

Relationship between DNA Repair and Formation of Sister Chromatid Exchanges and Chromatid Aberrations under the Influence of Poly(ADP-Ribose) Polymerase Inhibition by 3-Aminobenzamide

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Key Words

Base excision repair • Chromosomal aberrations • DNA repair • Homologous recombinational repair • Poly(ADP-ribose) polymerase • Sister chromatid exchanges • Spontaneous sister chromatid exchanges

Abstract

The mechanisms of formation of sister chromatid exchanges (SCEs) and chromosome aberrations following inhibition of poly(ADP-ribose) polymerase by 3-aminobenzamide were studied in Chinese hamster ovary cell lines deficient in different repair pathways. The results confirm earlier findings that (a) the 'spontaneous' SCEs are formed due to the incorporated BrdU in the DNA, (b) 'spontaneous' and induced SCEs originate from different mechanisms, and (c) SCEs and chromatid exchanges are formed by different pathways.

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Visualisation of sister chromatid exchanges (SCEs) in somatic cells was first demonstrated by Taylor [1958] in cells of *Vicia faba* and *Bellevia romana*. Latt [1973] and Kato [1974] demonstrated the use of halogenated pyrimidines followed by DNA-specific fluorochromes for dif-

ferentiating unifilarly and bifilarly substituted sister chromatids. Modification of these techniques for solid staining was introduced by Perry and Wolff [1974]. Most of the chemical carcinogens and mutagens, as well as UVC, have been shown to increase the frequencies of SCEs in a dose-dependent manner. In spite of the large number of studies, the mechanisms involved in the formation of SCEs are still not well understood. The frequencies of 'spontaneous' SCEs correlate with the DNA content of the cell type, e.g. very low in *Drosophila* and very high in *Vicia faba* [Uggla and Natarajan, 1982]. One factor which seems to be critical is the extent of 5-bromo-deoxyuridine (BrdU) incorporation in DNA, since there is a parallel increase in the frequencies of SCEs with the extent of thymine substitution with BrdU [Zwanenburg and Natarajan, 1984]. By incorporating very low concentrations of BrdU in DNA and immunodetection of SCEs with BrdU-specific antibodies, it could be demonstrated that about only 1 SCE occurs per Chinese hamster ovary (CHO) cell division [Natarajan et al., 1986], a frequency similar to the one found in Chinese hamster cells carrying a large ring chromosome, in which SCEs can be detected without incorporation of BrdU [Sutou, 1981].

Among the human syndromes deficient in different pathways of DNA repair, such as ataxia telangiectasia,

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