Cytogenet Genome Res 104:178–181 (2004)
DOI: 10.1159/000077485

Cytogenetic and Genome Research

Potassium bromate but not X-rays cause unexpectedly elevated levels of DNA breakage similar to those induced by ultraviolet light in Cockayne syndrome (CS-B) fibroblasts

P. Mosesso, S. Penna, G. Pepe, C. Lorenti-Garcia and F. Palitti

Università degli Studi della Tuscia, Dipartimento di Agrobiologia e Agrochimica, Viterbo (Italy)

Abstract. It has been previously reported that the elevated accumulation of repair incision intermediates in cells from patients with combined characteristics of xeroderma pigmentosum complementation group D (XP-D) and Cockayne syndrome (CS) XP-D/CS fibroblasts following UV irradiation is caused by an "uncontrolled" incision of undamaged genomic DNA induced by UV-DNA-lesions which apparently are not removed. This could be an explanation for the extreme sensitivity of these cells to UV light. In the present study, we confirm the immediate DNA breakage following UV irradiation also for CS group B (CS-B) fibroblasts by DNA migration in the "comet assay" and extend these findings to other lesions such as 8-oxodeoxyguanosine (8-oxodG), selectively induced by $KBrO_3$ treatment. In contrast, X-ray exposure does not induce differential DNA breakage. This indicates that additional lesions other than the UV-induced photoproducts (cyclobutane pyrimidine dimers, CPD, and 6-pyrimidine-4-pyrimidone products, 6-4 PP), such as 8-oxodG, specifically induced by $KBrO_3$, are likely to trigger "uncontrolled" DNA breakage in the undamaged genomic DNA in the CS-B fibroblasts, thus accounting for some of the clinical features of these patients.

Cockayne syndrome (CS) is a rare autosomal human genetic disease with features of premature aging and striking somatic and neurological defects. It is caused by mutations in the CS-A or CS-B genes which determine hypersensitivity to a number of DNA damaging agents including UV radiation, ionizing radiation and hydrogen peroxide (Cooper et al., 1997).

The nucleotide excision repair (NER) pathway is involved in a complex process that detects and repairs a wide range of DNA damage including removal of cyclobutane pyrimidine dimers (CPD) and 6-pyrimidine-4-pyrimidone products (6-4 PP) caused by UV irradiation, bulky DNA adducts and DNA cross links caused by chemical agents.

NER is known to operate through two sub-pathways with different kinetics, depending on the function of the damaged DNA: (1) transcription coupled repair (TCR) and (2) global genome repair (GGR) (for review, see Balajee and Bohr, 2000). The TCR sub-pathway repairs only DNA that is actively transcribed by RNA polymerase II (RNAPII). This type of DNA repair is more rapid and complete than GGR.

Both sub-pathways of NER are controlled by all genes involved in xeroderma pigmentosum (XP-A to XP-G) with the exception of XP-C, whose gene product is essential in the recognition and repair of DNA lesions in the overall genome and possibly (XP-E) where its equivalent in TCR-NER is a stalled RNA polymerase II (RNAPII) at a site of a DNA lesion in an actively transcribed gene.

The molecular mechanisms of removal of DNA damage in NER are very similar for the GGR and TCR sub-pathways. After initial recognition of damage and partial unwinding of double stranded DNA, a dual incision of DNA strands at either

The work was partially supported by grants from ASI (Contract No. IR11900) and FIRB (RBNED1RNN7).

Received 7 October 2003; accepted 28 November 2003.

Request reprints from: Prof. Pasquale Mosesso
Università degli Studi della Tuscia
Dipartimento di Agrobiologia e Agrochimica
Via San Camillo de Lellis s.n.c., IT–01100 Viterbo (Italy)
telephone: +39 0761 357205; fax: +39 0761 357242
e-mail: mosesso@unitus.it

KARGER

Fax + 41 61 306 12 34
E-mail karger@karger.ch
www.karger.com

0301–0171/04/1044–0178$21.00/0

Accessible online at:
www.karger.com/cgr