## Supplementary Materials and Methods

### Oligonucleotides and primers sequences

| Oligo/primers | Sequence (5’ to 3’) |
|---------------|---------------------|
| **Oligonucleotides** |                     |
| MALAT1-shRNA  | TCCTTGGGACGCAGCGACGAGTTGTGTGCTG |
| MALAT1-AS1    | mG*mG*mG*mA*mG*T*T*A*C*T*T*G*C*C*A*mA*mC*mU*mU*mU*mG |
| MALAT1-AS2    | mA*mU*mG*mG*mA*G*G*T*A*T*A*T*G*A*C*mA*mU*mA*mA*mU*mA*mA*mA*mA*U |
| Scrambled     | mU*mC*mA*mC*T*T*C*A*C*C*C*T*C*T*mC*mC*mA*mC*mU* |
| SBE-sense     | TCGATAGCCAGACAGGTAGCCAGACAGG |
| SBE-antisense | CCTGTCTGGCTACCTGTCTGGCTATCGA |
| **Primers**   |                     |
| MALAT1-forward  | TGTAGTTCA GTTGGGGCA |
| MALAT1-reverse   | GCTCAAATCCTGATCTGGTC |
| MEG3-forward   | GCCACGAGAGGATCCCTCACC |
| MEG3-reverse   | CGTGCTCTAGTCGCTCGTA |
| HOTAIR-forward  | CGTGGCAGAGGGCAAGACGG |
| HOTAIR-reverse  | GTGCGCAGCTAGGACCGGA |
| HULC-forward   | AGAAGCTCTGAAGTAAAGGCCGGA |
| HULC-reverse   | TGGCAGAAACTTCTTGCTTGATGC |
| HEIH-forward   | CCTCTTGTCGCCCTTTTCTT |
| HEIH-reverse   | ATGGCTTCTCGCATCCTAT |
| AFP-forward    | GCAGCACAAGTGAAGAGGAG |
| AFP-reverse    | TGTGTCTGCTTTGTGGT |
| Albumin-forward | GCCACAATGAAGTGAGGTAAC |
| Albumin-reverse | AGGCAATCAAACACCAAAG |
| CK-18-forward  | CTACATCAACAACCTTAGGC |
| CK-18-reverse  | TCCACATCTCTTGATCG |
| G-6P-forward   | TTCCCTGTAACCTGTGAGAC |
| G-6P-reverse   | ATTCAGACCGAAATCTCG |
| HNF-4a-forward | CCAAGTACATCCCCAGCTTTC |
| HNF-4a-reverse | TTGGCATTCTGGTCAAAG |
| TDO2-forward   | GGAACATCATCATTGTG |
| TDO2-reverse   | TCTCTGAAGTCATTGAAGTCC |
| TAT-forward    | ACTGTGTTTGGAACACCTGCC |
| TAT-reverse    | GCAGCACCATTGTCAAGATGA |
CYP3A4-forward  CCTACATACACACCCCTTTG
CYP3A4-reverse  GGTTGAAGAAGTCCTCCTAAGCT
CYP7A1-forward  CTGCCAATCCTTTGAGTTCC
CYP7A1-reverse  ACTCGGTAGCAGAAAGAATACATC
FOXA2-forward  TGCACTCGGCTCCAGTATG
FOXA2-reverse  CATGTTGCTACGGAGAGAT
GATA4-forward  GAACCTCCAGGCCCAGC
GATA4-reverse  TCTCTCCCTCGCAAGTCAAG
GAPDH-forward  GAGTCCACTGGCGTCTTC
GAPDH-reverse  GACTGTGGTCATGAGTCCTTC

Note: m: 2'O-Methyl bases; *: phosphorothioate bonds

Transfections with plasmids and oligonucleotides

Plasmids pGFP-V-RS-shMALAT1, pCMV6-AC-PPM1A, and their respective control were obtained from OriGene (Rockville, MD); pReceiver-M06-SETD2 and control from GeneCopoiea (Rockville, MD); pCS2-Flag-Smad2, pCS2-Flag-Smad3, pCS2-Flag-Smad3EP5M, and pCMV5-Flag-Smad2EP5M from Addgene (Cambridge, MA). MALAT1 (ID: n272238) and SETD2 (ID: s26423) SilencerSelect siRNA were purchased from Ambion. Transfections were carried out by using Lipofectamine2000 (for plasmids) and Oligofectamine (for siRNA) (Invitrogen Carlsbad, CA) as per manufacture instructions. Phosphorothioated 2'O-methyl modified oligonucleotides were synthesized by IDT DNA (Coralville, IA) and transfected to iPS cells by using Lipofectamine2000 as described previously(1).

Cells proliferation WST1 assay

Cells were cultured in serum-free medium for 24 hours to synchronize cell cycle. 2×10^3 cells were seeded into each well of 96-well plates in 200μl culture medium containing 1% fetal bovine serum. The medium was removed at indicated time points; 90μl serum-free medium mixed with 10μl WST-1 (Roche) was added to each well. Four hours after incubation, absorbance of each well was measured by an ELISA plate reader at wavelength of 450nm.

Luciferase activity assay
Twenty-four hours after p3TP-lux plasmid (Addgene) transfection, cells were incubated with TGF-β1 (5ng/mL) for additional 24 hours. The cells were then collected and analyzed by using the Dual-Luciferase reporter assay system (Promega, Madison, WI) as per user manual. Luciferase activity was measured by centro XS3LB960 microplate fluorescence reader (Berthold Tech, Ontario Canada). The pRL-TK plasmid with constitutive expression of Renilla luciferase was co-transfected with p3TP-lux as internal control.

**Quantitative real-time PCR**

Total RNA was prepared using Trizol reagent (Invitrogen). Reverse-transcription and quantitative PCR were performed by using SuperScript II Reverse Transcriptase (Invitrogen) and SYBR Green Supermix reagent (Qiagen, Valencia, CA).

**Immunoprecipitation (IP)**

The cells cultured in 100-mm dishes were fixed by 1% paraformaldehyde and then lysed in 1 ml RIPA buffer (1% Triton X-100, 0.1% sodium dodecyl sulfate, 50mM Tris-HCl pH 7.4, 150mM sodium chloride, 0.5% sodium deoxycholate, 1mM EDTA) containing phosphatase and protease cocktail inhibitors. Pre-cleared supernatants were rotated with 1µg antibodies and 50µl protein A/G-plus agarose beads at 4°C overnight; then samples were collected by centrifugation at 4°C 5000 rpm for 5 min, followed by five times wash with RIPA buffer; pellets were suspended in 2× SDS-PAGE sample loading buffer and subjected to Western blotting.

**DNA pull-down assay**

The cells in 100-mm dishes were lysed in RIPA buffer containing phosphatase and protease inhibitors. The samples were precleared with Streptavidin-agarose resin (Thermo) for 1 hour. The precleared supernatant was then incubated with 1µg biotinylated double-stranded SBE (Smad Binding Element) and 10µg poly (dI-dC) at 4°C for 24 hours. DNA-protein complex was collected by streptavidin-agarose resin incubation at 4°C for 1 hour. The complex was washed, boiled and subjected to West blotting.

**Western blotting**
The logarithmically growing cells were lysed in RIPA buffer with phosphatase and protease inhibitors. Centrifuged cell lysates were denatured at 95°C 5 min and subjected to SDS-PAGE gel. The separated proteins were transferred onto nitrocellulose membranes (BioRad, Hercules, CA); the membranes were blocked in 5% non-fat milk for 1 hour, followed by primary incubation with primary antibodies at 4°C overnight. IRDye 800CW or 680LT labeled antibody (1:10000) were used as secondary antibodies. The membranes were scanned and quantified with The Odyssey® Infrared Imaging System (LI-COR Biosciences, Lincoln, Ne).

**Fluorescent in situ hybridization (FISH)**

Probe set containing 48 different oligonucleotides for MALAT1 was designed and synthesized by Biosearch Technologies (Novato, CA) based on principles described by Raj et al(2). Cells on cover slide were fixed with 1% formaldehyde for 10 minutes at room temperature and permeabilized with 70% ethanol at 4°C overnight, followed by washing with Wash buffer (10% formamide, 2× saline-sodium citrate). Then, the cells were incubated with FISH probe and primary antibody diluted in Hybridization buffer (10% Dextran sulfate, 10% deionized formamide) in a dark humidified chamber at 37°C overnight. After washing with Wash buffer twice, the cells were incubated with secondary antibody in hybridization buffer for 1 hour at 37°C, followed by triple washings with Wash buffer, DAPI (5 ng/mL) counterstaining, and mounting with anti-fluorescence medium.

**Immunofluorescence (IF)**

Cells growing on coverslips (70% confluence) were washed twice with cold phosphate buffered saline and fixed in 2% paraformaldehyde for 10 min, followed by penetrating with 0.1% Triton X-100 and blocking with 5% BSA. Subsequently, the cells were incubated with primary antibodies at 4°C overnight, followed by three washings and incubation with Alexa488 or Alexa594 labeled secondary antibodies. After counterstaining with DAPI (0.1μg/ml) for 1min, the coverslips were applied with mounting medium for fluorescence; images were captured using fluorescence microscope.
1. Ma Y, et al. (2010) High-efficiency siRNA-based gene knockdown in human embryonic stem cells. *Rna* 16(12):2564-2569.

2. Raj A, van den Bogaard P, Rifkin SA, van Oudenaarden A, & Tyagi S (2008) Imaging individual mRNA molecules using multiple singly labeled probes. *Nat Methods* 5(10):877-879.