Abstract

Werner's syndrome (WS) is a recessive human genetic disorder associated with an elevated incidence of many types of cancer. The WS gene product, WRNp, belongs to the RecQ family of DNA helicases and is required for the maintenance of genomic stability in human cells. A possible interaction between helicases and topoisomerases that could co-operate in many aspects of DNA metabolism such as progression of the replication forks, recombination and repair has been recently suggested. In addition, sgs1 gene product in yeast, homologous to WS gene, has been shown to physically interact with topoisomerase types I and II. Earlier data from our laboratory suggested that WRN helicase might play a role in a G2 recombinational pathway of double strand breaks (DSBs) repair, co-operating with topoisomerase II. In this work, the effect of the topoisomerase I inhibitor camptothecin in WS cells has been investigated at the chromosomal level.

The data from the present work suggest that the inhibition of topoisomerase I activity by camptothecin results in a higher induction of chromosomal damage in WS cell lines in the G2-phase and in the S-phase of the cell cycle compared to normal cells, perhaps associated with the defects in DNA replication synthesis