MODIFICATION OF RADIOSENSITIVITY OF DNA-MEMBRANE COMPLEXES IN MAMMALIAN CELLS BY MEANS OF PROTECTORS

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Besides DNA itself, the DNA-membrane complex of mammalian was found to contain firmly bound RNA, nonhistone proteins and lipids (I). This complex is shown to be stable in vitro to RNAase, pronase, proteinase K, trypsine, sodium dodecylsylphate, EDTA. However, when treated with phospholipase C or 35% ethanol this complex destroys to release DNA subunits with the molecular weight of $I\text{-}2.IO^8$ daltons. The DNA-membrane complex of mammalian cells is suggested to consist of DNA subunits of $I\text{-}2.IO^8$ dalton (about 400 subunits per one chromosome) connected with each other by lipoprotein linkers (2). Irradiation in vivo acts analogously with ethanol and phospholipase C: it destroyes the lipoprotein linkers and releases the DNA subunits from the DNA-membrane complex, this reaction being accompanied by a very high radiation-chemical yield (IO^5 lipid molecules and IO^4 NHP per IOO eV).Therefore in the DNA-membrane complex there are specific nondesoxyribonucleotide linkers - the critical sites of a lipid nature - which are primarily damaged by radiation (2).

The physico-chemical criterion of nativity of DNA-membrane complex is elastoviscosity which we measured on the Struchkov capillary elastoviscosimeter (3). We suggest the rapidly changes in elastoviscosity of the DNA-membrane complex in irradiated rat tissues (minutes after irradiation) to be responsible for survival of cells and the organism as a whole (4). We stated the postirradiation recovery of DNA elastoviscosity in spleen of mice irradiated with sublethal doses of I50 and 600 rad (5). The protector AET, when introduced to mice during irradiation at a dose of I50 rad, produces a marked radioprotective effect on DNA: the DNA elastoviscosity of protected mice was recovered on the third or fourth day after irradiation whereas that of non-protected - only after I4 days. The spleen of irradiated mice restored its normal weight slower than DNA its elastoviscosity.

Recently we proposed a new method of radioprotection of mammalian organisms including humans by means of a hypoxic gas mixture containing IO% oxygen and 90% nitrogen (HGM-IO) (6). HGM-IO inhaled during irradiation increases survival of the animals (mice, rats, guinea pigs, dogs, monkeys). In this connection it was interesting to determine the efficiency of radioprotection of HGM-IO at the level of the DNA-membrane complex. The experiments were carried out on spleen and brain of rats. HGM-IO was found to have a pronounced radioprotective effect on elastoviscosity of DNA of rat spleen and brain upon the action of radiation at different doses (50, 200, 500, 900 rad) (7).

Simultaneously with the biochemical studies we investigated the radioprotective effect of HGM-IO on the frequency of chromosomal aberrations of monkey bone marrow and on the mitotic index of human skin cells produced by local irradiation with IOO-200 rad (7). By the test "chromosomal aberrations" the coefficient of protection for bone marrow at a dose of IOO rad was 9.I and, compared to the norm, the mitotic index for human skin cells was 3.5 and 5.5 times higher under the conditions of radioprotection with HGM-IO at doses IOO and 200 rad respectively.

Based on the facts that HGM-IO, adrenaline and AET themselves produce prolonged but reversible changes in the DNA-membrane complex structure (4,7,8), these protectors are suggested to have a molecular mechanism of action. It is probable that radioprotectors and HGM-IO transfer the DNA-membrane complex into a radioresistant form by physiological mechanisms. We are now studying the nature of this transfer which is not only interesting from the theoretical viewpoint but also important for optimization of the method of radioprotection of human organism which we have already begun to use since I975.

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