PRMT5 inhibition epigenetically regulates DNA repair pathways in cancer cells and sensitizes to chemotherapy and PARP inhibition

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INTRODUCTION

PRMT5 inhibition promotes DNA damage in breast and ovarian cancer cells

RESULTS

PRMT5 promotes alternative splicing and downregulates epigenetic marks associated with reduced DDR pathway gene expression

CONCLUSIONS

PRMT5 downregulates a DDR/dna repair gene signature and protein expression in cells by regulating DDN splicing (see supplemental data) and HRM326, associated with increased DNA damage in cancer cells.

PRMT5 preferentially inhibits proliferation of HR-deficient cancer cells.

Combination of PRMT5 and chemotherapy drugs or PARP inhibitors shows synergistic effects in both HR-proficient and HR-deficient cancer cells.