

Description of Additional Supplementary Files

Supplementary Data 1 – Genome-wide CRISPR-Cas9 screen in eHAP iCas9 wild type vs *EXO1* KO cells (n=3). MAGeCK analysis of sequencing from samples from day 6. Negative binomial model integrated in MAGeCK algorithm was used to calculate P values.

Supplementary Data 2 – Genome-wide CRISPR-Cas9 screen in eHAP iCas9 wild type vs *EXO1* KO cells (n=3). MAGeCK analysis of sequencing from samples from day 16. Negative binomial model integrated in MAGeCK algorithm was used to calculate P values.

Supplementary Data 3 – BLISS score analysis for validated synthetic lethal interactions from *EXO1* KO vs WT CRISPR dropout screen. Unpaired t-test was used for the statistical analysis of actual vs theoretical values (two-tailed P values).

Supplementary Data 4 – Rescue screen in eHAP iCas9 *EXO1* KO cells for synthetic lethal interaction with *FANCG* (n=3). MAGeCK analysis comparisons between '*EXO1* KO + sgNT' vs '*EXO1* KO +sg*FANCG*'. Negative binomial model integrated in MAGeCK algorithm was used to calculate P values.

Supplementary Data 5 – Rescue screen in eHAP iCas9 *EXO1* KO cells for synthetic lethal interaction with *ZRSR2* (n=3). MAGeCK analysis comparisons between '*EXO1* KO + sgNT' vs '*EXO1* KO +sg*ZRSR2*'. Negative binomial model integrated in MAGeCK algorithm was used to calculate P values.

Supplementary Data 6 – sgRNA target sequences used in this study.

Supplementary Data 7 – Oligos for cloning and sequencing used in this study.

Supplementary Data 8 – Oligos used for amplification of integrated sgRNAs in CRISPR screening.