Supplemental Materials and Methods:

**Microdissection** Microdissection was performed as previously described (1). Briefly, OCT-embedded snap-frozen tissue was cut into 10 μm cryosections, which were then mounted onto DEPC-treated sterile glass slides. One section from every 10 sequential sections was stained with hematoxylin for microdissection guidance. Then manual microdissection was done using a sterile blade under the microscope. About 100-200 μg target tissues of each case were collected for the following RNA or DNA extraction. Over 80% of the material prepared as above contains epithelial cells.

**Datasets** The endometrioid endometrial cancer data set was downloaded from “The Cancer Genome Atlas” data portal (https://tcga-data.nci.nih.gov/tcga). For methylation analysis, we selected 208 EEC patients and 34 normal controls from the dataset and obtained the methylation data generated on HumanMethylation 450 Beadchip. For association analysis between PCDH10 methylation intensity and expression, we retrieved corresponding gene expression RNAseq and methylation data of 196 EEC tumor samples and 9 normal controls (data generated from IlluminaGA_RNAseqV2 platform and HumanMethylation 450 Beadchip). For association analysis between the RNA expression of PCDH10 and MALAT1, we obtained the corresponding RNAseq data of 253 EEC tumor samples (data generated from IlluminaGA_RNAseqV2 platform).

**Xenograft mouse model.** For MALAT1 knockdown in xenograft model, $3 \times 10^6$ of HEC-1-B cells were subcutaneously injected into the mice (n = 5 for each group). At 14
days after implantation, si-NC or si-MALAT1 oligo was injected into the left or right tumor, respectively; and the injection was conducted twice a week for two weeks. Oligos were prepared by pre-incubating 0.5 nM of siRNA oligos with Lipofectamine 2000 (Life Technologies) for 15 mins and injections were made in a final volume of 60 μl in OPTI-MEM (Life Technologies). Tumor sizes were measured every three days and the tumor volume was calculated. The mice were sacrificed at day 18 (relative to the first siRNA injection), and tumors were excised, weighed, and snap-frozen for RNA extraction. The tumor mass was presented as mean ± S.D.

**MTS assay.** Cells (5 × 10³ per well) were cultured in 96-well plate. 48 h post-transfection, 10 μl of the CellTiter 96® AQueous One Solution Reagent (Promega, Madison, WI) was added to each well and incubated for 1 h at 37 °C. The absorbance at 490 nm was measured using a μQuant Microplate Reader (Bio-Tek Instruments, Winooski, VT). For MALAT1 rescue experiment, cells were transfected with empty vector or MALAT1 vector for 24 h and then re-seeded into 96-well plates. MTS assays were monitored over 4 days of incubation after seeding. All experiments were performed in triplicate.

**Colony formation assay.** Stable cell lines expressing PCDH10 or empty vector were seeded onto a 6-well plate (5000 cells/well) and cultured for 10 days. The resultant colonies were stained with 0.2% crystal violet and those larger than 1 mm in diameter were counted under the microscope.
**Wound healing assay.** Cells were seeded on 6-well plate and a linear scratch was introduced using a fine 200 µl pipette tip when cells reached 100% confluent monolayer. Photographs were taken at the indicated time points after the scratch to monitor the cell migration process (healing process). The “healing” area at each field was measured using Image-Pro Plus6.0 software (Media Cybernetics, Bethesda, MA) and the percentage of wound closure was calculated with respect to the wound area at 0 h.

**5-Aza-2’-Deoxycytidine treatment.** Endometrial cancer cells were seeded on 10 cm plate and after 24 hours, cells were treated with 2 µmol/L of the DNA demethylating agent 5-Aza-2’-deoxycytidine 5-Aza (Sigma-Aldrich, St. Louis, MO) for 72 or 144 hours. Cells then were collected for DNA and RNA extraction.

**FACS analysis.** For cell apoptosis analysis, cells seeded on a 6-well plate were transfected with the indicated siRNAs. Forty-eight hours post-transfection, cells were harvested and washed with PBS. Annexin V-FITC (5 µM, BD Pharmingen) and propidium iodide (50 µg/ml, Sigma-Aldrich) were added to stain the cellular suspension following the manufacturer’s instructions. The fluorescence of 10,000 cells was determined using a FACSCalibur flow cytometer (BD Biosciences) and analyzed by WinMDI 2.9 software (Scripps Institute, La Jolla, CA). Data were obtained from three independent experiments. Annexin V: FITC positive and PI negative cells were regarded as early apoptotic. Annexin V: FITC positive and PI positive cells were identified as late apoptotic or necrotic. For cell cycle analysis, cells were fixed with 70% ethanol, treated
with RNase, stained with propidium iodide, then sorted and quantified with FACSCalibur flow cytometer (BD Biosciences).

**TUNEL staining.** Cells were seeded onto poly-L-lysine-coated slides in a 6-well plate and transfected with vectors or siRNA oligos as described above. Forty-eight hours after the transfection, apoptotic cells were assessed using In Situ Cell Death Detection Kit, TMR red (TUNEL) (Roche, Mannheim, Germany) according to its procedure. Cell nuclei were counterstained with ProLong® Gold Antifade Reagent with DAPI (Invitrogen) and visualized on an Olympus fluorescence microscope. To analyze apoptosis on xenograft tumors, 5 μm paraffin-embedded tissue sections were dewaxed in xylene, rehydrated in graded alcohols and double distilled water and washed in PBS. Sections were then treated with protease K at the concentration of 10 μg/ml for 15 min at 37 °C. Following this, cell death was detected using In Situ Cell Death Detection Kit, TMR red as performed on adherent cells. Cell death was calculated as the number of TUNEL-positive cells per total number of cells (DAPI positive) in matched areas of five sections at 200× magnification (×20 objective and ×10 ocular).

**Luciferase reporter assay.** For Topflash reporter assay, cells were co-transfected (per 24-well) with 250 ng of PCDH10 expression vector or control, 100 ng Topflash vector, and 2.5 ng of Renilla luciferase (pRL-TK) as a normalizing control. For MALAT1 reporter assay, cells were co-transfected with 250 ng of PCDH10 expression vector or control, 100 ng MALAT1 WT reporter or Mutant, and 100 ng LacZ expression vector as a normalizing control. Luciferase activity was measured at 48 h after transfection using
Dual-Glo Luciferase Assay kit (Promega) according to the manufacturer’s instructions. Fifteen micro liters of cell lysate were used for β-Gal staining if LacZ vector was used as normalizing control. Firefly luciferase was normalized against Renilla luciferase or β-Gal readings. Transfections were performed in triplicates.

**Bisulfite genomic sequencing (BGS).** Genomic DNA was extracted from EEC samples or normal tissues and cell lines using DNeasy Tissue Kit (Qiagen, Valencia, CA USA) and subjected to modification with sodium bisulfate using a Zymo DNA Modification kit (Zymo Research, Orange, CA). For bisulfite genomic sequencing, 2 μl of sodium bisulfate-treated DNA was amplified using primers designated to span the *PCDH10* promoter region -328 to +8 bp relative to the transcription start site. Thermo cycle conditions were set as following: 95 °C for 5min; 40 cycles of 95 °C for 30 s, 54 °C for 45 s, and 72 °C for 45 s; 72 °C for 5 min. PCR products were then cloned into the T vector pMD20-T (Takara). Seven colonies from each treatment group were picked randomly for plasmid DNA extraction and analyzed by automated DNA sequencing. Sequences were analyzed using DNAMAN software. Primers used are listed in Supplemental Table S5.

**Cell Fractionation** Cytoplasmic and nuclear proteins were extracted from HEC-1-B cells as previously described (2). Briefly, cells were harvested and washed with cold PBS three times. Cell pellet was resuspended in RSB buffer (10 mM Tris, pH 7.4, 10 mM NaCl, 3 mM MgCl2) and incubated on ice for 3 min followed by centrifugation at 4 °C. Then cell pellet was resuspended in RSBG40 buffer [10 mM Tris, pH 7.4, 10 mM NaCl, 3 mM MgCl2, 10% glycerol, 0.5% Noidet P-40, 0.5 mM dithiothretol, and proteinase inhibitor
cocktail (Roche diagnostics, Mannheim, Germany)] followed by centrifugation. Supernatant was transferred to a new tube as cytoplasmic fraction and the remaining pellet was resuspended in RSGB40 buffer with 1/10 volume of detergent (3.3% sodium deoxycholate and 6.6% Tween 40) followed by centrifugation. The supernatant was pooled with previous cytoplasmic fraction. The nuclear pellets were dissolved with RIPA buffer (25 mM Tris-HCl, pH 7.6, 150 mM NaCl, 1% NP-40, 1% sodium deoxycholate, 0.1% SDS and proteinase inhibitor cocktail) and used as nuclear fraction. For total protein extraction, the harvested cells were directly lysed with RIPA buffer.

**RT-PCR and Real-time RT-PCR.** Total RNAs from tissues or cells were extracted using TRIzol reagent (Life Technologies). Expression of mRNA analysis was determined with SYBR Green Master Mix (Life Technologies) in a 7900HT system (Applied Biosystem). GAPDH or 18S was used for normalization. Primers used are listed in Supplemental Table S5.

**Sequencing and base calling.** Preparation of transcription libraries for sequencing on Illumina GAIIx platform was carried out using mRNA-seq sample preparation kit (Part no. 1004898 Rev. D) according to manufacturer's standard protocol. Briefly, Total RNA (10 µg) was subjected to two rounds of hybridization to Oligo (dT) beads. The resulting mRNAs were fragmented via incubation for 5 min at 94 °C with the Illumina-supplied fragmentation buffer. The first strand of cDNA was next synthesized by reverse transcription using random primers. Second-strand synthesis was conducted by incubation with RNase H and DNA polymerase I. The resulting double-stranded DNA fragments were subsequently end-repaired, and A-nucleotide overhangs were added by
incubation with Taq Klenow lacking exonuclease activity. After the attachment of anchor sequences, fragments were PCR-amplified using Illumina-supplied primers and loaded onto GAIIx flow cell. DNA clusters were generated with an Illumina cluster station with Paired-End Cluster Generation Kit v2 (Illumina), followed by 2 x 36 cycles of sequencing on GAIIx (Illumina) with Sequencing Kit v3 (Illumina). Genome Analyzer Sequencing Control Software (SCS) v2.5, which could perform real-time image analysis and base calling, was used to carry out the image processing and base calling during the chemistry and imaging cycles of a sequencing run. The default parameters within the data analysis software (SCS v2.5) from Illumina were used to filter poor-quality reads. In the default setting, a read would be removed if a chastity of less than 0.6 is observed on two or more bases among the first 25 bases.

Read mapping to genome with splice-aware aligner Sequenced. Fragments were mapped to reference genome NCBI36/hg18 using TopHat version 1.1.4. Cufflinks version 0.9.3 was then used to estimate transcript abundances of RNA-Seq experiments. Abundances were reported in FPKM (fragments per kilobase of transcript per million fragments mapped) which is conceptually analogous to the reads per kilobase per million reads mapped (RPKM) used for single end RNA-seq. Z score is calculated with the formation: Z = (R-M)/SD. Where: R is the expression abundance of a gene; M is the mean of the 25-75% of expression levels of all the genes; and SD is the standard deviation of the 25-75% portion defined above.
**MALAT1 in situ hybridization.** Briefly, in situ hybridization assays were performed as following: The paraffin-embedded tissue sections were dewaxed in xylene, rehydrated in graded alcohols and double distilled water and washed in PBS. Tissues were then bleached with 6% H$_2$O$_2$, digested with proteinase K (10 μg/ml), and refixed with 0.2% Glutaraldehyde /4% PFA. After pre-hybridization at 57 °C for 3 h, the sections were hybridized with 0.5 ng/μl digoxigenin (DIG)-labeled probe at 57 °C for at least 16 h, followed by sequential washing steps. Sections were incubated with 1:2000 anti-Digoxigenin-AP, Fab fragments (Roche Molecular Biochemicals) overnight at 4 °C. After the incubation, the signal was developed with BM Purple (Roche) to produce precipitate at the hybridization site. Sections were inspected under an Olympus microscope. Blinded for clinical parameters, slides were evaluated by two of the authors (YZ and JT) independently. Photographs were taken and nuclear staining was scored using a semi-quantitative staining index. In brief, positively stained cells were given an intensity score (0 none; 1 weak; 2 intermediate; 3 strong); a proportion score was assigned representing the estimated proportion of positively stained tumor cells (0, 0%; 1, <10%; 2, 10-50%; and 3, >50%). A final score ranging from 0-9 was generated by multiplying proportion score with intensity score. This classification system has been validated in several studies (3,4).

**Immunohistochemistry.** Immunohistochemistry was performed as previously described (1). IHC on paraffin-embedded sections was performed using the following antibodies: β-catenin (CST 9562, 1:200). For scoring the β-catenin IHC staining (Cytoplasmic and/or Nuclear), positively stained cells were given an intensity score (0 none; 1 weak; 2
intermediate; 3 strong) and an area score representing the estimated proportion of positively stained tumor cells (0, 0%; 1, 1–10%; 2, 10–50%; 3, 51–100%). A final score ranging from 0–9 was generated by multiplying area score with intensity score. Nuclear β-catenin staining was evaluated as the percentage of cells with nuclear β-catenin staining compared with total cells. The staining was considered to be nuclear when it is observed in over 5% tumor cells (5,6).