RADIATION SENSITIVITY OF CELLS FROM HETEROZYGOTES FOR ATAXIA-TELANGIECTASIA

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Ataxia-telangiectasia (AT), a recessive hereditary disease, is characterized in particular by increased sensitivity to x-ray irradiation both *in vivo* [3, 4, 6] and *in vitro* [5, 7]. The unusual sensitivity of patients with AT to radiation was discovered during x-ray therapy of such patients for neoplasms; after ordinary doses of irradiation these patients developed ulcers of the skin and mucous membranes, and unexpectedly serious complications or even death. Experiments *in vitro* showed that irradiation induces more aberrations in the cells of patients with AT (in cultures of peripheral blood lymphocytes and of skin fibroblasts) than in cells from control individuals. The same principle is observed at all stages of the cell cycle.

With regard to heterozygous carriers of the AT gene there are no data on sensitivity to irradiation.

In this paper the frequencies of chromosomal aberrations after irradiation of cells from heterozygotes for AT (parents of patients with AT) are compared with those of control blood donors.

LITERATURE CITED

Cultures of lymphocytes from four heterozygous carriers of the AT gene and five control blood donors were studied. The experiments were carried out in two stages as the patients were admitted. The main experimental conditions was simultaneous irradiation of cells from heterozygotes for AT and of a control donor. In this way the dose of irradiation given to each member of the heterozygote for AT—control pair was absolutely identical.

Irradiation was given on the Gupus apparatus (dose rate 650 rads/min). Whole blood was irradiated in doses of 40, 80, and 160 rads immediately before the beginning of culture. The conditions of culture and the method of obtaining and staining the preparations were those generally adopted. Cells were fixed at the 56th hour of culture. Colchicine was added 2 h before fixation. The preparations were coded. At each point 100 cells were analyzed. The data were subjected to statistical analysis by the dispersion method [2].

EXPERIMENTAL RESULTS

Data on the frequency of chromosomal aberrations in lymphocyte cultures from two groups of individuals — heterozygotes for AT and control — are given in Table 1. For dispersion analysis the data in Table 1 were grouped as follows: 1) the first and second pairs of individuals (the pair consisting of a heterozygote for AT and a control blood donor), dose of irradiation 40 and 80 rads; 2) third, fourth, and fifth pairs of individuals, dose of irradiation 80 and 160 rads; 3) first, second, third, fourth, and fifth pairs of individuals, dose of irradiation 80 rads.

Dispersion analysis revealed statistically significant differences between the two groups of individuals (heterozygotes for AT and control) only for analysis of the frequency of dicentrics and rings in the group of two pairs of individuals receiving irradiation in doses of 40 and 80 rads ($0.01 < P < 0.05$).

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TABLE 1. Action of Irradiation on Lymphocyte Cultures from Heterozygotes for AT and Control Blood Donors

Dose of irradiation, rads	Individuals	Heterozygotes for AT							
		No. of cells analyzed	No. of cells with aberrations	No. of breaks	dicentrics + rings	No. of cells analyzed	No. of cells with aberration	No. of breaks	dicentrics + rings
40	1	100	13	22	6	100	6	9	2
	2	100	8	15	5	100	8	15	6
80	1	100	15	29	9	100	11	18	5
	2	100	22	34	10	100	16	24	5
	3	100	15	27	9	100	12	28	11
		40	9	15	6	100	24	40	10
	4	100*	22,5	37,5	15	100			
	5	100	25	45	15	100	13	25	9
160	3	100	38	89	34	100	41	107	36
	4	100	42	105	44	89	36	73	22
						100*	40,5*	82*	24,7*
	5	100	46	120	41	100	35	91	33

*Data calculated for 100 cells.

Analysis of the remaining types of chromosomal aberrations and of the other groups of individuals (receiving doses of 80 and 160 rads) revealed no statistically significant differences ($P > 0.05$).

It follows from these results that two groups of individuals (heterozygotes for AT and control) differed only to a very slight degree, if at all, in their sensitivity to irradiation.

Previously the writers obtained data showing increased sensitivity of heterozygotes for AT to low concentrations of thiophosphamide [1].

If the data on sensitivity of heterozygotes for AT to irradiation and to thiophosphamide are generalized it can be concluded that the presence of a mutant AT gene in the genome in the heterozygous state has no significant effect on the defensive properties of the cell against the action of these mutagenic factors.

However, on the basis of the results of these experiments the following hypothesis seems likely. Increased sensitivity of heterozygotes for AT to mutagenic factors is manifested during exposure under conditions when the defensive properties of the cell can still perform their role (at levels of exposure comparable with the level of mutagenic factors in the external environment). The mechanism of realization of this property of the AT gene may differ under these circumstances: Mechanisms of the defensive properties of the cell may be disturbed and an intracellular mutagenic factor may be formed during metabolic activity of the cell [8].

LITERATURE CITED

1. Yu. E. Ivanova, N. P. Bochkov, and K. N. Yakovenko, Byull. Eksp. Biol. Med., No. 7, 95 (1980).
2. C. Hicks, Fundamental Concepts in the Design of Experiments, Holt, Rinehart, and Winston, New York (1964).
3. P. N. Cunliffe, J. R. Mann, A. H. Cameron, et al., Br. J. Radiol., 48, 374 (1975).
4. S. P. Gotoff, E. Amirmokri, and E. J. Leibner, Am. J. Dis. Child., 114, 617 (1967).
5. M. Higurashi and P. E. Conen, Cancer (Philadelphia), 32, 380 (1973).
6. J. L. Morgan, T. M. Holkomb, and R. W. Morrissey, Am. J. Dis. Child., 116, 557 (1968).
7. A. T. Natarajan and M. Meyers, Hum. Genet., 52, 127 (1979).
8. M. Shaham, Y. Becker, and M. M. Cohen, Cytogenet. Cell. Genet., 27, 155 (1980).