in the hormonal status of these animals. This interpretation is also supported by data on the different levels of sensitivity to tumors in females during lactation and in males. The considerably higher level of resistance to tumors in multiparous females, which the writer observed previously [1], may perhaps be due to selection of the animals for two features important for preservation of the species: a higher level of natural resistance to tumors and higher fertility.

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REVERSIBILITY OF THE STATHMOKINETIC REACTION AFTER MALIGNANT TRANSFORMATION OF CELLS

M. E. Aspiz and N. A. Starosvetskaya

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KEY WORDS: stathmokinetic reaction; colcemid; mitosis; tubulins; malignant transformation of cells.

There have been many observations of changes in the mitotic regime in tumors, including the presence of numerous pathological mitoses in them. Analysis of pathological forms of cell division in tumor tissue has shown that a high proportion of them are due to pathology of the division spindle [1-3, 5, 7].

The appearance of polyploid and aneuploid cells in tumors is also evidently the result of injury to their division spindle, which is responsible for the uniform distribution of the chromosomes to the poles of the dividing cells. The mechanisms of these disturbances are not yet clear. Previous investigations of differences in the sensitivity of normal and transformed cells to metaphase inhibitors showed [10] that increased sensitivity of transformed cells to colcemid compared with that of cells of primary cultures is due, not to a change in binding of the alkaloid with the tubulins of the transformed cells, but to a change in the permeability of their plasma membrane. This has been confirmed by biochemical studies also [8, 9]. It remained to be discovered whether the processes of polymerization of tubulins are disturbed in tumor cells.

In the investigation described below this question was studied on a model of reversibility of the stathmokinetic reaction induced by colcemid. The writers showed previously that the reversibility of this reaction is associated mainly with repolymerization of the microtubules of the spindle from tubulins of the precursor pool [4]. This model thus enables processes of tubulin polymerization in the cells to be judged during formation of the division spindle.

EXPERIMENTAL METHOD

Experiments were carried out on cells of line KOKh-1, which have undergone malignant transformation, generously provided by the K. I. Skryabin Veterinary Academy, where this strain was obtained as follows. A tumor (sarcoma) was induced in newborn Syrian hamsters by subcutaneous injection of type 3 bovine adenovirus (BA-3). Tumors developed in 50% of animals. The present culture was obtained from the 23rd passage of this tumor in vivo. This cell line proved to be highly tumorogenic for hamsters (the value of TD_{50} varied between 10^1 and $10^{3\cdot6}$). Tumors formed at the site of injection of KOKh-1 cells within a short time attained a large size in adult animals and quickly caused their death [6].

Institute of Human Morphology, Academy of Medical Sciences of the USSR, Moscow.

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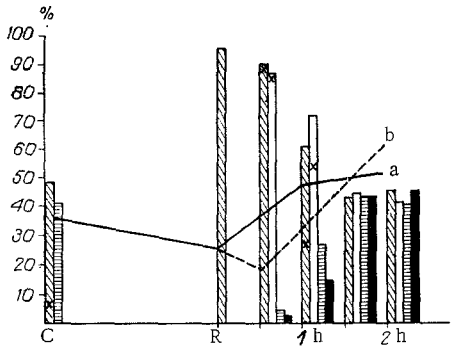

Fig. 1. Parameters of mitotic regime during reversal of stathmokinetic reaction induced by colcemid and after additional treatment with Cu^{++} ions. a) MI; b) MI after treatment with Cu^{++}. Obliquely shaded columns represent metaphases, unshaded columns metaphases with Cu^{++}; horizontally shaded columns sum of anaphases and telophases; black columns sum of anaphases and telophases with Cu^{++}. C) Time of addition of colcemid; R) rinsing out of colcemid and addition of Cu^{++}. Crosses indicate number of colchicine-like mitoses.

The cells were grown in medium No. 199 with 10% bovine serum. The seeding density was about 300,000 cells/ml. Colcemid (0.3 μg/ml) was added to the medium after 12-14 h of growth of the cells after seeding. After exposure for 2 h to the alkaloid, cover slips with cells that had settled on them were carefully washed in Hanks' solution and some cover slips were transferred to fresh medium, others to medium containing copper ions (in a final concentration of 10^{-5} M), which are known to inhibit polymerization of tubulins [12, 13]. The rate of reversibility of the stathmokinetic reaction was determined from the level of the mitotic index (MI) and the ratio between the phases of mitosis.

EXPERIMENTAL RESULTS

After exposure to colcemid for 2 h the percentage of cells at the metaphase stage was increased by 50-100% (Fig. 1). Under these circumstances MI was not higher than in the control, probably because of simultaneous delay of entry of the cells into mitosis. The final stages of mitosis (anaphases and telophases) had completely disappeared by this time. After transfer of the cells to the pure medium, the first anaphases and telophases began to appear after 30 min. In medium containing proper ions, normalization of the mitotic regime was delayed by comparison with cells kept in the pure medium. The number of final phases of mitosis in the presence of copper ions 1 h after rinsing off the alkaloid was only half of that without them, and a correspondingly larger number of cells were at the metaphase stage. Among the metaphase cells in the presence of copper ions, the percentage of colchicine-like metaphases was twice as high as in cells at the same stage of division, but kept in pure medium (54 and 27%, respectively). However, complete normalization of the mitotic regime took place after 2-2.5 h in cells cultured both in the pure medium and in medium with copper ions.

The character of restoration of the normal mitotic regime is thus evidence of activity of polymerization processes in the cells studied. The course of these processes in the presence of copper ions is evidence of involvement of the same mechanisms as in the case of cells which have not undergone malignant transformation. Although the results of these experiments show that repolymerization processes during the formation of the division spindle are completely preserved in tumor cells, the possibility cannot be ruled out that other stages of mitosis in them, connected with polymerization and depolymerization of tubulins, may be significantly altered. Such a possibility may also be suggested on the basis of the longer course of metaphase in these cells, the considerable number of colchicine-like mitoses in them, and the delayed course of anaphase [11], possibly due to a disturbance of polymerization–depolymerization processes.

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ATYPICAL INCOMPATIBILITY OF F-LIKE GENETIC TRANSFER FACTORS pAP22-4, pAP39, AND pAP41 WITH F-GROUP INCOMPATIBILITY PLASMIDS

A. P. Pekhov, V. P. Shipkov,
V. N. Reshetnikova, E. V. Gubar',
and N. A. Drobysheva

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When studying the plasmid complex found in cells of serologically typed (serogroup 06) strain Escherichia coli AP1 [1-3], we identified in it a genetic transfer factor pAP22-4 with a molecular weight of $39.3 \cdot 10^6$ daltons. Meanwhile in bacteria of strains AP25 (serogroup 076) and AP26 (serogroup 0121) transfer factors pAP39 and pAP41 with molecular weights of $42.6 \cdot 10^6$ and $90 \cdot 10^6$ daltons, respectively, were identified. All these factors are F-like plasmids.

The relationship of the identified transfer factors to F-group incompatibility plasmids was studied in the present investigation.

EXPERIMENTAL METHOD

Genetic marking of the transfer factors was carried out in crosses in which the donors were cells of E. coli 1553, carrying mutant temperature-sensitive plasmid RP4 [4] with transposon Tn1, containing the gene of resistance to ampicillin (Ap), served as donors and E. coli AP105 cells carrying one of the transfer factors under investigation, served as recipients. The transfer factors marked by the Tn1 transposon (resistance to ampicillin) were designated pAP22-4:: Tn1, pAP39:: Tn1, and pAP41:: Tn1. In experiments to determine compatibility (incompatibility) of the transfer factors with F-like plasmids, plasmids R386, R1-19, ColB-R3, R124, F_0lac, and Hly-P212, reference plasmids of the incompatibility group FI, FII, FIII, FIV, FV, and FVI respectively, were used. These experiments were carried out by a method according to which a given transfer factor

Department of Biology and General Genetics, Patrice Lumumba Peoples' Friendship University, Moscow.

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