

Abstract

PURPOSE: To investigate whether catalytic topoisomerase II activity by ICRF187, a compound that interferes with the catalytic cycle of topoisomerase II without causing DNA damage, could result in a modulation of X-ray-induced chromosomal damage in Werner's syndrome (WS) cell lines.

MATERIALS AND METHODS: Two WS (KO375, DJG) and one normal lymphoblastoid cell line (SNW646) were exposed to X-rays, post-treated with ICRF187 and harvested after various recovery times. Cell progression to mitosis was monitored by 5-bromo-2'-deoxyuridine (BrdUrd) and fluorescent immunodetection to analyse chromosomal damage in homogeneous treated cell populations in the G1, S or G2 phase of the cell cycle.

RESULTS: In WS cell lines, catalytic inhibition of topoisomerase II activity by ICRF187 resulted in potentiation of X-ray-induced chromosomal damage in the G2 phase of the cell cycle. This potentiation was not observed in the G1 or S phases of the cell cycle, neither in WS nor normal cells.

CONCLUSION: These results point out the possibility that Werner's syndrome protein (WRNp) might play a role in a G2 recombinational pathway of double-strand break repair, cooperating with topoisomerase II and thus contributing to maintain genomic integrity