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Role of *sn*-1 monounsaturated, *sn*-2 polyunsaturated phospholipid molecular species in temperature adaptation of membranes in poikilotherms

Summary of the Ph.D. Thesis

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INTRODUCTION

Biological membranes are delicately composed assemblies of lipids and proteins, and perform multifold function in living organisms. They separate cells and cell compartments from their environment providing an effective barrier against large variety of compounds, and preserving the particular composition of the cells and compartments. On the other hand, membranes ensure communication with the same environment by passively or actively transporting materials into and out of the cell. Membranes are also the sites of many important cell functions; they act as reaction surfaces and present matrices for enzyme functions, signal and energy transduction. Because membranes perceive and mediate the external signals to the cell machinery, their role is crucial in the adaptation of the cell to the ever-changing external conditions. To accomplish all these functions, a biological membrane has to form a physically solid, yet dynamic entity, establishing dynamic equilibrium between its constituents and between itself and its environment.

One of the most important environmental factors that affect living organisms is the change of temperature. Temperature influences the physical properties of the cell components, and also the rates of chemical reactions. Because temperature directly affects the rates of molecular motions, its change has great impact especially on the membranes whose integrity is maintained by a collection of weak, largely hydrophobic, non-covalent interactions. Therefore, it affects their phase state, physical strength and barrier properties as well.

Understanding the process of adaptation of living organisms to varying temperatures at the level of the cell and cell membranes has been the subject of interest since many years. Numerous studies revealed the importance of the physical state, referred as "fluidity", of the membranes in this process, and currently membrane fluidity is invoked as controlling the expression of stress, especially temperature, related genes. How exactly the adapting organisms compensate for the direct effects of temperature on the fluidity of membranes is still not clear and under investigation. The basic concepts such as the homeoviscous and homeophasic character of membrane adaptation, currently used to describe the cell's response to altering temperatures rose from the studies on the bacterium *Escherichia coli*. In these studies a strong correlation between fatty acid unsaturation and growth temperature, as well as between growth temperature and membrane fluidity was found, and the decisive

role of unsaturated fatty acids in fluidizing membranes at low temperatures was concluded. However, studies restricted to certain organisms did not give universal explanations for all aspects of adaptation phenomena even at the level of membrane lipids.

The problem of membrane stability is particularly important for poikilotherms such as fishes, whose body temperature varies over a wide range, adopting the temperature of the environment. Since the phase state and fluidity of the membranes are extremely sensitive to temperature variations it is intriguing to study how fishes can survive and function over a wide range of temperature. Fishes had been studied intensively in the last decade and the principle of homeoviscous adaptation was tested in different species and tissues. These investigations were, however, restricted mainly on fatty acid composition analysis of the membrane lipids. The changes occurring at the level of phospholipid molecular species compositions and the need for such a wide range of lipid species remained unknown.

Beside the environmental temperature, the fatty acid content of the diet may also affect the lipid composition of membranes of the animals. Studies showed that feeding various fish species with unsaturated fatty acids (UFA) resulted in their accumulation in liver polar lipids, and feeding rats with fish oil resulted an increase of polyunsaturated fatty acids (PUFA) in liver total phospholipids. As a response to temperature variation, homeoviscous adaptation (HVA) involves the control of the membrane lipid composition to ensure an optimal fluidity of the membranes. The possible contribution of the dietary fatty acids in HVA is not known.

The body temperature of amphibians, like frogs, follows the changes in the environmental temperature but they undergo hibernation during winter. Whether these organisms regulate their membrane lipid composition and physical properties in the same manner as the winter-active fishes upon their seasonal adaptation or not, is not yet known.

The present thesis attempts to contribute to the answering of the above mentioned questions, with the specific aim to refine the existing concept on the role of lipids in the process of temperature adaptation and to explain the need for specific phospholipids in a poikilothermic cell membrane.

OBJECTIVES

The aim of the studies presented is to investigate the role of membrane lipids during the process of temperature adaptation of those organisms whose body temperature varies with the ambient temperature.

Being the major part of the studies done on fresh-water fish, the scope of investigations was extended to other organisms, bacterial species and amphibians as well, to reveal which elements of the temperature adaptation strategy known so far at the level of lipids are universal, and whether there are other factors acting in the process of temperature adaptation.

In this view the major questions addressed and the specific objectives of the studies were as follows:

1. To investigate the relation between the fatty acid unsaturation and membrane order in bacterial species (symbiotic bacteria of nematodes, *Photorhabdus luminescens* and *Xenorhabdus nematophilus*, and the cyanobacterium, *Cilindrospermopsis raciborskii*) grown at different temperatures.

2. To investigate the relation between the fatty acid unsaturation and molecular species composition of phospholipids, and membrane order in fish.

a) To assess the changes in the liver fatty acid and molecular species composition of the fresh-water fish *Cyprinus carpio* L. in response to seasonal and short-term temperature adaptation.

b) To compare the physical characteristics of native and phospholipid membranes of livers of the fish *Cyprinus carpio* L. seasonally adapted and/or short-term acclimated to different temperatures.

c) To correlate the changes occurring in the lipid composition with the physical characteristics of the membranes upon seasonal and short-term temperature adaptation of the fish *Cyprinus carpio* L.

3. To reveal the influence of dietary fatty acids in the process of temperature adaptation of fresh-water fishes.

4. To characterize the seasonal adaptation of amphibians to summer and winter

temperatures at the level of phospholipids and lipid-membrane order.

a) To assess the changes in the liver fatty acid and molecular species composition of frogs (*Rana esculenta*) upon transition from active to hibernation state.

b) To correlate the changes in the lipid composition with the fluidity of the vesicles made of phospholipid extracts of liver.

5. To test the regulatory potential of specific phospholipids on the physical characteristics of membranes using model systems of synthetic lipids.

6. With the synthesis of the results obtained from the experiments, to find generalities regarding the role of lipids in temperature adaptation of the membranes.

MATERIALS AND MAJOR METHODS USED

Comparative studies were carried out on poikilotherms at their states of adaptation to distant temperatures. Samples were collected at the the differing temperatures for fatty acid and lipid molecular species analysis, as well as, for membrane "fluidity" measurements.

Lipid classes were separated from total lipid extracts by thin layer chromatography. Fatty acid compositions were analyzed by gas chromatography; lipid molecular species of major lipid classes were identified by high performance liquid chromatography.

The "fluidity" of the lipid vesicles and isolated membrane fractions were assessed either by electron spin resonance spectroscopy using 5- or 16- doxylstearic acid (5-SASL or 16-SASL) spin probe, or by steady-state fluorescence polarization spectroscopy using anthroyloxy fatty acid (2-AS, 12-AS, 16-AP) and DPH (1,6-diphenyl-1, 3, 5-hexatriene) fluorescent probes. In case of spin probes, the outer hyperfine splitting parameter and the rotational correlation time, while for fluorescent probes the steady-state anisotropy parameter were determined in a temperature scan (from 5 to 35°C, in general) and were used to characterize the physical state of the lipid phase of membranes. Both the hyperfine splitting and the steady-state anisotropy gives informayion about the membrane order, while the rotational correlation time about the rotational mobility of the molecules.

The bacterial species analyzed were *Photorhabdus luminescence* and *Xenorhabdus nematophilus* (symbionts of nematodes), and the cyanobacterium *Cilindrospermopsis raciborskii*. These species were cultured at cold (18°C for symbiotic bacteria and 25°C for cyanobacteria) and warm (28°C and 35°C, respectively) temperatures.

The thermal adaptation of poikilothermic animals was studied on the fresh water fish *Cyprinus carpio* L. Fishes were collected during their states of seasonal adaptation to summer and winter temperatures, and their livers were analyzed. Lipids were extracted either from the whole liver, or from isolated plasma membranes or mitochondrial membranes, and were analyzed for fatty acid and molecular species composition. The fluidity of phospholipid vesicles, plasma membranes and mitochondrial membranes were further analysed by the above-mentioned techniques.

Short-term acclimation experiments were carried out on *Cyprinus carpio* L. seasonally adapted to winter (5°C) and summer (25°C) temperatures. Fishes were collected at their adaptational temperature and were gradually cooled or warmed to the opposite temperature value. During short-term acclimation, the temperature was varied by 0.5°C/hour and samples were taken at the third day of the experiment. Plasma membranes and mitochondria were isolated from the liver and analyzed for their lipid composition and fluidity.

Four different fish species, living in the same habitat but consuming foods differing in fatty acid composition were chosen to study the impact of dietary fatty acids on HVA. The fish species were, *Hypopthalmichtys molitrix* (silver carp) feeding with phytoplanktons, *Aristichthys nobilis* (big head carp) feeding on zooplanktons, *Ctenopharyngodon idella* (grass carp) feeding on higher plants and *Cyprinus carpio* (common carp) which is omnivorous. The fatty acid content of triacylglycerols and phospholipids as well as molecular species composition of PC and PE lipid classes were analyzed. The fluidity of the vesicles made of extracted total phospholipids of the liver, and the fluidity of the isolated plasma membranes were determined and compared.

Frogs (*Rana esculenta*) were collected during hibernation and active periods. The liver phospholipids were analyzed as well as the fluidity of the vesicles made up of the extracted phospholipids of the liver were assessed and compared.

RESULTS

I. ABSENCE OF DIRECT RELATION BETWEEN FATTY ACID UNSATURATION, MEMBRANE ORDER AND GROWTH TEMPERATURE IN BACTERIAL SPECIES

1. *Photorhabdus luminescens* and *Xenorhabdus nematophilus* accumulated more unsaturated fatty acids in their total lipids at low (18°C) growth temperatures than at high (28°C) temperatures. The vesicles made of phospholipid extracts were, however, more ordered for the cultures grown at 18°C than at 28°C, which is contradictory to what could be expected according to the homeoviscous adaptation theory found to be valid for different bacterial species.
2. Despite the fact that the saturated-to-unsaturated (S/U) fatty acid ratio of phospholipids in primary cultures of *P. luminescens* was lower than that of *X. nematophilus* grown either at 18°C or at 28°C, phospholipid vesicles of the former showed more ordered structure than that of the latter.
3. After the transfer of the cell cultures of *Cilindrospermopsis raciborskii* grown at 25°C to 35°C, a gradual decrease of linoleic (18:2) acid and a concomitant increase of linolenic (18:3) and octadecatetraenoic (18:4) acids were observed in the major lipids of the thylakoid membrane. The S/U fatty acid ratio decreased at 25°C in the total lipid extract and changed differentially in the lipid classes. Neither the molecular mobility assessed by the rotational correlation time of 16-SASL, nor the membrane order assessed by 5-SASL spin probe showed major compensation for the change of the growth temperature in thylakoid membranes. These results suggest that while growing at different temperatures, *C. raciborskii* does not utilize the homeoviscous adaptation mechanism. The extent of the compensation was much less than in the case of *Synechocystis* PCC 6803, that is known to follow the HVA of the thylakoid membranes when grown at different temperatures.

II. CHARACTERISTICS OF SEASONAL ADAPTATION TO DIFFERENT TEMPERATURES AT THE LEVEL OF PHOSPHOLIPIDS OF THE LIVER OF THE FRESH WATER FISH *Cyprinus carpio* L.

1. Total phospholipids of winter-adapted carps showed a 25% accumulation of long chain PUFAs such as arachidonic (20:4n-6) and docosahexaenoic (22:6n-3) acids, and approximately 25% loss of saturated fatty acids such as palmitic (16:0) and stearic (18:0) acids. as a consequence, the S/U fatty acid ratio was lower in the winter-adapted carps as compared to their summer-adapted counterparts.
2. Monounsaturated fatty acids, 16:1 and 18:1 increased at cold-adaptation in the total phospholipid extracts of liver. In phosphatidylcholines (PC) the 16:1, while in phosphatidylethanolamines (PE) the 18:1 fatty acids accumulated at cold.
3. The most pronounced changes in the molecular species composition of PC upon cold-adaptation were the decrease of the levels of 16:0/16:0, 16:0/18:1, 18:0/22:6, and the increase of the 16:0/20:4, 18:1/20:4, 18:1/20:5, 18:1/22:6, 20:4/20:4 species. These changes resulted in a decrease of total saturated/unsaturated-to-monounsaturated/polyunsaturated PC molecular species.
4. The changes in the molecular species composition of PE upon cold-adaptation were similar to that of PC, and additionally, the levels of 16:0/22:6 and 18:0/20:4 also decreased. The increase of the ratio of monounsaturates/polyunsaturates was also more pronounced in PE, thus the ratio of the total saturated/unsaturated-to-monounsaturated/polyunsaturated PE molecules has decreased. In general, the levels of 16:0/18:1 were always lower in PE than in PC.
5. Vesicles made of total phospholipids of cold-adapted fish were less ordered than those of summer-adapted ones, as determined by the outer splitting parameter of 5-SASL-spin probe inserted into the lipid membrane.
6. The steady-state fluorescence anisotropy of anthroyloxy fatty acid probes (2-AS, 12-AS, 16-AP) were lower in the vesicles made from the total extract of liver phospholipids of the cold-adapted fish than those of summer-adapted fish. This indicates a more "fluid" lipid structure for the former.
7. The steady-state fluorescence anisotropy of anthroyloxy fatty acid probes (2-AS, 12-AS, 16-AP) in vesicles made of total PC of fish liver were also lower during cold-adaptation

than during warm-adaptation. However, this anisotropy difference between the two samples was progressively smaller at the deeper regions of the bilayer.

III. CHANGES IN THE LIPID COMPOSITION AND IN THE PHYSICAL PROPERTIES OF LIVER MEMBRANES DURING SEASONAL AND SHORT-TERM ACCLIMATION OF FISH TO VARYING TEMPERATURES

1. The amount of 16:0/18:1 PC and PE molecular species were sensitive to temperature variations. Their levels at seasonally warm-adapted (25°C) states were much higher than at cold (5°C), during winter-adaptation. The same changes could be triggered by short-term acclimation to 25 and 5°C, respectively. The variations were more pronounced in plasma membranes than in mitochondrial membranes.
2. In both membrane fractions, the level of 16:0/20:4 PC was higher in the seasonally warm-adapted states. Their level could also be increased in the cold-adapted membranes by short-term warm (25°C) acclimation. The 16:0/20:4 PE molecular species behaved similarly in mitochondrial preparations but in the plasma membranes decreased during warm-adaptation.
3. For both seasonal adaptation and short-term acclimation, in response to high (25°C) temperature, the amount of 18:0/20:4 molecular species decreased in PC and increased in PE. Interestingly, short-term cold-acclimation initiated changes in the same direction as warm-acclimation or adaptation, except in PE of mitochondria where its level increased during warm-adaptation and decreased during cold- adaptation.
4. The levels of 18:0/22:6 molecular species varied similarly in both membrane fractions within a lipid class. During seasonal adaptation to 25°C, its level increased in PC and decreased in PEs. As a response to short-term acclimation, the level of this species increased in both lipid classes regardless of the direction of temperature change.
5. 18:1/22:6 PC and PE were the most responsive lipid molecular species to the changes in temperature in the plasma membranes. During cold-adaptation and short-term cold-acclimation, their levels increased while during short-term warm-acclimation their levels decreased. In mitochondria, their response was similar with the exception of

short-term acclimation to cold temperatures where the level of 18:1/22:6 PE did not change.

6. During short-term acclimation, regardless of the direction of the temperature change, the amount of some molecular species like 16:0/20:4, 16:0/22:6 and 18:1/20:4 has increased.
7. With respect to the magnitude of change in the levels of the molecular species responding to the temperature variations, it was found that plasma membranes were more sensitive than mitochondrial membranes.
8. Steady-state fluorescence anisotropy of DPH, incorporated either into plasma membranes or mitochondrial was lower in the case of cold-adapted fish (indicating a more fluid structure) as compared to the summer-adapted fish.
9. In short-term acclimation experiments, the steady-state fluorescence anisotropy of DPH, incorporated into plasma membranes and mitochondria also showed more fluid structure during cold-acclimation. In plasma membranes, however, this difference was visible only at temperatures below 25°C between the thermotropic response curves of the DPH anisotropy.

IV. THE ROLE OF DIETARY FATTY ACIDS IN THE CONTROL OF MEMBRANE FLUIDITY

1. The fatty acid pattern of the diet was reflected in the fatty acid composition of triacylglycerols but not in the fatty acid composition of total phospholipids of liver or of isolated plasma membranes.
2. In all four species tested, the levels of long-chain polyunsaturated fatty acids (LcPUFA) in livers were much higher than in the consumed food. However, differences in its level existed among the tested species.
3. The steady-state anisotropy parameters of DPH in plasma membranes were similar in all four fish species.
4. The steady-state anisotropy parameters of DPH in vesicles made of total phospholipids of liver were higher in *C. idella* and *C. carpio* than those of *A. nobilis* and *H. molitrix* in temperature scans below 15°C, but above this temperature the differences diminished.

5. The molecular species compositions of PC and PE were qualitatively similar in extracts of total phospholipids of liver and in extracts of the isolated plasma membranes in case of all four species. Differences among the species existed with respect to the levels of the following molecules: 16:0/22:6 PC dominated the diacyl PC-s in *H. molitrix* and *A. nobilis* while in *C. idella* and *C. carpio* the dominating species were 16:0/20:4 PC and 18:0/20:4 PC. In PE-s, the major components were 18:1/22:6 PE in *H. molitrix* and *A. nobilis* and 18:1/20:4 PE in *C. idella* and *C. carpio.* The 16:0/22:6 PE and 18:0/22:6 PE molecules were also present in high levels in *H. molitrix* and *A. nobilis,* whereas 18:0/20:4 PE and 16:0/20:4 PE were present in high levels in *C. idella* and *C. carpio.*

V. TEMPERATURE ADAPTATION OF AMPHIBIANS, A STUDY ON THE FROG *R. esculenta*

1. In the total phospholipid, PC and PE extract of liver, the saturated to unsaturated fatty acid ratio decreased during hibernation.
2. The major changes in the molecular species composition of diacyl PC and PE lipid classes upon hibernation had occurred in the levels of saturated/polyunsaturated and polyunsaturated/polyunsaturated lipid species. In the PC fraction, there was a pronounced decrease of 16:0/18:2, 16:0/20:4, 16:0/22:6, 18:0/20:4 and 18:0/22:6 and an increase of the 18:0/20:5 species.Interestingly, the amount of *sn*-1 monounsaturated, *sn*-2 polyunsaturated species did not differ much at the two adaptational states. The level of 18:1/22:6 molecular species did not change in PC and PE of liver during hibernation of frogs. These species were the major species that increased in both PC and PE during cold-adaptation of fish.
3. At the region of the C-12 and C-16 carbon atoms of the fatty acids, the steady-state anisotropy of 12-AS and 16-AP fluorescent probes showed no difference between the lipid-membranes of active and hibernating states. At the region of the C-2 carbon atom, probed with 2-AS, phospholipid vesicles prepared from lipids of the hibernating species showed even more rigid structure than the active ones. This result is contradicting to the classical theory of fluidization at cold temperatures observed in winter-active fish species.

VI. THE ROLE OF SPECIFIC LIPIDS IN THE REGULATION OF MEMBRANE PHYSICAL PROPERTIES DURING COLD-ADAPTATION

1. The hyperfine splitting parameters of the 5-SASL spin label were similar in vesicles made of 18:0/22:6 PC and in ternary mixtures of 16:0/16:0, 20:4/20:4 and 18:0/22:6 PC-s when they were mixed in ratios corresponding to summer and winter adapted states of the fish *Cyprinus carpio* L. Therefore these changes in the lipid composition during cold-adaptation do not regulate membrane order during thermal adaptation.
2. The steady-state fluorescence anisotropy of the 2-AS, 12-AS, and 16-AP probes were similar in vesicles made of pure 18:0/22:6 PC or 16:0/18:1 PC or 22:6/22:6 PC. This means that the presence of 11 more double bond as compared to a single *cis* double bond in 16:0/18:1 PC does not render the vesicles more disordered. On the contrary, vesicles of 22:6/22:6 PC were more ordered at high temperatures than vesicles of 16:0/18:1PC.
3. The melting temperature of the gel phase as monitored by the temperature profile of the hyperfine splitting parameter of 5-SASL spin probe incorporated into vesicles made from 18:0/22:6 PC was up-shifted when the vesicles were made with the addition of 25% 16:0/18:1 PE, and downshifted when 18:1/22:6 PE was added.
4. The steady-state fluorescence anisotropy of the probes 2-AS, 12-AS, and 16-AP incorporated into the lipid vesicles of 16:0/22:6PC and in its mixture with either 16:0/18:1 PE or 18:1/ 22:6 PE, showed that 16:0/18:1 PE has ordering effect (higher anisotropy values) while 18:1/ 22:6 PE has fluidizing effect (lower anisotropy values) on the PC membranes.
5. The steady-state fluorescence anisotropy of the 2-AS, 12-AS, and 16-AP probes was much higher in vesicles made from 16:0/22:6 PC than in vesicles of 18:1/22:6 PC.

CONCLUSIONS

1. The increase of the amount of the unsaturated fatty acids of membrane lipids is not a general mechanism of adaptation to altered growth temperature in the case of the bacterial species studied. The differences in the fatty acid compositions do not correlate with the differences found in the phospholipid membrane fluidity. It is concluded that the gross amount of unsaturated fatty acids is not a decisive factor in determining membrane fluidity properties, and changing its amount is not always the method of adaptation to altered temperatures in prokaryotic systems.

2. The most characteristic changes in the phospholipid composition of the fresh water fish *Cyprinus carpio* upon its seasonal adaptation to cold was the decrease of the *sn*-1 saturated, *sn*-2 polyunsaturated and the increase of the *sn*-1 monounsaturated, *sn*-2 polyunsaturated phospholipid species of the liver. These changes were accompanied by the increased fluidity of vesicles made of total phospholipids and also of plasma membranes and mitochondrial membranes of liver during cold-adaptation. The 18:1/22:6 PE appeared to be the most responsive molecule for the temperature change both during seasonal and short-term acclimation.

3. Since the fluidity of the plasma membranes and phospholipid vesicles were largely independent of the fatty acid composition of the food ingested by the cold-adapted fishes, it can be concluded that the environmental temperature and not the fatty acid composition of the diet is the major factor controlling the physical state of the membrane.

4. Frogs are unable to regulate the level of *sn*-1 monounsaturated, *sn*-2 polyunsaturated phospholipid molecular species in their membranes which may explain the absence of lipid-membrane order compensation.

5. The 18:1/22:6 PE and PC molecular species exerted a disordering effect in each segment of the bilayer and lowered the gel to liquid crystalline phase transition temperature of 18:0/22:6 PC while 16:0/ 18:1 PE had just the opposite effect. Therefore it can be

concluded that the 18:1/22:6 PE and PC molecular species play major role in regulating membrane physical properties during cold-adaptation.

6. The regulation of *sn*-1 monounsaturated, *sn*-2 polyunsaturated PE molecular species, especially 18:1/22:6 PE has important role in keeping proper membrane physical characteristics during cold exposure in cold-active poikilotherms like fish.

7. On the basis of the presented results we can propose not the gross amount of long-chain polyunsaturated fatty acids, but their specific pairing with monounsaturated fatty acids in the position *sn*-1 is the most important factor in adjusting membrane architecture and physical properties during cold-adaptation in fish. In particular, the increase in *sn*-1-monounsaturated, *sn*-2-polyunsaturated phosphatidylethanolamine species are the major candidates to be responsible for the regulation of membrane "fluidity" in liver membranes of fresh-water fish adapted to cold temperatures.

LIST OF PUBLICATIONS

Publications on which the present thesis is based:

1. "Molecular architecture and biophysical properties of phospholipids during thermal adaptation in fish: An experimental and model study"
   E. Fodor, R. H. Jones, Cs. Buda, K. Kitajka, I. Dey and T. Farkas
   Lipids, Vol. 30, No.12, pp. 1119-1126 (1995). IF: 1.947

2. "Composition and biophysical Properties of lipids in *Xenorhabdus nematophilus* and *Photorhabdus luminescence*, symbiotic bacteria associated with entomopathogenic nematodes"
   E. Fodor, E. Szállás, Zs. Kiss, A. Fodor, L. I. Horváth, D. J. Chitwood and T. Farkas
   Applied and Environmental Microbiology, Vol. 63, No. 7, pp. 2826-2831 (1997). IF: 3.336

3. "Fatty acid composition of the ingested food only slightly affects physicochemical properties of liver total phospholipids and plasma membranes in cold-adapted fresh water fish"
   R. Roy, **E. Fodor**, K. Kitajka and T. Farkas
   Fish Physiology and Biochemistry, 20, pp.1-11 (1999). IF: 1.105

4. "Exception to seasonal adaptation: cyanobacterium *Cylindrospermopsis raciborskii*"
   E. Fodor, O. Zsíros, Zs. Várkonyi, Z. Gombos, L. I. Horváth, L. Hiripi, and T. Farkas
   (manuscript submitted to *Applied and Environmental Microbiology*).

Other publications:

5. "The effects of cadmium on the fluidity and H^+-ATPase activity of plasma membrane from sunflower and wheat roots"
   E. Fodor, A. Szabo-Nagy and L. Erdei
   Journal of Plant Physiology, Vol.147. pp.87-92 (1995). IF: 1.179

6. "Involvement of phospholipid molecular species in controlling structural order of vertebrate brain synaptic membranes during thermal evolution"
K. Kitajka, Cs. Buda, **E. Fodor**, J.E. Halver and T. Farkas
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7. "Search for the pathogenesis of the differing phenotype in two compound heterozygote Hungarian brothers with the same genotypic triosephosphate isomerase deficiency"
S. Hollan, M. Magócsi, **E. Fodor**, M. Horányi, V. Harsányi and T. Farkas
Proc. Natl. Acad. Sci. U.S.A, Vol. 94, pp. 10362-10366 (1997). IF: 9.04

8. "Role of lipid polymorphism in G protein-membrane interactions: Nonlamellar-prone phospholipids and peripheral protein binding to membranes"
P. V. Escriba, A. Ozaita, C. Ribas, A. Miralles, **E. Fodor**, T. Farkas and J. A. Garcia-Sevilla
Proc. Natl. Acad. Sci. U.S.A., Vol. 94, pp. 11375-11380 (1997). IF: 9.04

9. "Lipids affect the charge stabilization in wild type and mutant reaction centers of *Rhodobacter sphaeroides*"
L. Nagy , **E. Fodor**, J. Tandori, L. Rinyu, and T. Farkas
Austr. J. of Plant Physiol., (1999). 26, 465-473. IF: 2.185

10. "Lipids affect the charge stabilization in wild type and mutant reaction centers of *Rhodobacter sphaeroides*"
Sz. Gédelyi, Á. Kecskés, **E. Fodor**, T. Farkas, and L. Nagy
In Photosynthesis: Mechanisms and Effects, Ed. G. Garab, Kluwer Academic Publishers, Dordrecht, Netherlands, Vol. II. pp.893-896. (1998).

11. "Response of fish to environmental temperature at the level of membrane phospholipids"
T. Farkas, **E. Fodor**, K. Kitajka. (Accepted for publication in *Aquaculture Research*)

12. "Docosahexaenoic acid containing phospholipid molecular species in brains of vertebrates"
T. Farkas, K. Kitajka, **E. Fodor**, I. Csengeri, E. Lahdes, Y. K. Yeo, J. E. Halver. (Submitted manuscript to *P.N.A.S. U.S.A.*)

13. "Adaptation of composition and biophysical properties of phospholipids to temperature by the crustacean, *Gammarus* spp."
E. Lahdes, G. Balogh, **E. Fodor**, T. Frakas. (Submitted manuscript to *Lipids*)