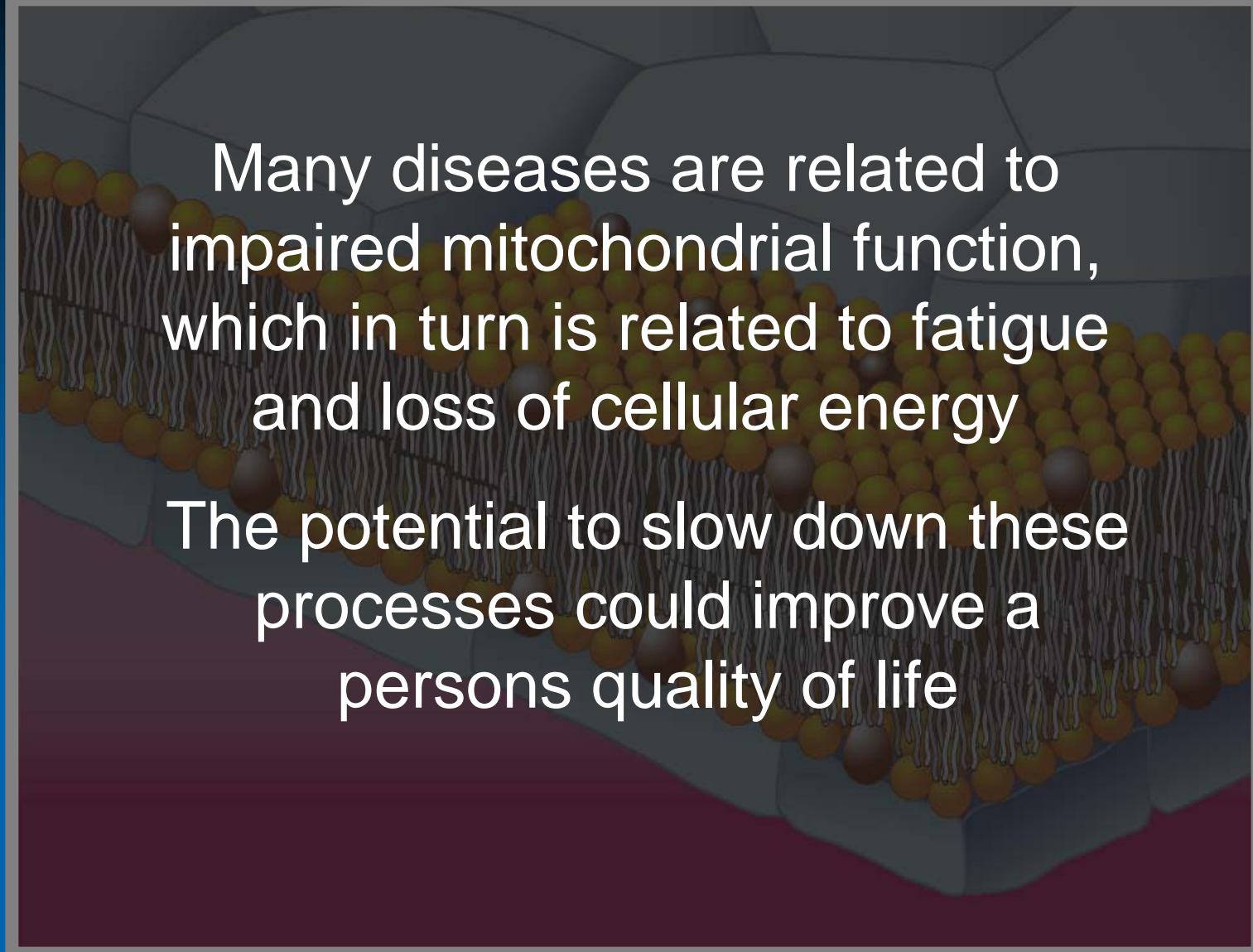


Lipid Replacement Therapy

**Validated To Restore
Mitochondrial Function, Restore
Membrane Potential.**

**Validated to Reduce & Eliminate
Clinically proven Fatigue Including
Severe Fatigue**



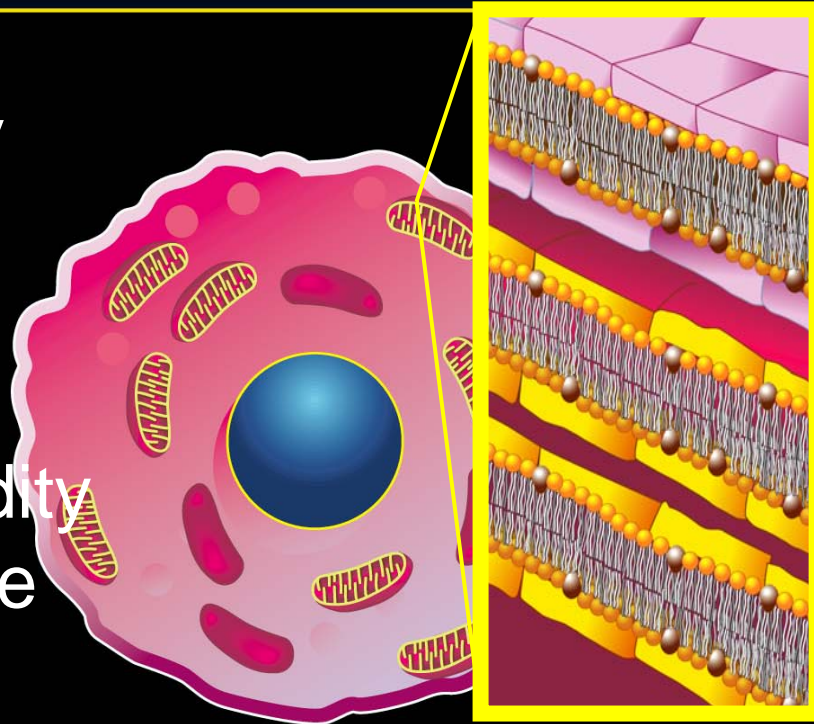
Many diseases are related to impaired mitochondrial function, which in turn is related to fatigue and loss of cellular energy

The potential to slow down these processes could improve a persons quality of life

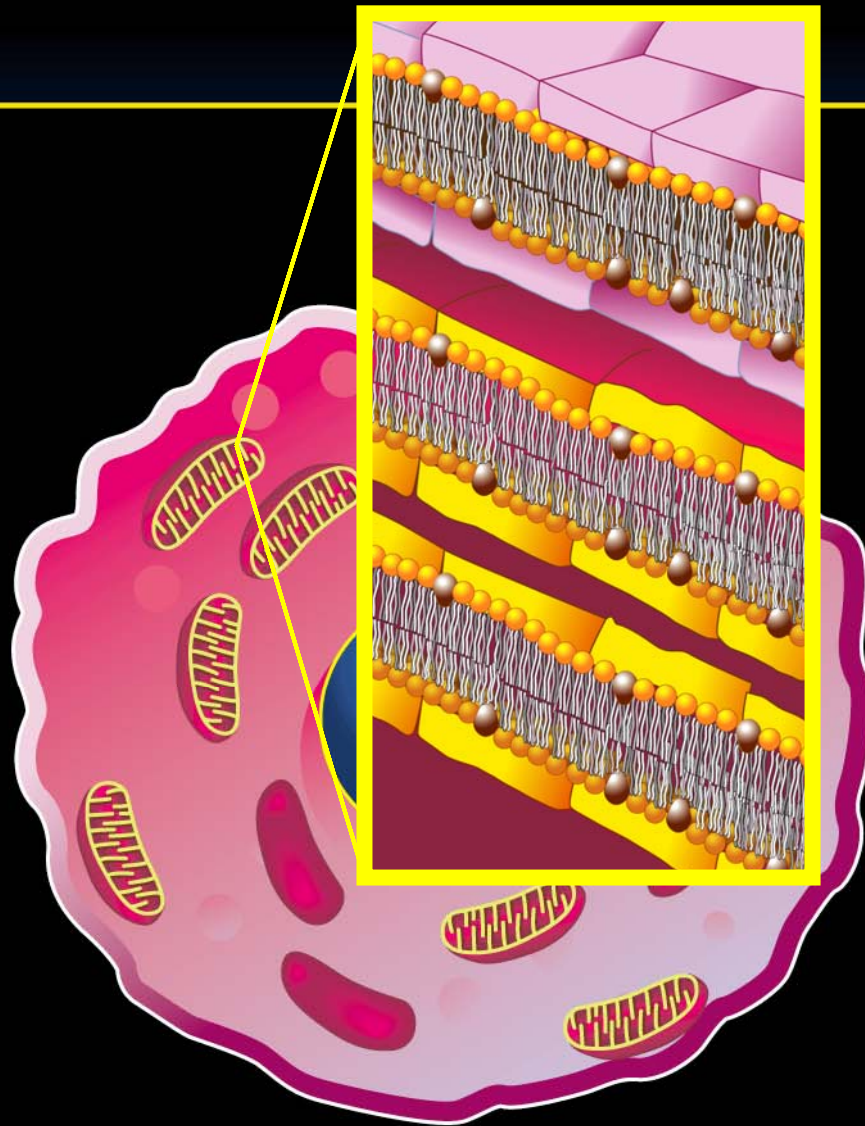
The Phospholipids that make up the fabric of the membranes will physically change and/or become oxidized with age and oxidative stress.

This will decrease the fluidity and electrical activity of the membranes.

Reactive Oxygen Species will begin changing mtDNA



The oxidation and morphing of the membrane accelerates the volume and quantity of Reactive Oxidative Species – free radicals that occur as a byproduct of energy metabolism. They are also called Reactive Oxygen Metabolites.

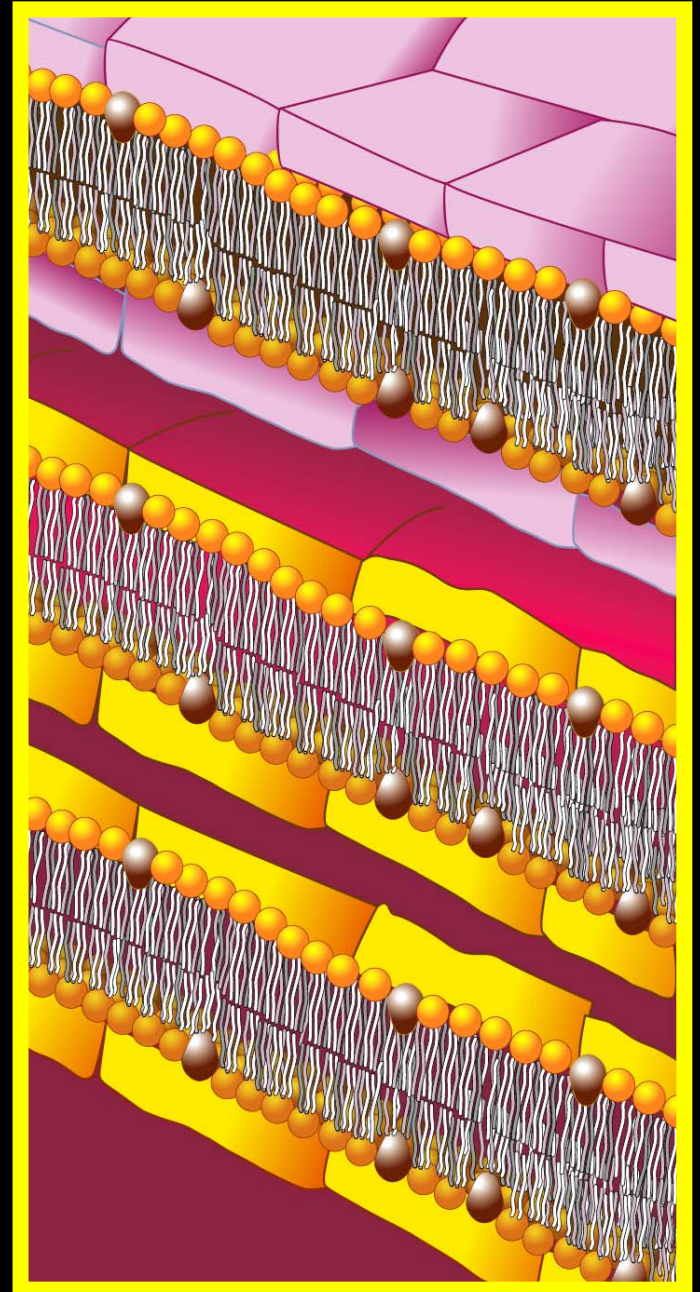


Human Cell Membrane Schematic

Cell Membrane



Mitochondria Membrane
(Outer)

Mitochondria Membrane
(Inner)



Phosphoglycolipids

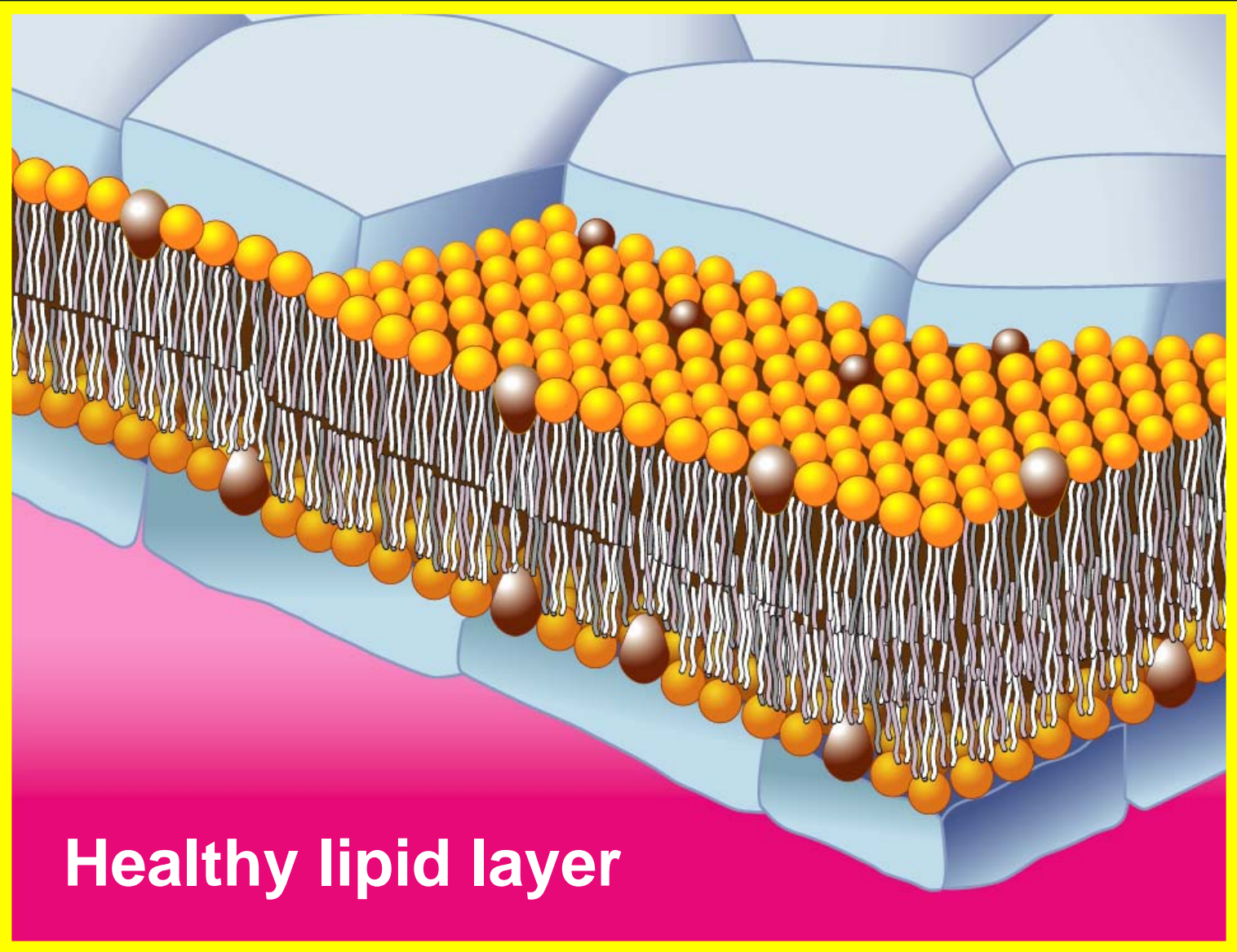
The cells are able to acquire phospholipids for their own repair through two methods:

-  **Through adequate mitochondrial function, the cell produces phospholipids itself**
-  **Cells acquire phospholipids from neighboring cells**

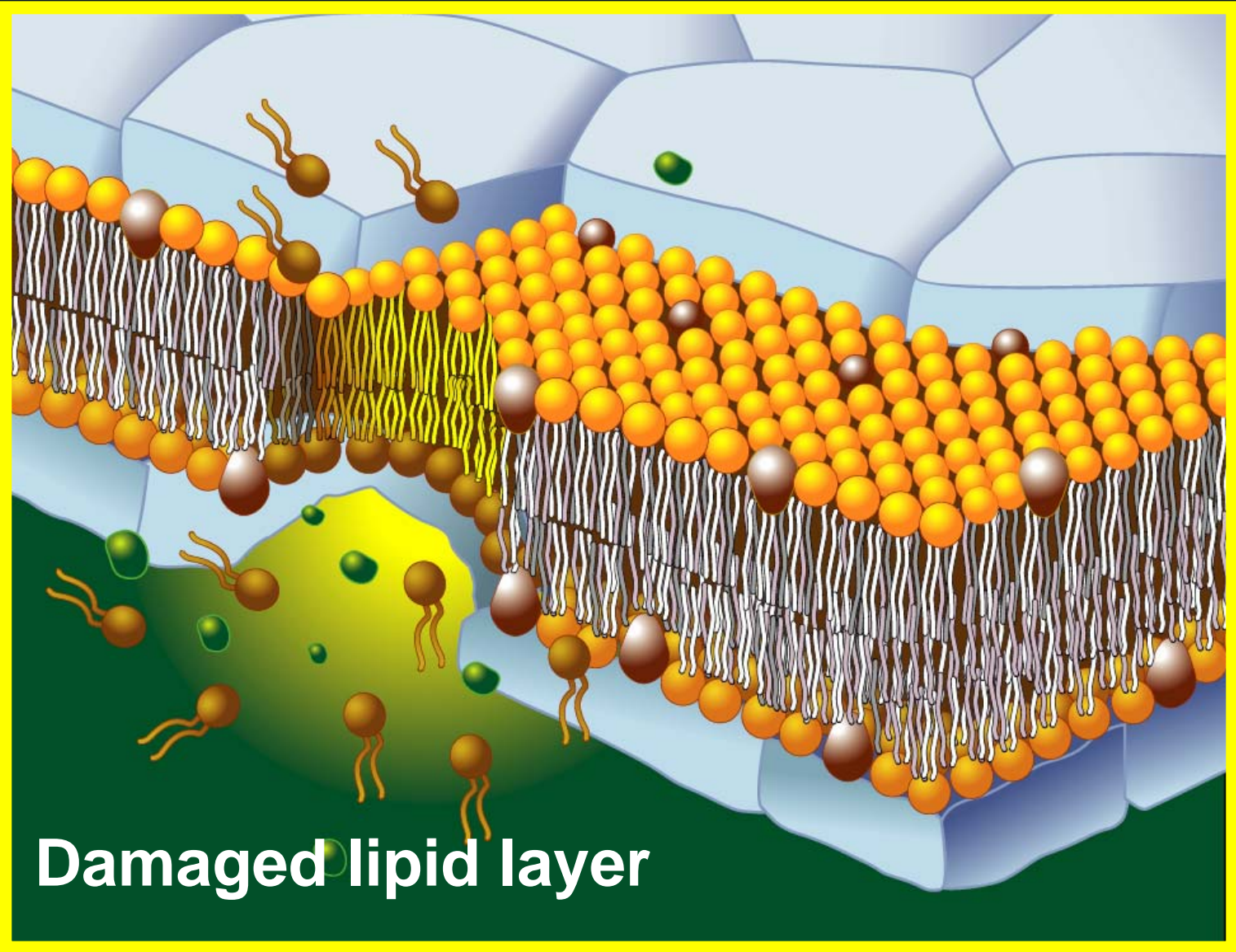
This is the proverbial 'Catch 22'

- If membrane potential and thereby energy output of the cell is reduced then it cannot manufacture PL for auto-repair.
- Traditionally phospholipids are broken apart in digestion. This process is one of the most efficient because of the bioactive potential of dual charged and amphiphilic molecules present in all food sources, i.e. phospholipids.

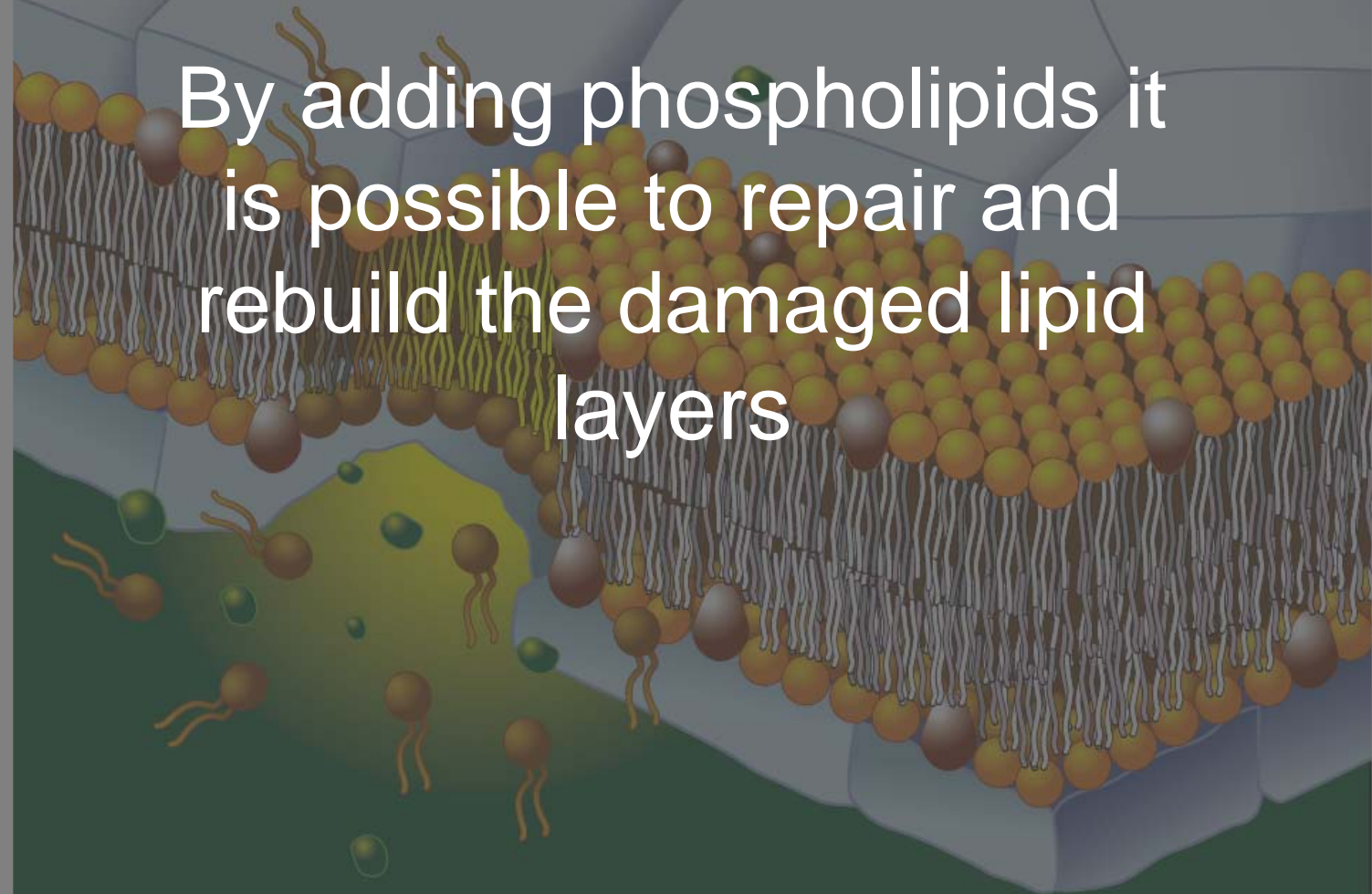
- **LIPID REPLACEMENT IS THE UNPRECEDENTED PROVISION OF UNOXIDIZED MEMBRANE MATCHING PHOSPHOGLYCOLIPIDS THAT ARE TAKEN UP UNOXIDIZED.**



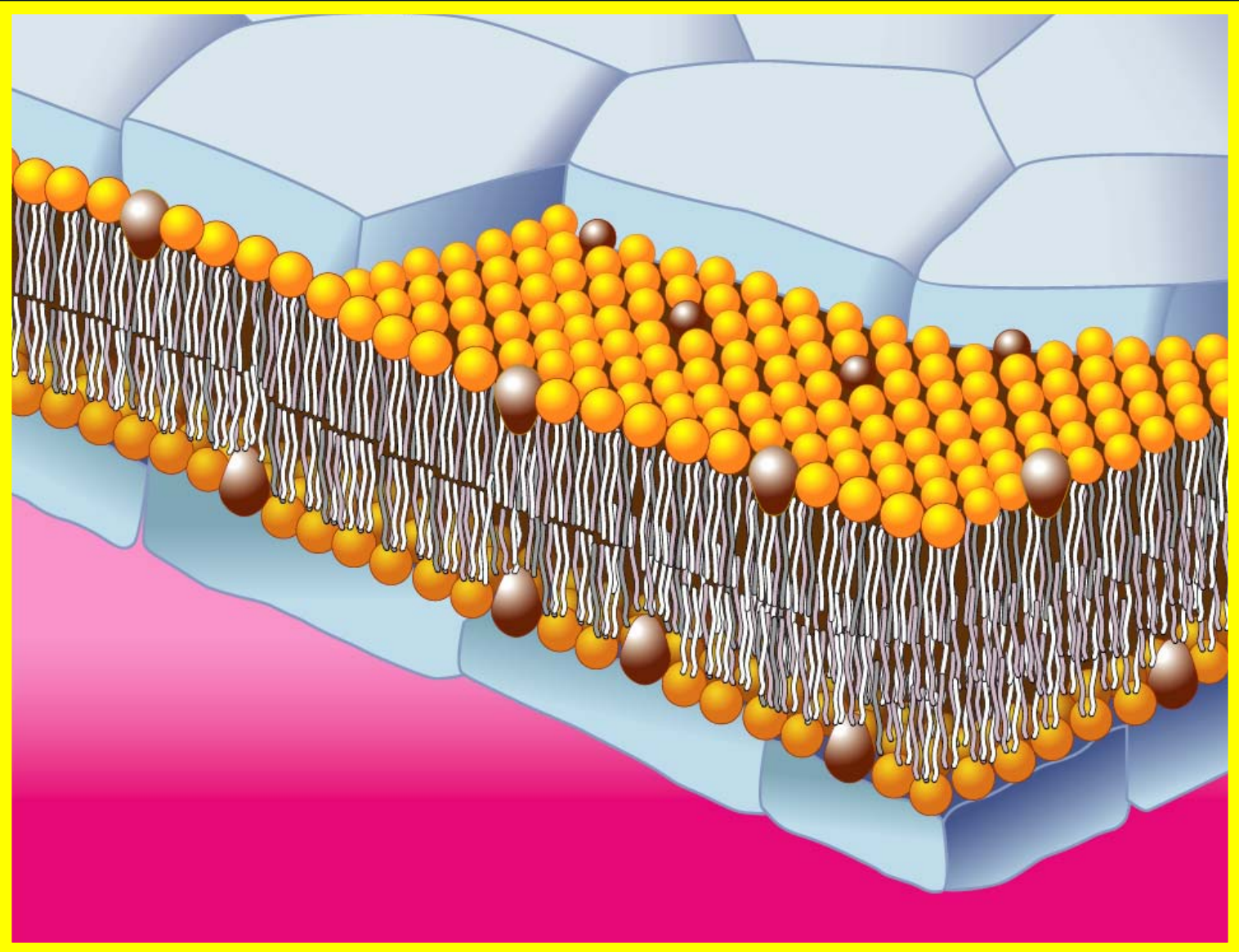
Healthy lipid layer



Damaged lipid layer



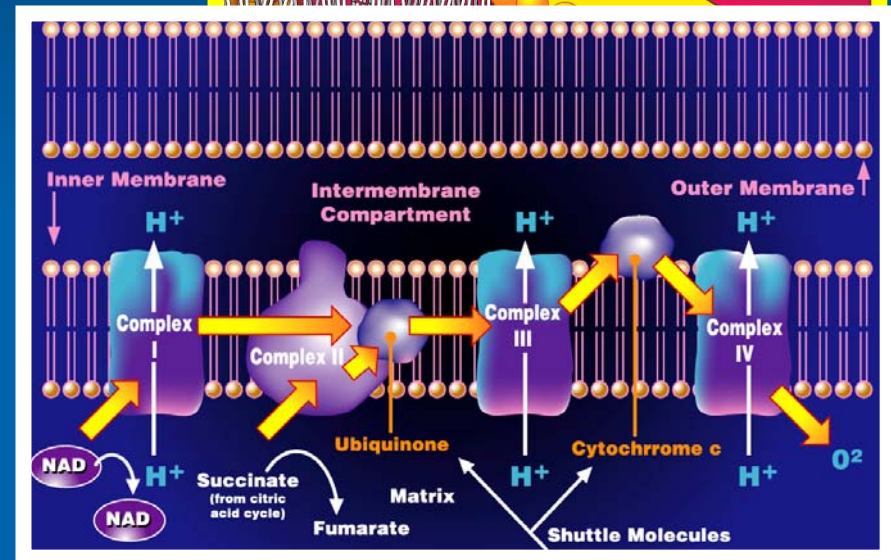
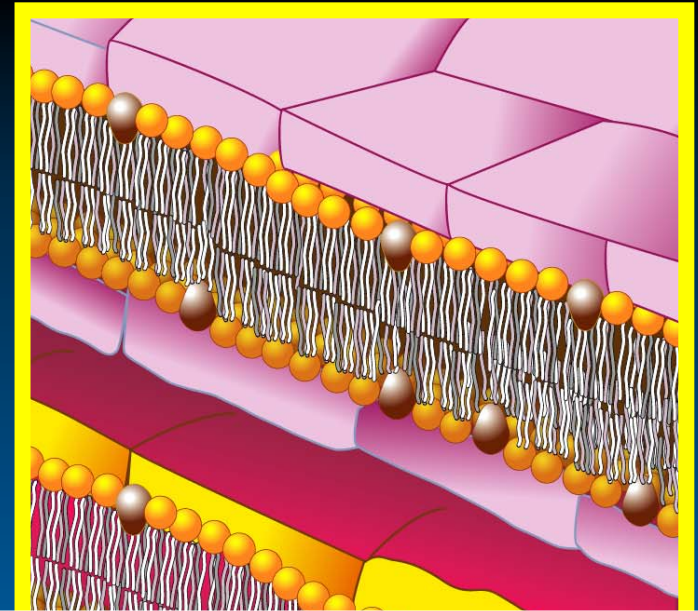
Lipid layer repaired



The **Electron Transport Chain** occurs in the mitochondrion inner membrane.

This can be commonly referred to as the

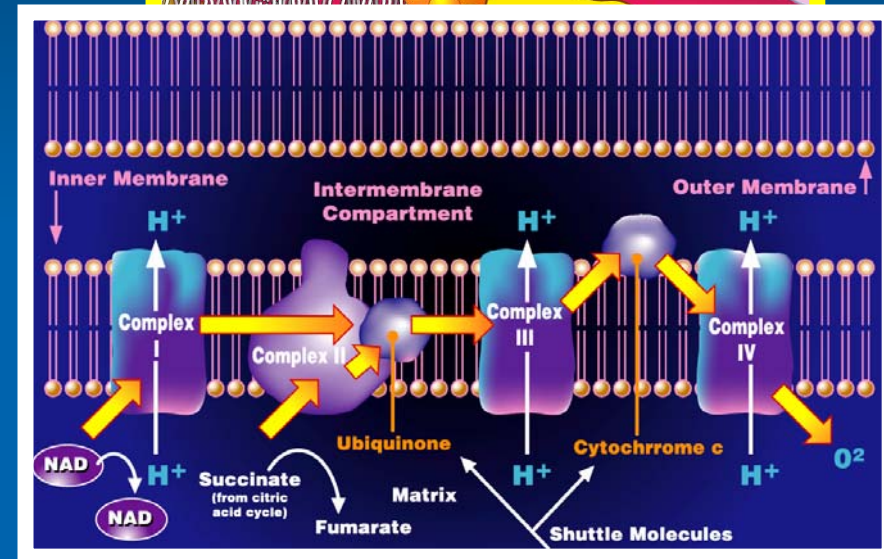
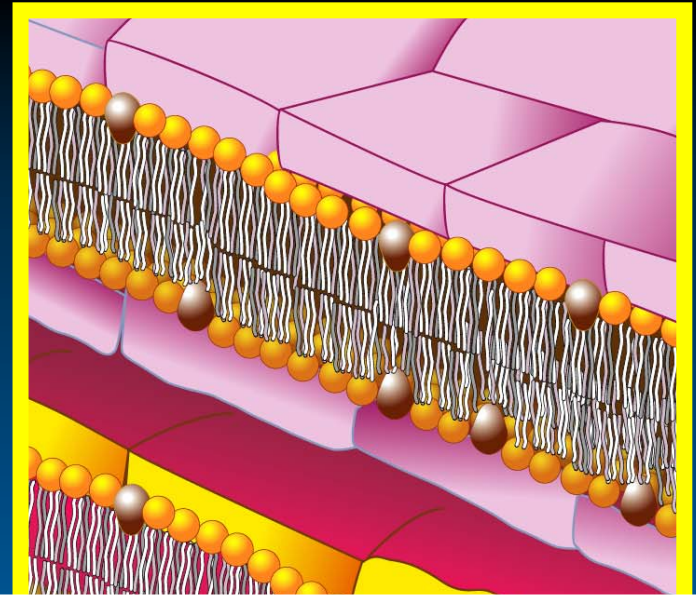
Oxidative Phosphorylation or **Cellular Respiration / Respiratory Chain.**



def: The process in cell metabolism by which respiratory enzymes in the mitochondria synthesize ATP from ADP and inorganic phosphate during the oxidation of NADH by molecular oxygen.

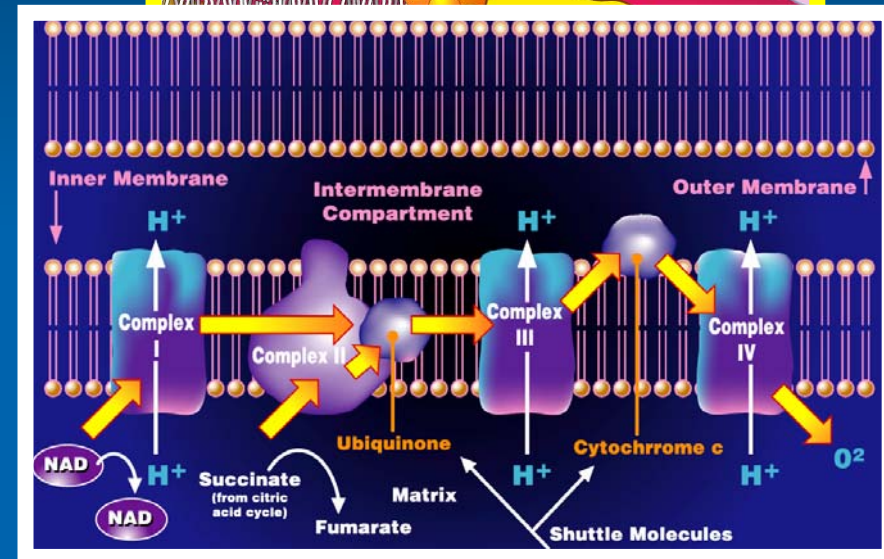
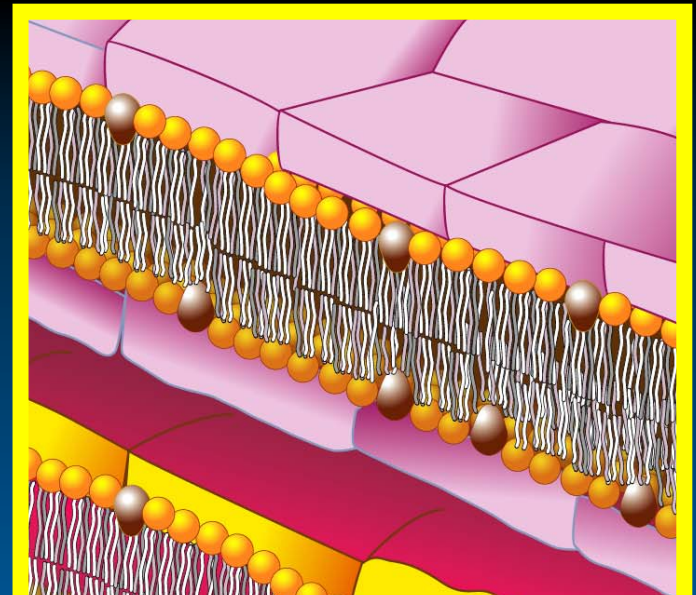
The importance of the inner membrane is that it contains the proteins & enzymes necessary for **Aerobic metabolism, the source of up to 90% of energy (e.g. cardiocyte) in a healthy cell.**

The fabric, i.e. the phospholipids, of the membrane is the housing or infrastructure in/on which this process occurs

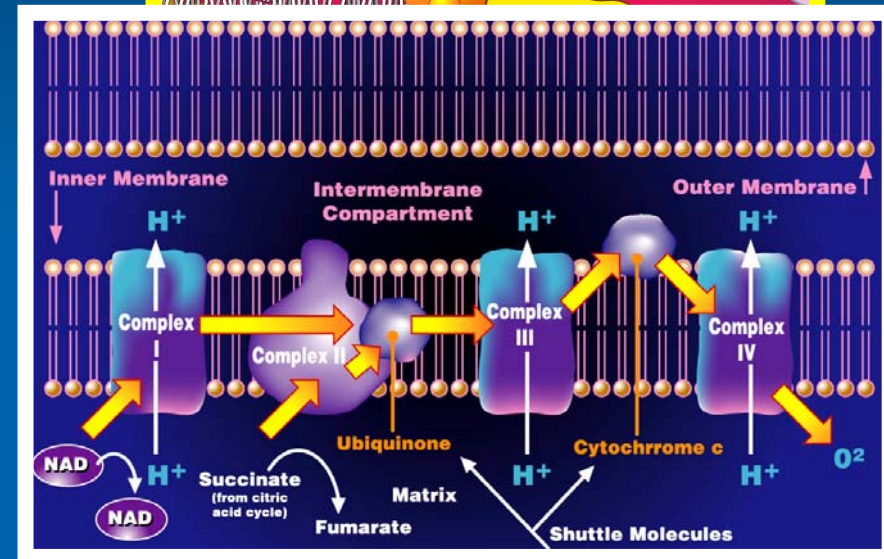
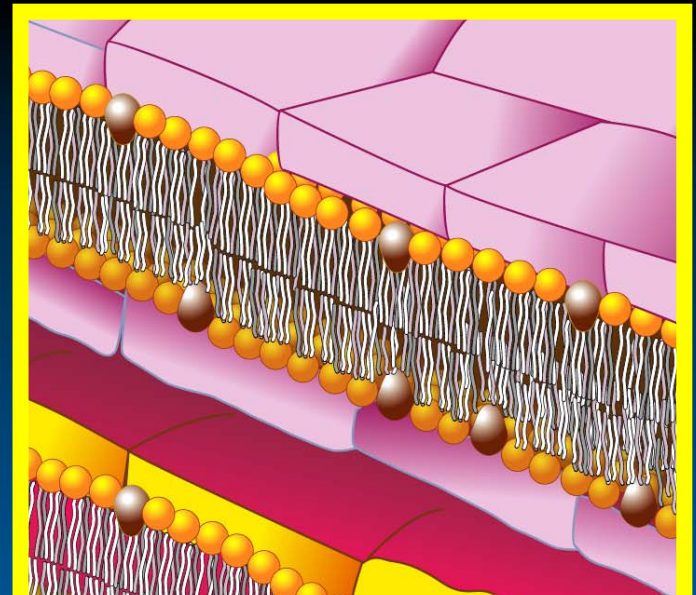


As phospholipids saturate the cell membrane they naturally partition into the mitochondria and as the outer membrane becomes saturated this extends into the inner membrane.

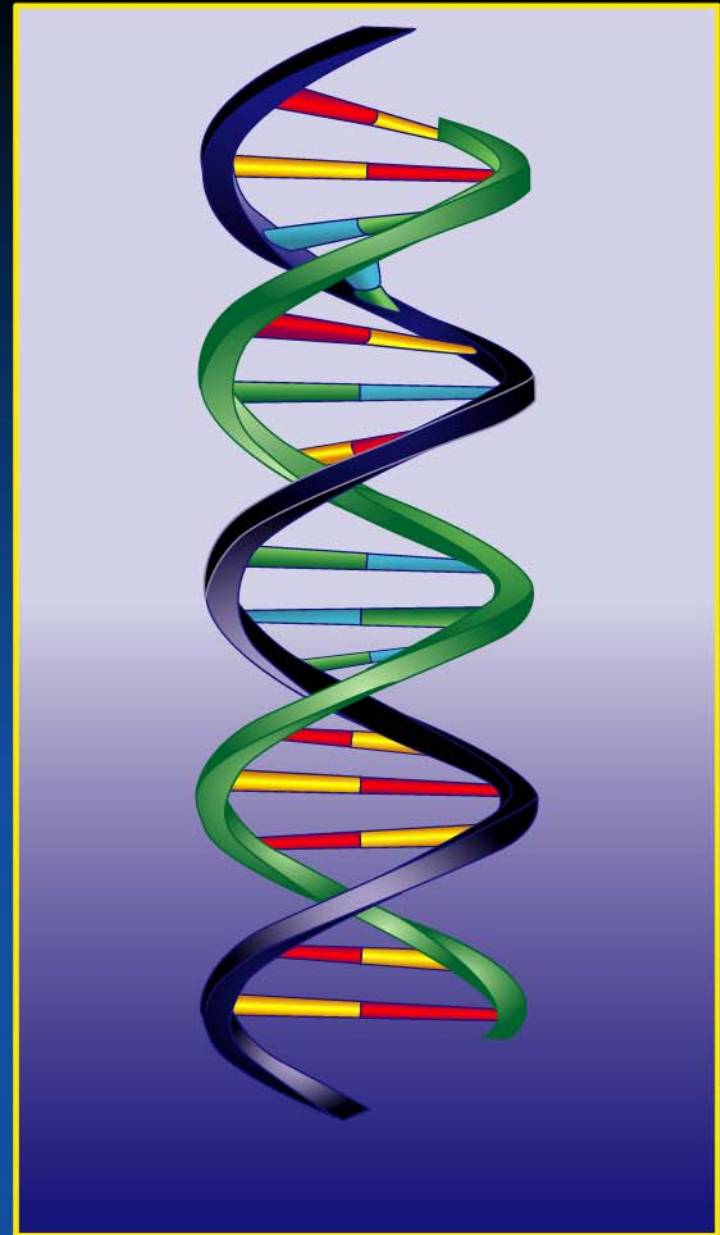
This is Dynamic Equilibrium of lipids in bio membranes.



As the inner membrane becomes more stabilized, more structurally sound and less leaky, better energy production occurs

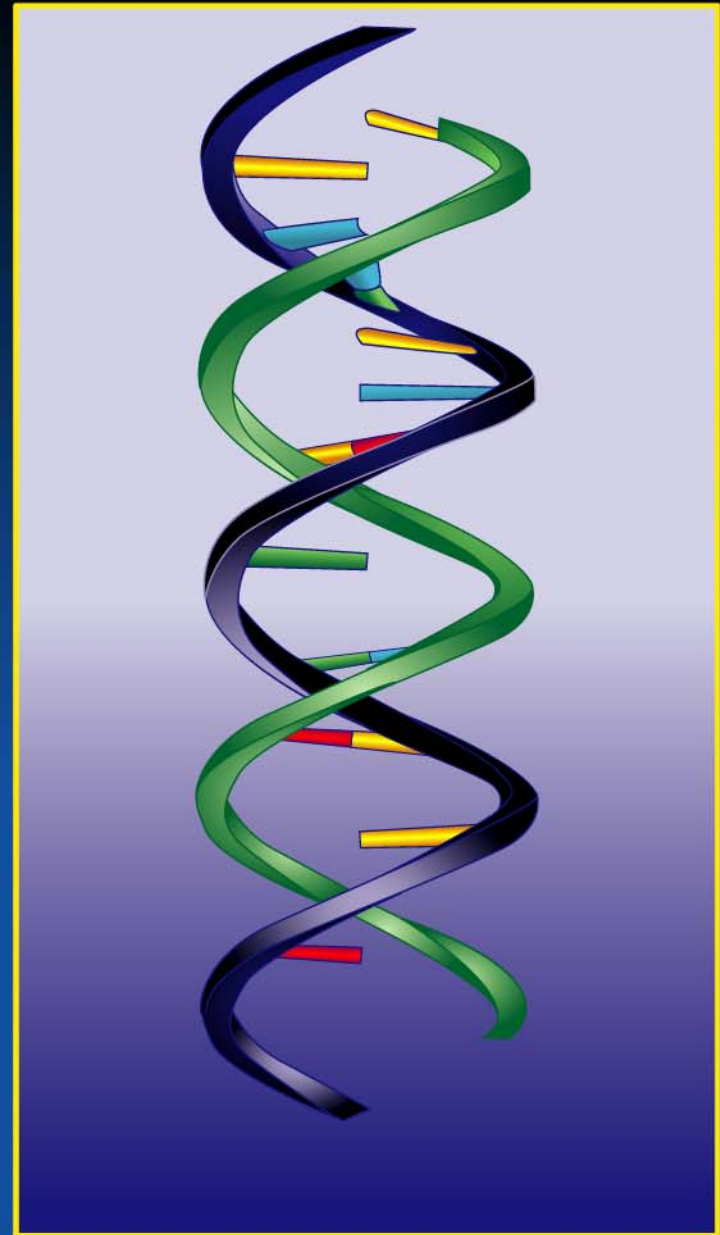


Addition of mitochondrial phospholipids to replace damaged lipids can reduce the rate of mitochondrial DNA (mtDNA) deletions. The mitochondria have a DNA structure that is distinct and separated from the nuclear DNA of the cell



Studies have shown that damage to the mtDNA is directly related to aging and disease of the cell.

Lipid Replacement Therapy has proven in animal studies to inhibit mtDNA deletions by half when introduced at the equivalent of middle age.



The Institute for Molecular Medicine

Lipid Replacement Therapy: Nutritional Supplement Restores Mitochondrial Function and Reduces Severe and Moderately Severe Fatigue

Ellithorpe *et al.* *JANA* 2003; 6(1): 23-28.

Agadjanyan *et al.* *J. Chronic Fatigue Syndr.* 2003;
11(3): 23-36.

Nicolson & Ellithorpe *J. Chronic Fatigue Syndr.* 2005;
13(2): *in press.*

What is Lipid Replacement Therapy?

It is the natural replacement of oxidized or damaged lipids using lipid supplements that are protected from oxidation/damage

Nicolson, G.L. *J Amer Nutraceut Assoc* 2003; 6(3):22-28.

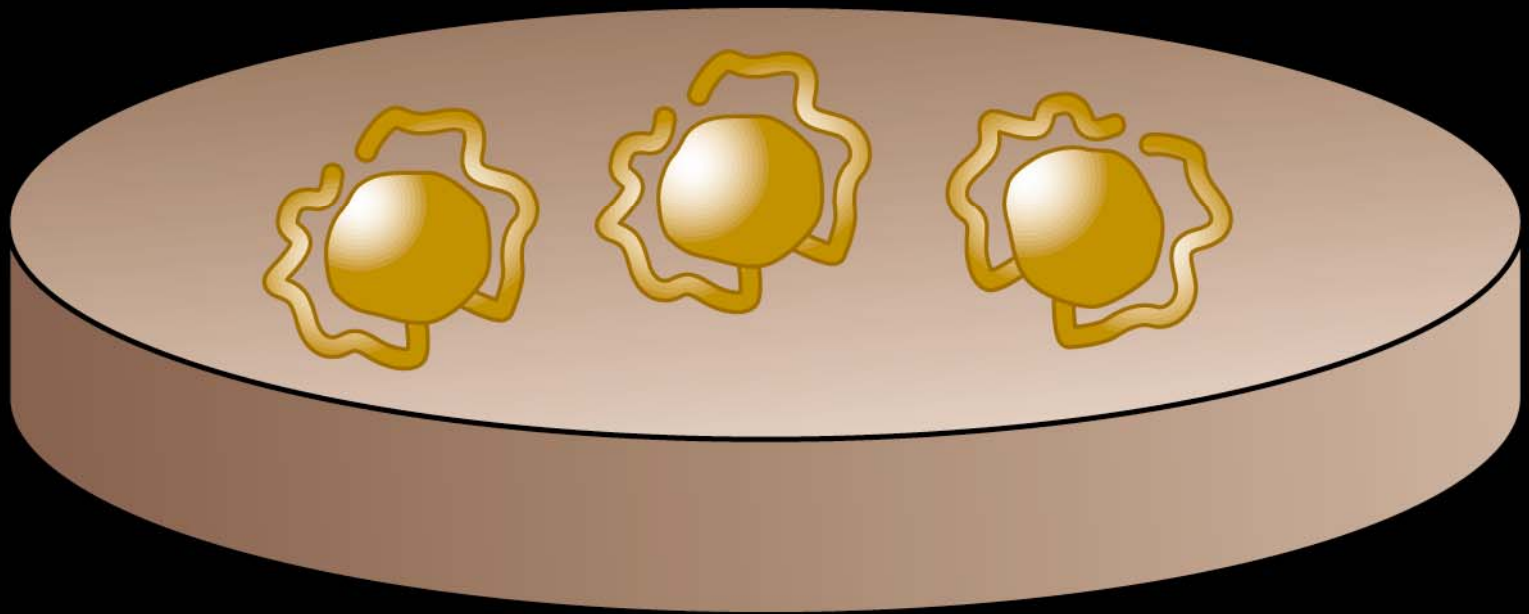
How NT Factor[®] Energy Restores Membranes

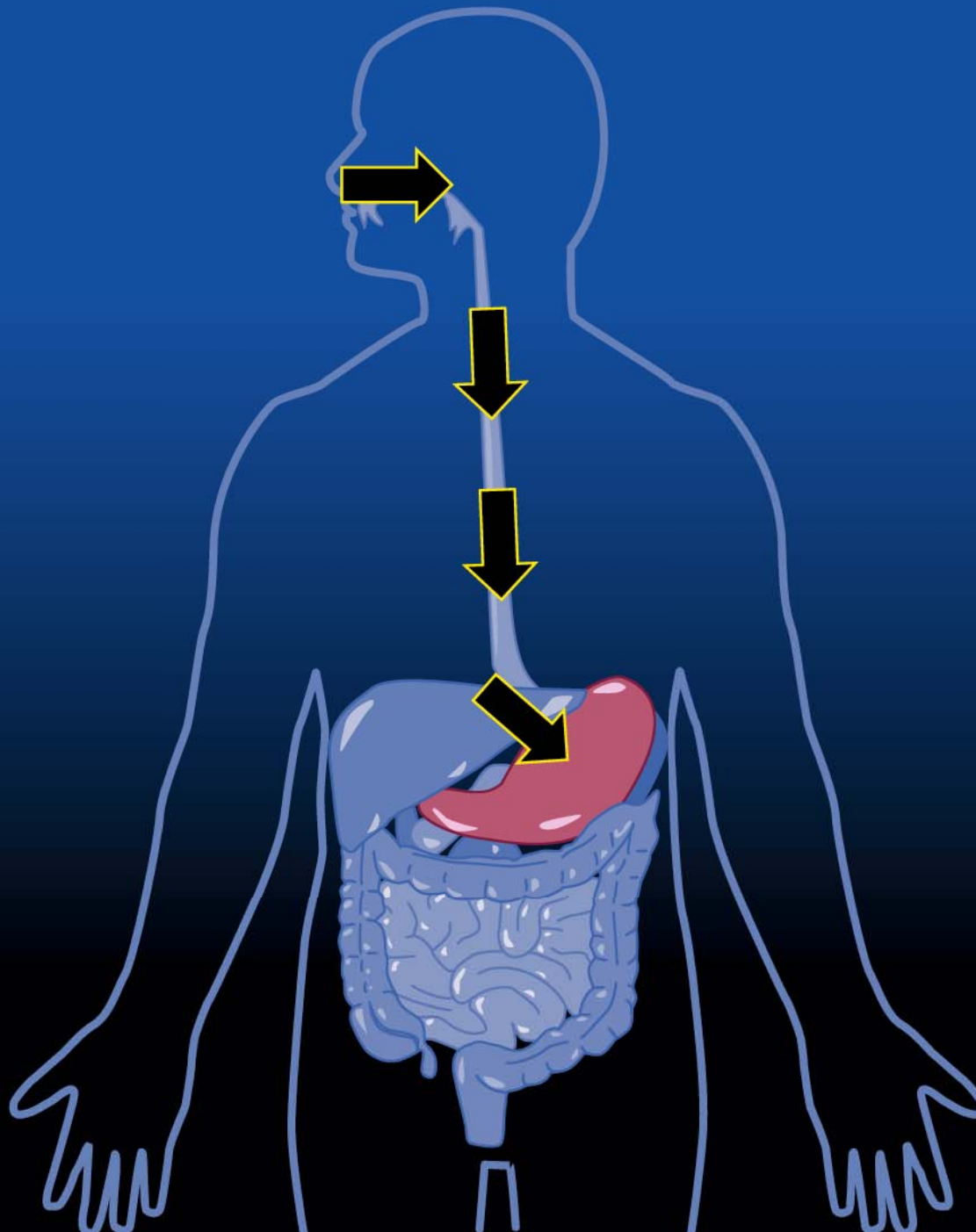
PHOSPHOGLYCOLIPIDS

The phosphoglycolipids are extracted from **soy**

The phosphoglycolipids are properly categorized as polyunsaturated nutrients

Through technological advancement, NTI has been able to **tablet stable UNOXIDIZED phosphoglycolipids**







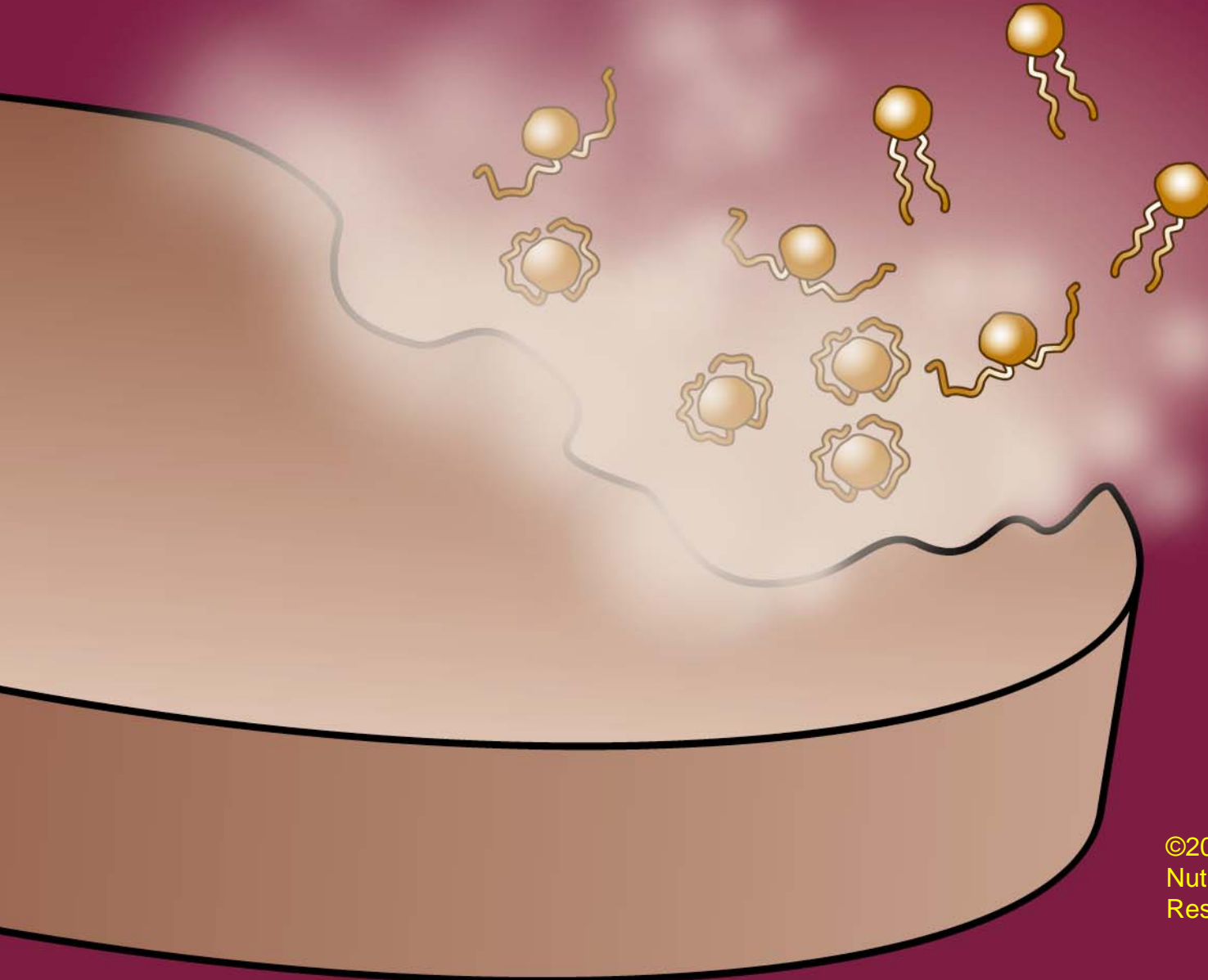
**Tablet immediately
starts to dissolve**

**The
phospholipids
are released**



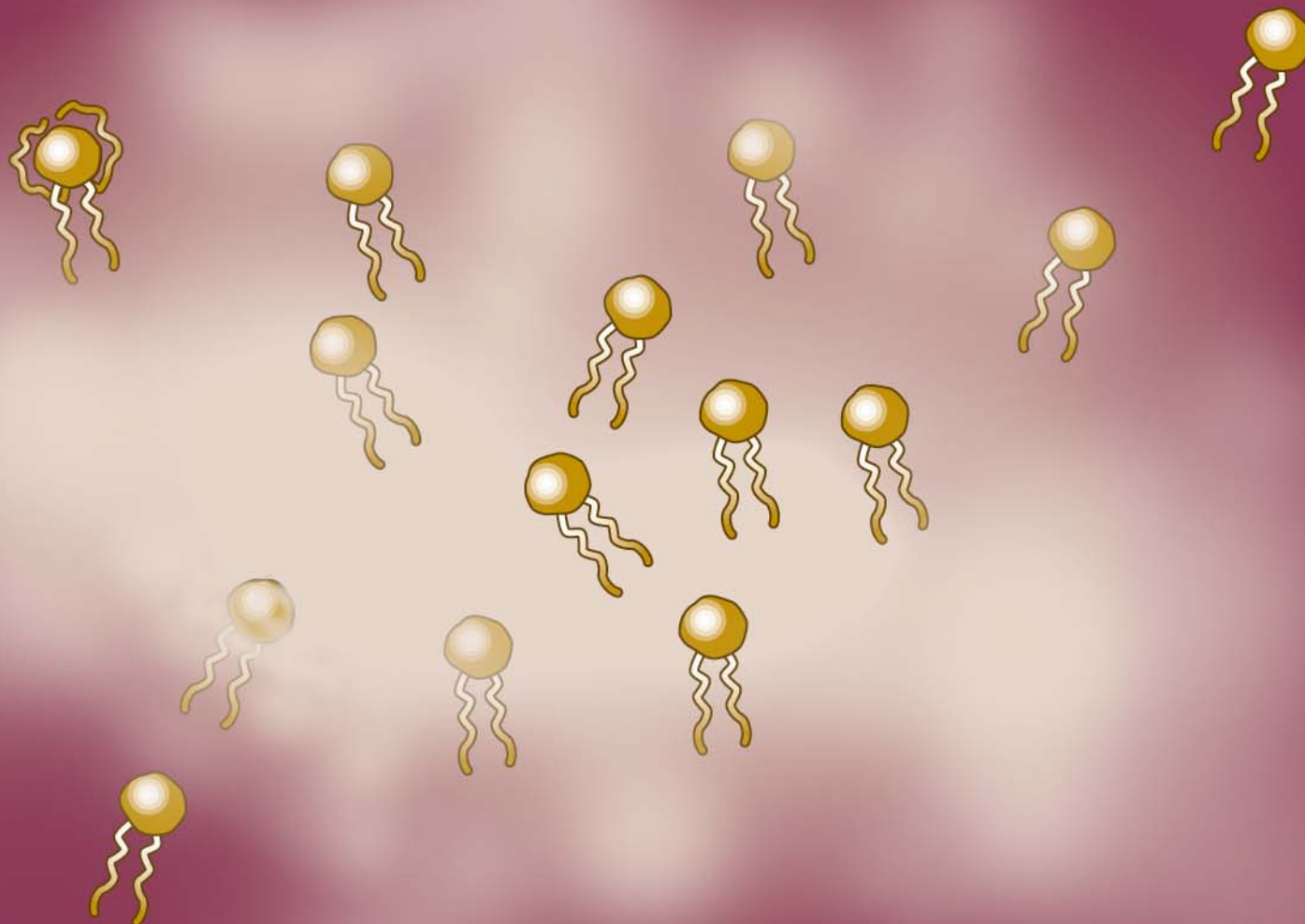
©2007 Researched
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Reserved.

And Are Immediately Available for Absorption into Gastro Intestinal Mucosa



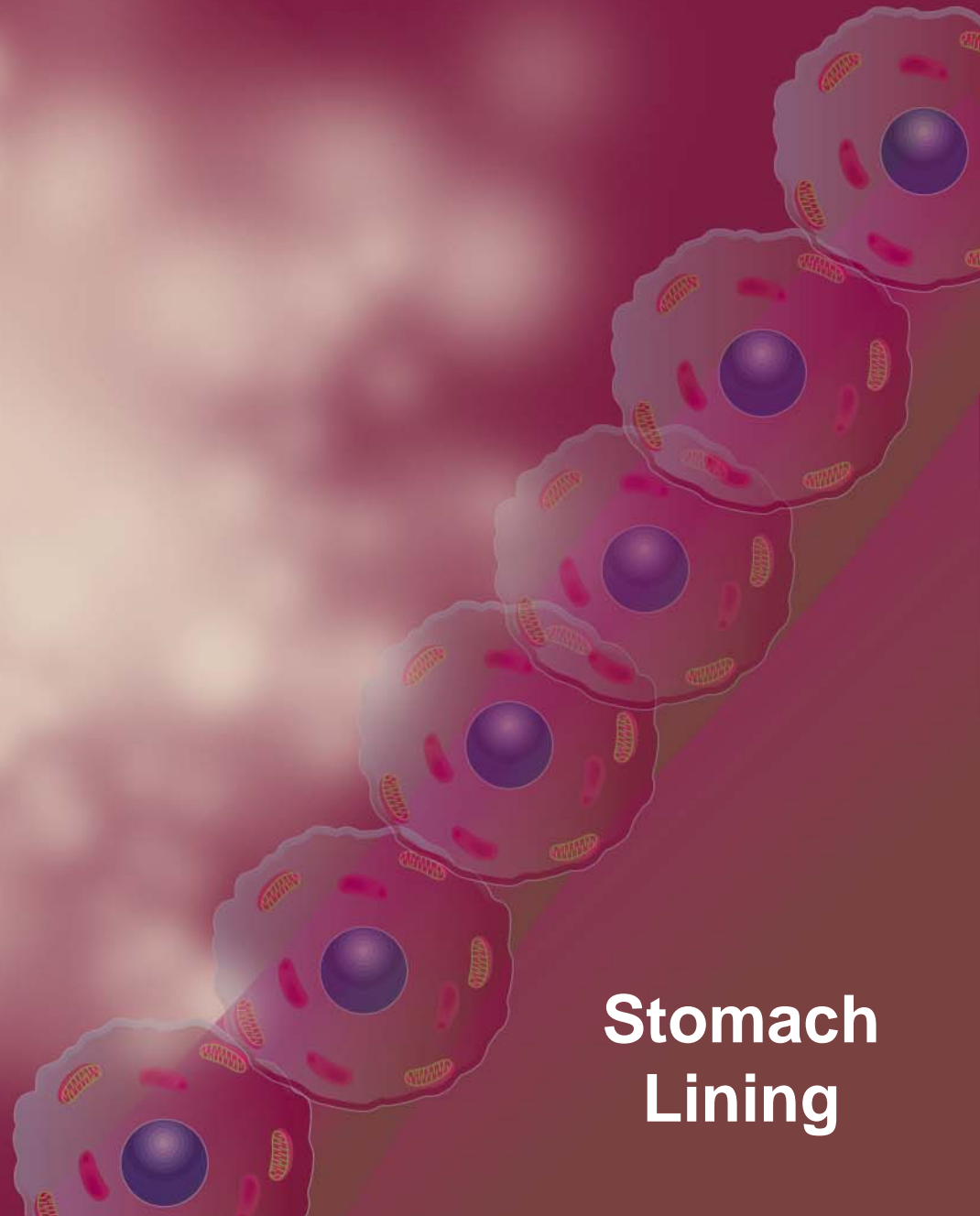
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Reserved.

**Since all nutrients work in combination with other nutrients,
this dispersal indicates a better potential to be utilized**



This cloud indicates a good homogenization of the nutrients

**Since the entire gastro-
intestinal lining is made
up of cells
phosphoglycolipids can
be taken up immediately**



**Stomach
Lining**

How NT Factor[®] Energy Restores Membranes

By providing a regular , or periodic, provision of the phospholipids we saturate the cells lining the gastrointestinal tract.

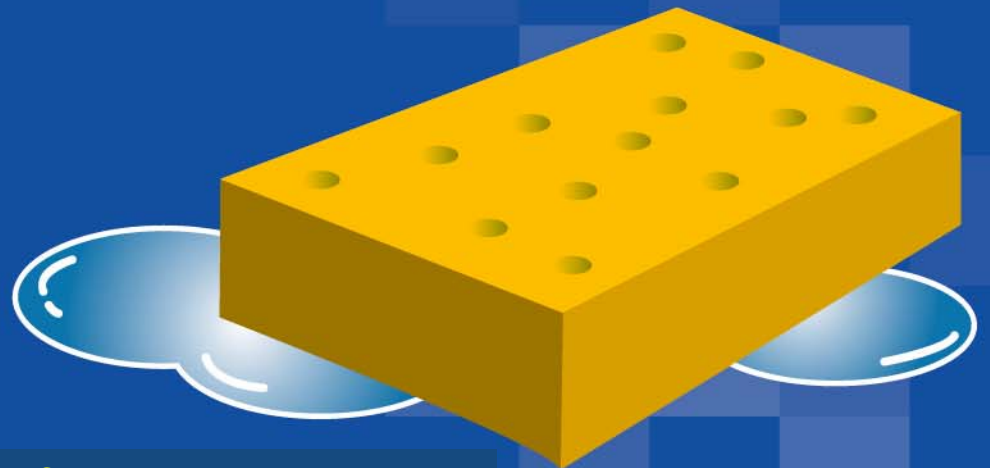
How NT Factor[®] Energy Restores Membranes

In time these cells take on a characteristic similar to a sponge at the bottom of the sink which water is dropping into



How NI Factor[™] Energy Restores Membranes

The sponge becomes so swollen with water that each time a new drop hits it disperses smaller droplets

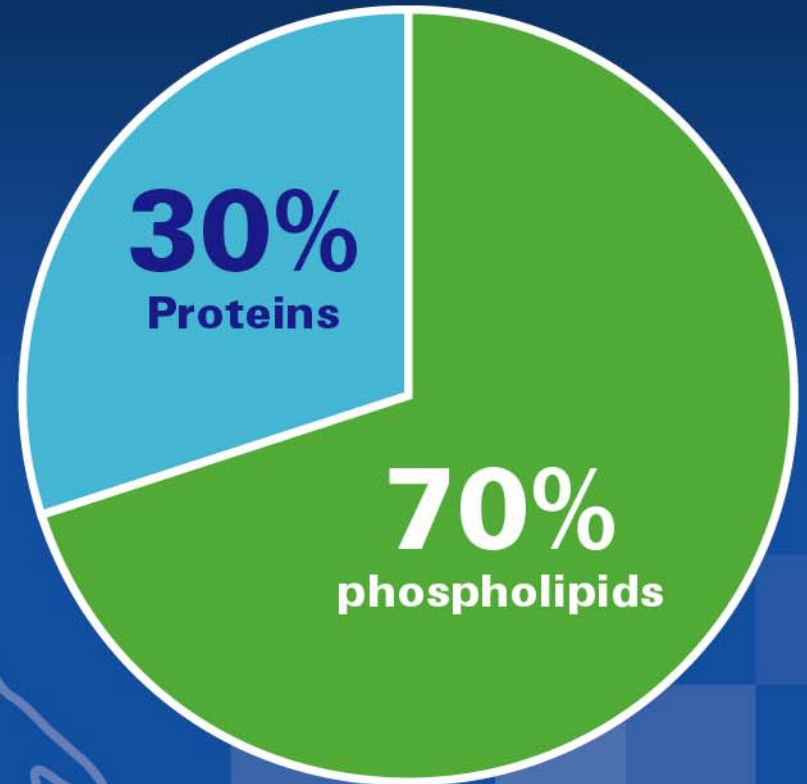


**Phospholipids are universal
to all the cells in the body**



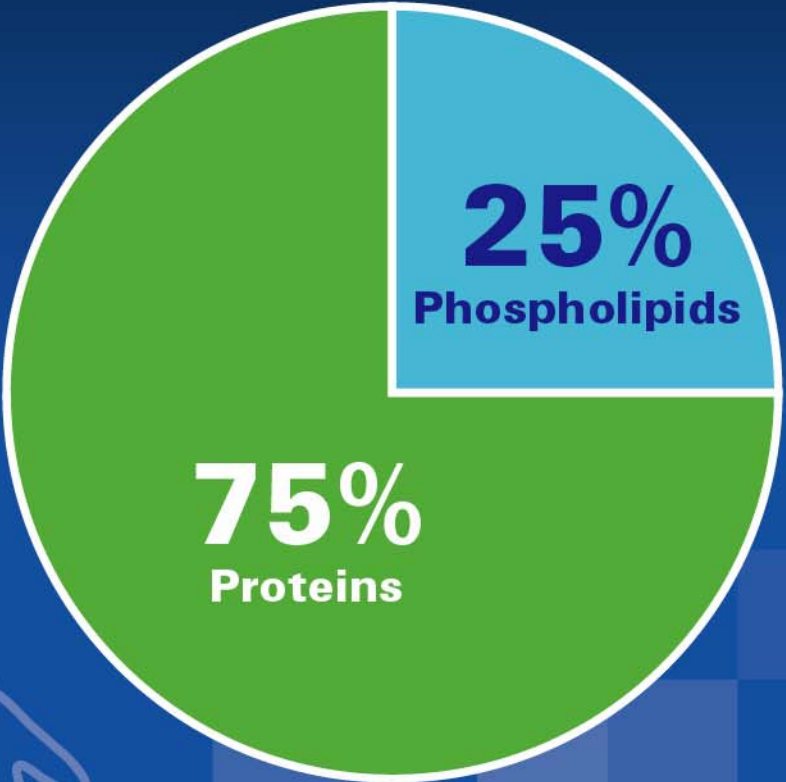
Phospholipids are universal to all the cells in the body

Cells of the body

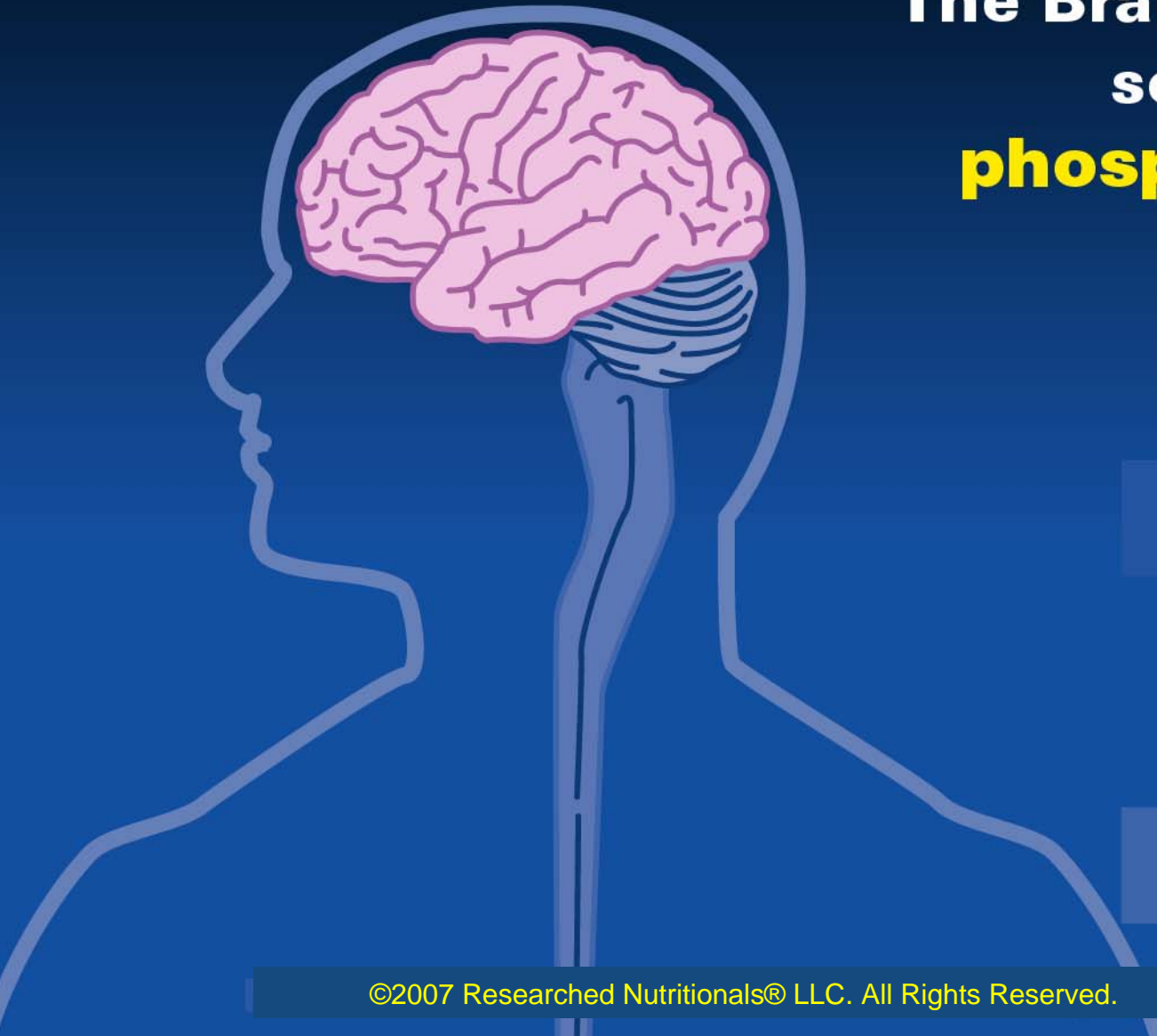


Phospholipids are universal to all the cells in the body

Cells of the Central Nervous System

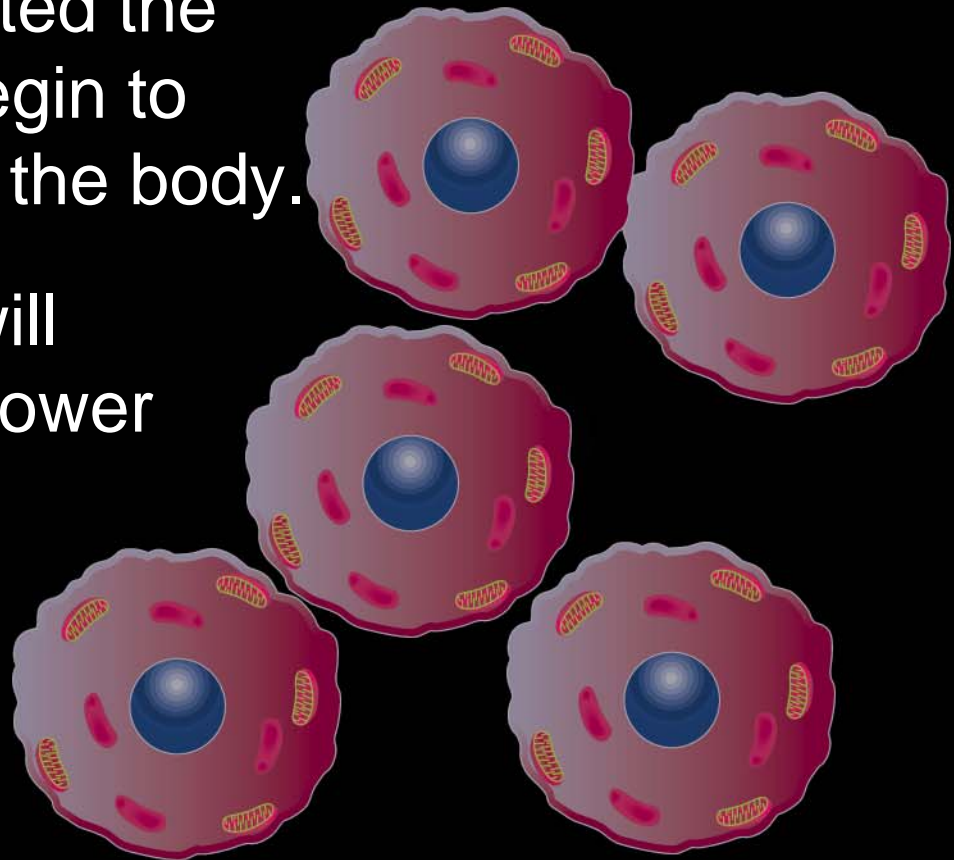
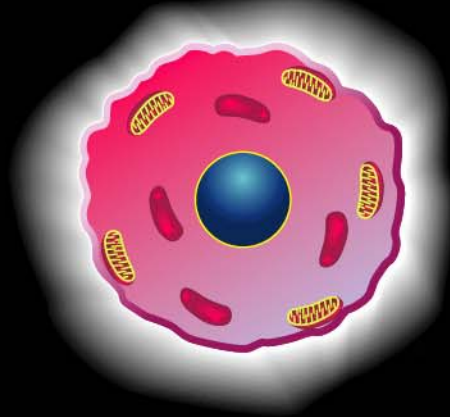


**The Brain is almost
solidly
phospholipids**

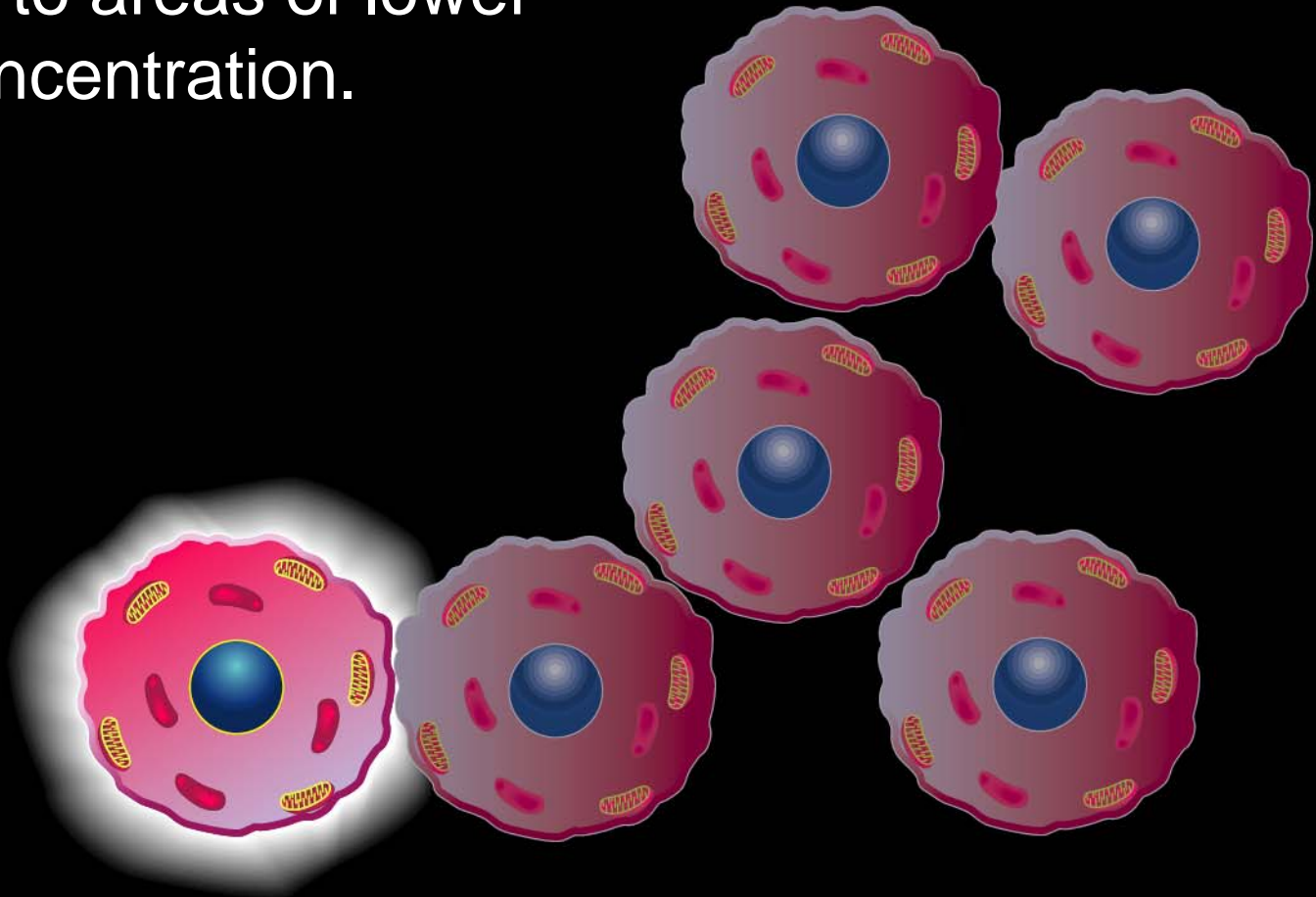


When the GI cells become sufficiently saturated the phospholipids begin to disperse throughout the body.

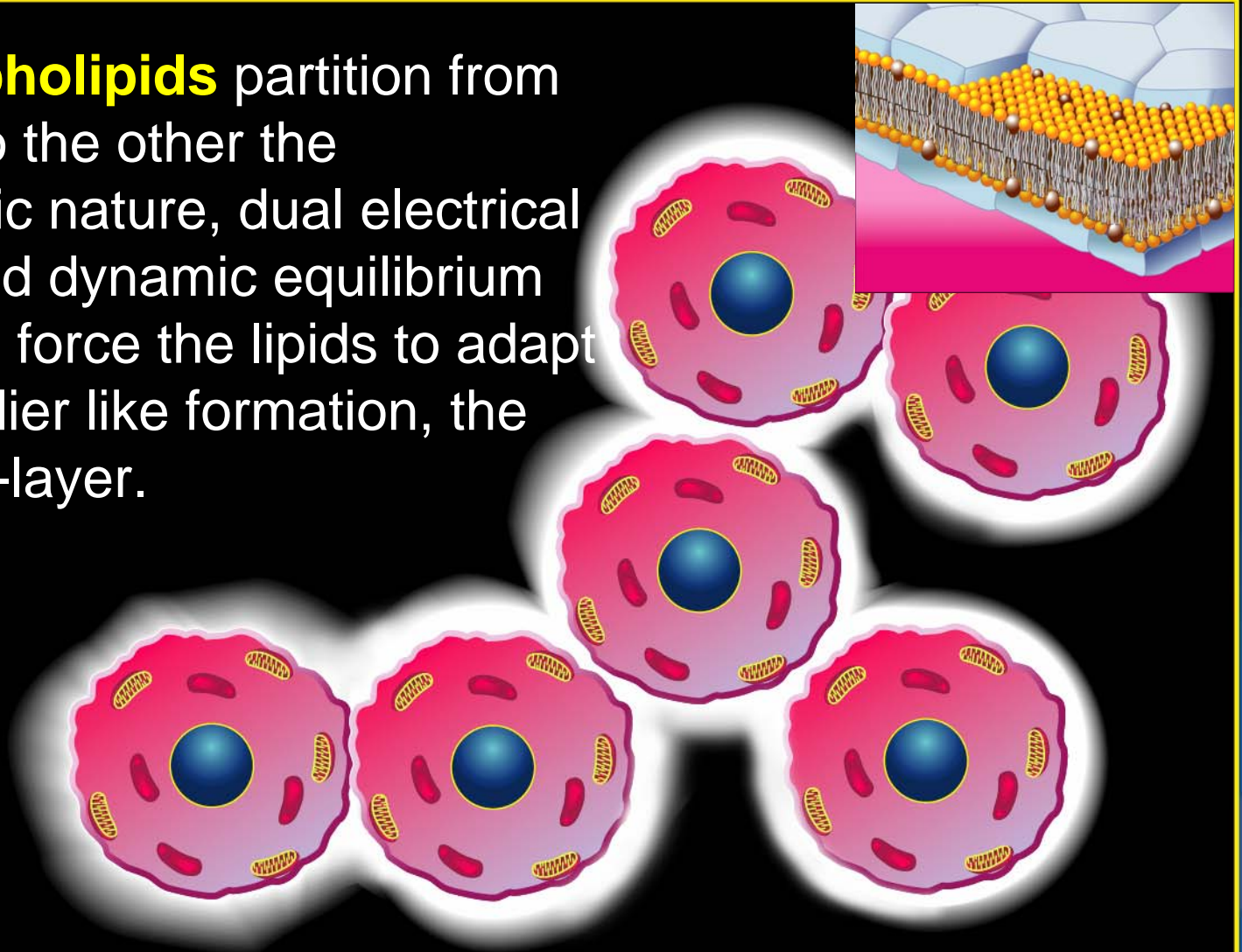
Phospholipids will partition to areas of lower concentration.



Phospholipids will
partition to areas of lower
concentration.



As **Phospholipids** partition from one cell to the other the amphiphilic nature, dual electrical charge and dynamic equilibrium properties force the lipids to adapt into a soldier like formation, the familiar bi-layer.



Validated & Proposed Clinical Uses of Lipid Replacement Therapy:

Fatigue-The most common medical complaint

**Anti-Aging-Restores mitochondrial function
and inhibits nuclear/mitochondrial mutations**

**Cytotoxic Therapy-Reduces drug/radiation
damage to normal tissues and membranes**

**Diabetes-Reduces ROS in mitochondria – the cause of
Insulin Resistance.**

Tissue Repair-Increases post-surgical healing

Validated & Proposed Clinical Uses of Lipid Replacement Therapy:

CardioVascular Disease – Restore aerobic metabolisms and alleviates ‘Energy Starvation’.




Neurodegenerative Disease-Reduces cell death /mitochondrial apoptosis, membrane damage

Chronic Infections-Reverses ROS damage to mitochondrial, nuclear and other membranes

Radiotherapy – Radiation therapy is dependent on aerobic metabolisms which LRT restores.

Lipid Metabolic Diseases-Lipid supplementation

NFACTOR[®] NUTRIENT COMPOUND COMPOSITION

-  **Phosphoglycolipids**
-  **Microencapsulated friendly bacteria**
-  **Growth media for friendly bacteria**

Phosphoglycolipids

A complex of
polyunsaturated
lipids extracted
from soy

Phosphoglycolipids

This group includes polyunsaturated phosphatidylcholine which are the principle lipids and structure of cell and mitochondrial membrane

Preclinical Results with NT Factor®

- NT Factor increased mitochondrial function in rat brains
- NT Factor decreased mtDNA deletions in some rat brain tissues (auditory nerve, stria vascularis)
- NT Factor significantly improved preservation of age-related auditory brainstem responses (ABR) in rats

Ref: Seidman, MD, et al. Otolaryngol Head & Neck Surgery 2002; 127:138-144

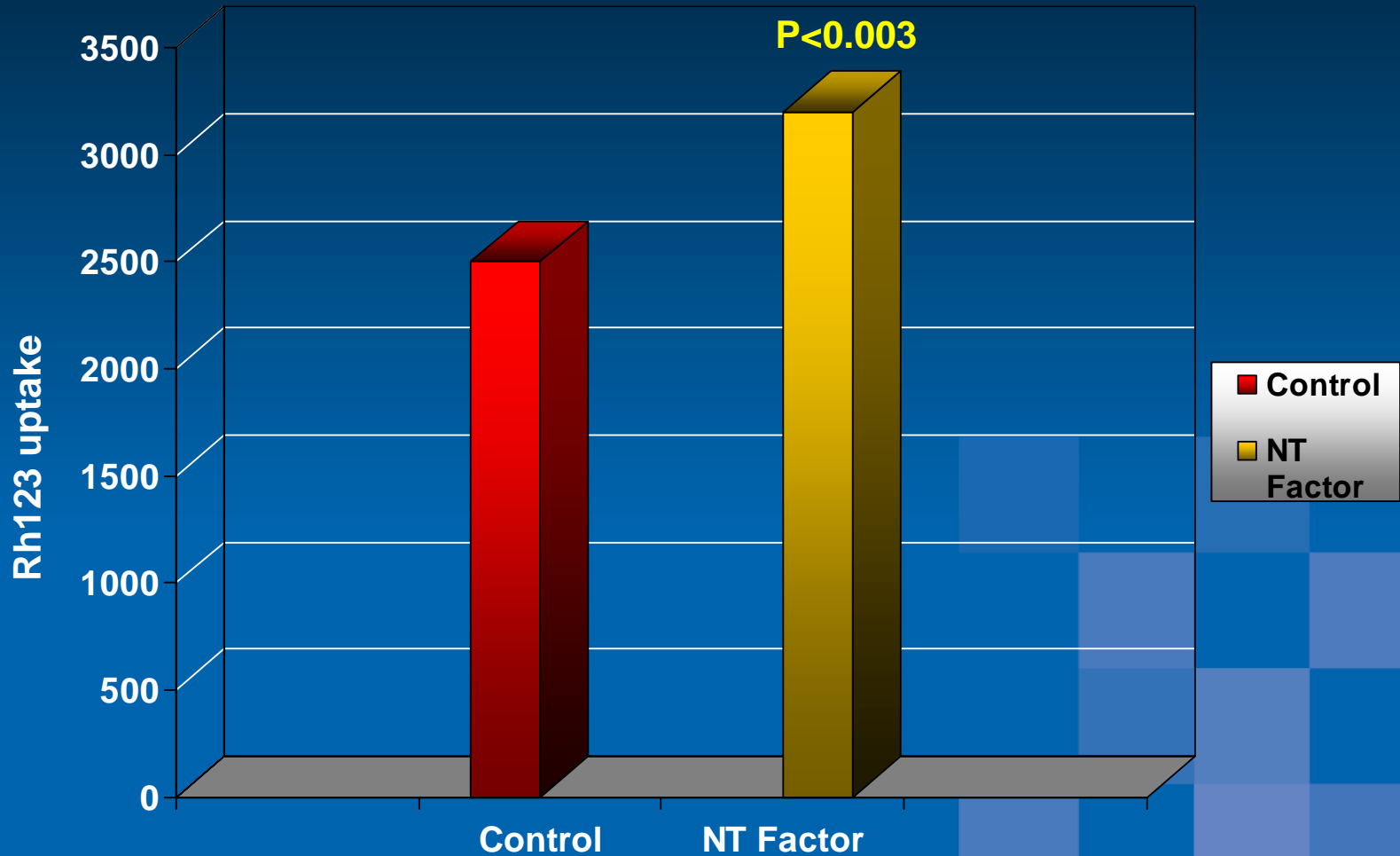
Animal Studies

Conducted at Henry Ford Hospitals, Bloomfield MI

Seidman M., Polyunsaturated Phosphatidylcholine in NT Factor Improves Mitochondrial Function, Auditory Sensitivity and May Slow Some Aspects of the Aging Process Anti-Aging Medical News 2001; Winter: 5,16,32,44

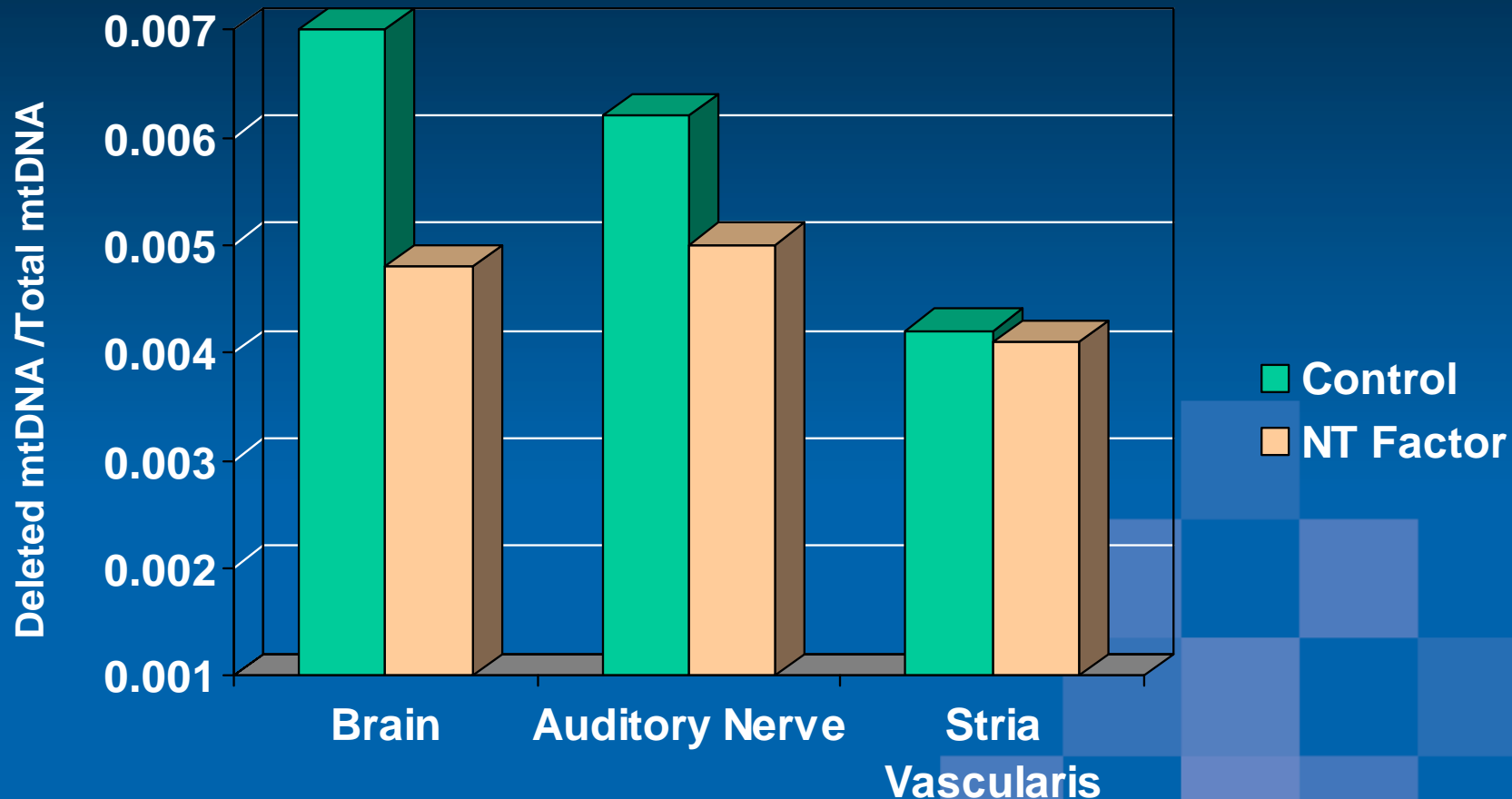
Seidman M., Khan M.J., Tang W.X., Quirk W.S., Influence of lecithin* on mitochondrial DNA and age-related hearing loss. Otolaryngol Head Neck Surg. 2002; 127:138-144
* [NT Factor ®]

Effects of Mitochondrial Function in Rats



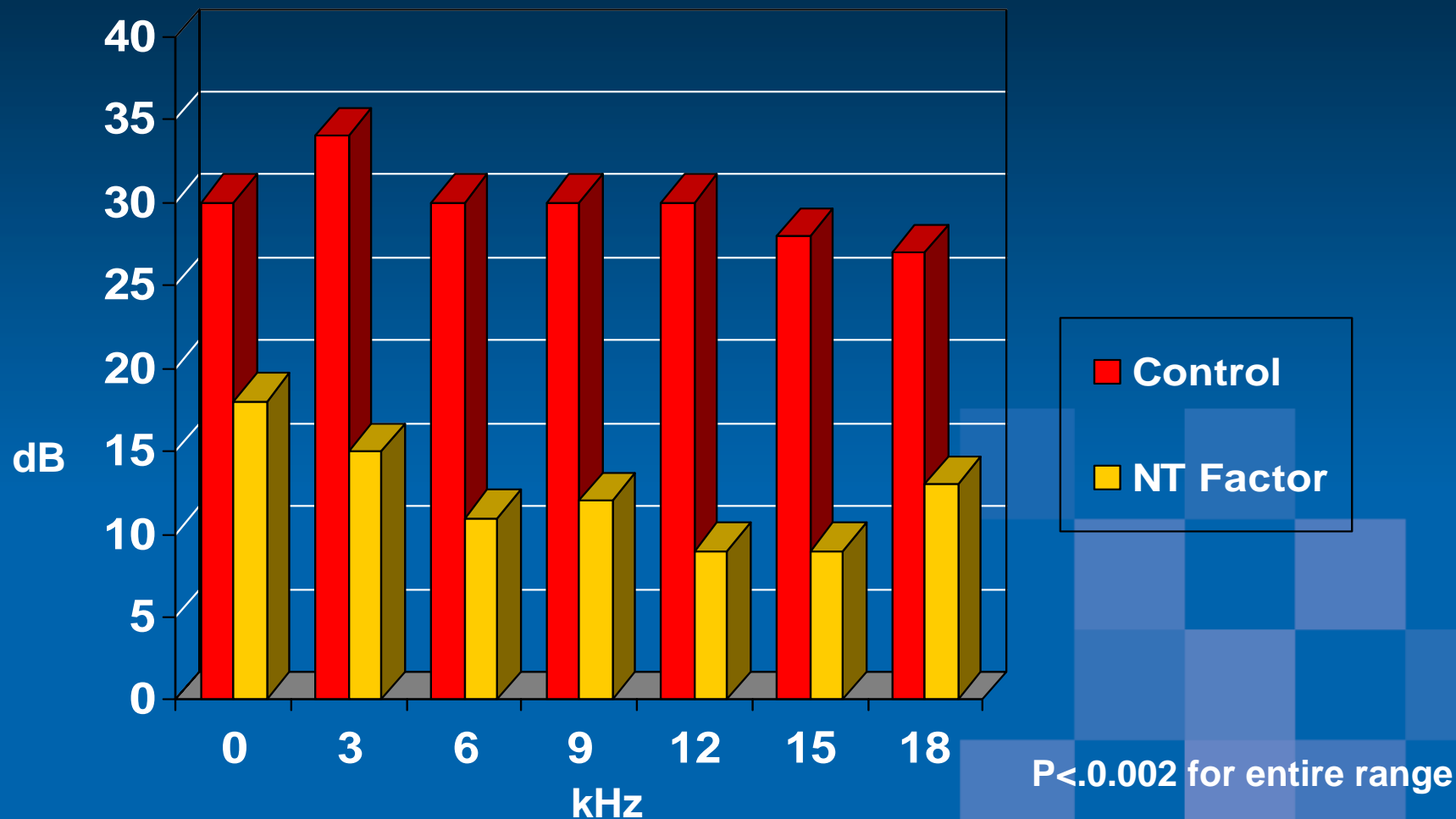
Ref: Seidman, MD, et al. Otolaryngol Head & Neck Surgery 2002; 127:138-144

Effects of NT Factor on mtDNA Deletions in Rat Brains



Ref: Seidman, MD, et al. Otolaryngol Head & Neck Surgery 2002; 127:138-144

Effects of NT Factor on Auditory Threshold (dB) In Rats: Preservation of Hearing Loss



Ref: Seidman, MD, et al. Otolaryngol Head & Neck Surgery 2002; 127:138-144

Conclusions From Pre-Clinical Publications

- *Polyunsaturated Phosphatidyl nutrients in NT Factor* preserves mitochondrial membrane potential and hence mitochondrial function
- *Polyunsaturated Phosphatidyl nutrients in NT Factor* appears to play a vital role in delaying the progression of age-related hearing loss

Clinical Trials

- **UCLA** – Multi Center Double Blinded, Placebo Controlled, Randomized Crossover to reduce the adverse , effects of cancer therapy, such as chemotherapy-induced fatigue, nausea, vomiting, malaise, diarrhea, headaches and other side effects.
- **Tustin Longevity Center, Institute of Molecular Medicine-** severe fatigue was reduced approximately 40.5% ($P < 0.0001$), to low moderate fatigue after eight weeks of supplementation with Lipid Replacement Therapy.
- **Institute of Molecular Medicine, UC Irvine** – Restored membrane potential and mitochondrial function in an aged population to levels normal for half a lifetime earlier. Reduced fatigue, protected cellular and mitochondrial membranes from damage by ROS.

- UCLA – Multi Center Double Blinded, Placebo Controlled, Randomized Crossover to reduce the adverse effects of cancer therapy.

- **Effects of Propax with NT Factor® on the adverse effects of chemotherapy in a cross-over trial†***

First Arm	Second Arm	<u>Average % patients on test supplement</u>		
		Improvement	No Change	worsening
Placebo	Propax w/NTFactor®	57	22	21
Propax w/NTFactor®	Placebo	70	6	24

† Data from; *Lipid replacement/antioxidant therapy as an adjunct supplement to reduce the adverse effects of cancer therapy and restore mitochondrial function*. Pathol Oncol Res. 2005;11(3):139-44. Epub 2005 Sep 29.

* The same regimen of 5-FU/methotrexate/leukovorin was used for colon, pancreatic or rectal cancers

§ The percent of patients reporting self adverse effects was averaged with the percent of patients with adverse effects reported by a research nurse.

Piper Fatigue Survey Scale

Study measurements

Fatigue Scoring

- Behavioral/severity
- Affective meaning
- Cognitive/mood
- Sensory

* Piper BF, et. al. *Oncol. Nurs. Forum.* 1998.

Piper Fatigue Survey Scale

Study Results: Clinical Trial-1

Fatigue Scoring

% Improvement

- Behavioral/Severity
- Affective Meaning
- Cognitive/Mood
- Sensory

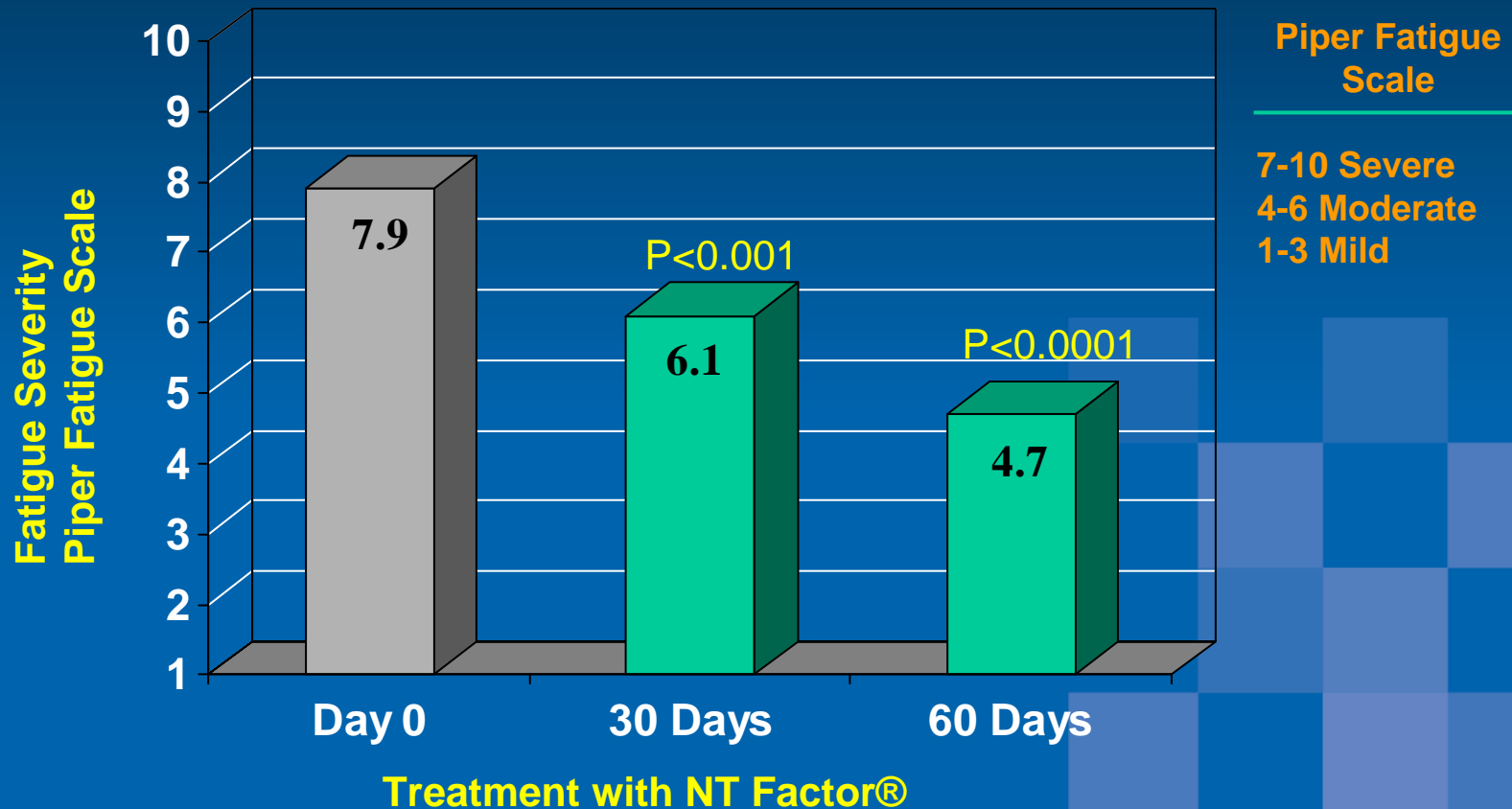
37

31

27

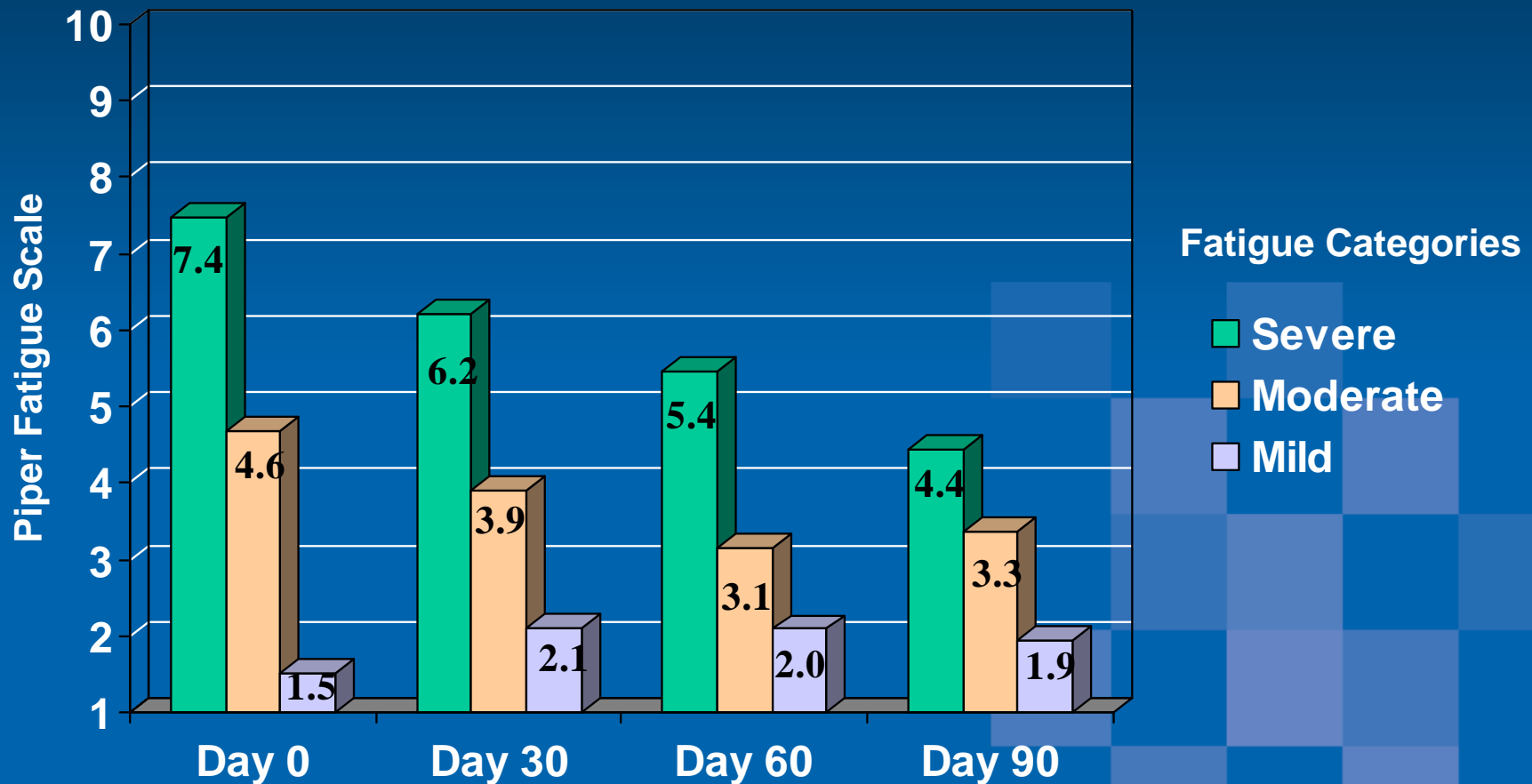
34

Tustin Longevity Center, Institute of Molecular Medicine- Severe Fatigue Reduced Approximately 40.5% ($P < 0.0001$ after Eight Weeks Of Supplementation With Lipid Replacement Therapy.



Institute of Molecular Medicine, UC Irvine – Restored membrane potential and mitochondrial function in an aged population to levels normal for half a lifetime earlier with corresponding reduction in fatigue.

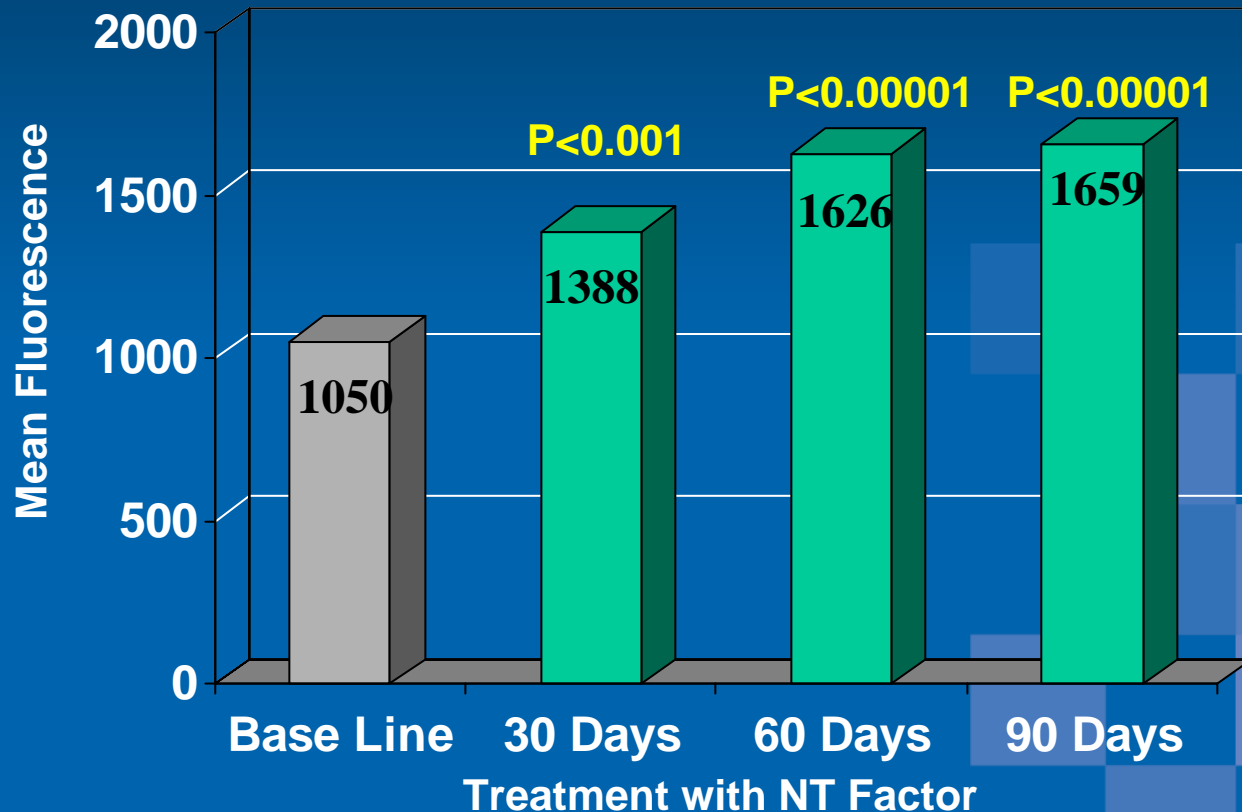
Effects of NT Factor on Fatigue Reduction Using Piper Fatigue Scale



Mitochondrial Function Assay

- Rhodamine 123 uptake into mitochondria and its subsequent fluorescence is a measure of mitochondrial function and membrane potential
- Mitochondria are isolated from the blood leukocytes of aged subjects and Rhodamine 123 is added; function is assessed by uptake and reduction of dye
- Changes in mean fluorescence intensity are recorded in replicate samples

Mitochondrial Function in Subjects Treated with NT Factor Determined by Uptake of 2uM Rh123



Mitochondrial Function Results

- NT Factor resulted in an average of ~40% increase in mitochondrial function using the Rhodamine 123 assay within a 60 day period.
- This was approximately the loss in mitochondrion output over the previous 40 years. Test population was 70 years of age average.
- Most subjects responded within 30 days to the NT Factor supplementation
- A washout period of 90 days resulted in a decline back to pre-NT Factor levels

Conclusions - NT Factor® Energy Can Restore Mitochondrial Function And Improve Fatigue Scores In Aging Human Subjects

- Reductions In Fatigue Paralleled Significant Gains In Mitochondrial Function.
- After Only Eight Weeks Of NT Factor, Mitochondrial Function Was Significantly Improved ($P < 0.001$).
- After Twelve Weeks Of NT Factor Use, Mitochondrial Function In Elderly (aver age 70) was Found To Be Similar To That Of Young, Healthy Adults (aver age 29)
- Continued Use Of NT Factor Is Probably Required To Maintain Lower Fatigue Scores And Improvements In Mitochondrial Function.