RAMA UNIVERSITY

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DEPARTMENT OF BIOTECHNOLOGY
FACULTY OF ENGINEERING & TECHNOLOGY

X-ray – Mechanism of radiation carcinogenesis

Content outline

1. X-Ray

X-Ray Mechanism

➢An *X-ray*, or *X*-radiation, is a penetrating form of high-energy electromagnetic radiation. Most *X-rays* have a wavelength ranging from 10 picometres to 10 nanometres, corresponding to frequencies in the range 30 petahertz to 30 exahertz (3×10^{15} Hz to 3×10^{18} Hz) and energies in the range 124 eV to 124 keV.

•Carcinogenesis is viewed as a multistep process in which two or more intracellular events are required to transform a normal cell into a cancer cell. The concept that carcinogenesis involves more than one step is derived from three main lines of evidence: (1) the rate of mortality from cancer increases as a power function of age, (2) a long latent period typically intervenes between exposure to a known carcinogen and the appearance of cancer, and (3) three distinct and separate stages have been identified in experimental carcinogenesis: initiation, promotion, and progression.

Mechanism

•The mechanisms by which radiation may produce carcinogenic changes are postulated to include the induction of: (1) mutations, including alterations in the structure of single genes or chromosomes; (2) changes in gene expression, without mutations; and (3) oncogenic viruses, which, in turn, may cause neoplasia. Although controversy persists as to the relative importance of these hypothetical mechanisms in the induction of carcinogenesis, they are not mutually exclusive, since different mechanisms may be involved at successive stages in carcinogenesis.

•The somatic mutation theory of carcinogenesis, proposed by Boveri in 1914 (Bo14), has received further support from the high correlation between the carcinogenicity and the mutagenicity of different agents. In a few types of cancer (e.g., retinoblastoma), moreover, the same specific gene mutation or deletion is found both in familial and nonfamilial cases. suggesting that the mutation or the deletion of the gene plays a causative role.

Initiation, Promotion, and Progression in Carcinogenesis

The following generalizations about the process of carcinogenesis are noteworthy: (1) The effects of radiation and chemical carcinogens which lead to cancer are dose dependent and generally irreversible; (2) the carcinogenic process is dependent on cell proliferation; (3) the changes that initiate carcinogenesis in a cell are passed on to daughter cells; (4) the subsequent events in carcinogenesis can be profoundly influenced by various noncarcinogenic factors; and (5) tumors tend to become increasingly malignant with time through the stepwise outgrowth of progressively more malignant subpopulations of tumor cells

•Radiation itself also can enhance tumor promotion, tumor progression, and the conversion of benign growths to malignant growths (Ja87). To the extent that the effects of radiation are mediated by free radicals (Li77), which can also mediate the effects of promoting agents (Co83), sequential exposures to radiation may serve to promote tumorigenesis through mechanisms similar to those of chemical promoting agents.

Radiobiological Factors Affecting Oncogenic Transformation

Dose Response

The dose-response relationship for the induction of radiogenic transformation reflects a balance between an increase with dose in the proportion of cells that are transformed and a decrease in cell survival.

Dose Rate and Dose Fractionation

For low-LET radiations, the consensus is that cell survival is enhanced by a decrease in the dose rate or separation of the dose into a number of fractions. Effects on the yield of transformants, however, are more complex. It has been reported that for low-LET radiations, splitting or fractionating the dose or reducing the dose rate can either enhance (Bo74, Ha81, Li79) or decrease (Hi84) the transformation frequencies.

Effects of radiations

Recessive Breakage and Repair Disorders

•These disorders, which include xeroderma pigmentosum, ataxia telangiectasia, Fanconi's anemia, and Bloom's syndrome, are recessively inherited conditions that predispose the chromosomes of an individual to breakage and/or defective repair of DNA damage (Han86). They do not involve cancer genes of the types discussed above but can be viewed as conditions that increase the probability of a cancer-producing mutation.

•Thus, in xeroderma pigmentosum a defect in excision repair permits an increased rate of mutations at all genetic loci in cells exposed to sunlight. Ataxia telangiectasia predisposes the chromosome to breakage, especially in lymphocytes.

Genetic Polymorphism for Metabolism of Carcinogens

In contrast to the aforementioned DNA repair disorders, in which the response to an environmental agent is altered, there are cases in which the response may be normal but the amount of radiant energy imparted is increased. Thus, albinos are sensitive to ultraviolet light because they absorb more of it, not because they have a defective DNA repair mechanism. Such a genetic predisposition is also known for many chemical carcinogens

References & Further reading

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