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Synthesis of Lipids in Isolated Nuclei from Rat Thymus and Liver Cells

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Abstract—Synthesis of lipids was studied in isolated nuclei from rat thymus and liver cells. On incubation of the isolated nuclei with [2-^{14}C]acetate and [1-^{14}C]glycerol, the label was intensively incorporated into phospholipids and with a significantly lower intensity into fatty acids and cholesterol. Only trace amounts of radioactivity were detected in the lipids of chromatin prepared from isolated thymus nuclei after their incubation, and this suggested that lipids were mainly synthesized on the nuclear membrane. On the preincubation of thymus tissue homogenate with [2-^{14}C]acetate and the subsequent isolation of the nuclei and chromatin, the radioactivity of chromatin lipids was comparable to the radioactivity of nuclear lipids. The findings suggested that in the isolated nuclei the newly synthesized lipids were not transported into chromatin from the nuclear membrane. The specific radioactivities of individual phospholipids and fatty acids were different in the isolated nuclei and in nuclei obtained from preincubated homogenate. Mechanisms of lipid synthesis in isolated nuclei and causes of the different radioactivities of lipids in the isolated nuclei and in the nuclei obtained from the preincubated homogenate are discussed.

Key words: phospholipids, fatty acids, synthesis, nuclei, chromatin, thymus, liver

Studies on the role of lipids in functions of the nuclear apparatus of the cell are interesting because of their effects on the structure and functions of chromatin [1, 2] and also of their involvement in the nuclear signal systems, such as the sphingomyelin [3, 4] and phosphoinositol [5, 6] cycles. We found earlier that lipids of chromatin from rat liver and thymus cells had higher specific radioactivity than lipids of the intact nuclei [7, 8]. The radioactivities of fatty acids and cholesterol were compared in the nuclei, nuclear membrane, and chromatin from rat thymocytes, and the specific radioactivity of these lipids in the nuclear membrane was lower than in chromatin [9]. These findings suggested either the existence of a directed transport of the newly synthesized lipids from the endoplasmic reticulum where they had been synthesized into chromatin without averaging their radioactivity with that of the nuclear membrane lipids, or the presence in the nuclei of their own systems for lipid synthesis. Literature data on the possible synthesis of individual lipids in the isolated nuclei from mammalian cells are scarce. The incorporation of labeled glycerol into lipids of the isolated nuclei from calf thymus was first shown by Rose and Frenster [10]. The incorporation of labeled choline into phosphatidylcholine of isolated nuclei from liver cells was shown [11, 12]. The synthesis of polyphosphoinositol lipids was shown *in vitro* in purified nuclei from Friend cells [5]. Activities of acyl-CoA-synthetase [13] and phosphatidylinositol synthetase [14] were found in neuronal nuclei from rabbit brain, and sphingomyelin synthetase was found in the nuclear membrane and chromatin from liver cells [4]. However, there are no reports about lipid synthesis in isolated nuclei from mammalian cells with [2-^{14}C]acetate used as a precursor, although this would allow us to study the synthesis of cholesterol, free fatty acids, and phospholipids into which these fatty acids could be included. Therefore, the purpose of this work was to study the possibility of lipid synthesis in nuclei from rat thymus and liver cells using [2-^{14}C]acetate and [1-^{14}C]glycerol and to compare the incorporation of the labeled precursors into lipids of the isolated nuclei and into lipids of the nuclei inside the cell.

MATERIALS AND METHODS

Male Wistar rats with body weight of 180-200 g were used. The animals were sacrificed by decapitation, and the thymus and liver were rapidly isolated and placed into

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cold saline. From the thymus tissue nuclei were isolated as described in [15], from the liver tissue as described in [16] with an obligatory purification in the sucrose density gradient. The purity of the nuclear preparations was monitored by electron microscopy and by the presence in them of admixtures of marker enzymes from the plasma membrane, endoplasmic reticulum, and mitochondria: 5′-nucleotidase, glucose-6-phosphatase [17], and succinate dehydrogenase [18], respectively. The nuclei from thymus were incubated at 37°C in 0.01 M Tris buffer (pH 7.4) supplemented with 0.25 M sucrose and 3 mM $MgCl_2$. The nuclei from liver were incubated in the presence of 0.32 M sucrose. The concentration of nuclei was ~1.5 mg DNA per 1 ml of the incubation mixture. To study effects of the cytoplasmic factors on the label incorporation into nuclear lipids, the filtered homogenate of the thymus tissue was incubated with labeled acetate with subsequent isolation of the nuclei from the homogenate and the isolation of chromatin from these nuclei. [2-^{14}C]Acetate and [1-^{14}C]glycerol with specific radioactivities of 1.8 and 0.4 GBq/mmol, respectively, were added into the incubation medium at the concentration of 0.4 MBq/ml. After the incubation, chromatin was isolated from the nuclei as described in [19], the protein was determined by the Lowry method, the concentration of DNA was determined spectrophotometrically, the ratio DNA/protein in chromatin was 1 : 1.4. Lipids were extracted by the method of Folch. The lipids were separated by thin layer chromatography using plates with silica gel 60 (Merck, Germany). Neutral lipids were separated in the system of hexane–diethyl ether–glacial acetic acid (73 : 25 : 2 v/v) [20]. Phospholipids were separated using the system methyl acetate–*n*-propanol–chloroform–methanol–0.25% KCl (25 : 25 : 25 : 10 : 9 v/v) [21]. Amounts of cholesterol and fatty acids were determined as described in [22], and lipid phosphorus was determined as described in [23]. Radioactivities of the specimens were determined in a standard toluene scintillator (4 g PPO, 0.1 g POPOP per 1 liter of toluene) with a Beckman LS 6500 counter. The results were processed by methods of variation statistics using Student's *t*-test.

RESULTS

Lipid synthesis in isolated nuclei from rat thymus and liver. Highly purified isolated nuclei from thymus and liver cells were used. The purification was monitored by electron microscopy and by the activities of marker enzymes of the plasma membrane, endoplasmic reticulum, and mitochondria. In the liver nuclei the activity of glucose-6-phosphatase was 18% of its activity in the endoplasmic reticulum, the activity of succinate dehydrogenase was 1% of its activity in mitochondria, and the activity of 5′-nucleotidase was 14.2% of its activity in the homogenate. In the nuclei from thymus the activity of glucose-6-phosphatase was 3%, the activity of 5′-nucleotidase was 14%, and the activity of succinate dehydrogenase was 46% of the activities of these enzymes in the homogenate. The activity of succinate dehydrogenase in the nuclei from thymus purified in the sucrose density gradient was not decreased even after washing with 0.01 M Tris-HCl buffer (pH 7.5) supplemented with 3 mM $MgCl_2$. This washing removed not only fragments of membranes of other organelles from the surface of the nuclear membrane but partially the nuclear membrane itself. This suggested that thymus nuclei should have inherent succinate dehydrogenase activity, in agreement with the literature [24].

To determine the incorporation of labeled acetate and glycerol into phospholipids, cholesterol, and fatty acids, the nuclei isolated from liver and thymus were incubated with the labeled precursors for 5 and 30 min. Even after the incubation for 5 min the radioactivity of virtually all lipids became maximal and retained this level for 30 min (Table 1). The lipid synthesis in the isolated nuclei from thymus and liver was characterized by the highest radioactivity of phosphatidylethanolamine due to incorporation of both the labeled acetate and glycerol. The total fraction of fatty acids had very low radioactivity on the incubation of the isolated nuclei, whereas the radioactivity of phospholipids was rather high, suggesting possible synthesis of fatty acids in the nuclei, despite the classical concept on the cytoplasm as the place of synthesis of fatty acids responsible for radioactivity of phospholipids with [2-^{14}C]acetate as a precursor.

Lipid synthesis in nuclei in the presence of cytoplasm. Specific features of lipid synthesis in isolated nuclei can be due to the loss of some endogenous factors and/or proteins in the course of isolation and purification of the nuclei. Therefore, in the next series of experiments the homogenate of thymus tissue was incubated with [2-^{14}C]acetate for 10 min, the nuclei were obtained from the homogenate, and the radioactivity of lipids was determined. The isolated nuclei were also incubated for 10 min. In the nuclei incubated in the homogenate the radioactivity of the combined fraction of lipids, cholesterol, and fatty acids was significantly higher than in the case of incubation of the isolated nuclei, whereas the radioactivity of the total phospholipid fraction was nearly the same (Table 2). The amounts of lipids in the isolated nuclei and in the nuclei obtained from the homogenate after its incubation were not significantly different (Table 3). Although the radioactivity of the total phospholipid fraction in the isolated nuclei and in the nuclei incubated in the homogenate was approximately the same (Table 2), the specific radioactivities of individual phospholipids varied. In the isolated nuclei the specific radioactivity of phosphatidylcholine was significantly decreased and the radioactivity of phosphatidylethanolamine was increased relatively to radioactivities of these lipids in the nuclei obtained from the homogenate after its incubation.

Table 1. Incorporation of [2-^{14}C]acetate and [1-^{14}C]glycerol into lipids of isolated nuclei from rat thymus and liver cells on incubation for 5 and 30 min (cpm/mg protein) (n = 3)

Lipid under study	Thymus				Liver			
	[2-^{14}C]acetate		[1-^{14}C]glycerol		[2-^{14}C]acetate		[1-^{14}C]glycerol	
	5 min	30 min	5 min	30 min	5 min	30 min	5 min	30 min
Sphingomyelin	26 ± 10	21 ± 6	190 ± 40	130 ± 30	20 ± 8	10 ± 2	90 ± 10	100 ± 20
Phosphatidylcholine	29 ± 10	32 ± 6	250 ± 50	200 ± 50	150 ± 20	120 ± 20	110 ± 10	130 ± 10
Phosphatidylserine	28 ± 2	41 ± 10	290 ± 100	120 ± 30	110 ± 10	110 ± 3	60 ± 10	60 ± 2
Phosphatidylinositol	32 ± 6	40 ± 8	260 ± 70	210 ± 60	140 ± 20	110 ± 20	50 ± 9	60 ± 2
Phosphatidylethanolamine	110 ± 20	160 ± 6	7370 ± 1450	7260 ± 820	510 ± 150	360 ± 110	2390 ± 190	1980 ± 460
Cardiolipin	32 ± 10	23 ± 7	1090 ± 360	1390 ± 270	190 ± 30	100 ± 20	170 ± 20	200 ± 40
Cholesterol	3.8 ± 0.1	4.7 ± 0.6	26 ± 1	29 ± 1	28 ± 5	13 ± 3	50 ± 20	50 ± 8
Fatty acids	1.8 ± 0.6	2.5 ± 0.5	4.0 ± 1.4	2.8 ± 0.8	9.0 ± 2.0	9.3 ± 4	11.1 ± 2.9	6.5 ± 0.5

Furthermore, the specific radioactivity of phosphatidylcholine in the isolated nuclei was significantly decreased as compared to the radioactivity of sphingomyelin, phosphatidylserine, phosphatidylethanolamine, and cardiolipin. In the nuclei incubated in the homogenate the specific radioactivity of phosphatidylcholine and phosphatidylethanolamine was significantly decreased as compared to the radioactivities of sphingomyelin and cardiolipin (Table 4). These findings suggested that the nucleus should have its own system for the lipid synthesis but that it also could use the lipids synthesized in the cytoplasm and transferred into the cell nucleus by a special transporting system.

Incorporation of [2-^{14}C]acetate into lipids of chromatin from thymus nuclei. The incorporation of [2-^{14}C]acetate in chromatin lipids was studied using nuclei from thymus cells. Nuclei from liver cells were unsuitable for this study because of high activity of endonucleases which caused a significant fragmentation of chromatin. The incubation time of 10 min was chosen based on the label incorporation into lipids of the isolated nuclei and also on the absence of degradation of chromatin in the isolated thymus nuclei during a 20-min incubation in medium containing Mg^{2+} and lacking Ca^{2+} [25].

On incubation for 10 min of the isolated nuclei from thymus with subsequent isolation of chromatin the

Table 2. Radioactivities (cpm/mg protein) of lipids of nuclei and chromatin from rat thymus on incubation of thymus homogenate and of isolated nuclei with [2-^{14}C]acetate for 10 min (n = 3)

Fraction under study	Total fraction of proteins and lipids	Total lipid fraction	Total phospholipid fraction	Fatty acids	Cholesterol
Homogenate	33270 ± 3830	2830 ± 420	830 ± 160	18 ± 1	32 ± 5
Nuclei					
fraction 1*	8450 ± 450	1040 ± 270	340 ± 60	13 ± 5	38 ± 11
fraction 2*	34060 ± 10090	450 ± 130	390 ± 110	1.2 ± 0.5	8 ± 3
Chromatin					
fraction 1*	11400 ± 1520**	900 ± 170**	320 ± 60**	8 ± 2**	36 ± 11**
fraction 2*	250 ± 60	45 ± 10	35 ± 10	0.0	1.4 ± 0.2

* Here and further: fraction 1, nuclei obtained from incubated homogenate and chromatin isolated from these nuclei; fraction 2, isolated nuclei and chromatin isolated from the incubated nuclei.

** The difference between the radioactivities of chromatin lipids in fractions 1 and 2 is significant, $p < 0.05$.

Table 3. Amount of lipids (μg/mg protein) in the nuclei and chromatin from rat thymus after incubation of thymus homogenate and of isolated nuclei for 10 min ($n = 3$)

Lipid under study	Homogenate	Nuclei		Chromatin	
		fraction 1*	fraction 2*	fraction 1*	fraction 2*
Sphingomyelin	1.7 ± 0.3	1.9 ± 0.3	2.2 ± 0.3	1.0 ± 0.2	1.6 ± 0.4
Phosphatidylcholine	24.7 ± 3.3	19.3 ± 2.1	22.5 ± 1.5	21.7 ± 3.0	18.2 ± 2.0
Phosphatidylserine	3.5 ± 0.1	3.6 ± 0.4	3.3 ± 0.1	2.1 ± 0.1	2.2 ± 0.1
Phosphatidylinositol	3.3 ± 0.4	3.6 ± 0.2	4.0 ± 0.2	3.6 ± 0.3	4.2 ± 0.1
Phosphatidylethanolamine	13.3 ± 1.2	9.0 ± 0.8	9.5 ± 0.8	8.2 ± 1.1	7.0 ± 0.6
Cardiolipin	2.1 ± 0.3	1.5 ± 0.2	1.8 ± 0.4	1.3 ± 0.1	1.6 ± 0.4
Cholesterol	12.1 ± 0.1	7.3 ± 0.6	6.0 ± 0.6	6.2 ± 1.5	5.5 ± 0.3
Fatty acids	23.8 ± 5.8	10.1 ± 0.8	8.8 ± 0.9	6.4 ± 1.7	6.0 ± 1.7

* As in Table 2.

radioactivity of cholesterol and the combined fraction of lipids and phospholipids of chromatin was ~10% of the radioactivity of these lipids in the nuclei, the radioactivity of the combined fraction of proteins and lipids was less than 1%, and no radioactive fatty acids were found in chromatin (Table 2). It was suggested that the incubation of isolated nuclei under conditions of the experiment was associated with disorders in mechanisms of synthesis of neutral lipids, in particular, of cholesterol and fatty acids, because the radioactivities of the combined fraction of lipids and phospholipids differed insignificantly. Disorders in the synthesis of cholesterol and fatty acids on the incubation of the isolated nuclei could be also interrelated with the lack of transport of newly synthesized proteins and lipids into chromatin.

Disorders in the transport of newly synthesized radioactive lipids into chromatin could be also associated either with the absence in the isolated nuclei of cofactors and/or proteins required for the transport and which enter from the cytoplasm, or with the loss by the nuclei of

Table 4. Specific radioactivity (cpm/μg lipid) of phospholipids and fatty acids in the nuclei and chromatin on the incubation of thymus homogenate and of isolated nuclei with [2-^{14}C]acetate for 10 min ($n = 3$)

Lipid under study	Homogenate	Nuclei		Chromatin	
		fraction 1*	fraction 2*	fraction 1*	fraction 2*
Sphingomyelin	73 ± 5	18 ± 3*****	13 ± 3.2	22 ± 3**,*****	2.4 ± 0.7
Phosphatidylcholine	5 ± 2	6 ± 1***	2 ± 0.4****	5 ± 2**	0.3 ± 0.1
Phosphatidylserine	16 ± 3	17 ± 5	7 ± 0.01	24 ± 5**,*****	0.7 ± 0.04
Phosphatidylinositol	13 ± 2	9 ± 2	6 ± 2.6	10 ± 3**	0.2 ± 0.1
Phosphatidylethanolamine	5 ± 1	5 ± 1***	11 ± 1.5	5 ± 3**	0.6 ± 0.2
Cardiolipin	10 ± 2	13 ± 2*****	14 ± 2.3	20 ± 5**,*****	1.5 ± 0.7
Fatty acids	0.9 ± 0.1	1.5 ± 0.6	0.1 ± 0.04	1.3 ± 0.7	0.0

* Similarly to Table 2.

** The difference between the radioactivities of chromatin lipids in fractions 1 and 2 is significant, $p < 0.05$.

*** The difference between the radioactivities of phosphatidylcholine and phosphatidylethanolamine of the nuclei in fractions 1 and 2 is significant, $p < 0.05$.

**** The difference between the radioactivity of phosphatidylcholine and the radioactivities of sphingomyelin, phosphatidylserine, phosphatidylethanolamine, and cardiolipin of the nuclei in fraction 2 is significant, $p < 0.05$.

***** The difference of radioactivity is significant relative to phosphatidylcholine and phosphatidylethanolamine of the fraction under consideration, $p < 0.05$.

these factors and/or proteins in the course of isolation and purification in the sucrose density gradient. Therefore, in the next series of experiments the thymus tissue homogenate was incubated with [2-^{14}C]acetate for 10 min, then the nuclei were isolated from it, chromatin was isolated from the nuclei, and the radioactivity of lipids was determined in the isolated specimens. In this case the radioactivity of lipids was nearly the same in the chromatin and nuclei (Table 2) which suggested a recovery of the transport of the newly synthesized lipids into chromatin under conditions similar to those in the native cell. Moreover, in the chromatin obtained from the nuclei incubated in the homogenate the radioactivity of the combined fraction of lipids, cholesterol, and fatty acids was significantly higher than in the chromatin of the incubated isolated nuclei. The amount of lipids was also the same in both the chromatin of the isolated nuclei and of the nuclei obtained from the incubated homogenate (Table 3). The specific radioactivity of individual phospholipids in chromatin from the isolated nuclei was extremely low, possibly because of disorders in the mechanisms of lipid transport in these nuclei (Table 4). Values of specific radioactivity of phospholipids in the chromatin from the nuclei incubated in the homogenate were nearly the same as the radioactivity values of these phospholipids in the nuclei themselves, and the radioactivities of phosphatidylcholine and phosphatidylethanolamine in the chromatin were significantly decreased as compared to the radioactivities of sphingomyelin, phosphatidylserine, and cardiolipin (Table 4) that was not specific for *in vivo* conditions [7]. This suggested specificity of lipid synthesis in the nucleus when the cell integrity was damaged.

DISCUSSION

We have compared lipid synthesis in isolated nuclei and in nuclei in the presence of cytoplasm (the nuclei were incubated in the tissue homogenate). From these nuclei incubated under different conditions chromatin was obtained and radioactivity of total lipids, total phospholipids, individual phospholipids, in free fatty acids, and cholesterol was determined. The radioactivity of the combined fraction of lipids, cholesterol, and fatty acids was significantly higher in the nuclei incubated in the homogenate and in chromatin obtained from these nuclei than in the isolated nuclei and in chromatin obtained from these nuclei. It was suggested that fatty acids synthesized in the cytoplasm and cholesterol synthesized in the microsomal fraction of the homogenate could be transferred into nuclei and chromatin and cause the higher radioactivity of their lipids. In the isolated purified nuclei lipids seemed to be synthesized on the nuclear membrane the external leaf of which is an extension of the endoplasmic reticulum, which is the place of lipid synthesis. Our findings suggested that the nuclei isolated from thymus and liver had enzymatic systems responsible for synthesis of lipids. Earlier the enzymes of acylation and trans-acylation of endogenous phospholipids were found in nuclei of mammalian cells [26, 27], and the synthesis of phospholipids in the isolated nuclei with [1-^{14}C]glycerol as a labeled precursor could be easily explained. However, according to the classical concept, the synthesis of fatty acids providing the radioactivity of phospholipids with [2-^{14}C]acetate as a precursor occurs in a soluble enzymatic complex located in the cytoplasm. There are no reports in the literature about the presence in nuclei of enzymes responsible for synthesis of fatty acids. However, notwithstanding a very low radioactivity of the total fraction of fatty acids on the incubation of the isolated nuclei, phospholipids displayed a rather high radioactivity that suggested the possible synthesis of fatty acids in the nuclei.

Along with the significantly different radioactivities of fatty acids, the radioactivities of the total phospholipid fractions from the isolated nuclei and from the nuclei incubated in homogenate were nearly the same (Table 2). This finding can be explained only by the suggestion that in the isolated nuclei two metabolically separate pools of fatty acids should exist. One pool, a small one, consists of highly radioactive newly synthesized fatty acids which are incorporated into phospholipids and provide their radioactivity. Another, a significantly greater pool, consists of nonradioactive fatty acids which are responsible for the strongly decreased radioactivity of the total fraction of fatty acids in the isolated nuclei. The specific radioactivities of individual phospholipids of the nuclei were compared, and the radioactivity of phosphatidylcholine was significantly decreased in the isolated nuclei and the radioactivity of phosphatidylethanolamine was increased relative to the radioactivities of these lipids in the nuclei isolated after the incubation of the homogenate. The literature data [10] and results of our experiments *in vivo* and on isolated thymocytes suggested that the maximal radioactivity in the nuclei determined by the incorporation of labeled acetate was inherent in phosphatidylcholine. The radioactivity of phosphatidylethanolamine was lower or neared that of phosphatidylcholine but was never higher [7, 28]. Moreover, the specific radioactivity of phosphatidylcholine in the isolated nuclei was significantly decreased as compared to the radioactivities of sphingomyelin, phosphatidylserine, phosphatidylethanolamine, and cardiolipin. The difference in the radioactivities of lipids in the isolated nuclei and in the nuclei incubated in the homogenate seemed to depend on the incubation conditions of the nuclei. It was likely that on incubation of the isolated nuclei the metabolic changes associated with the internucleosomal fragmentation of chromatin and preceding it should be manifested earlier than in the case of incubation of the nuclei in the homogenate. It seemed that on the mechanical dis-

integration of the cell with retention of the nuclear integrity the mechanisms of nuclear death by the apoptotic pathway were switched on. The activation of sphingomyelin and cardiolipin metabolism in the nuclei incubated in the homogenate and in chromatin from these nuclei where the phosphatidylserine metabolism was also activated, on the background of a decreased metabolism of phosphatidylcholine and phosphatidylethanolamine, seemed to be caused by triggering signal mechanisms of apoptosis into which these phospholipids were involved [6]. Changes in the specific radioactivity of phospholipids found on the incubation of the isolated nuclei seemed to be determined by the later stage of this process (Table 4). Therefore, the data on changes in the fatty acid composition of phospholipids in the culture of hippocampus neurons on induction of apoptosis by hypoxia and starvation are interesting [29]. The authors found that prior to the appearance of morphological manifestations of apoptosis the fraction of saturated fatty acids increased in phospholipids of the cell. And saturated fatty acids were incorporated into phosphatidylethanolamine, phosphatidylinositol, and phosphatidylserine. No incorporation of saturated fatty acids into phosphatidylcholine was recorded. On the contrary, on mitogenic stimulation of T-lymphocytes of rabbit thymus the fraction of unsaturated fatty acids increased in phospholipids of the plasma membrane of the cells [30]. This increase was observed for phosphatidylcholine, phosphatidylinositol, and phosphatidylserine, whereas the fatty acid composition of phosphatidylethanolamine was not significantly changed. The differently directed changes in the fatty acid composition of phospholipids, especially in the composition of the main membrane lipids phosphatidylcholine and phosphatidylethanolamine during apoptosis and cell proliferation confirmed our hypothesis on the existence of two metabolically separate pools of fatty acids in the isolated nuclei from thymus. The pool of newly synthesized radioactive fatty acids seems to consist of saturated fatty acids which are incorporated into phosphatidylethanolamine, phosphatidylserine, sphingomyelin, and cardiolipin, and are scarcely incorporated into phosphatidylcholine. The changes found by us in the fatty acid composition of phospholipids of the nuclear membrane seemed to be associated with changes in its permeability and other properties during apoptosis. In this connection, attention should be paid to the significantly higher radioactivity of phosphatidylethanolamine on incubation of the isolated nuclei as compared to their incubation in the homogenate (Table 4). Phosphatidylethanolamine was shown to produce in local regions of the membrane bilayer nonlamellar hexagonal structures which could destabilize the membrane bilayer [31]. Under certain conditions, these structures seemed to be produced in the cell and to influence the membrane permeability [32] and activities of some membrane-bound enzymes [33]. Phosphatidylcholine, which is believed a stabilizer of the membrane bilayer [34], was shown to be mainly located on the external leaf of the bilayer of some membranes, whereas phosphatidylethanolamine and phosphatidylserine were mainly located on the internal leaf [29]. Changes in the fatty acid composition of phosphatidylethanolamine and other phospholipids could change the rigidity of membranes and influence the changes in their morphology during apoptosis.

Thus, cell nuclei possess a sufficiently large set of enzymes responsible for synthesis of lipids to ensure their autonomous synthesis under critical conditions of apoptosis and cell proliferation because the composition of membrane lipids determines its morphology and the regulation of membrane-bound and lipid-dependent enzymes. Moreover, membrane phospholipids are sources of secondary messengers which transmit signals directly into the genetic matter located in the nucleus.

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