Detection of functional protein domains by unbiased genome-wide forward genetic screening

Mareike Herzog¹, #, Fabio Puddu¹, #, Julia Coates¹, Nicola Geisler¹, Josep V Forment¹, †, * and Stephen P. Jackson¹, *

¹ The Wellcome/CRUK Gurdon Institute and Department of Biochemistry, University of Cambridge, Tennis Court Road, CB2 1QN, Cambridge, UK

# these authors contributed equally to this work

* to whom correspondence should be addressed: Stephen P. Jackson, Tel: +44 1223 334088 (email: s.jackson@gurdon.cam.ac.uk); correspondence may also be addressed to: Josep V. Forment, Tel: +44 1223 334088 (email: j.forment@gurdon.cam.ac.uk)

† Current address: AstraZeneca, Oncology DNA damage response group, Hodgkin Building, 310 Cambridge Science Park Milton Road, CB4 0WG, Cambridge, UK (josep.forment@astrazeneca.com)
Supplementary Figures

Supplementary Figure 1. (a) Examples of two camptothecin resistant yeast strains, which each carry a large deletion in the TOP1 gene. (b) Nonsense mutations are depicted as in Figure 2D. Superimposed is the frequency of codons that can be mutated to a stop codon by one nucleotide change. (c) Frameshift mutations are depicted as in Figure 2E. Above the locations of homopolymers of a length of at least 3nt in the TOP1 gene are plotted, their length indicated on the y-axis.

Supplementary Figure 2. (a) Integrative Genomics Viewer (IGV) panels of the sequencing data for clones A9 and H10 showing the Parp1 mutation (Parp1 Δ341) that did not pass the filters. (b) Integrative Genomics Viewer (IGV) panels of the sequencing data for clones A7 and B7 showing the Parp1 mutation (Parp1 R138C) that did not pass the filters.

Supplementary Figure 3. (a) Western blots for PARP1 protein for olaparib resistant clones. (b) PARP1-DNA binding assays in olaparib resistant clones. Two exposure each are shown.
