

**Supplementary Figure S4- ER overexpression converts E2 from a growth promoter to a growth suppressor.** (A) Lysates from hormone-deprived HCC-1428 (HD x 3 d), HCC-1428/LTED, HCC-1428/vec (HD x 3 d), HCC-1428/FLAG-ESR1, MDA-MB-415/vec, MDA-MB-415/FLAG-ESR1, and T47D/pInd20-ESR1 cells (HD x 3 d, then treated  $\pm$  dox x 2 d) were analyzed by immunoblot. (B) HCC-1428/vec and MDA-MB-415/vec cells (HD x 3 d), and HCC-1428/FLAG-ESR1 and MDA-MB-415/FLAG-ESR1 cells (propagated in HD) were seeded and then treated  $\pm$  E2 for 4 wk. T47D/pInd20-ESR1 cells (HD x 3 d) were treated  $\pm$  dox for 2 wk, then reseeded and treated  $\pm$  dox  $\pm$  E2 for 2 wk. Relative cell growth was measured. Data are shown as mean of triplicates  $\pm$  SD. (C) HCC-1428/LTED cell lines expressing dox-inducible shRNA targeting *ESR1* (two independent constructs) or non-silencing control were treated  $\pm$  dox for 2 d, and lysates were analyzed by immunoblot. \* $p$ <0.05, \*\* $p$ <0.005, \*\*\* $p$ <0.0005.

