**Supplemental Figure Legends**

**Supplemental Figure 1. HPV(+) cell lines express high levels of HER3. (A)** HPV(+) and HPV(-) cell lines were examined for HER3 abundance by immunoblot analysis. Two-exposure times differentiate the expression patterns observed between HPV(+) and HPV(-) cell lines. -actin was used as a loading control. **(B)** HPV positivity was confirmed in HPV(+) cell lines by immunoblot analysis for E6 and E7. -Tubulin was used as a loading control.

**Supplemental Figure 2. Transient knockdown of E6 and E7 increases apoptosis without abrogating MAPK or Src Family Kinase signaling.** HPV(+) HNSCC cell lines were transfected with siE6/E7 (30 nM) or non-targeting (NT) siRNA for 72 hours prior to annexin-V analysis via flow cytometry **(A)** or immunoblot analysis for the indicate proteins **(B)**. Data points are represented as mean ± s.e.m. (n = 2). \*\*, P<0.01.

**Supplemental Figure 3. HPV(+) cell lines are sensitive to HER3 knockdown with a second independent siRNA.** HPV(-) and HPV(+) HNSCC cell lines were transfected with siHER3 (30 nM) or non-targeting (NT) siRNA for 72 hours before performing proliferation assays. Proliferation is plotted as a percentage of growth relative to siNT transfected cells (n=3 replicates in three independent experiments). Whole cell lysates were harvested at the same time point to confirm HER3 knockdown and differential expression changes in phospho-AKT. -actin was used as a loading control.

**Supplemental Figure 4. Knockdown of EGFR and HER2 does not completely block the phosphorylation of HER3 in HPV(+) cell lines.** HPV(+) cell lines (SCC47, 93-VU-147T, and SCC90) were transfected with siEGFR, siHER2, or a non-targeting (NT) siRNA for 72 hours before harvesting whole cell lysates and immunoblotting for the indicated proteins. GAPDH was used as a loading control.

**Supplemental Figure 5. Neuregulin-1 expression in a panel of HPV(-) and HPV(+) HNSCC cell lines.** Whole cell lysate **(A)** andtotal RNA **(B)** was extracted from the indicated HPV(-) and HPV(+) cell lines and analyzed for NRG1 expression by immunoblotting and quantitative RT-PCR. NRG1 expression was normalized to the endogenous control TBP for each cell line in (B). Data points are represented as mean ± s.e.m (n=3 in three independent experiments).