THE STUDY OF THE SYNTHESIS OF PROTEIN AND RNA BY THE DIVIDING ACINAR CELLS OF THE PANCREAS

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The hypothesis of antagonism between work and division of the cell [8] is based on observations that secretory cells cease to form granules and vacuoles during mitotic division. During recent years, however, facts have been discovered which suggest that during mitosis the working activity of the cell is not completely suspended. By means of the method of autoradiography, for example, several authors [7, 9] have shown that despite the lower level of protein synthesis by dividing cells, it nevertheless still continues, and in fact amounts to 25-30% of the interphase value. Other workers [6] have found that during mitosis protein synthesis may even be intensified in the initial stage of division (prophase), but in all subsequent stages it falls to the interphase level, at which it stays until the end of division.

As the author's earlier investigation showed, the dividing secretory cell of the pancreas retains the functions of accumulation and secretion of zymogen granules. Because of the decrease in the size of the prozymogen granules during mitosis it was postulated that the processes of synthesis of the secretion are depressed, although they probably remain partly preserved.

The object of the present investigation, in which the synthesis of protein and RNA was studied in the dividing acinar cells of the pancreas, was to test this hypothesis.

EXPERIMENTAL METHOD

Experiments were carried out on albino mice weighing 5-6 g, divided into two groups. Group 1 consisted of mice deprived of food for 10-12 h, in which the ability of the acinar cells to synthesize protein and RNA in a resting state was studied. In the mice of group 2 the ability of the secretory cells to synthesize protein and RNA in a state of increased secretory activity (recovery stage) was studied. The mice of this group received food 1 h before sacrifice. The animals of both groups were sacrificed at 8 a.m., in the period of maximal mitotic activity.

Leucine-H^3 was used to study the protein synthesis by the dividing acinar cells of the pancreas. The isotope was injected intraperitoneally into the mice in a dose of 5 μCi/g body weight. The mice were sacrificed 10 min after injection of the isotope, thus preventing the possibility of progress from one stage of mitotic division to another by the cells with incorporated precursor. The material was fixed for 48 h in Bouin's fluid, then thoroughly washed in several portions of 70° alcohol, embedded in paraffin wax, and sections were cut from it to a thickness of 5 μ. Liquid emulsion of type M (Motion Picture Institute—NIKFI) was used for preparing autoradiographs. The exposure for the fed animals was 42 days and for the fasting animals 64 days. After development, the sections were stained with Mayer's hematoxylin. The level of synthetic activity was judged from the number of tracks on a cell. In each preparation the tracks were counted over the interphase cells and over the cells in the various stages of mitosis (20-30 cells in each of the various phases of mitosis).

For the study of RNA synthesis, uridine-H^3 (its specific precursor) was used in a dose of 5 μCi/g body weight. The total dose was 25-30 μCi per animal. The material was fixed by Brodskii's method. The same technique of autoradiography was used as in the investigation of protein synthesis. The results were subjected to statistical analysis.

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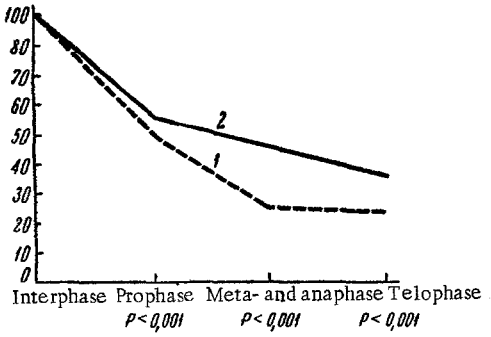

Fig. 1. Intensity of incorporation of leucine-H^3 during mitotic division of the secretory cells of the pancreas. Abscissa—stages of mitotic division; ordinate—number of tracks over dividing cells (in %) of fasting (1) and fed (2) mice.

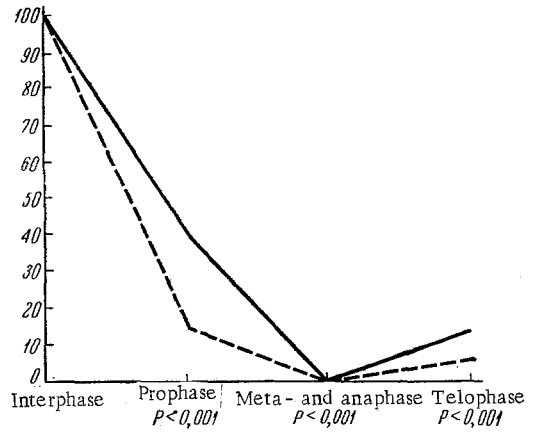

Fig. 2. Intensity of incorporation of uridine-H^3 during mitotic division of the secretory cells of the pancreas. Legend as in Fig. 1.

EXPERIMENTAL RESULTS

Analysis of the results showed that with the onset of mitosis in the acinar cells of the pancreas the incorporation of leucine-H^3 fell to 50% of the interphase level in the fasting mice and to 56% in the fed animals. In metaphase and anaphase protein synthesis continued to fall, reaching 24% in the fasting and 45% in the fed mice. In telophase a further fall in protein synthesis was observed, to 22% of the interphase level in the fasting mice and 30% in the fed animals. The dynamics of the changes in the incorporation of leucine-H^3 in the dividing acinar cells of the pancreas can be clearly followed in Fig. 1.

The results of these experiments thus showed that during mitosis the functional activity of the cell continued. The cell remained capable of synthesizing protein during mitotic division. The theory of the unconditional antagonism between work and division of the cell cannot be accepted unreservedly, for during mitosis only the synthetic processes are depressed, whereas the other functions are fully maintained [2].

It is a very interesting fact that the level of protein synthesis in the dividing acinar cells of the pancreas is determined by the functional state of these cells. As Fig. 1 shows, during mitosis of the secretory cells of the fed mice whose cells were in the recovery stage, the level of protein synthesis was relatively higher than in the fasting mice, whose acinar cells were in a resting state. The effect of functional loads on protein synthesis by interphase cells has been described. Hyden [3], for example, found that during moderate motor activity the protein content in the motor neurons of the ventral horns of the spinal cord in albino mice rose sharply. V. Ya. Brodskii [1] used the methods of interference microscopy and ultraviolet cytophotometry to study the dynamics of the protein content in the nuclei and cytoplasm of the ganglion cells of the frog's retina. If this neuron is brought from a state of physiological rest to one of activity by photic stimulation, marked activation of protein synthesis was observed in the cell.

The results thus show that not only are the processes of protein synthesis partially preserved in the dividing acinar cells of the pancreas, but as in the interphase cells, with an increase in functional activity, the intensity of synthesis is also increased. When a functional load is applied to the organ, not only the interphase cells, but the cells undergoing mitotic division are also involved in the general activity. The level of synthesis in the latter cells is fairly high, high enough for stimulation of synthesis in the dividing cells to be regarded as a reserve mechanism providing for the increased functional activity of the organ.

Since protein synthesis continued in the dividing acinar cells of the pancreas, the study of the RNA synthesis during mitotic division was of considerable interest. The results of the investigation of this problem showed that profound changes take place in RNA synthesis during mitotic division. As Fig. 2 shows, with the onset of mitosis the RNA synthesis fell to 39% of the interphase level in the fed mice and to 15% of that level in the fasting mice. In the metaphase and anaphase RNA synthesis ceased, but in the telophase it began to recover, reaching 6.4% of the interphase level in the fasting and 11% in the fed animals. The cessation of RNA synthesis during mitosis was evidently connected with changes in the chromosomes during mitotic division and with disappearance of the nucleolus. According to reports in the literature [4], all the

RNA of the cell is synthesized in the nucleus, and the changes taking place in the nucleus during mitosis are bound, therefore, to have some effect on the level of RNA synthesis.

It appears to be a very interesting fact that protein synthesis continues in the dividing acinar cells of the pancreas in the period of metaphase and anaphase, when the synthesis of RNA stops completely. Observations have been reported, showing that in various experimental conditions, when the transmission of genetic information from nucleus to cytoplasm is interrupted, protein synthesis may still continue for a long time. These results suggest the existence of a stable messenger RNA, capable of maintaining protein synthesis in the absence of genetic information.

Consequently, contrary to the hypothesis of antagonism between division and work of the cell, these results show that functional activity continues at a certain level in dividing secretory cells. The functions of maintaining the accumulated zymogen granules and of their liberation in the period of mitosis do not differ essentially from these functions of interphase cells. The function of the formation of secretory granules (protein synthesis), although depressed during mitosis, does not cease completely, and if increased functional loads are applied, it may attain high levels in the dividing cells.

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