

Oncogene Addiction and Synthetic Lethality in BRCA-Mutant Cancers

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ABSTRACT

Synthetic lethality exploits tumour-specific dependencies. We performed genome-wide CRISPR screens in BRCA-mutant cancer lines to map DNA-repair vulnerabilities beyond PARP. Loss of POLQ and USP1 emerged as the strongest selective dependencies, and combined inhibition overcame acquired PARP-inhibitor resistance in patient-derived xenografts.

KEYWORDS

synthetic lethality, BRCA, CRISPR screen, DNA repair

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