

SUPPLEMENTAL FIGURE LEGENDS

Supplemental Figure 1: Relationship between Cdc7 expression and clinico-pathological parameters. Box-Whisker plots showing Cdc7 labeling indices (LI) in relation to (A) tumor grade (grade 1, n=21; grade 2, n=75; grade 3, n=75), (B) tumor DNA ploidy status (aneuploid, n=85; diploid, n=81), (C) lymph node status (positive, n=68; negative, n=91) and (D) breast cancer subtype (luminal, n=135; Her2, n=8; triple-receptor negative, n=28). The median (solid black line), interquartile range (boxed) and range (enclosed by lines) of Cdc7 expression are shown (outliers are depicted by isolated points).

Supplemental Figure 2: Relationship between Cdc7 expression and NPI score. Box-Whisker plots showing Cdc7 labeling indices in relation to low (<3.4), medium (3.4-5.4) and high (>5.4) NPI scores. The median (solid black line), interquartile range (boxed) and range (enclosed by lines) of Cdc7 expression are shown (outliers are depicted by isolated points).

Supplemental Figure 3: Cdc7 depletion causes apoptosis in MDAMB157 (triple-receptor negative) breast cancer cells. (A) At the indicated time points, cell number was measured in UT, CO and Cdc7-depleted (Cdc7^{KD}) MDAMB157 cell populations. The graph shows fold-increase in cell numbers calculated for each time point relative to the number of cells seeded. (B) DNA content of Cdc7^{KD} MDAMB157 cells at the indicated time points. (C) Cell death and fragmented apoptotic nuclei (inset) were detected by phase contrast microscopy in Cdc7^{KD} but not in CO MDAMB157 cells. (D) Apoptotic cell death was confirmed in Cdc7^{KD} cells but not in UT and CO cells by immunoblot analysis of WCE prepared 72 hours post-transfection with the indicated antibodies (Actin – loading control).

Supplemental Figure 4: Cdc7 depletion causes apoptosis in MDAMB453 (Her2-amplified) breast cancer cells. (A) At the indicated time points, cell number was measured in UT, CO and Cdc7-depleted (Cdc7^{KD}) MDAMB453 cell populations. The graph shows fold-increase in cell numbers calculated for each time point relative to the number of cells seeded. (B) DNA content of Cdc7^{KD} MDAMB453 cells at the indicated time points. (C) Cell death and fragmented apoptotic nuclei (inset) were detected by phase contrast microscopy in Cdc7^{KD} but not in CO MDAMB453 cells. (D) Apoptotic cell death was confirmed in Cdc7^{KD} cells but not in UT and CO cells by immunoblot analysis of WCE prepared 72 hours post-transfection with the indicated antibodies (Actin – loading control).

Supplemental Figure 5: Cdc7 depletion causes cell cycle arrest in immortalized untransformed MCF10A cells. (A) Immunoblot analysis of WCE prepared from untreated (UT), control-siRNA (CO), and CDC7-siRNA (Cdc7^{KD}) transfected MCF10A cells probed with antibodies against Cdc7 and Actin (loading control). (B) At the indicated time points, cell number was measured in UT, CO and Cdc7^{KD} MCF10A cell populations. (C) DNA content of CO and Cdc7^{KD} MCF10A cells at the indicated time points. (D) Percentage of CO and Cdc7^{KD} MCF10A cells incorporating BrdU at the indicated time points. (E) WCE prepared from untreated, CO, and Cdc7^{KD} MCF10A cells 72 hours post-transfection were analysed by immunoblotting with the indicated antibodies (Actin – loading control). (F) Cell death and fragmented apoptotic nuclei (inset) were detected by phase contrast microscopy in Cdc7^{KD} but not in CO MCF10A cells.