

**Supplementary Data 1.** MS Protein-level Quantitation for Breast Cancer cell lines. Label Free quantitation of proteins per replicate across the breast cancer panel (related to Figure 1d and Supplementary Figure 1b-f).

**Supplementary Data 2.** Differentially expressed proteins per cell line. Pairwise differentially present proteins between different cell lines based on the triplicate quantitation (related to Supplementary Figure 1f).

**Supplementary Data 3.** Aggressiveness Regression Linear regression of protein abundance in each cell line across the ranked order of aggressiveness of the different cell lines (related to Figure 1d).

**Supplementary Data 4.** Differentially present protein on chromatin following Etoposide treatment. Proteins found to be differentially present on chromatin of U2OS cells upon etoposide treatment and 24hr release (related to Supplementary Figure 3a).

**Supplementary Data 5.** TOP2 and PARP1 OpenCell interactors. Proteins found to physically interact with the TOP2 and PARP1 proteins, under endogenous expression in HEK293T (related to Figure 4a).

**Supplementary Data 6.** Differential Gene Expression analysis of KO(-G), KO(+G), KO-WT, KO-NLS relative to WT condition (related to Fig. 5).

**Supplementary Data 7.** Hallmark\_G2M\_checkpoint gene set from the Molecular Signatures Database, MSigDB (related to heatmap Fig. 5b).

**Supplementary Data 8.** Hallmark\_reactome\_Senescence\_Associated\_Secretory\_Phenotype SASP gene set from the Molecular Signatures Database, MSigDB (related to heatmap Fig. 5b).

**Supplementary Data 9.** Hallmark\_DNA\_repair gene set from the Molecular Signatures Database, MSigDB (related to heatmap Fig. 5b).

**Supplementary Data 10.** Gene Ontology (GO) Apoptotic process (related to heatmap Fig. 5g). GO terms from GO.db R package.

**Supplementary Data 11.** Gene Ontology (GO) Necrotic process (related to heatmap Fig. 5g). GO terms from GO.db R package.

**Supplementary Data 12.** Gene Ontology (GO) Necroptotic Process (related to heatmap Fig. 5g). GO terms from GO.db R package

**Supplementary Data 13.** NAD<sup>+</sup> ADP-ribosyltransferase activity (GO:0003950) expanded to include SIRT1-7 family (related to heatmap Fig. 5i).

**Supplementary Data 14.**  $\log_2FC$  for SIRT family (SIRT1-7) in KO-WT and KO-NLS relative to WT condition (related to Fig. 5i).