Supplementary Legends

**Supplementary Figure S1.** Microdissection of (A) normal ovarian tissue and (B) high-grade serous ovarian tumor samples. After fixation, slides were stained with methyl green to visualize the histologic features of the tissue sections (left panels). Stromal and epithelial components in both normal and cancerous tissue were dissected for RNA extraction. During dissection, areas of interest were carefully outlined (middle panels). Areas with immune cell or blood vessel infiltration were avoided in the outlining to minimize contamination. The areas of interest were recovered from the slides for further processing (right panels).

**Supplementary Figure S2.** Immunostaining of ovarian tissue sections for TGF-β receptor type 1 and 2. (A and B) Normal ovary tissue sections \((n = 8)\) and (C and D) ovarian tumor tissue sections from high-grade serous ovarian cancer patients \((n = 15)\) were stained for both receptors. Quantification of receptor-staining intensities revealed lower protein expression levels for both (E) TGF-β receptor type 1 and (F) TGF-β receptor type 2 in ovarian cancer cells than in normal ovarian epithelial cells \((P < 0.001)\). Under high magnification, expression of (G) TGF-β receptor type 1 and (H) TGF-β receptor type 2 in ovarian cancer stroma by CAFs was visualized. Expression of TGF-β receptor in CAFs suggesting that stromal fibroblasts were responsive to TGF-β.
**Supplementary Figure S3.** A primary CAF line treated with TGF-β in the presence or absence of TGF-β pathway inhibitor. Treatment with the TGF-β receptor inhibitors and SMAD inhibitor abrogated the effect of TGF-β on induction of VCAN expression.

**Supplementary Figure S4.** The proposed model of TGF-β-modulated cross-talk between ovarian cancer cells and CAFs in the ovarian tumor microenvironment. (A) Diagram showing the VCAN promoter sequence. Examination of the 1000 bases upstream of the transcription start site of VCAN using a promoter analysis software program, the ExPlain data analysis system (Biobase Biological Databases), identified a potential VCAN minimal promoter at around 500 base pairs upstream of the transcription start site. Further analysis of the sequence revealed four potential Sp1-binding sites and one AP1-binding site. Involvement of Sp1 and the upstream TGF-β signaling pathway in controlling VCAN expression has not been described. Because the SMAD/Sp1 complex is an important mediator of TGF-β–regulated gene expression (33-35), the roles of SMAD and Sp1 in regulating VCAN expression, especially in CAFs, should not be overlooked. (B) Figure showing the proposed mechanism of enhancement of the motility and invasion potential of ovarian cancer cells by the interaction between epithelial cancer cells and stromal CAF components in the tumor microenvironment. TGF-β is a key initiator and regulator of this cross-talk.

**Supplementary Figure S5.** Expression of EMT markers in ovarian cancer cells co-cultured with fibroblasts. Four high-grade serous ovarian cancer cell lines were co-
cultured with ovarian fibroblasts in the absence or presence of TGF-β-neutralizing antibody. Total RNA was extracted from ovarian cancer cells, and the gene expression levels for the mesenchymal markers (A) N-cadherin and (B) vimentin and for the epithelial marker (C) E-cadherin were examined. Significant inhibition of EMT by the TGF-β-neutralizing antibody was not observed.

**Supplementary Table S1.** TGF-β concentrations in conditioned media of the co-culture system. The TGF-β1 and 2 concentrations in the ALST/NOF151-hTERT co-culture system were determined using ELISA. Conditioned culture medium was harvested at 24 and 48 hours and the concentrations of TGF-β were measured.

**Supplementary Table S2.** Complete list of CAF-specific, TGF-β-regulated genes identified in NOF151-hTERT fibroblasts treated with TGF-β. 71 upregulated genes with relative changes in expression greater than a factor of 2 and \( P \) values less than 0.05 were identified.

**Supplementary Table S3.** Complete list of VCAN-regulated genes identified in OVCA433 cells treated with VCAN. In this microarray experiment, we identified a total of 141 upregulated genes and 147 downregulated genes.