INTRODUCTION

An analysis of the mechanisms of radiation induced biological effects (cell death, mutation or transformation) has to describe the individual steps of the events that follow the absorption of radiation energy, i.e. the primary events leading to the damage of biomolecules, especially the DNA, as well as the subsequent repair reactions, which are either error-free leading to recovery, or error-prone, leading possibly to an altered nucleotide sequence and under certain circumstances to mutation or transformation of the cell. Recent review articles are published by Hüttermann et al., 1978; Hutchinson, 1985; Cadet and Berger, 1985; Ward, 1985; Hagen, 1985; v. Sonntag, 1987; Teoule, 1987.

CHEMICAL ASPECTS

In contrast to chemical agents the biological effects of ionizing radiation, i.e. X-rays, γ-rays or of various particles are due to a distinct spatial distribution of primary ionisations events in the cell. There can be single events of energy absorption in DNA as well as multiple events (Ward, 1981). We must consider this when analysing the reactions that follow the primary events in the cell.

Ionizing radiation produces radicals; in water:

\[ \text{H}_2\text{O} \rightarrow \text{H}^\cdot, \text{OH}^\cdot, \text{H}_2\text{O}^+, \text{e}^-_\text{aq} \]

as well in the biomolecules of the cell directly:

\[ \text{RH} \rightarrow \text{R}^\cdot + \text{H}^\cdot, \]

or via the water radicals:

\[ \text{RH} + \text{OH}^\cdot \rightarrow \text{R}^\cdot + \text{HOH} \] (H-Abstraction) or
\[ \text{R'} + \text{OH}^\cdot \rightarrow \text{R'}\text{OH}^\cdot \] (OH-Addition).

In the presence of oxygen, these radicals can be transformed into peroxyradicals:

\[ \text{R}^\cdot + \text{O}_2 \rightarrow \text{ROO}^\cdot. \]

This reaction prevents recombination:

\[ \text{R}^\cdot + \text{H}^\cdot \rightarrow \text{RH}, \]
and therefore increases the radical yield in the medium. In addition, O$_2$ reacts very fast with the solvated electron; thus recombination to the original molecules:

$$\text{RH}^\cdot + e^-_{aq} \rightarrow \text{RH}$$

is prevented (Henglein et al., 1969; v. Sonntag, 1987).

As a result of these reactions, the radiation effect depends strongly on the oxygen concentration in the cell during radiation, leading to an "oxygen-enhancement-ratio" (OER) of about 3 (cf. Dertinger and Jung, 1970). The actual yield of radicals formed in biomolecules is determined by the kinetics of these reactions. It is necessary to consider the relative reactivities of the various radicals when analysing the various steps of the chemical events that follow absorption of radiation energy.

PROTEINS

Proteins and nucleic acids are of special interest when analysing radiation effects on biomolecules. For proteins, the reactions on RNase has been studied. In contrast to nucleic acids, breaks in the peptide bonds are rarely found. Moreover there are dimerisations (crosslinks), leading to inactivation of the enzymatic center. In the presence of oxygen, dimerisation is prevented, probably due to formation of peroxyradicals (Schüssler and Jung, 1967, Dertinger and Jung, 1970).

Chemical reactions on the side-chains of amino acids can produce various types of damage; cysteine, methionine, tyrosine and phenylalanine being the most sensitive. Changes in the amino acid content is observed in all fractions of the protein, in the dimer, in the denatured inactive monomer but also in the molecules still active in the enzymatic function. With increasing dose, there is a linear rise of amino acids destruction in all fractions. Studies on the Michaelis-Menten kinetics have shown, that irradiation leads to non-competitive inhibition, due to changes in the molecule not located in the active center (Adelstein and Mee, 1961).

It should be pointed out, however, that damage on proteins in irradiated cells is not responsible for cell death or for the genetic effect of radiation.

RADIOLYSIS OF DNA IN VITRO

With respect to the genetic effects of radiation, we are interested in the primary reactions in DNA that lead to defective bases as well as to breaks of the sugar phosphate backbone.

Primary events and radical reactions have been analysed by electron spin resonance, thymidine being most susceptible to damage. Chemical studies show that there is a great variety of base damage characterized by H or OH-addition to the C5-C6-double bond in pyrimidines or opening of the heterocyclic ring of purines leading to various formamidopyrimidines. These compounds are only examples; there are many other products not yet identified (Dertinger and Jung, 1976; Cadet and Berger, 1985; Hagen, 1986; Teoule, 1987).