2019 ILADS Annual Scientific Conference

Abridged – Applicable to Numerous Indications

<u>A New Modality in Treating Disease</u>: Calibrated, <u>Ingestible</u>, Plant-Based <u>ESSENTIAL EFAs</u> Significantly Help Patients

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Focus: Improving Patient Outcomes With <u>Calibrated</u> <u>Lipid Formulation</u> of <u>Essential</u> <u>EFAs</u>

INCREASE:

- Immune Support
- Cellular Oxygenation
- Gut Integrity
- Blood Flow

Utilize State-of-the-Art Life-Sciences:

- Physiology
- Biochemistry

• Epigenetic Solutions – Applicable to all modalities as an Adjuvant w / NO Contraindications.

• State-of-the-art medical science many health professionals have not seen before

Ingestible <u>Plant-Based</u> <u>Essential EFA</u> Insight

LA (**Essentia**l EFA ω -6) and **ALA** (**Essential** EFA ω -3) are the **only 2** essential fats the **body can't synthesize**.

 ∞ -6 oils are <u>ALWAYS</u> <u>USED</u> for cooking / baking: <u>To increase shelf-life</u> ∞ -6 is <u>highly processed</u> / <u>adulterated</u>, <u>nonfunctional</u> (unless organic) :

> * *Trans*fat **Interesterifed* fat,

*Etc.

<u>
 ω-3 is Never Used</u> for cooking — far too reactive

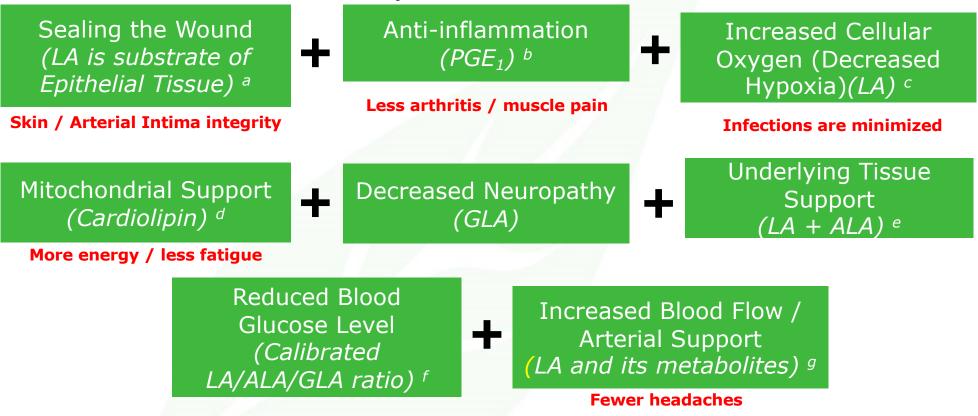
The Superiority of Plant-Based Essential EFA Seed Oils

- They MUST come from food LA is highly processed causing impaired functionality
- 100 TRILLION cells... Every cell's lipid portion contains 25% - 33% Essential EFAs.¹
- Mitochondrion (<u>cellular energy production</u>) 100s-1,000s in each cell — <u>cardiolipin is 100%</u> Essential Omega-6).¹

 ** 2017: "...[S]ecretory cells are <u>hypersensitive</u> to changes of their membrane lipids induced by the diet [Cells sense adulterated oils and respond with stress and chronic inflammation]."²

- Alberts, B., et al., Molecular Biology of the Cell (3rd edition), Garland Science, 1994, p 428; Murray, Robert K, et al., Harper's Illustrated Biochemistry (26th edition), McGraw-Hill, New York, 2003: p 97; Guyton, Arthur C & Hall, John E, Textbook of Medical Physiology (9th ed.), W.B. Saunders Co. 1996: 16, pp 861–862; Alberts, B., et al., Molecular Biology of the Cell (3rd edition), Garland Science, 1994, p 428; Murray, Robert K, et al., Harper's Illustrated Biochemistry (26th edition), McGraw-Hill, New York, 2003: p 97; Guyton, Arthur C & Hall, John E, Textbook of Medical Physiology (9th ed.), W.B. Saunders Co. 1996: 16, pp 861–862.
- 2. Halbleib, K., et al., "Activation of the Unfolded Protein Response by Lipid Bilayer Stress," Molecular Cell, Vol. 67, Issue 4, pp 673-684.e8, August 17, 2017.

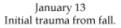
Critical Pathways w / Extensive References



- a. "Current results show that substituting ω-3 fatty acid [fish oil] for w-6 fatty acids in the diet is deleterious to the mechanical properties of wounds at 30 days." Ref.: Albina E et al. Detrimental effect of an ω-3 fatty-acid enriched diet on wound healing. J Parenter Enteral Nutr. 1993;17(6):519–521.
- b. Libby P. Inflammation in atherosclerosis. Nature. 2002 Dec 19–26;420(6917):868–874.
- c. Guo S, DiPietro LA. "Factors affecting wound healing." J Dent Res. 2010;89(3):219-229.
- d. Peskin BS. Cancer and mitochondrial defects: new 21st century research, Townsend Letter, August/September 2009:87–90; Murray RK et al. Harper's Illustrated Biochemistry. 26th ed. New York: McGraw-Hill; 2003:97; Guyton AC, Hall JE. Textbook of Medical Physiology. 9th ed. W.B. Saunders Co.; 1996:16,861–862; Krebs, JJ, Hauser H, Carafoli E, Asymmetric distribution of phospholipids in the inner membrane of beef heart mitochondria. J Biol Chem. 1979;254:5308–5316; Zhang M et al. Gluing the respiratory chain together: cardiolipin is required for supercomplex formation in the inner mitochondrial membrane. J Biol Chem. 2002;277:43553–43556.
- e. Alberts B et al. Molecular Biology of the Cell. 3rd ed. Garland Science; 1994:428.
- f. Asp ML et al. Time-dependent effects of safflower oil [LA] to improve glycemia, inflammation and blood lipids in obese, post-menopausal women with type 2 diabetes: A randomized, double-masked, crossover study. Clin Nutr. 2011 Aug;30(4):443–449.; Kahleova H et al. Vegetarian diet-induced increase in linoleic acid [LA] in serum phospholipids is associated with improved insulin sensitivity in subjects with type 2 diabetes. Nutr Diabetes 2013;3(6)e 75; Dutta-Roy A. Effect of evening primrose oil feeding on erythrocyte membrane properties in diabetes mellitus. In: Horrobin D, ed. Omega-6 Essential Fatty Acids: Pathophysiology and Roles in Clinical Medicine. New York: Wiley-Liss; 1990:505–511.
- g. Das UN. A defect in the activity of D6 and D5 desaturases may be a factor in the initiation and progression of atherosclerosis. Prostaglandins Leukot Essent Fatty Acids. 2007;76(5):251– 268; "[O]mega-6 PUFAs also have powerful anti-inflammatory properties that counteract any proinflammatory activity,' say the advisory authors. 'It's incorrect to view the omega-6 fatty acids as "proinflammatory."" Ref.: Farvid MS et al. Dietary linoleic acid [LA/ parent omega-6] and risk of coronary heart disease: a systematic review and meta-analysis of prospective cohort studies. Circulation. 2014;130:1568–1578; Terano T et al. Effect of oral administration of highly purified eicosapentaenoic acid on platelet function, blood viscosity and red cell deformability in healthy human subjects. Atherosclerosis. 1983;46:321–331.

Science Predicts Clinical Outcome ESSENTIAL EFA Healing Progression in Crushing Fall in <u>86-Year-Old Patient</u>







January 23 10 days after fall.



January 30 17 days after fall.

"This 86-year-old patient experienced a significant bilateral orbitofrontal and nasal crushing injury in a fall. She incurred the anticipated bilateral upper and mid-facial swelling and ecchymosis, but surprisingly had much less nasal injury than expected, including no fractured/comminuted nasal bones or orbital rim/floor fracture. Within 10 days, she

demonstrated remarkable resolution of the facial edema and bruising and guickly thereafter eliminated the remainder over the ensuing weeks. So not only did it seem that her facial soft tissues and bones were more resilient and the bones also not brittle. but her overall recovery was unusually expedited and uncomplicated."

Geoffrey L. Robb, M.D., F.A.C.S. Professor / Past Chairman (1998-2013) Department of Plastic Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX

DISEASE PATIENTS will benefit from Multiple Metabolic Pathways positively affected by Essential EFAs, responsible for this "remarkable" healing progression.



February 7 24 days after fall.



February 13 31 days after fall.



39 days after fall.

February 28 46 days after fall.



March 8 54 days after fall.

ESSENTIAL EFAs & Non-Essential EFAs — The Essential Difference

LA and ALA are the only 2 essential (body can't synthesize) fats.

Omega-6 (LA) – essential

Omega-3 (ALA) – essential

- DHA from fish oil is NOT an EFA <u>NOT essential</u> body makes AS NEEDED
- EPA from fish oil is NOT an EFA <u>NOT essential</u> body makes AS NEEDED

21st Century Newsflash: < 1% of Essential EFAs Converted into Derivatives ^{a,b,c}

Contrary to popular belief, your body <u>makes the derivatives AS NEEDED</u>, such as DHA and EPA, <u>with at least 99% staying in Essential EFA form</u>.

Fish oil supra-pharmacologic overdose of of 20x-500xs per day^b

* Brain uses only 7.2mg DHA / day **^b

- a. Salem N, Lin Y, Brenna JT, Pawlosky RJ. Alpha-linolenic acid conversion revisited. PUFA Newsletter, December 2003.
- b. Pawlosky RJ, Hibbeln JR, Novotny JA, Salem N Jr. Physiological compartmental analysis of alpha-linolenic acid metabolism in adult humans. *J Lipid Res* **2001**;42:1257-65
- c. Goyens PL, Spilker ME, Zock PL, Katan MB, Mensink RP. Conversion of alpha-linolenic acid in humans is influenced by the absolute amounts of alpha-linolenic acid and linoleic acid in the diet and not by their ratio. *Am J Clin Nutr* **2006**;84:44-53.

Fish Oil's EPA / DHA Impedes Healing

- "Current results show that <u>substituting ω-3 fatty acid</u>
 [fish oil] for ω-6 fatty acids in the diet is highly deleterious to the mechanical properties of wounds [impedes healing] at 30 days."¹
- Fish Oil's Horrific Inflammatory oxidation: "675% (6xs) increase in basal oxidation / 2624% (26xs) increase in auto-oxidation / 4244% (42xs) increase in iron-ascorbic catalyzed oxidation compared with omega-6."²
- <u>2018 Cochrane Systematic Reviews</u>: Fish Oil is Worthless in Preventing All CVD-Related Conditions.³
- Albina, JE, et al., "Detrimental Effect of an ω-3 Fatty–Acid Enriched Diet on Wound Healing," Journal of Parenteral and Enteral Nutrition, Vol. 17, No. 6, 1993, pages 519-521.
- 2. R.S. Meta, et al., "High fish oil diet increases oxidative stress potential in mammary gland of spontaneously hypertensive rats," Clin Exp Pharmacol Physiol. 1994 Nov;21(11):881-9.
- 3. cochranelibrary-wiley.com/doi/10.1002/14651858.CD003177.pub3/full

Fish Oil (EPA/DHA) DECREASES IMMUNITY ^{1,2} <u>Acts as Long-Term Steroid</u>

2006

• Fish Oil (EPA/DHA) Damages Cellular Mitochondria³

2018

 DHA From Fish Oil [Omega-3 DERIVATIVE] Ruins <u>Mitochondrial</u> <u>Cardiac Enzymes</u> (up to 50% decrease)⁴

- The International Society for the Study of Fatty Acids and Lipids (ISSFAL) 4th Congress, June 4-9, 2000 in Tsukuba, Japan, "Omega-3 Polyunsaturated Fatty Acids, Inflammation and Immunity," Philip Calder, Institute of Human Nutrition, University of Southampton, Bassett Crescent End, Southampton, UK.
- 2. © 2005 "Introducing The Body of Evidence," Reliant Pharmaceuticals, Inc. (September 2005), page 17.
- 3. Fantin, VR, et al., "Attenuation of LDH-A expression uncovers a link between glycolysis, mitochondrial physiology, and tumor maintenance. *Cancer Cell* 2006;9:425-434, Proc Natl. Acad. Sci. USA 87 1990.
- 4. Sullivan, E. Madison, et al., "Docosahexaenoic acid lowers cardiac mitochondrial enzyme activity by replacing linoleic acid in the phospholipidome," *Journal of Biological Chemistry*, **2018**, 293: 466-2018 Jan 12;293(2):466-483.

<u>2009 / 2014</u>: American Heart Association
 Champions Omega-6 to Counter Popular Nutritional Advice^{1,2}
 <u>"INCORRECT about LA and AA being inflammatory...</u>"

<u>2017 Confirmation</u>: Omega-6 <u>Beneficial, NOT HARMFUL³</u>

"<u>Omega-6 fatty acids do not promote low-grade inflam-</u> <u>mation</u>. The higher the serum linoleic acid [Essential Omega-6] level, the lower the CRP [inflammation]."

 AHA Heartwire 2009, © 2009 Medscape, January 28, 2009 (Dallas, Texas), based on *Journal of the American Heart Association*, Ref.: A Science Advisory From the American Heart Association Nutrition Subcommittee of the Council on Nutrition, Physical Activity, and Metabolism; Council on Cardiovascular Nursing; and Council on Epidemiology and Prevention, Harris WS, et al., "Omega-6 fatty acids and risk for cardiovascular disease," *Circulation*. 2009;119:902-907.

2. Farvid, M.S., et al., "Dietary Linoleic Acid [Parent omega-6] and Risk of Coronary Heart Disease: A Systematic Review and Meta-Analysis of Prospective Cohort Studies," *Circulation,* (on-line pre-publication) August 26, 2014, pages 1-22.

3. Virtanen, JK, et al., "The associations of serum n-6 polyunsaturated fatty acids with serum C-reactive protein in men: the Kuopio schaemic Heart Disease Risk Factor Study," European Journal of Clinical Nutrition, online accessed November 18, 2017, https://doi.org/10.1038/s41430-017-0.

Processed Essential Omega-6 Causes Decreased Cellular Oxygen^{1,2}

Essential Omega-6 = Cellular HBOT 24-hours-a day

Bacterial infections / mold spores) are microaerophilic — *die or rendered inactive in high oxygen* environments.³

1. Campbell, IM, et al., "Abnormal fatty acid composition and impaired oxygen supply in cystic fibrosis patients," *Pediatrics*, 57:480-486, 1976.

2. Anton SD, et al., "Differential effects of adulterated versus unadulterated forms of linoleic acid on cardiovascular health," *J Integr Med*, 2013; 11(1): 2–10.

3. Fife, Freeman, DM, Treatment of Lyme Disease with Hyperbaric Oxygen Therapy, 1998: http://archive.rubicon-foundation.org/xmlui/handle/123456789/654

Lipids are the #1 (Modifiable) Variable in Tissue Composition with Potential to Impact Healing^{1,2}

- 1. E. Wainwright, Y. S. Huang, et al., "The effects of dietary n-3/n-6 ratio on brain development in the mouse: a dose response study with long- chain n-3 fatty acids," *Lipids,* vol. 27, no. 2, pp. 98–103, 1992.
- 2. W. E. M. Lands, et al., "Quantitative effects of dietary polyunsaturated fats on the composition of fatty acids in rat tissues," *Lipids*, vol. 25, no. 9, pp. 505–516, 1990.

 ESSENTIAL Omega-6 is the #1 lipid functionally impaired by food processors to increase shelf-life.¹

Impairment of Fully Functional Essential Omega-6
 Lack of Oxygen = Chronic Fatigue.²

- 1. Anton SD, et al., "Differential effects of adulterated versus unadulterated forms of linoleic acid on cardiovascular health," *J Integr Med*, 2013; 11(1): 2–10.
- 2. Campbell, IM, et al., "Abnormal fatty acid composition and impaired oxygen supply in cystic fibrosis patients, Pediatrics, 57:480-486, 1976.

PATHWAY SUMMARY

- <u>PGE1</u> is body's most potent anti-inflammatory & bronchial / vasodilator.
- PGI2 (<u>Prostacyclin</u>) is body's natural "blood thinner." *

* S. Bunting, S. Moncada, and J.R. Vane, "Prostacyclin-Thromboxane A2 Balance: Pathophysiological and Therapeutic Implications," *British Medical Journal*, (1983), Vol. 39, No. 3, pages 271-276.

Crucial for Optimal Vascular Function

EICOSANOID PATHWAYS **Eicosanoids from Omega-6 Fatty Acids Omega-6 Fatty Acids PGE1** \leftarrow (20:3w6) DGLA \leftarrow Desaturase Elongase 20:4w6 (Archidonic Acid) Cyclooxygenase Lipoxygenase **Prostanoids: Thromboxanes** Leukotrienes: Lipoxins PGE₂ TXA₂ **5HPETE 12-HPETE** PGI₂ (prostacyclin) **5HETE 12-HETE** PGD₃ LTA₄ PGF series LTB_{A} $LTC_{\mathbf{\Lambda}}$ **Eicosanoids from Omega-3 Fatty Acids Omega-3 Fatty Acids** Desaturase Elongase 20:5w3 (Eicosapentaenoic Acid) Cyclooxygenase Lipoxygenase **Prostanoids: Thromboxanes** Leukotrienes: TXA₃ PGE₂ LTB5 LTC, D, E₂ PGI₃

<u>Mitochondrial Maximization</u> via Fully Functional Essential Omega-6's Cardiolipin (CL)^{1,2,3,4} <u>decreasing cancer risk, too</u>.⁵

- "...Our findings in mouse <u>brain</u> tumors provide evidence linking <u>abnormal CL to *irreversible respiratory injury*."
 </u>
- Impaired LA→Impaired CL →Insufficient cellular energy required for a strong immune system.
- Science Daily (January 14, 2009) and Kiebish MA, Han X, Cheng H, Chuang JH, Seyfried TN. "Cardiolipin and electron transport chain abnormalities in mouse brain tumor mitochondria: lipidomic evidence supporting the Warburg theory of cancer." *J Lipid Res* 2008;49:2545-66.
- 2. Krebs JJ, Hauser H, Carafoli E. Asymmetric distribution of phospholipids in the inner membrane of beef heart mitochondria. *J Biol Chem* 1979;254:5308-16.
- Scottish Crop Research Institute (MRS Lipid Analysis Unit, Invergowrie, Dundee DD2 5DA, Scotland). Cardiolipin (diphosphatidylglycerol). Structure, occurrence, biology and analysis. Retrieved January 20, 2009 from: <u>http://www.lipidlibrary</u>. co.uk/Lipids/dpg/index.htm.
- 4. "Oxygen uptake in mitochondria," *Journal of Experimental Biology* 2007; 210:i-ii. Ref.: Wittenberg, J. B. and Wittenberg, B. A. (2007). Myoglobin-enhanced oxygen delivery to isolated cardiac mitochondria. J. Exp. Biol. 210, 2082 -2090.
- 5. Warburg, O, "On the origin of cancer cells," Science, 1956 Feb 24;123(3191):309-14.

Digestive Tract Lining / Epithelial (Skin) / Arterial Intima Structure are both Essential Omega-6^{1,2}

"Leaky gut" syndrome is caused by this defect of functionally impaired Essential Omega-6. Many skin maladies are also caused by lack of fully functional Essential Omega-6.

- 1. Chapkin RS, Ziboh VA, Marcelo CL, Voorhees JJ. Metabolism of essential fatty acids by human epidermal enzyme preparations: evidence of chain elongation. J Lipid Res 1986; 27:945-954.
- 2. Andersson A, Sjödin A, Hedman A, Olsson R, Vessby B. Fatty acid profile of skeletal muscle phospholipids in trained and untrained young men. AmJ Physiol Endocrinol Metab 2000;279:E744-E751.

Oxidized Essential Omega-6 from food,¹ causes cellular toxicity assault.²

1% oxidized Essential Omega-6 consumption

100,000-fold / cell toxicity assault

** healing becomes impaired / impossible **

- Staprãns, I, et al., "Oxidized cholesterol in the diet is a source of oxidized lipoproteins in human serum," *J. Lipid Res.* 2003. 44: 705–715; "Consumption of oxidized PUFA-cholesterol esters [LA] seems to be responsible for the initial damage to endothelial cells [inner arterial lining, i.e., intima]." Ref.: Spiteller G, "Peroxyl radicals: Inductors of neurodegenerative and other inflammatory diseases. Their origin and how they transform cholesterol, phospholipids, plasmalogens, polyunsaturated fatty acids, sugars, and proteins into deleterious products," *Free Radical Biol Med*, 2006;41:362.
- 2. The molecular weight of a triglyceride (any EFA-containing oil; good or bad) is approximately 1,000. A liter (quart) of oil contains approximately 1,000 grams (about 2 pounds), and from chemistry a mole (gm molecular weight) of any substance contains about 6 x 10²³ molecules. Therefore, there is a mole of triglycerides in a liter of cooking oil. There are 64 Tablespoons per liter—approximately 100 tablespoons (instead of 64) per liter to keep it easy to calculate, yet get the point across. Therefore, there are on the order of 10²¹ per Tablespoon (10²³ molecules per 100 Tbl.= 10²¹ molecules). Just a 1% defective amount is therefore (1/100) or 10¹⁹ defective molecules. [The body contains about 100 trillion cells (10¹⁴ cells).] Overload = 10^(19/14) = 100,000 nonfunctional EFAs overwhelming each cell.

Remarkable Cardiovascular Clinical Improvement with Essential EFAs

2008: "I previously wrote you about the remarkable **cause / effect** relationship in **reversing plaque** volume in a (smoking) patient taking conventional treatment (i.e. statins, aspirin, Co-Q10, etc.). In reading over [the patient's] scans I have never seen such a remarkable result.

"When he [the patient] stopped the Essential EFAs the plaque came back.

"As you can see, for the first time from 2007 to 2008, the volume of **plaque** decreased from 39 to 30, which is a **decrease of 22% when annualized on a yearly basis**. I have never seen a decrease of coronary **artery plaque volume by more than 5% in one year**."



Robert Kagan, MD Radiologist, USA

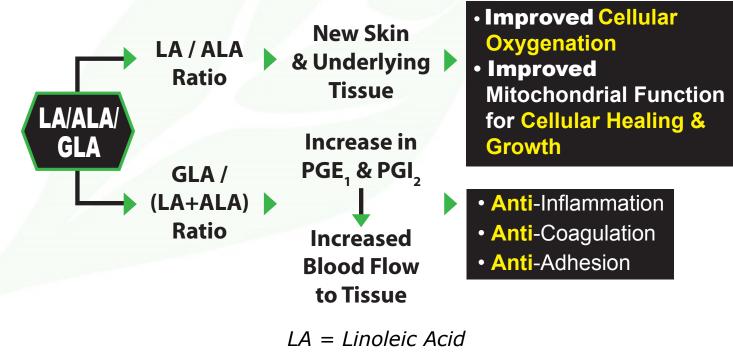
Former Chairman of the Board of Nuclear Medicine Resource Committee of the College of American Pathologists / Past President of the Florida Association of Nuclear Physicians / President Clinton appointee as the sole physician commissioner on the White House Fellowship Commission



Requirements for Effectively Treating Infections and a Helpful Adjuvant in Numerous Chronic Conditions

Utilizing Novel Dual Mechanisms of Action

Multiple Key Metabolic Pathways Maximized Simultaneously



ALA = Alpha-Linolenic Acid GLA = Gamma-Linolenic Acid

Plant-Based Seed Oils (Essential EFAs) Are a Significant **Adjuvant Helpful in Treating Many Chronic Conditions to** Name a Few.....

- ANTI-DIABETES ¹
- ANTI-AGING²
- REDUCED CANCER Risk ³
- LESS DEMENTIA (vascular-capillaries) ⁴
- LESS Cardiovascular Disease ⁵

Karlström, BE, et al., "Fatty fish in the diet of patients with type 2 diabetes: comparison of the metabolic effects of foods rich in n-3 and n-6 fatty acids," Am J Clin Nutr 2011;94:26-33.

O'Rourke, Eyleen, J., et al., ω-6 Polyunsaturated fatty acids extend life span through the activation of autophagy," *Genes & Development* (2013). Published in advance February 7, 2013, http:// genesdev.cshlp.org/content/27/4/429.full. Brasky, Theodore, M., et al., "Plasma Phospholipid Fatty Acids and Prostate Cancer Risk in the SELECT Trial," *Journal of the National Cancer Institute*, Vol. 105,

No. 15, 2013, pp. 1132–1141.

[&]quot;Low Plasma N-3 Fatty Acids and Dementia in Older Persons: The InCHIANTI Study, *J Gerontol A Biol Sci Med Sci.* 2007 October; 62(10): 1120–1126. Das, U.N., "A defect in the activity of D6 and D5 desaturases may be a factor in the initiation and progression of atherosclerosis," *Prostaglandins, Leukotrienes and Essential Fatty Acids*, 76 (2007) 251-268.



Requirements for LYME Disease Healing?

Essential EFAs Organically

grown and processed seed oils

Essential Omega-6/-3 Ratio REQUIRED 2.5:1 – 1:1
 Omega-6 Derivative GLA REQUIRED

- High linoleic (LA) REQUIRED with minimum oleic content
- Hard gel cap
- NO fish oil / NO Borage oil
- P-Anisidine (Secondary Aldehyde) <6.0 <u>Note</u>: P-A values of even pristine fish oil's EPA/DHA are approx. 19.0 (borderline toxic)

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