

Abstract

Werner's syndrome (WS) is a rare autosomal recessive human disorder and the patients exhibit many symptoms of accelerated ageing in their early adulthood. The gene (WRN) responsible for WS has been biochemically characterised as a 3'–5' helicase and is homologous to a number of RecQ superfamily of helicases. The yeast SGS1 helicase is considered as a human WRN homologue and SGS1 physically interacts with topoisomerases II and III. In view of this, it has been hypothesised that the WRN gene may also interact with topoisomerases II and III. The purpose of this study is to determine whether the loss of function of WRN protein alters the sensitivity of WS cells to agents that block the action of topoisomerase II. This study deals with the comparison of the chromosomal damage induced by the two anti-topoisomerase II drugs, VP-16 and amsacrine, in both G1 and G2 phases of the cell cycle, in lymphoblastoid cells from WS patients and from a healthy donor. Our results show that the WS cell lines are hypersensitive to chromosome damage induced by VP-16 and amsacrine only in the G2 phase of the cell cycle. No difference either in the yield of the induced aberrations or SCEs was found after treatment of cells at G1 stage. These data might suggest that in WS cells, because of the mutation of the WRN protein, the inhibition of topoisomerase II activity results in a higher rate of misrepair, probably due to some compromised G2 phase processes involving the WRN protein