REPORT

Report for Nutritional Therapeutics, Inc.

Effects of Phosphoglycolipid Extract (NT Factor) on Normal and Cancerous Cells

David S. Newburg, Ph.D.*

Director, Program in Glycobiology, Shiever Center for Mental Retardation, 200 Trapelo Road, Waltham, Massachusetts 02452-6368
Biochemist (Neurology), Massachusetts General Hospital, Harvard Medical School
Boston, Massachusetts

CANCEROUS CELLS OF TUMORS IMPORT PHOSPHOLIPIDS FROM NORMAL CELLS

One of the fundamental biochemical differences between tumor cells and normal cells is the composition of the membrane lipid, including glycophospholipid and phospholipids. The phospholipid content of tumor cell membranes in known to be distinct from that of normal cells.[3,8,9,16,27] The difference in phospholipid content has been attributed to differences in rates of phospholipid transfer to the plasma membrane of aggressive tumors. There are two components to this difference in the ability of tumor membranes to acquire phospholipids from neighboring cells: first is a difference in phospholipids exchange due to phospholipids exchange protein (PLEP); second is a difference in phospholipids exchange rates due to the intrinsic lipid composition of the membrane. Over 90% of the Phosphatidylcholine in hepatoma microsomes can be exchanged within two hours at 37°C.[23] In Morris hepatoma cells, the transfer activity of phosphatidylcholine was 2 to 3 times higher thank in controls.[24] However, only some of this difference could be accounted for by an increase in PLEP activity, the rest being attributed to intrinsic differences in membrane lipids. Clearly, many types of tumors are able to incorporate extrinsic phospholipids into their membranes at the expense of normal cells of the body with the potential to deplete the phospholipids in the normal cells.

*Correspondence:
David S. Newburg, Ph.D.
Director, Program in Glycobiology
Shriver Center for Mental Retardation
200 Trapelo Road
Waltham, Massachusetts 0245-6368
Phone: 781-642-0025 Fax: 781-893-4018
E-mail: dnewburg@shriver.org

REDUCED LEVELS OF PHOSPHOLIPIDS IN NORMAL CELLS CAN LIMIT METABOLIC ACTIVITY AND LIMIT AVAILABLE ENERGY

Phospholipids, as part of the membrane structure, maintain membrane integrity, and, through changes in membrane fluidity, also regulate enzyme activities and membrane transport processes.[28,29] Phospholipids can have other specific functions. Signal transduction utilizes phospatidylcholine and phosphatidylinositol for the production of diacyl glycerol (DAG) by phospholipase C^5 and for the production of inositol triphosphate (IP_3).[18,19,25] One of the choline phospholipids (1-alkyl-2acetyl-*SN*-glycerol-3-phosphocholine) is the substrate for the synthesis of platelet activating factor (Synder 1989). The arachidonic acid found as part of the structure of choline or inositol phospholipid is utilized for the production of prostaglandin and leukotriene.[22] The choline of phosphatidylcholine may be used in neural tissue for the synthesis of acetylcholine.[6]

Plasma brain and neuronal choline concentrations were elevated by oral administration of choline, which also causes the release of acetylcholine in the neuromuscular system.[10,13] Furthermore, muscle function has been shown to decrease during choline deficiency.[36] Physical stress depresses plasma choline concentration, e.g., individuals in the Boston Marathon of 1986 showed 40% decreases in

plasma choline levels during the race.[11] Providing phosphatidylcholine prior to exercise can compensate for these choline losses.[34] Even with shorter and less strenuous forms of exercise, a supplemental supply of lecithin results in an increase in performace.[33]

When tumor cells sequester large amounts of the phosphatidylcholine produced by normal cells, this could lead to a loss of choline homeostasis, producing decreases in plasma, brain, and muscle choline that would be expected to result in muscle fatigue. This could account for some of the malaise and chronic fatigue that is known to accompany certain forms of cancer. Under these circumstances, exogenous oral supplements would be expected to provide some measure of relief from cancer-associated fatigue.

THE RATE OF PHOSPHOLIPID ACCUMULATION IN CANCER CELLS IS INDEPENDENT OF EXOGENOUS SUPPLY

In general, adult tissues contain more phosphatidylcholine than immature tissues.[30,35] Like immature developing tissues, some tumors contain lower levels of phospholipid than corresponding normal tissue.[4] However the phospholipid content varies greatly from tumor to tumor. Many varieties of cancerous tissue contain more phosphatidylcholine with increased amounts circulating in the blood and available for use by the tumor.[1,21,31] Thus, some tumors can deplete normal tissue of phospholipid.

NT FACTOR™ PHOSPHOGLYCOLIPID IMPROVES CELL MAINTENANCE AND METABOLIC ACTIVITY OF NORMAL CELLS

The integrity of mitochondria and their ability to produce energy can be measured by isolating lymphocytes, treating them with Rhodamine 123 (a mitochondrial stain), and analyzing them using FACSCAN, a flow cytometer modified for analysis of mitochondria. In rats, there is a measurable decrease in mitochondrial function as the rat ages. However, in rats fed a diet that contains NT Factor™ phosphoglycolipid, mitochondria showed a 20% improvement over those fed the identical diet without the NT Factor™, as measured by Rhodamine flow cytometry. (Michael Seidman, personal communication)

Assuming that the degradation of mitochondrial function with age is caused by cumulative chemical toxicity, it would appear that NT Factor™ phosphoglycolipid is able to protect normal tissue from this type of chemical induced damage.

NT FACTOR™ PHOSPHOGLYCOLIPID CONTAINS HIGH CONCENTRATIONS OF LYSOLECITHINS

When NT Factor™ phosphoglycolipid was analyzed in our laboratory and its composition compared to that of the parent soy-derived material from which it was extracted, we found that NT Factor™ phosphoglycolipid contains substantially more phosphatidylcholine than the parent material. Although the fatty acid composition of the phosphatidylcholine from NT Factor™ phosphoglycolipid was not different from that of the parent compound, by virtue of concentrating the phosphatidylcholine the extraction process also concentrated polyunsaturated phosphatidylcholine. The greatest difference between the preparations was that NT Factor™ phosphoglycolipids had over 6 times the lysolecithin content of the parent compound. This suggests that any unique biological activity of NT Factor™ may be due in part to its lysolecithin content, either acting alone or in concert with other of its components.

LYSOLECITHIN DERIVATIVES DISRUPT CANCER CELLS AT CONCENTRATIONS THAT DO NOT AFFECT NORMAL CELLS.

Lysolecithin-like molecules are selectively cytotoxic to cancer cells in vitro.[12,15] Such compounds inhibit HL60 leukemic cells at a dosage that has no effect on normal human marrow cells, the tissue from which the leukemic cells are derived. Normal cells were able to tolerate 4 times higher dosage than the leukemic cells during 24 hours incubation with the phospholipid preparation.[2] There was up to a 5-fold difference in sensitivity between the normal and tumor cells with breast, ovarian, and lung cancer cells, as well as with mesothelioma cells.[20]

In summary, some cancerous cells are able to deplete normal cells of phospholipids, causing a degradation in function, and possibly leading to lethargy. NT Factor™ phosphoglycolipid is a very rich source of phospholipids, and also contains high levels of lysolecithin. Lysolecithin-like molecules are able to inhibit tumors at doses that do not affect normal cells.

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