

## ABSTRACT

Werner's syndrome (WS) is a rare autosomal recessive disorder that arises as a consequence of mutations in a gene coding for a protein that is a member of RecQ family of DNA helicases, WRN. The cellular function of WRN is still unclear, but on the basis of the cellular phenotypes of WS and of RecQ yeast mutants, its possible role in controlling recombination and/or in maintenance of genomic integrity during S-phase has been envisaged. With the use of two drugs, camptothecin and hydroxyurea, which produce replication-associated DNA damage and/or inhibit replication fork progression, we find that WS cells have a slower rate of repair associated with DNA damage induced in the S-phase and a reduced induction of RAD51 foci. As a consequence, WS cells undergo apoptotic cell death more than normal cells, even if they arrest and resume DNA synthesis at an apparently normal rate. Furthermore, we report that WS cells show a higher background level of DNA strand breaks and an elevated spontaneous induction of RAD51 foci. Our findings support the hypothesis that WRN could be involved in the correct resolution of recombinational intermediates that arise from replication arrest due to either DNA damage or replication fork collapse