**Supplementary Figure Legends**

**Supplementary Fig. S1**

ΔNp63α function in CSCC cell lines. **A,** Representative images of p63, ΔNp63α by western blots in four cervical cancer cell lines. B, Proliferation curves of the four cervical cancer cell lines. **C,** Colony formation assays of the four cervical cancer cell lines. Quantification of colony number is shown (lower). **D,** Representative images of wound healing in the four cervical cancer cell lines. Quantification of healing rate is also shown (lower). \*\*\*p< 0.001 is based on the Student’s *t*-test. In C-H, data are means ± SEM. Error bars, SD. Scale bar: 40 μm.

**Supplementary Fig. S2**

**A,** H&E staining of p63 expression by immunohistochemistry in SiHa/p63-derived tumors from the xenograft mice. **B,** H&E staining of p63 expression by immunohistochemistry in ME-180/shp63-derived tumors from the xenograft mice. n=6 pairs. \*\*p< 0.01, \*\*\*p< 0.001 are based on the Student’s *t*-test. Data are means ± SEM. Error bars, SD. Scale bar: 40 μm.

**Supplementary Fig. S3**

Heatmap of RNA-seq analyses. **A,** Heatmap of top 200 most affected genes in ME-180/shp63 RNA-seq. **B,** Heatmap of the genes in ME-180/shp63 RNA-seq. Cutoff of two-fold enrichment and p<10-5.

**Supplementary Fig. S4**

Validation of the 33 overlapped direct targets of ΔNp63α in both SiHa/p63 cells and ME-180/shp63 cells. Note: All the mRNA expressions were all consistent with the RNA-seq analyses except SHROOM2, JAM2, and PTX3. All the experiments were performed in triplicates and normalized to GAPDH. Error bars, SD, data are means ± SEM. n.s., not significant, \*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001, are based on the Student’s *t*-test.

**Supplementary Fig. S5**

Survival curves of 12 genes related to cervical squamous cell carcinoma analyzed by Kaplan-Meier Plotter . p value was calculated by log-rank test.

**Supplementary Fig. S6**

**A,** ΔNp63α ChIP-seq (red) and input DNA signals (blue) in the genomic regions of CLDN1 and ZNF385B. ΔNp63α binding sites are indicated with green arrows. Gene orientations were indicated with black arrows. **B,** Confirmation of CLDN1 and ZNF385B in p63α ChIP-seq. DCP2 was used as a positive control and GAPDH was used as a negative control. **C,** ΔNp63α ChIP-seq (red) and input DNA signals (blue) in the genomic regions nearby NFATC1. ΔNp63α binding sites are indicated with green arrows. The black arrows indicate gene orientation. Normalized read counts are indicated to the left of the tracks. **D,** Confirmation of CLDN1 and ZNF385B in p63α ChIP-seq. DCP2 was used as a positive control and GAPDH was used as a negative control. For **B** and **D,** the experiments were performed in triplicates. Error bars, SD, data are means ± SEM. n.s., not significant, \*\*p < 0.01, \*\*\*p < 0.001, are based on the Student’s *t*-test.

**Supplementary Fig. S7**

Function of CLDN1 and ZNF385B in EMT. Expression of epithelial (E-cadherin) and mesenchymal (Vimentin) markers were analyzed by western blot upon **A,** CLDN1 overexpression in SiHa and the control, **B,** ZNF385B knockdown in SiHa and the control. **C,** CLDN1 knockdown in ME-180 and the control, **D,** ZNF385B overexpression in ME-180. The experiments were performed in triplicates. Data are means ± SEM.

**Supplementary Fig. S8**

Fold change of relative NFATC1 expression after siRNA knockdown, normalized to GAPDH. Error bars, SD, data are means ± SEM. \*\*\*p < 0.001 is based on the Student’s *t*-test.

**Supplementary Table S1**

All the primers and antibodies used in this study were shown.