

Abstract

PURPOSE: To investigate whether in Werner's syndrome cells the G2 phase of the cell cycle has some abnormal response to post-treatment with agents such as caffeine and hydroxyurea known to interfere with cellular response to DNA damage.

MATERIALS AND METHODS: Two Werner's syndrome lymphoblastoid cell lines (KO375 and DJG) and the normal cell line SNW646 were exposed to 50 cGy of X-rays or mitomycin-C and posttreated with caffeine or hydroxyurea in the G2 phase of the cell cycle.

RESULTS: Hydroxyurea post-treatment potentiated the X-ray-induced aberration levels both in the normal and Werner's syndrome (KO375 and DJG) cell lines; in contrast caffeine was only effective in the normal cell line. Similar results were observed when Werner's syndrome cells were treated in the G1 phase with the S-dependent agent mitomycin-C and post-treated with caffeine in G2, extending the observation that Werner's syndrome cells are unaffected by caffeine G2 post-treatment.

CONCLUSIONS: These results show a lack of caffeine effect in Werner's syndrome cells, suggesting an involvement of the Werner's syndrome protein in the signal transduction pathway by which caffeine could override the DNA damage induced G2 checkpoint