Supplementary Materials and Methods

Histology, Immunofluorescence and Immunohistochemistry

Ovarian and tumor tissues were fixed in 4% paraformaldehyde (PFA) and embedded in paraffin. 5-μm sections were processed for staining with hematoxylin and eosin (H&E) or for immunofluorescent (IF) or immunohistochemistry (IHC) analyses. IF or IHC analyses were performed with primary antibodies specific for cytokeratin 8 (KRT8) (TROMA-I, Developmental Studies Hybridoma Bank, Department of Biology, The University of Iowa, Iowa City, Iowa), phospho-S10-histone H3 (pHH3) (ab5176, Abcam Inc, Cambridge, MA), estrogen receptor alpha (ESR1) (sc-542, Santa Cruz Biotechnology Inc), TRP53 (sc-6243, Santa Cruz Biotechnology Inc), MUC5AC (mouse IgG, Clone 45M1, Imgenex), FOXL2 (generated and generously provided by Dagmar Wilhelm, Monash University, Melbourne, Australia), and PAX8 (10336-1-AP, Proteintech), using procedures previously described (50). For IF, cell nuclei were counterstained with 5μg/ml Hoechst 33342 dye (Sigma Aldrich). Digital images of H&E and IHC staining were captured using a Zeiss AxioPlan2 microscope in the Integrated Microscopy Core and images of IF staining were captured with Zeiss LSM780 confocal microscope in the Optical Imaging and Vital Microscopy Core at Baylor College of Medicine.

Laser-capture microdissection of human mucinous tumor samples

Frozen tissues were obtained from the Multidisciplinary Gynecologic Cancer Translational Research Tissue Bank at MD Anderson Cancer Center. All specimens had been collected, archived, and handled under protocols approved by the Institutional Review Board. Frozen sections embedded in optimal cutting temperature compound (OCT) were cut as 10 micrometers sections onto PEN-membrane slides (Leica Microsystems, Wetzlar, Germany). Tissue sections were immediately fixed in 70% ethanol and then stained with 1% methyl green to visualize the histologic features. A Leica AS LMD Laser Capture Microdissection System

(Leica Microsystems) was used to microdissect and retrieve tumor cells from different regions of the sections.

RNA extraction, Real-time RT-PCR and Microarray analyses

For microarray analyses, RNA quality was assessed and hybridization was performed using Mouse 430.2 microarray chips (Affymetrix) in the Microarray Core Facility of the Baylor College of Medicine. Microarray data were analyzed using the MultiExperiment Viewer (MeV) software and the average fold differences in RNA were analyzed using tools provided in the Ingenuity Pathway Analyses system. The microarray data have been deposited to GEO with the accession number GSE65206.

Injection of Tumor Cells into Syngenic Mice and Hormone Pellet Implants

$PKP53^{H/+}$ and $PKP53^{H/H}$ cells were trypsinized, washed, re-suspended in Hanks' Balanced Salt Solution (GIBCO, Carlsbad, CA), and injected as single cell suspension at $1x10^6$ cells/animal in a total volume of 0.1 ml into the peritoneal cavities, in 0.01 ml into the ovarian stroma, or in 0.1 ml of 1:1 mixture of DMEM-F12 and Matrigel (BD Biosciences) into the subcutaneous space of syngenic recipient mice.