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Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed	
☐	☒	The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒	For null hypothesis testing, the test statistic (e.g. F, t, r) with confidence intervals, effect sizes, degrees of freedom and P value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐	Estimates of effect sizes (e.g. Cohen's d, Pearson's r), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	BMG Clariostar plate reader software; V5.70 R2
Data analysis	GraphPad Prism 8

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

Raw data files for all the Figures, Supplementary Figures, Tables, and Supplementary Tables have been submitted to Nature Communications and are also available from the authors without any restrictions.

Field-specific reporting

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	We chose to examine the eight (8) most common clinically relevant PARP1 inhibitors that exhibit some significant differences with respect to structure and potency. We also included the non-PARPi iniparib as a negative control. Since we are interested in the better understanding how and why PARP inhibitors work in the clinic, we did not include non-clinically relevant PARP inhibitors. To clarify, this study is not a randomized clinical trial.
Data exclusions	No data were excluded in the replicate experiments.
Replication	All experiments were performed at least in triplicate and actual n values are indicated in the text and/or tables. For the experiments using labeled HPF-1, different preparations were used, and quantitation of extent of labeling was found to be the largest source of error.
Randomization	Samples were collected in different order on different days. That is, at most, 3 different complete time-courses of 2.5 h could be collected on one day. These would be for 3 different inhibitors plus./minus HPF1. Different inhibitors were tested on different days. Inhibitors were chosen randomly until sufficient replicates were collected for each. Each experiment is on its own a whole complete set including positive and negative controls. That is, there is no effect of what other inhibitor was tested earlier or later in the day, or the next day. To clarify, this study is not a randomized clinical trial.
Blinding	There was no blinding because this was not a randomized controlled trial.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
✗	☐ Antibodies
✗	☐ Eukaryotic cell lines
✗	☐ Palaeontology and archaeology
✗	☐ Animals and other organisms
✗	☐ Human research participants
✗	☐ Clinical data
✗	☐ Dual use research of concern

Methods

n/a	Involved in the study
✗	☐ ChIP-seq
✗	☐ Flow cytometry
✗	☐ MRI-based neuroimaging