

Top1-PARP1 association and beyond: from DNA topology to break repair

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Selective trapping of human topoisomerase 1 (Top1) on the DNA (Top1 cleavage complexes; Top1cc) by specific Top1-poisons triggers DNA breaks and cell death. Poly(ADPribose) polymerase 1 (PARP1) is an early nick sensor for trapped Top1cc. New mechanistic insights have been developed in recent years to rationalize the importance of PARP1 beyond the repair of Top1-induced DNA breaks. This review summarizes the progress in the molecular mechanisms of trapped Top1cc-induced DNA damage, PARP1 activation at DNA damage sites, PAR-dependent regulation of Top1 nuclear dynamics, and PARP1-associated molecular network for Top1cc repair. Finally, we have discussed the rationale behind the synergy between the combination of Top1 poison and PARP inhibitors in cancer chemotherapies, which is independent of the 'PARP trapping' phenomenon.