0.01) and (J) caspase 3/7 activity (n=3, * P<0.05, # P<0.01).

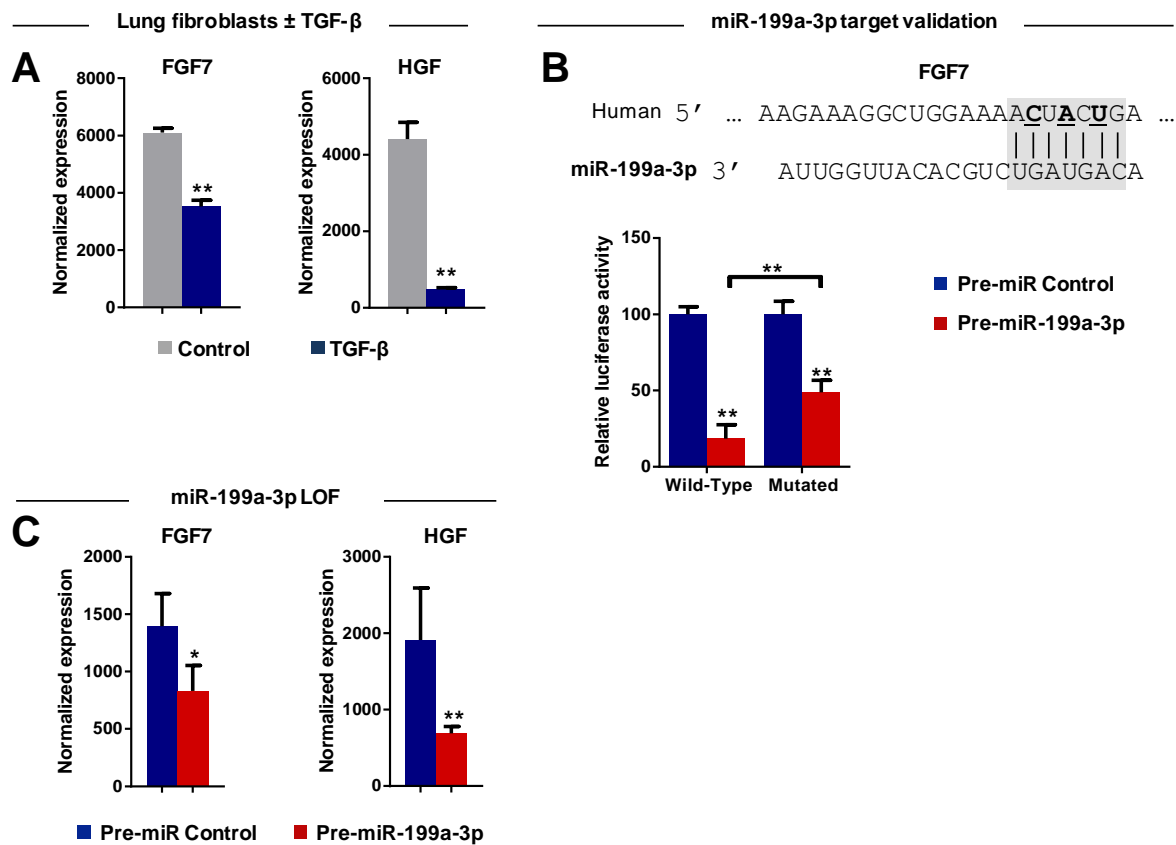
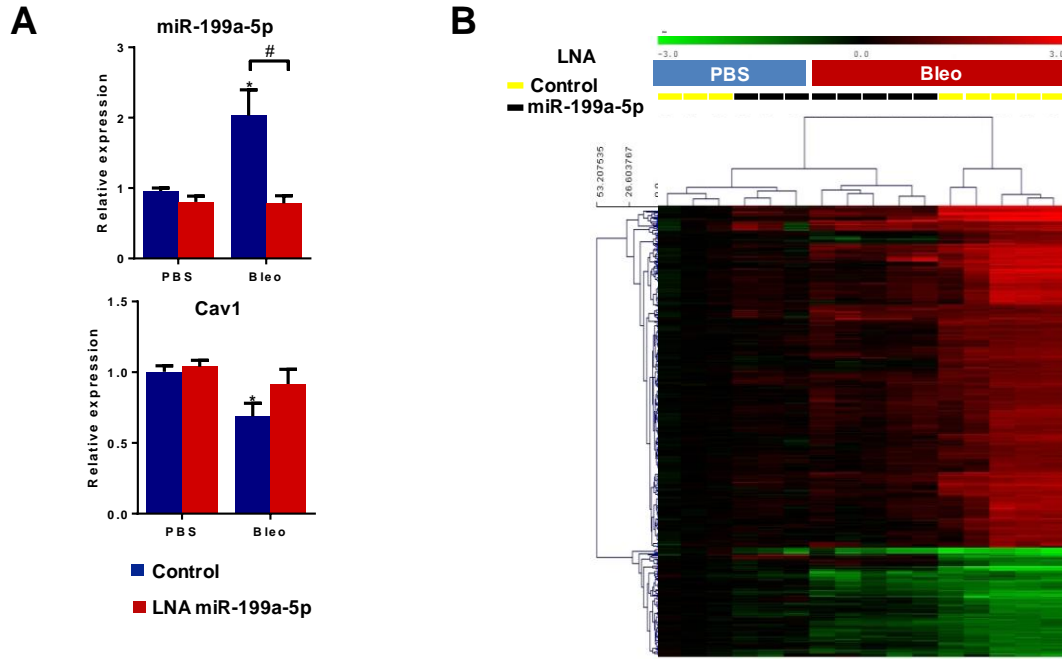


Fig. S6. KGF/FGF7 and HGF are direct targets of miR-199a-3p. (A) HGF and KGF/FGF7 transcripts are down-regulated by TGF-β in lung fibroblasts. Normalized expression from transcriptomic studies are shown. (B) Position of miR-199a-3p functional target site in hFGF7 3' UTR and validation of the functional interaction between miR-199a-3p and FGF7 using luciferase reporter assay. The “seed” region of the miRNA is highlighted in grey. Bases that have been mutated in the psiCHECK-2 construct are underlined. Pre-miR-199a-3p or control and hFGF7 3'UTR-derived psiCHECK-2 constructs were transfected in HEK293 cells. All renilla luciferase activities were normalized with firefly luciferase activity. (n=3) ** P<0.01. (C) Bar charts showing the normalized expression values of KGF and HGF in MRC5 lung fibroblasts after transfection with pre-miR-199a-3p using microarray data. Data are expressed as mean ± SEM (n=2). * P<0.05 ** P<0.01.

LNA-miR-199a-5p intratracheal administration



Cav1 TSB intratracheal administration



Fig. S7. Interfering with miR-199a-5p function prevents lung fibrosis in vivo. (A) Bar charts showing the relative pulmonary expression of miR-199a-5p (compared to SNO251) as well as Cav1 (compared to PPIA) in the LNA-miR-199a-5p protocol. Data are expressed as mean \pm SEM. $n=4-6$ mice in each group. * $P<0.05$, # $P<0.05$. (B) Heatmap representing the differential transcriptomic response to bleomycin in the lungs of mice treated with LNA-miR-199a-5p or LNA-control ($n=3-5$ mice in each group, Dataset 6). (C) Position and alignment of the two Cav1 TSB used in vivo with Cav1 3'UTR. (D) Ponceau staining of the membrane used in Fig. 4e showing equal loading of the samples.

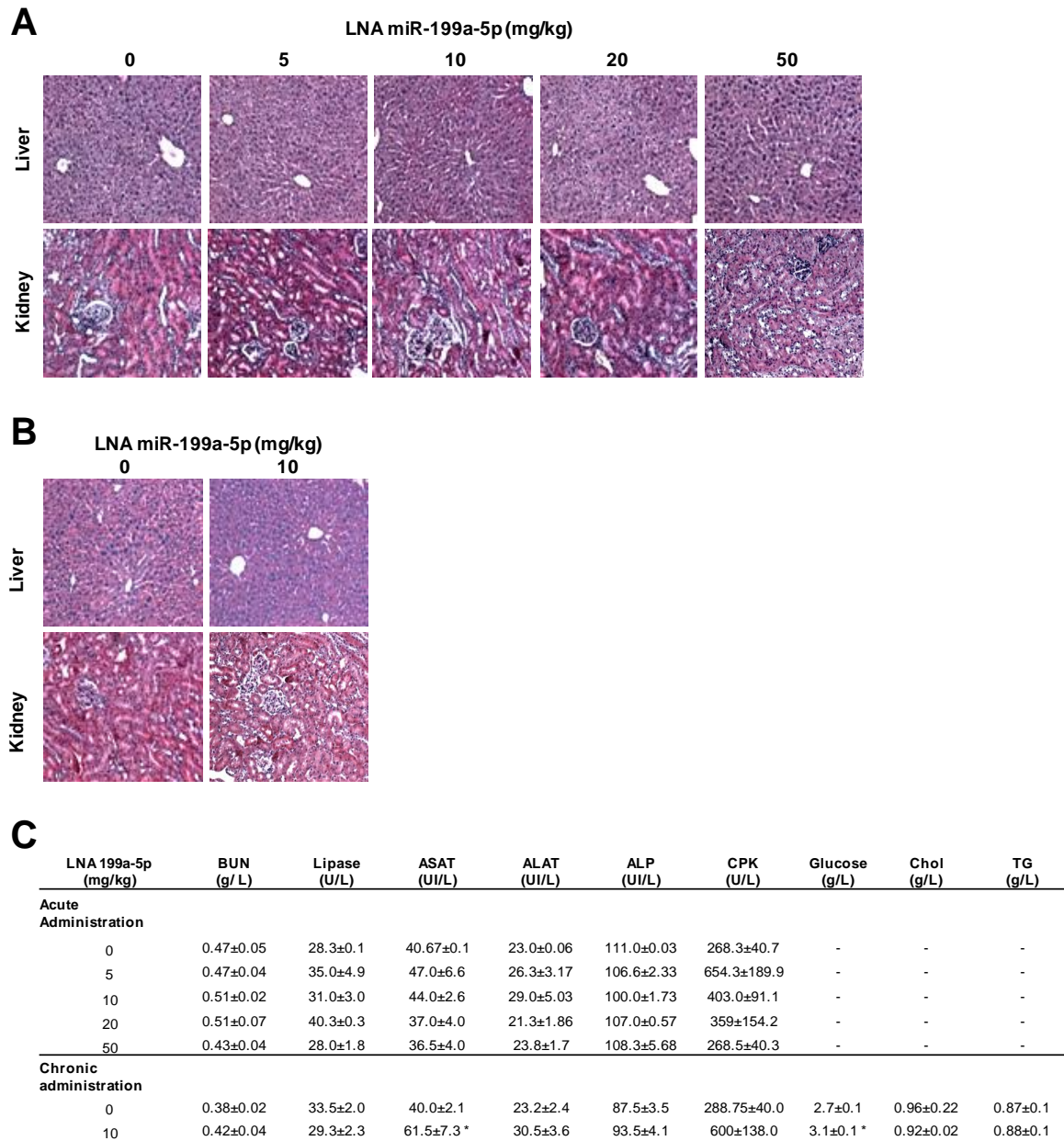


Fig. S8. Acute and chronic systemic administration of LNA-199a-5p inhibitor does not induce major side effects. (A) Acute toxicity study. LNA-miR-199a-5p antisense probe was administered intraperitoneally in mice (n=3 per group) at dose rate of 0, 5, 10, 20 and 50 mg/kg body weight. 4 days after injection, kidneys and livers were collected and processed for histological analysis. One representative H&E section is shown for each condition at x 10 magnification. (B) Chronic toxicity study. LNA-miR-199a-5p antisense probe was repeatedly administered intraperitoneally in mice (n=3 mice per group) at dose rate of 10 mg/kg body weight once a week for 4 weeks. Kidneys and livers were collected and processed for histological analysis. One representative H&E section is shown for each condition at x 10 magnification. (C) Clinical chemistry measurement after acute and chronic systemic administration of LNA-miR-199a-5p antisense probe (n=3 per group). Data are expressed as mean ± SEM, *P<0.05. BUN: Blood Urea Nitrogen, ASAT: aspartate aminotransferase, ALAT: alanine aminotransferase, ALP: Alkaline Phosphatase, CPK: Creatine Phosphokinase, Chol: cholesterol, TG: triglycerides.

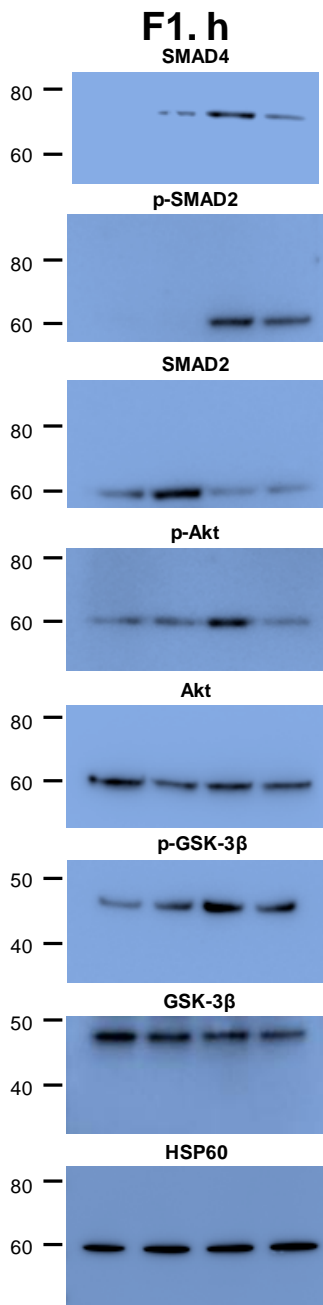


Fig. S9. Raw gel images corresponding to western blot shown on Figure 1.

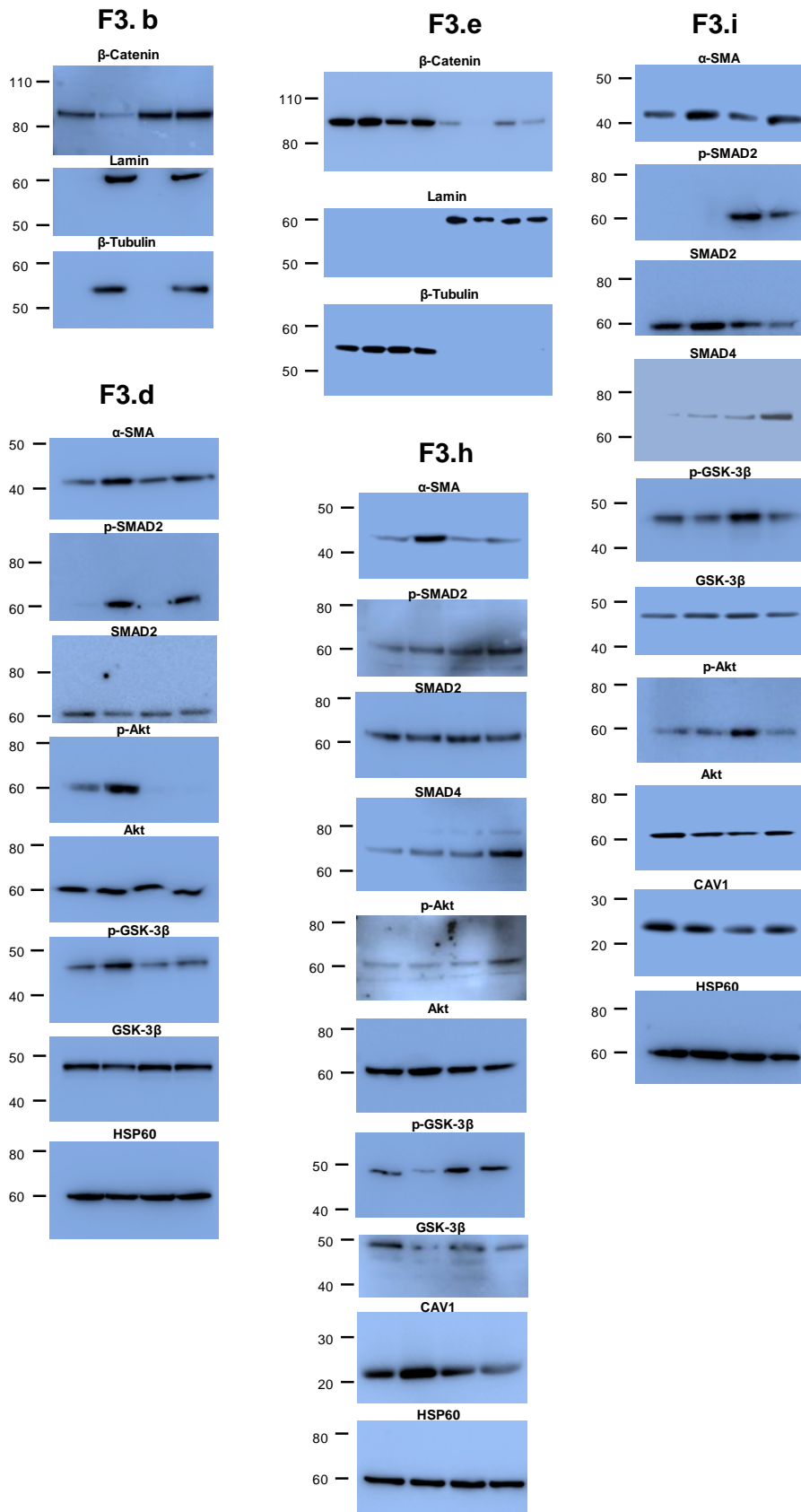


Fig. S10. Raw gel images corresponding to western blot shown on Figure 3.

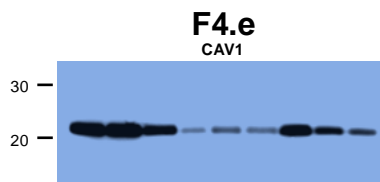


Fig. S11. Raw gel images corresponding to western blot shown on Figure 4.

Table S1. List of the TGF- β core signature of 419 coding genes significantly modulated by TGF- β in lung fibroblasts, as identified by Ingenuity Pathway analysis (dataset 1). The table indicates the Log Ratio (TGF- β / control), and the predicted activation state of the TGF- β pathway (ie: activated, inhibited or affected when the modulation has not been clearly demonstrated).

Name	Log2 FC	Prediction
AASS	-1.51	Affected
ABCE1	0.787	Affected
ABCG2	-2.331	Activated
ACLY	1.114	Activated
ACSL3	0.835	Affected
ACTA2	3.885	Activated
ACTC1	8.242	Activated
ACTG2	2.631	Activated
ACTN1	0.931	Activated
ACVR1	1.053	Activated
ACVRL1	-1.329	Inhibited
ADAM12	4.923	Activated
ADAM19	3.183	Activated
ADAMTS2	0.804	Activated
ADI1	-0.797	Activated
ADM	-2.302	Activated
ADORA2B	-0.825	Affected
AKR1C1	-2.899	Affected
ALDH18A1	1.145	Activated
ALDH2	-1.057	Activated
AMD1	1.007	Affected
ANGPT1	-0.784	Activated
ANGPTL4	-3.925	Inhibited
ANKH	1.756	Activated
ANKLE2	1.517	Affected
ANKRD1	4.075	Activated
ANPEP	-1.546	Activated
ANXA11	-0.859	Affected
ANXA2	1.014	Activated
ANXA8	0.877	Activated
APOE	-0.704	Inhibited
AQP1	0.772	Affected
ARF4	1.199	Activated
ARL4A	2.127	Affected
ARPC2	0.796	Activated
ASNS	2.345	Activated
ASS1	1.53	Activated
ASUN	1.539	Inhibited
ATF4	0.976	Affected
ATXN1	1.14	Affected
BAMBI	-0.964	Affected
BCL2	-1.701	Inhibited
BCL2L11	-0.879	Inhibited
BGN	1.85	Activated
BHLHE40	3.156	Activated
BIN1	-0.892	Affected
BMP1	0.738	Activated
BMP2	-2.535	Inhibited
BMP4	-2.35	Affected
BRIP1	0.767	Inhibited
BTG1	-0.989	Inhibited
C1S	-0.769	Inhibited
C5	-1.066	Affected
C9orf3	1.271	Affected
CADM1	0.796	Affected
CALCOCO2	0.89	Affected
CALCR	0.941	Affected

CALD1	2.632	Activated
CALM2	1.001	Activated
CAMK2N1	-0.791	Inhibited
CAP1	1.222	Activated
CARS	0.732	Affected
CASP1	-1.775	Inhibited
CASP4	-1.004	Activated
CASP8	-1.014	Affected
CASP9	-1.06	Affected
CAT	-1.508	Activated
CAV2	0.912	Activated
CBFB	0.944	Affected
CCDC85B	-1.357	Affected
CCL2	-3.442	Inhibited
CCNA2	0.849	Inhibited
CCND1	-0.773	Inhibited
CCNG2	-1.118	Inhibited
CD4	-0.888	Activated
CD44	-1.139	Activated
CDC42EP4	-1.616	Affected
CDH11	0.809	Affected
CDH2	2.97	Activated
CDH4	-0.798	Inhibited
CDKN1C	-1.599	Inhibited
CDKN2B	4.303	Activated
CDT1	-1.342	Affected
CELF2	-1.596	Affected
CHST11	1.463	Activated
CITED2	-1.353	Activated
CKS2	-1.009	Affected
CLIC4	0.909	Activated
CLU	-0.845	Inhibited
CNN1	2.547	Activated
CNN3	0.716	Activated
COL11A1	1.932	Activated
COL16A1	0.985	Activated
COL18A1	-0.863	Affected
COL1A1	1.545	Activated
COL1A2	0.747	Activated
COL4A1	2.652	Activated
COL4A2	1.466	Activated
COL4A6	-2.537	Inhibited
COL5A1	1.905	Activated
COL6A1	-0.884	Inhibited
COL7A1	1.415	Activated
COL8A1	1.819	Activated
COMP	3.37	Activated
CORIN	-0.797	Affected
COTL1	0.774	Activated
CPXM1	-2.175	Affected
CREB3	0.702	Affected
CSF1	-0.891	Inhibited
CSPG4	0.961	Activated
CSRP1	1.334	Activated
CSRP2	2.004	Activated
CTGF	1.443	Activated
CTPS1	2.446	Activated
CTSC	-1.542	Affected
CTSH	-0.843	Inhibited
CTSK	-1.246	Inhibited
CXCL12	-1.276	Activated
CYR61	1.262	Activated
DAD1	0.822	Activated

DCN	-1.038	Activated
DDB2	-0.761	Affected
DDIT4	1.62	Affected
DDR2	0.753	Affected
DDX21	1.137	Affected
DEPTOR	-1.115	Activated
DES	2.107	Activated
DKC1	0.856	Affected
DNAJB4	1.014	Affected
DOCK4	-1.122	Inhibited
DOK1	-0.862	Inhibited
DPYSL3	0.9	Affected
DSG2	0.779	Affected
DSP	2.164	Affected
DTX4	-3.173	Affected
DUSP4	-2.578	Inhibited
DYRK2	1.863	Affected
E2F1	-0.773	Inhibited
EDN1	3.829	Activated
EDNRA	-1.148	Activated
EGR2	6.015	Activated
EHMT2	-0.964	Affected
ELN	2.7	Activated
EPHB2	1.259	Activated
EPRS	1.53	Activated
F2R	-1.479	Inhibited
FAM110B	-0.893	Affected
FAM3C	0.722	Activated
FAP	0.833	Activated
FBLN5	1.372	Activated
FBN1	0.857	Activated
FDXR	-0.77	Affected
FERMT2	1.835	Activated
FGF2	1.382	Activated
FGF5	-0.724	Inhibited
FGF9	-2.547	Affected
FHL1	-1.351	Activated
FILIP1L	0.74	Activated
FLNA	0.727	Activated
FLNB	2.09	Activated
FN1	2.231	Activated
FNBP1	-0.861	Affected
FNDC3B	0.849	Activated
FOSL2	-0.815	Inhibited
FOXC1	-1.532	Inhibited
FOXC2	1.656	Activated
FSTL3	2.372	Activated
FTH1	-1.096	Activated
FTL	-1.204	Activated
FZD1	-1.411	Inhibited
GADD45B	2.706	Activated
GAL	1.229	Activated
GALM	-1.826	Activated
GARS	1.675	Activated
GAS1	-2.466	Affected
GBP1	1.147	Inhibited
GBP2	-0.897	Affected
GCLC	-0.745	Activated
GDF6	1.11	Activated
GFPT2	0.863	Affected
GLI1	2.005	Activated
GLI2	0.97	Activated
GLRX2	1.399	Affected

GMPR	-1.477	Affected
GNA13	1.037	Activated
GNB4	0.854	Activated
GNG2	-1.3	Inhibited
GPRC5A	-2.206	Affected
GRIA1	-2.273	Inhibited
GYG1	-0.989	Affected
H1FX	-0.715	Affected
H6PD	-0.924	Activated
HADH	-0.896	Affected
HAPLN3	0.919	Activated
HBEGF	2.932	Activated
HEBP1	-0.99	Affected
HGF	-2.305	Activated
HIF1A	0.912	Activated
HLA-DMA	-1.294	Affected
HMGA1	-1.09	Activated
HMGA2	-0.738	Inhibited
HMOX1	-1.145	Inhibited
HOXB5	-1.085	Activated
HSD17B6	2.473	Affected
HSPA5	0.985	Activated
HSPB1	1.263	Activated
HTRA1	1.331	Activated
IARS	0.895	Activated
ID1	0.988	Activated
IER3	1.106	Activated
IFIT3	-2.159	Affected
IFRD1	1.375	Affected
IGF1	6.399	Inhibited
IGFBP2	-1.159	Activated
IGFBP3	4.697	Activated
IGFBP4	-1.908	Affected
IGFBP5	-1.983	Activated
IGFBP6	-1.398	Activated
IGFBP7	0.847	Activated
IL11	2.779	Activated
IL12A	-1.267	Inhibited
IL17D	0.77	Inhibited
IL1R1	-1.794	Activated
IL21	0.895	Activated
IL23A	0.89	Activated
IL6	0.823	Activated
IL6R	-2.952	Inhibited
IMPDH1	1.631	Inhibited
INHBA	2.441	Activated
IRAK3	-0.707	Inhibited
ITGA1	2.213	Activated
ITGA11	1.801	Activated
ITGA5	1.219	Activated
ITGAV	1.119	Activated
ITGB1	0.863	Activated
ITGB3	2.266	Activated
ITGB5	0.758	Activated
ITGBL1	1.9	Activated
ITIH3	0.837	Inhibited
ITPR1	0.75	Inhibited
JADE2	-1.55	Affected
JAG1	-1.136	Inhibited
JUN	-1.394	Inhibited
JUNB	2.095	Activated
KCNG1	2.23	Affected
KDEL2	1.03	Activated

KDELR3	1.027	Activated
KIAA1199	-2.147	Affected
KIT	-3.025	Inhibited
KITLG	-2.299	Activated
KLF10	2.008	Activated
KRT18	2.162	Activated
LDHA	0.864	Activated
LIFR	-1.493	Inhibited
LIMK2	1.646	Affected
LIMS1	2.468	Activated
LOX	2.648	Activated
LOXL2	0.718	Activated
LPAR1	-2.315	Activated
LTBP1	1.015	Activated
LTBP2	1.946	Activated
MAOA	-1.274	Affected
MAPK6	1.229	Activated
MCM2	-1.064	Activated
MFAP2	2.221	Activated
MFAP4	1.156	Activated
MGAT3	-1.047	Activated
MGMT	-1.027	Inhibited
MID1	-1.301	Affected
MITF	-1.716	Activated
MLXIP	0.749	Activated
MMP10	0.802	Activated
MMP11	0.876	Activated
MMP2	0.749	Activated
MPV17L	-0.794	Activated
MRE11A	1.818	Affected
MSN	0.966	Activated
MTHFD2	2.249	Affected
MXI1	-0.939	Inhibited
MYH11	4.228	Activated
MYH9	0.826	Activated
MYL12A	0.829	Activated
MYOCD	0.885	Activated
NCOA3	0.716	Activated
NDRG4	-1.015	Affected
NDST1	0.971	Activated
NEDD9	1.22	Activated
NEGR1	0.842	Activated
NFATC2	-0.91	Inhibited
NGF	2.6	Activated
NIPA2	0.846	Affected
NME1	1.158	Activated
NNMT	2.112	Activated
NOV	-2.859	Activated
NOX4	4.454	Activated
NPAS2	1.275	Affected
NPTXR	-0.89	Activated
NR1H3	-1.387	Affected
NRP1	-1.406	Inhibited
NT5E	-0.74	Inhibited
NUAK1	4.079	Affected
NUCB2	0.827	Activated
NUPR1	0.831	Activated
OLFM2	0.854	Activated
P2RX6	-1.725	Affected
P4HA1	1.368	Activated
PAPPA	-1.778	Affected
PATZ1	-1.063	Affected
PAX8	-1.187	Activated

PDGFA	2.088	Activated
PDGFRA	-1.761	Inhibited
PDGFRB	0.726	Activated
PDHB	0.87	Activated
PDLIM4	1.302	Activated
PDLIM5	2.374	Affected
PDLIM7	0.812	Activated
PFN2	-0.987	Activated
PGRMC2	1.734	Affected
PHGDH	1.139	Inhibited
PI4K2B	0.928	Activated
PKIG	-0.849	Inhibited
PLAT	-2.171	Inhibited
PLAU	-2.166	Inhibited
PLAUR	0.738	Activated
PLEK2	1.125	Activated
PLK2	-1.482	Affected
PLOD1	0.745	Activated
PLOD2	2.398	Activated
PLS3	1.261	Activated
PLSCR1	-1.492	Activated
PLXNC1	-3.358	Inhibited
PMEPA1	2.224	Activated
PPARG	-2.769	Activated
PPP1R3C	1.186	Affected
PPP2R2A	0.803	Activated
PRDM1	1.771	Activated
PRKCA	0.943	Affected
PRPS1	1.879	Activated
PSME4	0.961	Affected
PSPH	1.422	Inhibited
PTEN	0.942	Inhibited
PTGER2	-2.637	Inhibited
PTH1R	-0.905	Inhibited
PTHLH	1.373	Activated
PTPRN	1.109	Activated
PTX3	-3.459	Affected
RAB18	0.801	Activated
RAB1A	0.807	Activated
RAB6A	0.782	Activated
RAPGEF3	0.732	Affected
RASGRP1	0.702	Activated
RASGRP3	3.782	Activated
RASL11B	1.22	Activated
RDH11	0.8	Inhibited
RGCC	-3.176	Inhibited
RHOU	-1.164	Inhibited
RIN1	-1.824	Activated
ROR1	-1.147	Affected
RRAD	1.034	Activated
RSU1	1.133	Activated
RUNX1	1.37	Activated
RYBP	0.936	Affected
S100A10	-0.785	Inhibited
S100A4	-0.769	Inhibited
S1PR3	-1.449	Inhibited
SALL2	-0.784	Activated
SAR1B	0.799	Inhibited
SCD	1.356	Activated
SDC4	-0.931	Affected
SDPR	-1.227	Inhibited
SEC61B	0.845	Affected
SELENBP1	-1.341	Activated

SEMA3A	-1.64	Activated
SEMA3B	-0.726	Inhibited
SEMA7A	2.857	Activated
SERP1	1.515	Affected
SERPINB1	-0.706	Inhibited
SERPINE1	2.758	Activated
SERPINE2	3.799	Activated
SFRP1	-1.751	Affected
SHOC2	1.902	Affected
SLC12A7	-2.267	Affected
SLC39A14	2.146	Affected
SMAD3	-2.523	Inhibited
SMAD6	-2.389	Inhibited
SNAI2	-1.043	Inhibited
SOCS1	-2.693	Inhibited
SOCS3	-1.758	Inhibited
SOD3	-1.423	Inhibited
SPRY1	-3.154	Affected
ST3GAL5	-0.956	Affected
STC2	-1.038	Affected
STRAP	0.743	Affected
SVEP1	-2.171	Affected
TCN2	-1.35	Affected
TGFB2	1.467	Inhibited
TGFB3	1.819	Inhibited
TGFBR2	-0.995	Inhibited
TGM2	-1.414	Inhibited
TNFAIP3	-0.759	Inhibited
TNFRSF11B	-1.976	Inhibited
TNFRSF14	-1.672	Affected
TRIM9	0.789	Affected
TSC22D3	1.404	Affected
TUBB3	-0.94	Inhibited
TWIST1	-0.811	Inhibited
TWIST2	-1.295	Inhibited
TXNIP	-1.594	Inhibited
TXNRD1	-0.796	Affected
UBE2J1	1.379	Affected
UCK2	1.193	Affected
UNC119	-0.761	Affected
USO1	0.748	Inhibited
VEGFC	-1.049	Inhibited
XRCC4	1.365	Affected
ZEB2	-0.703	Inhibited
ZFP36	-1.074	Inhibited
ZFP36L2	-1.492	Affected
ZNF365	2.187	Affected

Table S2. List of putative lncRNAs significantly modulated by TGF- β in lung fibroblasts (dataset 1). The thresholds used for selection of the lncRNA candidates are log₂ Base Mean >5, Log₂ FC>1 and adj.Pval <0.01.

Gene Name	Length	ENTREZ ID	Description	BIOTYPE	Base Mean	log ₂ FC	Adj. P Value
ANXA2P2	1310	304	annexin A2 pseudogene 2	pseudogene	48741	1.01	1.04E-20
APCDD1L-AS1	4940	149773	APCDD1L antisense RNA 1 (head to head)	antisense	373	1.82	2.69E-27
ATF4P4	2136	100127952	activating transcription factor 4 pseudogene 4	pseudogene	922	1.04	1.89E-14
BAIAP2-AS1	4590	440465	BAIAP2 antisense RNA 1 (head to head)	lincRNA	759	-1.45	9.82E-24
BLZF2P	1130	317729	basic leucine zipper nuclear factor 2 pseudogene	pseudogene	41	1.25	1.19E-03
C17orf82	1530	388407	chromosome 17 open reading frame 82	lincRNA	55	-1.12	1.60E-03
C1orf132	15647	100128537	chromosome 1 open reading frame 132	lincRNA	81	-1.25	2.48E-05
C1orf220	2775	400798	chromosome 1 open reading frame 220	lincRNA	33	-1.43	8.22E-04
CAP1P2	1409	399748	CAP1 pseudogene 2	pseudogene	1296	1.26	2.20E-22
CCDC144CP	8558	348254	coiled-coil domain containing 144C, pseudogene	pseudogene	119	1.76	4.96E-12
CMAHP	4328	8418	cytidine monophospho-N-acetylneuraminic acid hydroxylase, pseudogene	pseudogene	64	1.11	1.05E-03
COX20P1	357	100507102	COX20 cytochrome c oxidase assembly factor pseudogene 1	pseudogene	248	1.20	2.18E-09
DAOA-AS1	2482	282706	DAOA antisense RNA 1	antisense	164	-1.95	2.16E-16
DCAF13P1	1330	100129009	DDB1 and CUL4 associated factor 13 pseudogene 1	pseudogene	94	1.02	6.68E-04
DNAJC27-AS1	5651	729723	DNAJC27 antisense RNA 1	antisense	40	-1.41	6.50E-04
DNM3OS	7956	100628315	DNM3 opposite strand/antisense RNA	antisense	418	2.36	6.58E-33
EIF2S2P4	1342	728350	eukaryotic translation initiation factor 2 subunit 2 beta pseudogene 4	pseudogene	2574	1.19	1.31E-18
ELL2P1	1906	646270	elongation factor for RNA polymerase II 2 pseudogene 1	pseudogene	716	-1.00	7.47E-12
ENTPD1-AS1	12528	728558	ENTPD1 antisense RNA 1	antisense	256	1.87	7.33E-19
FAM212B-AS1	2131	100506343	FAM212B antisense RNA 1	antisense	73	-1.02	1.23E-03
FAM86EP	3476	348926	family with sequence similarity 86, member A pseudogene	pseudogene	159	-1.91	3.18E-17
FAM86FP	994	653113	family with sequence similarity 86, member A pseudogene	pseudogene	187	-1.59	5.39E-14
FAM86HP	1301	729375	family with sequence similarity 86, member A pseudogene	pseudogene	95	-1.12	1.13E-04
FAM92A1P1	890	729073	family with sequence similarity 92, member A2 (pseudogene)	pseudogene	418	-1.81	2.94E-23
FENDRR	6785	400550	FOXF1 adjacent non-coding developmental regulatory RNA	lincRNA	7294	-2.28	2.51E-91
FER1L4	9212	80307	fer-1 like family member 4, pseudogene	pseudogene	74	-1.41	5.42E-06
FTH1P10	930	2502	ferritin, heavy polypeptide 1 pseudogene 10	pseudogene	3148	-1.06	5.58E-18
FTH1P11	551	2503	ferritin, heavy polypeptide 1 pseudogene 11	pseudogene	3005	-1.09	5.00E-19
FTH1P23	550	100420300	ferritin, heavy polypeptide 1 pseudogene 23	pseudogene	1859	-1.01	1.14E-13
FTH1P5	545	2509	ferritin, heavy polypeptide 1 pseudogene 5	pseudogene	640	-1.08	2.74E-13
FTH1P7	552	2500	ferritin, heavy polypeptide 1 pseudogene 7	pseudogene	2183	-1.01	5.36E-16
FTH1P8	1028	2501	ferritin, heavy polypeptide 1 pseudogene 8	pseudogene	3215	-1.08	1.05E-17
FTLP2	528	392437	ferritin, light polypeptide pseudogene 2	pseudogene	962	-1.18	1.93E-13
FTLP3	540	284764	ferritin, light polypeptide pseudogene 3	pseudogene	17604	-1.15	3.32E-19
GBP1P1	2352	400759	guanylate binding protein 1	pseudogene	139	1.15	3.13E-06

GRK6P1	1775	2871	pseudogene 1 G protein-coupled receptor kinase 6	pseudogene	51	1.21	1.23E-03
GTF2IRD2P1	3217	401375	pseudogene 1 GTF2I repeat domain containing 2	pseudogene	545	-1.12	1.76E-13
H1FX-AS1	3420	339942	pseudogene 1 H1FX antisense RNA 1	antisense	69	-1.62	4.56E-07
HERC2P8	6014	440366	hect domain and RLD 2	pseudogene	58	-1.17	5.82E-04
HMGA1P1	1062	203477	pseudogene 8 high mobility group AT-hook 1	pseudogene	73	-1.12	3.46E-04
HMGA1P2	324	171559	pseudogene 1 high mobility group AT-hook 1	pseudogene	170	-1.12	3.67E-07
HMGA1P8	321	100130009	pseudogene 2 high mobility group AT-hook 1	pseudogene	161	-1.07	2.66E-06
HOXA-AS2	5281	285943	pseudogene 8 HOXA cluster antisense RNA 2	antisense	147	-1.19	4.59E-07
HS6ST1P1	1235	388605	heparan sulfate 6-O- sulfotransferase 1 pseudogene 1	pseudogene	413	-2.12	4.59E-30
HSFY6P	403	106480722	heat shock transcription factor, Y- linked 6, pseudogene	pseudogene	42	1.44	1.83E-04
HSP90B2P	2384	7190	heat shock protein 90kDa beta family member 2, pseudogene	pseudogene	560	1.14	2.28E-13
HSP90B3P	1796	343477	heat shock protein 90kDa beta family member 3, pseudogene	pseudogene	287	1.23	1.93E-11
HSPA9P1	2029	266724	heat shock protein family A (Hsp70) member 9 pseudogene 1	pseudogene	352	1.07	3.37E-10
HSPB1P1	256	653553	heat shock protein family B (small) member 1 pseudogene 1	pseudogene	1014	1.30	2.81E-18
HSPB1P2	1092	653364	heat shock protein family B (small) member 1 pseudogene 2	pseudogene	325	1.21	1.85E-08
HTR7P1	2299	93164	5-hydroxytryptamine receptor 7	pseudogene	295	-1.25	1.03E-11
JHDM1D-AS1	2380	100134229	pseudogene 1 JHDM1D antisense RNA 1 (head to head)	antisense	47	1.42	1.21E-04
KCNJ2-AS1	2442	400617	KCNJ2 antisense RNA 1 (head to head)	antisense	50	-4.38	8.08E-22
KRT18P10	1287	360019	keratin 18 pseudogene 10	pseudogene	170	2.06	2.07E-19
KRT18P11	1283	3876	keratin 18 pseudogene 11	pseudogene	201	2.07	1.68E-20
KRT18P15	1291	729211	keratin 18 pseudogene 15	pseudogene	52	1.98	1.85E-08
KRT18P17	1279	344866	keratin 18 pseudogene 17	pseudogene	51	1.32	3.49E-04
KRT18P28	1332	343326	keratin 18 pseudogene 28	pseudogene	62	2.11	1.95E-09
KRT18P29	1267	729050	keratin 18 pseudogene 29	pseudogene	34	1.72	3.59E-05
KRT18P38	1282	441133	keratin 18 pseudogene 38	pseudogene	81	1.86	7.84E-10
LHFPL3-AS1	3039	645591	LHFPL3 antisense RNA 1	antisense	1524	-2.04	6.44E-61
LIFR-AS1	5098	100506495	LIFR antisense RNA 1	antisense	49	-2.68	4.38E-12
LINC00265	3115	349114	long intergenic non-protein coding RNA 265	lincRNA	77	-1.86	5.68E-10
LINC00320	2325	387486	long intergenic non-protein coding RNA 320	lincRNA	1242	1.06	1.00E-14
LINC00346	585	283487	long intergenic non-protein coding RNA 346	lincRNA	39	-1.34	1.13E-03
LINC00472	3443	79940	long intergenic non-protein coding RNA 472	lincRNA	44	-1.01	9.74E-03
LINC00475	3858	158314	long intergenic non-protein coding RNA 475	lincRNA	1380	-1.34	3.30E-24
LINC00476	5100	100128782	long intergenic non-protein coding RNA 476	lincRNA	96	-1.30	1.79E-06
LINC00535	2595	642924	long intergenic non-protein coding RNA 535	antisense	38	-3.11	4.16E-13
LINC00607	5628	646324	long intergenic non-protein coding RNA 607	lincRNA	111	3.29	2.49E-27
LINC00641	5715	283624	long intergenic non-protein coding RNA 641	lincRNA	256	1.00	1.55E-07
LINC00643	2871	646113	long intergenic non-protein coding RNA 643	lincRNA	37	2.45	2.73E-09
LINC00662	7958	148189	long intergenic non-protein coding RNA 662	lincRNA	653	1.83	3.62E-36
LINC00880	2018	339894	long intergenic non-protein coding RNA 880	lincRNA	44	4.16	3.12E-19
LINC00900	4766	283143	long intergenic non-protein coding	lincRNA	233	-1.24	1.79E-10

LINC00957	2703	255031	RNA 900 long intergenic non-protein coding RNA 957	lincRNA	43	1.16	2.29E-03
LINC00968	2840	100507632	long intergenic non-protein coding RNA 968	lincRNA	40	-1.15	4.59E-03
MAPK6PS4	2142	286065	mitogen-activated protein kinase 6 pseudogene 4	pseudogene	35	1.20	5.37E-03
MBNL1-AS1	6585	401093	MBNL1 antisense RNA 1	antisense	1051	1.46	2.09E-24
MESTP1	994	338470	mesoderm specific transcript pseudogene 1	pseudogene	1242	2.21	2.16E-65
MESTP3	968	645641	mesoderm specific transcript pseudogene 3	pseudogene	301	2.11	7.89E-31
MESTP4	1204	131572	mesoderm specific transcript pseudogene 4	pseudogene	40	1.91	1.82E-06
MFI2-AS1	1139	100507057	MFI2 antisense RNA 1	antisense	52	-1.69	2.39E-06
MIR155HG	1600	114614	MIR155 host gene	lincRNA	36	-1.53	3.18E-04
MIR181A1HG	3250	100131234	MIR181A1 host gene	lincRNA	113	1.70	3.69E-10
MIR181A2HG	662	100379345	MIR181A2 host gene	antisense	122	1.49	1.56E-09
MIR210HG	2321	100506211	MIR210 host gene	lincRNA	111	1.10	6.58E-05
MIR22HG	2968	84981	MIR22 host gene	lincRNA	3225	1.49	9.29E-32
MSTO2P	2647	100129405	misato family member 2, pseudogene	pseudogene	167	1.01	9.63E-06
MTHFD2P5	844	442707	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase pseudogene 5	pseudogene	45	1.69	7.24E-06
MTHFD2P7	983	442098	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase pseudogene 7	pseudogene	320	2.05	1.21E-23
MYO15B	12862	80022	myosin XVb	pseudogene	127	-1.24	6.51E-07
NBPF2P	710	343381	neuroblastoma breakpoint family member 2, pseudogene	pseudogene	417	-1.28	1.12E-13
NEXN-AS1	2583	374987	NEXN antisense RNA 1	antisense	83	-1.87	4.55E-10
NRBF2P4	850	728381	nuclear receptor binding factor 2 pseudogene 4	pseudogene	45	1.42	1.19E-04
OFD1P9Y	1491	386693	OFD1 pseudogene 9, Y-linked	pseudogene	86	1.56	1.36E-07
OSTCP2	444	646567	oligosaccharyltransferase complex subunit pseudogene 2	pseudogene	97	1.17	1.67E-04
OSTCP4	449	645264	oligosaccharyltransferase complex subunit pseudogene 4	pseudogene	121	1.38	3.40E-08
PDCL3P4	720	285359	phosducin-like 3 pseudogene 4	pseudogene	70	1.24	6.78E-05
PDCL3P5	722	644850	phosducin-like 3 pseudogene 5	pseudogene	99	1.11	6.06E-05
PGDP1	1441	342705	phosphogluconate dehydrogenase pseudogene 1	pseudogene	303	-1.07	8.88E-09
PPP1R14BP3	445	100507617	protein phosphatase 1 regulatory inhibitor subunit 14B pseudogene 3	pseudogene	2524	1.02	1.32E-13
PRPS1P2	937	100421295	phosphoribosyl pyrophosphate synthetase 1 pseudogene 2	pseudogene	57	2.08	9.42E-10
PSAT1P3	1111	729779	phosphoserine aminotransferase 1 pseudogene 3	pseudogene	182	1.99	2.37E-19
PSAT1P4	529	100287630	phosphoserine aminotransferase 1 pseudogene 4	pseudogene	62	1.85	2.73E-08
PSMG3-AS1	6264	114796	PSMG3 antisense RNA 1 (head to head)	lincRNA	240	-1.01	5.37E-06
RASA4DP	1199	100133005	RAS p21 protein activator 4CD, pseudogene	pseudogene	4425	2.26	4.03E-85
RBMY2WP	894	379011	RNA binding motif protein, Y-linked, family 2, member W pseudogene	pseudogene	33	1.23	4.62E-03
RPSAP52	1144	204010	ribosomal protein SA pseudogene 52	pseudogene	58	-1.32	2.76E-04
RUSC1-AS1	3516	284618	RUSC1 antisense RNA 1	antisense	58	-1.18	8.92E-04
SBDSP1	3736	155370	Shwachman-Bodian-Diamond syndrome pseudogene 1	pseudogene	944	1.12	7.67E-14
SCDP1	1081	645313	stearoyl-CoA desaturase (delta-9- desaturase) pseudogene 1	pseudogene	280	1.39	3.76E-14

SEC63P1	1258	100420341	SEC63 homolog, protein translocation regulator pseudogene 1	pseudogene	260	1.09	1.60E-06
SERPINH1P1	1249	158172	serpin peptidase inhibitor, clade H1, pseudogene 1	pseudogene	228	1.29	6.43E-10
SERTAD4-AS1	1004	574036	SERTAD4 antisense RNA 1	antisense	94	1.52	2.99E-08
SH3RF3-AS1	1604	100287216	SH3RF3 antisense RNA 1	lincRNA	119	1.69	1.23E-11
SLC2A1-AS1	3364	440584	SLC2A1 antisense RNA 1	lincRNA	84	-1.25	1.84E-05
SLC9A7P1	3311	121456	solute carrier family 9 member 7 pseudogene 1	pseudogene	76	1.22	8.35E-05
SNX29P1	1341	100652781	sorting nexin 29 pseudogene 1	pseudogene	55	-1.40	8.63E-05
SNX29P2	9520	440352	sorting nexin 29 pseudogene 2	lincRNA	167	-2.74	1.54E-26
SOCS2-AS1	3816	144481	SOCS2 antisense RNA 1	antisense	60	-1.77	1.88E-06
TLR8-AS1	1349	349408	TLR8 antisense RNA 1	antisense	103	-1.08	3.35E-04
TMPRSS4-AS1	453	100526771	TMPRSS4 antisense RNA 1	antisense	78	1.13	1.50E-04
TTY6	590	84672	testis-specific transcript, Y-linked 6 (non-protein coding)	lincRNA	59	1.07	3.05E-03
UBE2Q2P2	1862	100134869	ubiquitin conjugating enzyme E2Q family member 2 pseudogene 2	pseudogene	564	1.03	1.24E-10
USP32P3	1943	347716	ubiquitin specific peptidase 32 pseudogene 3	pseudogene	39	1.41	3.33E-04
USP9YP18	695	106480424	ubiquitin specific peptidase 9, Y-linked pseudogene 18	pseudogene	59	1.42	1.87E-05
XPOTP1	2398	170559	exportin, tRNA pseudogene 1	pseudogene	652	1.42	1.54E-19
ZBED5-AS1	1995	729013	ZBED5 antisense RNA 1	antisense	133	-1.52	3.26E-10
ZNF674-AS1	2078	401588	ZNF674 antisense RNA 1 (head to head)	lincRNA	231	1.21	7.90E-10

Table S3. List of the best mature miRNAs significantly modulated by TGF- β in lung fibroblasts following small RNA-seq analysis (Dataset 2). The thresholds used for selection are: Base Mean >100 rpkm, Log₂ FC>0.5 and adj.Pval <0.05.

Name	description	coord	TGF- β regulation
hsa-miR-10a-5p	MIMAT0000253	17:46657266-46657288(-)	Down
hsa-miR-10b-5p	MIMAT0000254	2:177015057-177015079(+)	Down
hsa-miR-127-5p	MIMAT0004604	14:101349338-101349359(+)	Down
hsa-miR-145-3p	MIMAT0004601	5:148810262-148810283(+)	Up
hsa-miR-145-5p	MIMAT0000437	5:148810224-148810246(+)	Up
hsa-miR-146b-5p	MIMAT0002809	10:104196277-104196298(+)	Down
hsa-miR-148a-3p	MIMAT0000243	7:25989542-25989563(-)	Up
hsa-miR-155-5p	MIMAT0000646	21:26946295-26946317(+)	Down
hsa-miR-181a-2-3p	MIMAT0004558	9:127454797-127454818(+)	Up
hsa-miR-181a-3p	MIMAT0000270	1:198828198-198828219(-)	Up
hsa-miR-181b-5p	MIMAT0000257	9:127456004-127456026(+)	Up
hsa-miR-185-5p	MIMAT0000455	22:20020676-20020697(+)	Down
hsa-miR-197-3p	MIMAT0000227	1:110141562-110141583(+)	Down
hsa-miR-199a-3p	MIMAT0000232	19:10928105-10928126(-)	Up
hsa-miR-199a-5p	MIMAT0000231	19:10928145-10928167(-)	Up
hsa-miR-199b-3p	MIMAT0004563	9:131007024-131007045(-)	Up
hsa-miR-21-3p	MIMAT0004494	17:57918672-57918692(+)	Up
hsa-miR-218-5p	MIMAT0000275	5:168195216-168195236(-)	Down
hsa-miR-221-5p	MIMAT0004568	X:45605649-45605670(-)	Down
hsa-miR-224-5p	MIMAT0000281	X:151127103-151127123(-)	Down
hsa-miR-23a-3p	MIMAT0000078	19:13947409-13947429(-)	Up
hsa-miR-23b-3p	MIMAT0000418	9:97847547-97847567(+)	Up
hsa-miR-27a-3p	MIMAT0000084	19:13947261-13947281(-)	Up
hsa-miR-27a-5p	MIMAT0004501	19:13947301-13947322(-)	Up
hsa-miR-27b-3p	MIMAT0000419	9:97847787-97847807(+)	Up
hsa-miR-27b-5p	MIMAT0004588	9:97847745-97847766(+)	Up
hsa-miR-28-3p	MIMAT0004502	3:188406622-188406643(+)	Down
hsa-miR-30a-5p	MIMAT0000087	6:72113298-72113319(-)	Down
hsa-miR-30c-5p	MIMAT0000244	6:72086706-72086728(-)	Down
hsa-miR-30d-5p	MIMAT0000245	8:135817162-135817183(-)	Down
hsa-miR-30e-5p	MIMAT0000692	1:41220043-41220064(+)	Down
hsa-miR-330-3p	MIMAT0000751	19:46142267-46142289(-)	Down
hsa-miR-335-3p	MIMAT0004703	7:130136003-130136024(+)	Up
hsa-miR-335-5p	MIMAT0000765	7:130135967-130135989(+)	Up
hsa-miR-345-5p	MIMAT0000772	14:100774213-100774234(+)	Down
hsa-miR-34c-5p	MIMAT0000686	11:111384176-111384198(+)	Down
hsa-miR-409-3p	MIMAT0001639	14:101531683-101531704(+)	Down
hsa-miR-424-3p	MIMAT0004749	X:133680674-133680694(-)	Up
hsa-miR-424-5p	MIMAT0001341	X:133680710-133680731(-)	Up
hsa-miR-450a-5p	MIMAT0001545	X:133674594-133674615(-)	Down
hsa-miR-450b-5p	MIMAT0004909	X:133674261-133674282(-)	Down
hsa-miR-455-3p	MIMAT0004784	9:116971767-116971787(+)	Up
hsa-miR-490-3p	MIMAT0002806	7:136587989-136588010(+)	Down
hsa-miR-539-3p	MIMAT0022705	14:101513706-101513727(+)	Up
hsa-miR-629-5p	MIMAT0004810	15:70371766-70371786(-)	Down
hsa-miR-769-5p	MIMAT0003886	19:46522219-46522240(+)	Down

Table S4. List of themes corresponding to “canonical pathways” annotations associated with TGF- β stimulation of MRC5 lung fibroblasts in presence of a control or DNM3OS-specific gapmer identified by Ingenuity Pathway Analysis. MRC5 cells were stimulated with TGF- β in presence of a control or a DNM3OS-specific gapmer. ($n=3$). Expression profiles were determined with Agilent whole genome microarrays (Dataset 3). Z-scores calculated for each pathway (TGF- β versus control) in the presence of a control or a DNM3OS-specific gapmer (Gp) are indicated. Significant pathways are shown in progressively brighter shades of blue (repression) and orange (activation) according to their significance.

Canonical Pathway	Gp Control	Gp DNM3OS
Actin Cytoskeleton Signaling	3.92	3.57
cAMP-mediated Signaling	-3.00	-3.27
Protein Kinase A Signaling	-2.53	-3.16
RhoGDI Signaling	-3.27	-1.22
Interferon Signaling	-2.12	-1.67
Signaling by Rho Family GTPase	3.18	1.86
VEGF Signaling	1.51	2.84
Intergrin Signaling	2.56	2.72
Rac Signaling	2.11	2.40
RhoA Signaling	2.45	2.13
Paxillin Signaling	2.33	2.32
Regulation of Actin-Based Motility by Rho	1.70	1.09
PAK Signaling	1.60	1.15
ILK Signaling	1.30	2.20
IL-6 Signaling	1.50	2.06
IGF-1 Signaling	1.51	1.94
PTEN Signaling	0.83	0.47
Wnt/Ca+ Pathway	1.26	0.30
Thrombin Signaling	1.00	0.73
PDGF Signaling	1.21	0.94
Death Receptor Signaling	-0.33	-1.29
Chemokine Signaling	0.00	-1.21
Inflammasome Pathway	-1.34	0.00
NRF2-mediated Oxidative Stress Response	-1.50	1.07

Table S5. List of themes corresponding to “canonical pathways” annotations identified by Ingenuity Pathway Analysis in response to overexpression of miR-199a-3p, miR-199a-5p or miR-214-3p in human MRC5 pulmonary fibroblasts MRC5. MRC5 cells were transfected with pre-miR-Control, pre-miR-199a-3p, pre-miR-199a-5p or pre-miR-214-3p ($n=3$). Expression profiles were determined with Agilent whole genome microarrays (Dataset 4). The probability to obtain the number of genes in a certain pathway in the list of differentially expressed genes between the different conditions was compared with the representation of the same pathway among all the genes on the microarray; $-\log_{10}$ of the Fisher exact probability is indicated. Significant pathways are shown in progressively brighter shades of orange according to their significance.

Canonical Pathway	miR-199a-3p	miR-199a-5p	miR-214-3p
PI3K/AKT signaling	4.05	3.60	1.20
Cell Cycle: G2/M DNA Damage Checkpoint Regulation	0.88	5.29	2.48
Superpathway of Cholesterol Biosynthesis	0.28	8.07	0.00
Ephrin B Signaling	1.94	1.92	3.81
FGF Signaling	2.06	1.85	3.58
Regulation of the Epithelial-Mesenchymal Transition pathway	0.66	2.16	4.57
HGF Signaling	3.10	2.44	1.75
ERK/MAPK Signaling	3.16	1.63	2.16
HIPPO Signaling	3.43	1.13	2.11
Signaling by Rho Family GTPases	2.7	2.02	1.93
Protein Kinase A Signaling	2.53	2.87	1.14
Cyclins and Cell Cycle Regulation	1.29	3.97	1.02
Adipogenesis Pathway	1.23	2.33	2.52
AMPK Signaling	1.99	1.82	2.01
PTEN Signaling	2.43	2.78	0.46
Telomerase Signaling	1.17	2.57	1.84
RAN Signaling	2.13	2.41	0.87
STAT3 Signaling	1.39	1.92	2.04
Cell Cycle Control of Chromosomal Replication	1.13	3.01	1.18
Phospholipase C Signaling	2.05	2.90	0.31
Pyridoxal 5'-phosphate Salvage Pathway	1.08	0.87	2.99
Glucocorticoid Receptor Signaling	1.15	3.23	0.31
RhoGDI Signaling	2.74	0.92	1.04
Mitotic Roles of Polo-Like Kinase	0.62	3.35	0.56
SAPK/JNK Signaling	1.28	2.33	0.89
ErbB2-ErbB3 Signaling	0.58	1.14	2.75
Wnt/ β -catenin Signaling	0.83	1.54	2.06

Table S6. LNA-modified oligonucleotides used for *in vivo* experiments

Name	Sequence
LNA-negative Control	5'-TCAGTATTAGCAGCT-3'
LNA-miR-199a-5p	5'-TAGTCTGAACACTGG-3'
CAV1 Target Site blocker N°1	5'-TGTGACCGTACCGGTG-3'
CAV1 Target Site Blocker N°2	5'-GTCTGTGACCGTAC-3'

Table S7. Characteristics of 3'UTR psiCHECK-2 plasmid constructions

Construction	RefSeq	Position on human 3'UTR
GSK3β	NM_002093	1072 - 1503
PTGS2	NM_000963	1565 - 2527
FGF7	NM_002009	1 -245

Table S8. TaqMan assays used for miRNAs expression analysis

Assay name	Assay ID
miR-199a-5p	000498
miR-199a-3p	002304
miR-214-3p	002306
RNU44	0010921
SNO251	001236

Table S9. qPCR primers used for gene expression analysis

Gene name	Human Primers	Mouse Primers
PPIA	F: GACCCAACACAAATGGTTCC R: GGCCTCCACAATATTCATGC	F: GACCAAACACAAACGGTTCC R: TTCACCTTCCCAAAGACCAC
COL1A1	F: TTCTGCAACATGGAGACTGG R: AATCCATCGGTCATGCTCTC	F: GGCAAGAATGGAGATGATGG R: ACCATCCAAACCACTGAAGC
FN1	F: ATGAGCTGCACATGTCTTGG R: TGGCACCGAGATATTCCTTC	F: TGAGGAACATGGCTTTAGGC R: ATTCGGCAGGTATGGTCTTG
ACTA2 (α -SMA)	F: ACTGGGACGACATGGAAAAG R: GAGTCATTTTCTCCCGGTTG	F: TTGCTGACAGGATGCAGAAG R: TGATCCACATCTGCTGGAAG
DNM3OS	F: AGCATCCATGCTCGGTAAAG R: TTGTGATGGGTGGGCTATTC	F: TGAGAATGGCTGCTGTTACC R: TTCACAAGACCTCTGCATCTC
PTGS2 (COX2)	F: GAATCATTACCAGGCCAAATTG R: CTTTCTGTACTGCGGGTGGAA	
CAV1	F: TTTCCCTGCCTCTCATCAAC R: CCGGTGATGGATTAGTTTGG	F: TTGTACCGTGCATCAAGAGC R: AAAGAGTGGATCGCAGAAGG