**Supplementary methods**

**Cell culture**

Human renal cortical epithelial cells (HRCE, CC-2554) were purchased from Lonza (Basel, Switzerland), and maintained in renal epithelial cell growth medium with supplements (REGM, CC-3190, Lonza). HEK293T (CRL-3216), human PKD epithelial cells isolated from cyst linings (WT9-7, CRL-2830; WT9-12, CRL-2833), and mouse inner medullary collecting duct-3 cells (mIMCD-3, CRL-2123) were obtained from ATCC (VA, USA). mIMCD-3 cells were cultured in DMEM/F12 (LM002-04, Welgene, Inc., Gyeongsan-si, South Korea) with 10% fetal bovine serum (FBS, 16000-044, Gibco, MA, USA). Both HEK293T and PKD cell lines were cultivated in DMEM (LM001-05, Welgene, Inc.), supplemented with 10% FBS. Human renal glomerular endothelial cells (HRGEC, #4000) were purchased from ScienCell (CA, USA), and cultured in endothelial cell medium provided with supplements (ECM, #1001, ScienCell). HRGEC was only used at passage 2–8. With the exception of HRCE, HEK293T, PKD epithelial cells, and HRGEC were maintained on Poly-L-lysine (P6282, Merck, NJ, USA), bovine collagen Ⅰ (354231, Corning, NY, USA), and fibronectin (341631, Calbiochem, CA, USA)-coated culture vessels, respectively.

**Mouse kidney samples**

Mouse PKD tissues were isolated from Pkd1f/f:*HoxB7*-Cre mice at 7days after birth. Control tissues were harvested from age-matched Pkd1f/f mice. Care and genotyping for this mouse model are described previously [[1](#_ENREF_1)]. All animal experiments were reviewed and approved by Institutional Animal Care and Use Committee of Sookmyung women’s university.

**Transfection**

Negative control and target specific siRNAs were purchased from Bioneer (Daejeon, South Korea). Sequences of siRNAs are presented in Supplementary Table 1. First, 2×105 of WT cells were seeded on a 100 mm dish and treated with a mixture of siRNA #1 and #2 (20 nM each). siRNA transfection was performed with LipofectamineTM RNAiMAX (13778, Thermo Fisher scientific, MA, USA) in accordance with the manufacturer’s instructions. For DNA transfection, 6×105 of HEK293T cells were seeded on a 100 mm dish. Next, 10 μg DNA with the FuGENE HD transfection reagent (E2311, Promega, WI, USA) was introduced to the cells as described in the manufacturer’s protocol.

**RNA preparation, reverse transcription-PCR (RT-PCR), and real-time qPCR**

RNA was isolated using TRIzol® (15596018, Thermo Fisher scientific) or Nucleospin® RNA/Protein kit (740933, Macherey-Nagel GmbH & Co., Dueren, Germany) in accordance with the manufacturer’s protocol. RNA (0.5–1 μg) was used for RT-PCR. cDNA was synthesized using M-MLV reverse transcriptase (M170B, Promega) as described in the manufacturer’s manual. The diluted cDNA was mixed with SYBR green premix (PB20.15-05, PCR Biosystems, London, UK) and target-specific qPCR primers. Reactions were run using the LightCycler® 96 (Roche, Basel, Switzerland). Relative transcript levels were calculated using the 2-ΔΔCt method. Sequences of the qPCR primers are provided in Supplementary Table 2.

**Protein extraction and Western blot**

Protein was extracted using RIPA buffer (89900, Thermo Fisher scientific), or Nucleospin® RNA/Protein kit(740933, Macherey-Nagel GmbH & Co.) as described in the manufacturer’s protocol. Protein concentration was determined by BCA assay. The protein (20-200 μg) was loaded on 8–10% SDS-PAGE gel. Separated protein was transferred to a polyvinylidene fluoride (PVDF) membrane (AE-6667-P, Atto, Tokyo, Japan), and the membrane was blocked with 5% skim milk (232100, BD, CA, USA) in PBST (0.1% tween-20 in PBS). The membrane was incubated with primary antibodies at 4℃, overnight. After washing with PBST three times, the membrane was incubated with HRP-conjugated secondary antibodies at room temperature for 1 h. Chemiluminescent signal was induced by EzWestLumi plus (2332637, Atto), and detected by LAS3000 (Fujifilm, Tokyo, Japan). Band density was measured using Image J (NIH, free to download). Information pertaining to the antibodies used is provided in Supplementary Table 3.

**Enzyme-linked immunosorbent (ELISA) assay**

Cells (4×105) were plated in a 100 mm culture dish. After 24 h, the media was collected and filtered through 0.45 μm syringe filter. The amount of SEMA3C secreted was measured using SEMA3C ELISA kit (SEL919Hu, Cloud-Clone corp., TX, USA) in accordance with the manufacturer’s instruction.

**Flow cytometry**

Apoptosis was analyzed using the FITC-annexinV apoptosis detection kit Ⅰ (556547, BD Pharmingen). The trypsinized cells were washed with cold PBS and re-suspended with 1× annexinV binding buffer. The cells were stained with FITC-annexinV and PI at room temperature for 15 min. The analysis was conducted using FACS Canto Ⅱ (BD Biosciences, CA, USA) and FlowJo X software (FlowJo, LLC, OR, USA). More than 20000 cells were read.

**Reference**

1. Woo YM, Kim DY, Koo NJ, Kim YM, Lee S, Ko JY, et al. Profiling of miRNAs and target genes related to cystogenesis in ADPKD mouse models. Scientific reports. 2017 Oct 26;7(1):14151.