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Identifying noble factors and their functions in DNA damage response pathway

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To prevent genomic instability disorders, cells have developed a DNA damage response. The response involves various proteins that sense damaged DNA, transduce damage signals, and effect DNA repair. Among various types of DNA damage, double-stranded breaks are highly toxic to genomic integrity. Homologous recombination (HR) repair is an essential mechanism that fixes DNA damage because of its high level of accuracy. Although factors in the repair pathway are well established, pinpointing the exact mechanisms of repair and devising therapeutic applications requires more studies. RAP80 is one of key molecules in DNA damage response pathway. This protein localizes to sites of DNA insults to enhance the DNA-damage responses. I identified TRAIP/RNF206 as a novel RAP80-interacting protein and found that TRAIP is necessary for translocation of RAP80 to DNA lesions. Biochemical analysis revealed that the N terminus of TRAIP is crucial for RAP80 interaction, while the C terminus of TRAIP is required for TRAIP localization to sites of DNA damage through a direct interaction with RNF20-RNF40. My research demonstrated that the novel RAP80-binding partner TRAIP regulates recruitment of the damage signaling machinery and promotes homologous recombination.

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