Supplemental information

Figure S1 Suppression of miR-765 level accelerates the proliferation and EMT of UCEC.

A Level of miR-765 after treated with miR-765 mimics in KLE by RT-qPCR. B KLE cell viability was measured by CCK-8 at 12 h, 24 h, 36 h, 48 h after treated with miR-765 mimics. C After treated with miR-765 mimics, KLE cell proliferation was determined with Ki67 by flow cytometry. D Tumor volume growth and of NC and LV-miR-765 KLE cells xenografts in mice were measured every day. E Survival curves of NC and LV-miR-765 KLE cells xenografts-bearing mice. F mRNA levels of EMT related markers (COL1A, COL3, FNI, CDHI, CDH2, S100A, MMP2, MMP9, SNAIL, VIMENTIN, ZEB1, TJP1) in NC and miR-765 mimics treated KLE cells by RT-qPCR. Data were presented as mean ± SEM and analyzed by t test or ANOVA. * P < 0.05, ** P < 0.01, *** P < 0.001, **** P < 0.0001, NS: no significance.

Figure S2 MiR-765 negatively regulates PLP2 expression of UCEC in a miRNAs cluster regulatory manner.

A The ratio of PLP2 to GAPDH was quantified after Ishikawa and KLE cells were treated with miR-765 mimics according to the images of western blotting in Figure 2D. B Potential transcription factors downstream miR-765 predicted by bioinformatics analysis. C Levels of target miRNAs (miR-3584-5p, miR-7-5p, miR-150-5p and miR-124-3p) after treated with miR-765 mimics in KLE cells by RT-qPCR. D Levels of PLP2 after treated with miR-3584-5p, miR-7-5p, miR-150-5p and miR-124-3p mimics in KLE cells by RT-qPCR. E Levels of target miRNAs (miR-3584-5p, miR-7-5p, miR-150-5p and miR-124-3p) were
assessed to evaluated the efficiency of miRNA inhibitors in KLE cell by RT-qPCR. 

F Levels of PLP2 after treated with miR-765 mimics and/or miRNA inhibitors in KLE cell by RT-qPCR. Data were presented as mean ± SEM and analyzed by t test or ANOVA. * P < 0.05, ** P < 0.01, *** P < 0.001, **** P < 0.0001, NS: no significance.

Figure S3 PLP2 promotes the EMT process and invasion of UCEC.

A-B RT-qPCR and western blotting were performed to evaluate the efficiency of siPLP2 respectively in Ishikawa and KLE. The ratio of PLP2 to GAPDH was quantified in (C). 

D-E The ratios of EMT related markers (Vimentin and E-cadherin) to GAPDH in NC or siPLP2 Ishikawa and KLE cells were quantified according to the images of western blotting in Figure 3C. * P < 0.05, ** P < 0.01, *** P < 0.001, **** P < 0.0001, NS: no significance.

Figure S4 PLP2 enhances the EMT process of UCEC by activation of Notch signaling.

A-B mRNA and protein levels of Notch-related molecules (Notch1, NID, Hes1) in NC and OE-PLP2 KLE cells by RT-qPCR. After NC or PLP2-OE KLE cells after treated with DART or not, levels of EMT related markers (E-cadherin and Vimentin) (C), cell invasion (D) and cell viability (E) was detected. Data were presented as mean ± SEM and analyzed by t test or ANOVA. * P < 0.05, ** P < 0.01, *** P < 0.001, **** P < 0.0001, NS: no significance.

Figure S5 Estrogen regulates the miR-765/PLP2 level in UCEC through the ERβ.

A The ratio of PLP2 to GAPDH was quantified according to the images of western blotting in Figure 5G. 

B-C The ratio of PLP2 to GAPDH was quantified according to the images of
western blotting in Figure. 5H-I. **D-E** The ratio of PLP2 to GAPDH was quantified according to the western blotting images of Figure. 5L-M. **F** Levels of ESR2 were assessed after Ishikawa and KLE cells were treated with Fulvestrant by RT-qPCR. **G** Levels of ESR1 were assessed after Ishikawa and KLE cells were treated with Fulvestrant by RT-qPCR. **H** Levels of miR-765 were assessed after Ishikawa and KLE cells were treated with Fulvestrant by RT-qPCR. **I-J** Levels of PLP2 were assessed after Ishikawa and KLE cells were treated with Fulvestrant by RT-qPCR and western blotting. The ratio of PLP2 to GAPDH was quantified in (**K**). **L** Levels of miR-765 were measured after NC or si-ERβ transfected Ishikawa and KLE cells were treated with Fulvestrant or not by RT-qPCR. **M** Levels of PLP2 were assessed after NC or si-ERβ transfected Ishikawa and KLE cells were treated with Fulvestrant or not by immunofluorescence. Data were presented as mean ± SEM and analyzed by t test or ANOVA. * P < 0.05, ** P < 0.01, *** P < 0.001, **** P < 0.0001, NS: no significance.

**Figure S6** CD45RO⁻CD8⁺ T cell-derived exosomal miR-765 partly suppressed PLP2 in UCEC cells.

**A** Sorting strategy of CD45RO⁺CD8⁺ and CD45RO⁻CD8⁺ T cells by flow cytometry. **B** Histogram showing the particle diameter (nm) of the exosomes. **C** Exosome markers, CD63, TSG101, and GRP78, were assayed in exosomes and lysate using western blotting. The ratio of CD63/TSG101/GRP78 to PSMA was quantified in (**D-F**). **G** Levels of miR-765 in KLE were tested after treated with CD45RO⁻CD8⁺ T cells exosomes by RT-qPCR. **H** Levels of PLP2 in KLE were tested after treated with CD45RO⁻CD8⁺ T cell-derived exosomes by RT-qPCR. **I** The ratio of PLP2 to GAPDH was quantified according to images of western
mRNA and protein levels of PLP2 in KLE were tested after treated with CD45RO−CD8+ T cell-derived exosomes and/or GW4869 by RT-qPCR and western blotting. Data were presented as mean ± SEM and analyzed by t test or ANOVA. * P < 0.05, ** P < 0.01, *** P < 0.001, **** P < 0.0001, NS: no significance.

Figure S7 Exosomes originated from CD45RO−CD8+ T cell partly suppress UCEC development in a miR-765/PLP2-dependent manner.

After KLE cells were treated with estrogen and/or CD45RO−CD8+T cell-derived exosomes for 24h, A Levels of miR-765 were tested by RT-qPCR. B-C Levels of PLP2 were tested by RT-qPCR and western blotting. D Cell viability was measured by CCK-8 at 12 h, 24 h, 36 h, 48 h. E Cell proliferation was determined with Ki67 by flow cytometry. F Levels of EMT related markers (Vimentin and E-cadherin) were measured by western blotting and were quantified in (G-H), respectively. I Cell invasion was detected by transwell assays. Scale bars: 100 μm. J Ultimate tumor volume of Ishikawa cells xenografts in mice were measured. K Survival curves of KLE cells xenografts-bearing mice was plotted. Data were presented as mean ± SEM and analyzed by t test or ANOVA. * P < 0.05, ** P < 0.01, *** P < 0.001, **** P < 0.0001, NS: no significance.
Figure S1
Figure S2
Figure S3
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Figure S6
