RAD27 encodes a multi-functional nuclease involved in processing Okazaki fragments during DNA replication, base excision repair, and maintaining genome stability. Its 5'-flap endonuclease activity is required to cleave the 5' flap from Okazaki fragments that is generated during lagging strand synthesis and to remove the 5'-deoxyribosephosphate end that is formed at apurinic/apyrimidinic sites during BER. A double-flap structure with a 1-nt 3' tail has been proposed as the optimal substrate for its endonucleolytic activity. The 5' to 3' exonuclease of Rad27p is involved in preventing the expansion of di- and trinucleotide repeats by removing secondary structures that are formed by the repeated sequences. RAD27 has also been implicated in double-strand break repair via non-homologous end-joining.Despite its role in many aspects of DNA metabolism, rad27 null mutants are viable but grow slowly. rad27 null mutants are sensitive to UV radiation and methylmethane sulfonatebut not ionizing radiation, consistent with its role in processing intermediates that are formed during BER. rad27 mutants confer an increased rate of recombination and are synthetically lethal with mutations in genes involved in homologous recombination, suggesting that 5' flaps can be removed via homologous recombination. RAD27 expression is cell-cyle regulated.Rad27p is highly conserved in bacteria, other fungi, and mammals. It contains three highly conserved domains, two of which are conserved in prokaryotes. Because deletion of RAD27 in S. cerevisiae leads to expansion of repetitive DNA and trinucleotide repeat instability, RAD27has been implicated in the triplet repeat expansions that lead to Huntington disease and fragile X.