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INTERPRETIVE GUIDE

FAp - Fatty Acids Profile™

Our mission: to deliver innovative, accurate and clinically relevant diagnostic testing in a timely and cost-effective manner



FATTY ACIDS PROFILE



FIRST OF ALL
THANK YOU
FOR CONSIDERING US!

“At Diagnostic Solutions Laboratory, we’re not content with the range of clinical testing currently available to practitioners. We believe that every patient should achieve optimal health, and we’re driven to give clinicians the tools to do so. Our mission, therefore, is to use our resources to bring the most advanced, innovative, and clinically relevant testing to healthcare providers worldwide.”

Tony Hoffman
CEO

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INTRODUCTION

Fatty acids (FAs) are major constituents of lipids and play essential roles in the diverse biological functions of the human body. They are key components of the cell membrane, provide an essential source of cellular fuel and energy storage, and are involved in critical signal transduction pathways.

Fatty acids are classified based on their chemical structure, number and position of double bonds, and number of carbons in their chain.

- Saturated FA (SFA):
no double bonds
- Monounsaturated FA (MUFA):
one double bond
- Polyunsaturated FA (PUFA):
more than one double bond
- Short chain (SCFA): < 6 carbons
- Medium chain (MCFA):
6–12 carbons
- Long chain (LCFA): 14–20 carbons
- Very long chain (VLCFA):
> 20 carbons

Fatty acids come both from diet and endogenous production. Composition of dietary fats contributes to levels of plasma fatty acids. Endogenous production depends on fatty acid synthase, elongation, and desaturation enzymes.

There are 2 essential fatty acids, meaning they must be obtained through the diet and cannot be synthesized in the human body. These essential fatty acids are:

- Alpha-linolenic (ALA) — precursor to omega-3, also known as 18:3n3
- Linoleic acid (LA) — precursor to omega-6, also known as 18:2n6

Beyond the essential fatty acids, the body can synthesize all other fatty acids endogenously using the essential fatty acids as precursors. This happens via **desaturation and elongation reactions**. Desaturation reactions add double bonds, while elongation reactions add carbons to the chain. Fatty acids up to 16 carbons (C16) in length are produced by fatty acid synthases (FASs), while fatty acids beyond C16 use elongase enzymes. Fatty acid desaturases (also called unsaturases) add double bonds to the fatty acid carbon chain and convert saturated fatty acids into unsaturated fatty acids and polyunsaturated fatty acids.



HOW TO READ THE REPORT



QUANTIFYING FATTY ACID VALUES

Individual fatty acids are measured in plasma and reported as **quantitative** values. Plasma fatty acids are understood to reflect consumption through the diet and supplementation of short-term dietary fat intake, over the previous weeks/months.¹ Totals, ratios, and enzyme activities are calculated from the individual fatty acids within the report.

STATISTICAL REFERENCE RANGES

Reference ranges are based on statistical distribution. By convention, 95% of results fall within the normal range, and the outer 5% are considered clinically significant outliers. When both very high and very low values are clinically relevant, a **two-tailed model** is used.

- The lowest 2.5% of results represent the bottom reference limit (≤ 2.5 th percentile)
- The highest 2.5% represents the upper reference limit (≥ 97.5 th percentile)

When only one direction of change is considered clinically significant (e.g., only high levels or only low levels are a concern). This is called a **one-tailed model**, in which the full 5% cutoff is applied only to the high end (≥ 95 th percentile) or low end (≤ 5 th percentile) depending on the clinical interpretation.

Values just outside the normal range but not within the clinically significant tails are classified as borderline. These typically include the 10th–20th percentiles on the low end and the 80th–90th percentiles on the high end.

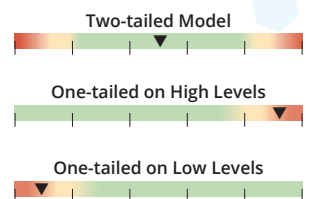


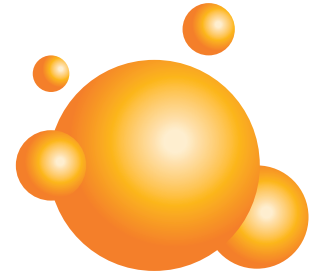
Figure 1. Reference models.

FATTY ACID LEVELS

Plasma concentrations of fatty acids are largely influenced by dietary intake and supplementation, along with fatty acid metabolism and adipose tissue activity. Always consider food sources and supplementation first line to correct levels of fatty acid imbalances.



SATURATED FATTY ACIDS



Saturated fatty acids (SFA) contain no double bonds in their carbon chain, which makes them structurally stable and solid at room temperature. They are found primarily in animal products such as red meat, butter, and full-fat dairy, but also in tropical oils like coconut and palm.

SFAs provide a dense source of energy and play essential roles in membrane structure and cell signaling. Their health effects are complex and depend on the specific type of SFA, the food matrix, and overall dietary and lifestyle patterns.

TOTAL SATURATED FATTY ACIDS (SFA)

Levels are highly impacted by dietary composition and enzyme functionality.

For all HIGH or LOW levels, examine intake from dietary sources and adjust accordingly. Consider the quantities of individual SFAs as some saturated fatty acids have better evidence and correlations with health outcomes than others. Eight saturated fatty acids are tested, and six are reported on the FAp.

- High levels: Mixed evidence
- Low levels: Monitor total intake of dietary fat

MARKER	IMPLICATIONS/EVIDENCE	FOOD SOURCES ⁴⁻⁶
Myristic 14:00	<ul style="list-style-type: none"> • Myristic acid levels have been positively associated with cancer risk.^{3,7} • Negative associations have been observed between dietary myristic acid and the risk of type 2 diabetes.⁸ 	<ul style="list-style-type: none"> • Palm kernel oil • Coconut oil • Butter • High fat dairy (cheese, cream) • Some red meat (beef)
Palmitic 16:00	<ul style="list-style-type: none"> • The most common saturated fatty acid in diet. • Palmitic acid intake and elevated levels increase cholesterol fractions more than other saturated fatty acids.⁹ Elevated blood levels are positively associated with risk for cardiovascular disease and ischemic heart disease.⁹ • Higher levels linked to increased cancer risk.³ • Lower levels of palmitic acid are seen in conjunction with lowering saturated fat in the diet and are associated with improved clinical outcomes such as lower LDL-C and blood glucose.⁹ • Palmitic acid is converted to steric acid by ELOVL6 enzyme. 	<ul style="list-style-type: none"> • Palm oil (processed foods with palm oil) • Butter • Red meat (beef, pork, lamb) • High-fat dairy (cheese, cream, milk) • Salmon • Egg yolks • Cocoa butter



MARKER	IMPLICATIONS/EVIDENCE	FOOD SOURCES ⁴⁻⁶
Stearic 18:00	<ul style="list-style-type: none"> Higher levels of stearic acid and intracellular accumulation can be proinflammatory and lipotoxic.⁹ Elevated blood levels of stearic acid are correlated with frailty index¹⁰ and have been linked to increased cancer risk.³ Stearic acid is converted to Arachidic acid by ELOVL1,3,7.¹¹ Higher levels have been associated with increased HbA1c.¹² 	<ul style="list-style-type: none"> Cocoa butter Red meat (beef and lamb) Butter Egg yolk Some dairy
Arachidic 20:00	<ul style="list-style-type: none"> Arachidic acid is converted to docosanoic acid by ELOVL1,3,7. 	<ul style="list-style-type: none"> Present in very small amounts in the diet Peanuts/peanut oil richest dietary sources Canola oil Some nuts, including macadamia (trace) Cocoa butter Corn oil
Docosanoic 22:00	<ul style="list-style-type: none"> Very long chain saturated fatty acid (VLSFA). Also known as behenic acid. Increased with higher total and saturated fat intake and nut intake.² Large studies have shown that higher levels of 22:0 are associated with lower incidence of type 2 diabetes and cardiovascular disease, and decreased mortality.² Circulating levels of 22:0 may have a protective effect against the risk of depression and have been associated with reduced cognitive decline.^{6,13} Docosanoic acid is converted to lignoceric acid by ELOVL1,3,7. 	<ul style="list-style-type: none"> Present in very small amounts in the diet Peanuts/peanut oil Canola oil Sunflower oil Macadamia nuts (trace)
Lignoceric 24:00	<ul style="list-style-type: none"> Very long chain saturated fatty acid (VLSFA). Increased with higher total and saturated fat intake and nut intake. Associated with a lower incidence of type 2 diabetes and cardiovascular diseases.² Circulating levels of 24:0 and total VLSFAs may have a protective effect against the risk of depression⁶ and have been associated with reduced cognitive decline.¹³ 	<ul style="list-style-type: none"> Present in very small amounts in the diet Peanuts/peanut oil Corn oil Cocoa butter Some nuts and seeds (trace)

Historical evidence has linked certain SFAs to adverse cardiometabolic outcomes and dyslipidemias. However, recent studies have shown that certain very long chain saturated fatty acids (VLSFAs) may be linked with positive cardiometabolic and mental health outcomes at higher levels.² Increased total SFA levels have been correlated with higher risks of breast, prostate, and colorectal cancers, but not with lung, pancreatic, ovarian, or stomach cancers.³

Emerging evidence suggests that SFAs from whole foods (e.g. dairy) may have different cardiometabolic effects compared to those from processed foods. Thus, the impact of SFAs on health is nuanced, and context—including dietary balance, lifestyle, and metabolic status—plays a critical role in determining risk or benefit.



MONOSATURATED FATTY ACIDS



Monosaturated Fatty Acids (MUFAs) are fatty acids that contain a single double bond in their carbon chain.

They are abundant in foods such as olive oil, avocados, nuts, and certain animal fats. They are often touted as a cornerstone of heart-healthy diets such as the Mediterranean diet.

MUFAs are involved in many physiological processes in the human body including energy metabolism, lipid biosynthesis, the maintenance of membrane integrity, antioxidant reactions, apoptosis, and aging. They are generally associated with beneficial effects including improvements in lipid profiles, insulin sensitivity, improved longevity, and cardiovascular health outcomes.¹⁴ There are even positive correlations with higher levels of MUFAs and changes in gut microbiota populations with increased production of butyrate-producing species.¹⁵ However, not all MUFAs are associated with the same physiological outcomes.

Certain MUFAs, when elevated in circulation, may reflect metabolic dysfunction, increased risk for insulin resistance, and even certain cancers.³



TOTAL MONOSATURATED FATTY ACIDS (MUFA)

Levels are highly impacted by dietary composition and enzyme functionality. For all HIGH or LOW levels, examine intake from dietary and supplement sources and adjust accordingly. Consider the quantities of individual MUFAs as some fatty acids have more evidence and better correlations with positive health outcomes than others. Seven monounsaturated fatty acids are tested, and four are reported on the FAP.

MARKER	IMPLICATIONS/EVIDENCE	FOOD SOURCES ⁴⁻⁵
Palmitoleic 16:1n7	<ul style="list-style-type: none"> Palmitoleic acid blood levels are significantly and positively correlated with percentage of body fat.¹⁶ 	<ul style="list-style-type: none"> Macadamia nuts Sea buckhorn berries/oil Oily fish (salmon, mackerel, anchovies, sardines) Avocado oil Dairy products
Vaccenic 18:1n7	<ul style="list-style-type: none"> Higher levels have been associated with increased HbA1c¹⁶ although research suggests a bidirectional etiology associated with diabetes risk.^{17,18} 	<ul style="list-style-type: none"> Dairy, particularly grass-fed dairy (butter, milk, cheese) Grass-fed beef and lamb fat
Oleic 18:1n9	<ul style="list-style-type: none"> Also called stearyl CoA. The major fatty acid in mammalian adipose triglycerides and is also used for phospholipid and cholesteryl ester synthesis. Produced from the saturated fat stearic acid (18:00) by delta-9-desaturase enzyme. The ratio of oleic acid to stearic acid is used to calculate delta-9-desaturase enzyme activity reported on this test. Higher levels are generally associated with better health and lower diabetes risk.¹⁶ 	<ul style="list-style-type: none"> Olive oil is largest dietary source Avocado/avocado oil Canola oil Sunflower oil Almonds, hazelnuts, macadamia nuts, pecan (nuts and oils)
Eicosenoic 20:1n9	<ul style="list-style-type: none"> Also called gondoic acid. 	<ul style="list-style-type: none"> Plant oils Nuts Jojoba oil



POLYUNSATURATED FATTY ACIDS: OMEGA-3 & OMEGA-6

When two or more double bonds are present, fatty acids are classified as polyunsaturated fatty acids (PUFAs). PUFAs are especially important because they:

- Modulate immune and inflammatory reactions
- Influence gene expression and cell signaling
- Are essential structural components of cell membranes¹⁹⁻²¹

There are two main families of PUFAs:

- Omega-3 (n-3)
- Omega-6 (n-6)

The dietary essential fatty acids serve as the entry points:

- Alpha-linolenic acid (ALA, 18:3n3) → omega-3 pathway
- Linoleic acid (LA, 18:2n6) → omega-6 pathway

These are converted into longer chain, more unsaturated derivatives through Delta-6-desaturase, elongase, and Delta-5-desaturase steps.



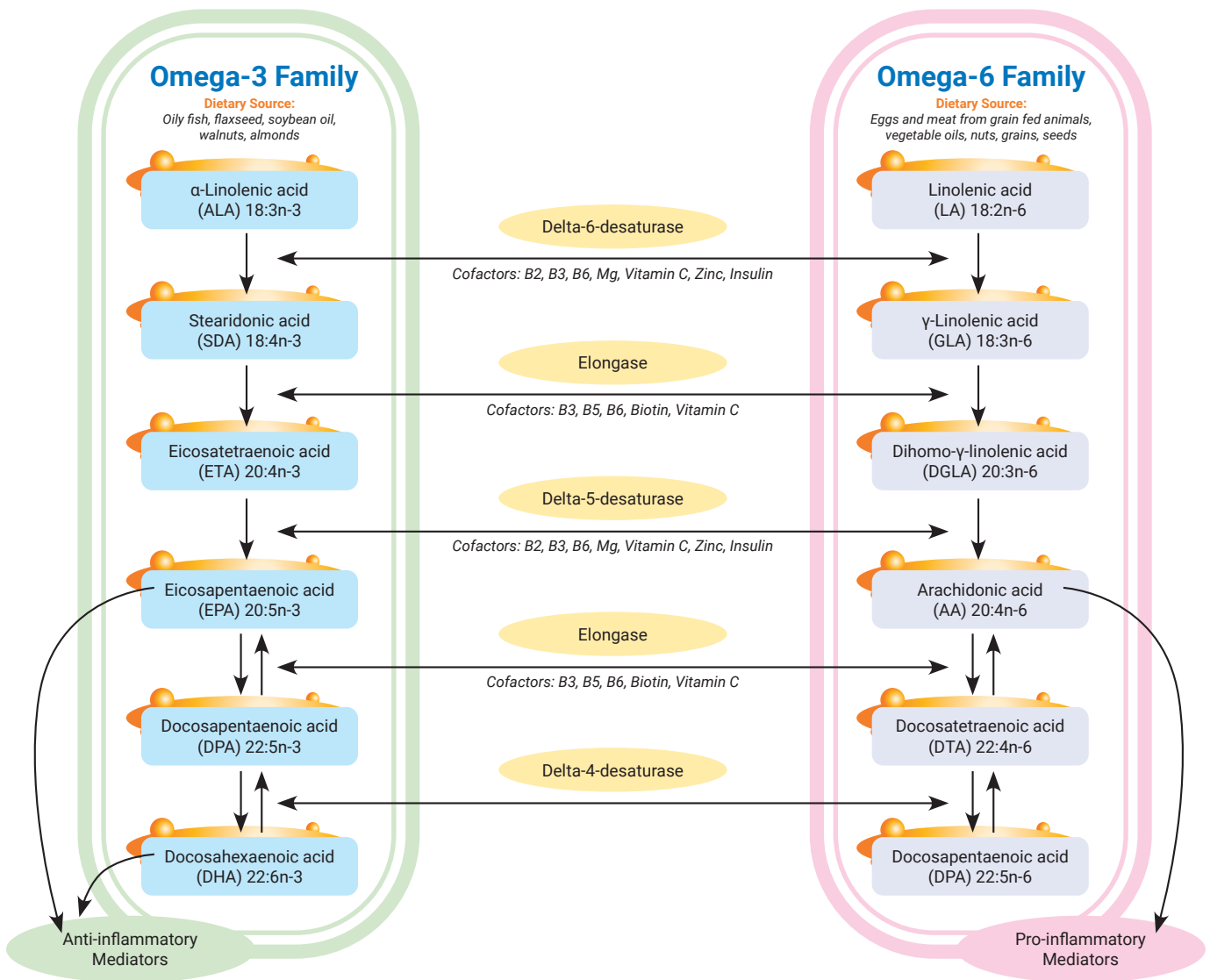


Figure Adapted From²²

Figure 2. PUFA Fatty Acid Metabolism

- Biological mediators are synthesized from omega-3 and omega-6 polyunsaturated fatty acids (PUFAs).
- The conversion of precursor omega-3 and omega-6 PUFA to their respective derivatives is catalyzed by desaturase and elongase enzymes in the presence of appropriate cofactors.
- Anti-inflammatory mediators are derived from EPA and DHA.
- Pro-inflammatory mediators are derived from arachidonic acid (AA).

PUFA PATHWAYS AND PRODUCTS

- **Omega-3 Pathway:**

ALA → stearidonic acid → eicosatetraenoic acid → eicosapentaenoic acid (EPA) → docosahexaenoic acid (DHA)

- » EPA and DHA are precursors for series-3 prostaglandins, series-5 leukotrienes, resolvins, protectins, and maresins — molecules with **anti-inflammatory and inflammation-resolving properties**, often referred to as **pro-resolving mediators**.

SPECIALIZED PRO-RESOLVING MEDIATORS (SPMs)

SPMs (resolvins, protectins, maresins) are bioactive lipid molecules derived primarily from EPA and DHA. They actively resolve inflammation, regulate immune cell activity, and promote tissue healing and regeneration. Thus, omega-3 fatty acids are important not just for preventing inflammation, but for completing the inflammatory cycle and returning tissues to balance (homeostasis).

- **Omega-6 Pathway:**

LA → γ-linolenic acid (GLA) → dihomo-γ-linolenic acid (DGLA) → arachidonic acid (AA)

- » AA is the precursor for series-2 prostaglandins, thromboxanes, and series-4 leukotrienes, generally **pro-inflammatory mediators**.

OMEGA-3 ENZYME COMPETITION

Because the same desaturation and elongation enzymes act on both omega-3 and omega-6 substrates, there is direct **competition** within these pathways.

- A high omega-6 to omega-3 ratio, typical of Western diets, favors AA-derived, pro-inflammatory mediators.
- Adequate omega-3 intake (fish, seafood, algae oils) shifts metabolism toward EPA/DHA and **anti-inflammatory production of pro-resolving mediators**.

Cofactors such as zinc, magnesium, and B vitamins are required for optimal desaturase and elongase activity. Deficiencies in these cofactors can impair conversion efficiency.



OMEGA-3 POLYUNSATURATED FATTY ACIDS

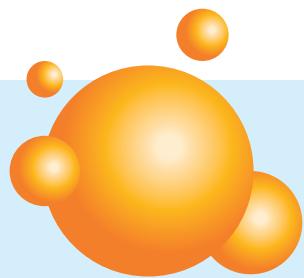
Higher levels of omega-3 fatty acids are generally favorable and associated with reduced risk of all-cause mortality.²⁵ Omega-3 fatty acids have been associated with lower rates of CVD, diabetes, Alzheimer's, mood disorders, MAFLD, brain function, skin health etc.²⁶⁻²⁸

MARKER & DESCRIPTION	IF HIGH	IF LOW	FOOD SOURCES ^{4-5,23-25}
<p>Total Omega-3 Fatty Acids</p> <ul style="list-style-type: none"> Total of all omega-3 fatty acids measured: ALA, EPA, DPA, DHA. Omega-3 fatty acids are converted to bioactive mediators, termed specialized pro-resolving mediators (SPM), that can limit inflammation. 	<ul style="list-style-type: none"> Evaluate diet changes or supplementation. Check omega-6/omega-3 ratio. 	<ul style="list-style-type: none"> Referred to as Total Omega-3 Insufficiency (low ALA, EPA or DHA with normal AA). Evaluate levels of individual fatty acids: ALA, EPA, DPA, DHA. Evaluate levels of omega-6 fatty acids and omega-6/omega-3 ratio. Consider diet changes or supplementation. 	<ul style="list-style-type: none"> EPA & DHA-rich foods: <ul style="list-style-type: none"> » Salmon, mackerel, and sardines ALA-rich foods include plant sources: <ul style="list-style-type: none"> » Flaxseeds, chia seeds, and walnuts ALA can be converted to EPA and DHA, though conversion rates can be low in some people, so a diet rich in EPA and DHA is typically advised.
<p>Alpha-Linolenic α-linolenic acid (ALA) 18:3n3</p> <ul style="list-style-type: none"> One of two essential fatty acids. ALA can convert to EPA, DPA, and DHA but the conversion is limited. ALA conversion to EPA depends on delta-6-desaturase + zinc, B2, B3, B6, vitamin C, Mg. 	<ul style="list-style-type: none"> Higher ALA levels are associated with reduced risk of mortality from all causes and cardiovascular disease. ALA regulates blood lipids, reduces blood viscosity, lowers blood pressure, suppresses allergic reactions, and inhibits inflammation. A high ALA with low EPA or DHA may be a desaturase enzyme issue. <ul style="list-style-type: none"> » Elevated omega-6 fatty acids may decrease the conversion. » Check delta-6-desaturase enzyme cofactors: zinc, B3, B6, vitamin C, Mg. 	<ul style="list-style-type: none"> Inadequate ALA is associated with inadequate intake. Increase food sources. High dietary LA intake, typical for the modern Western-type dietary pattern, can reduce the conversion rate of ALA. 	<ul style="list-style-type: none"> Flaxseeds Chia seeds Walnuts Soybean Nuts Canola oil



OMEGA-3 POLYUNSATURATED FATTY ACIDS

MARKER & DESCRIPTION	IF HIGH	IF LOW	FOOD SOURCES ^{4-5,23-25}
<p>Eicosapentaenoic (EPA) 20:5n3</p> <ul style="list-style-type: none"> EPA is an intermediate polyunsaturated fatty acid made from ALA by desaturation and elongation reactions and competes with AA for these enzymes. EPA produces anti-inflammatory and anti-aggregatory metabolites. Produces SPM. Known to reduce blood clotting, pain and swelling, triglycerides, blood pressure, and CVD.²⁹ EPA is further metabolized to DPA and DHA by ELOVL2 and ELOVL5 enzymes. 	<ul style="list-style-type: none"> High levels strongly correlated to diet and/or supplementation. Consider elongase enzyme nutrient cofactors: B3, B5, B6, biotin, vitamin C. EPA intake can improve blood lipid profiles and vascular inflammatory biomarkers and also helps lower levels of vascular inflammatory biomarkers.^{9,30} A higher EPA/AA ratio was associated with lower CRP and IL-6 and better COVID outcomes.³⁰ 	<ul style="list-style-type: none"> Increase intake of EPA-rich foods. Consider supplementation (EPA/fish oil). Evaluate B6 status. 	<ul style="list-style-type: none"> Cod liver oil Herring Mackerel Salmon Menhaden Sardines Algae oil
<p>Docosapentaenoic (DPA) 22:5n3</p> <ul style="list-style-type: none"> Intermediate compound between EPA and DHA. Structurally similar to EPA. DPA omega-3 metabolizes to SPMs. Metabolized to DHA (22:6n-3) by delta-4-desaturase. 	<ul style="list-style-type: none"> No clinical issues noted in research. Levels are higher with SNP variations on ELOVL-2 enzyme.³¹ 	<ul style="list-style-type: none"> Increase intake of DPA-rich foods. Supplementation with omega-3 or marine oil increases SPMs. 	<ul style="list-style-type: none"> Fish oil Salmon Grass-fed beef



MARKER & DESCRIPTION	IF HIGH	IF LOW	FOOD SOURCES ^{4-5,23-25}
<p>Docosahexaenoic (DHA)</p> <p>22:6n3</p> <ul style="list-style-type: none"> Required for brain growth, function, and development. DHA metabolizes to SPMs. ELOVL2 is involved in the elongation of DHA. DHA lowers blood triglyceride levels by reducing the activity of liver enzymes. It can reduce the inflammatory markers IL1-β, TNF-α, and IL-6.⁹ 	<ul style="list-style-type: none"> Levels strongly correlate with diet. Higher levels are associated with lower all-cause mortality and dementia.²¹ Higher levels of DHA have been shown to be associated with lower rates of Alzheimer’s disease in a long-term Framingham study (n=1490).³² 	<ul style="list-style-type: none"> Increase intake of DHA-rich foods. A low DHA blood level may be a biomarker of endothelial dysfunction.⁹ 	<ul style="list-style-type: none"> Salmon Caviar Anchovies Herring Mackerel Algae oil
<p>Index of Omega-3</p> <p>Total % EPA+DHA/ Total Fatty Acids</p> <ul style="list-style-type: none"> The percentage of the key omega-3 fatty acids EPA and DHA compared to all the other circulating fatty acids tested in this lab report. This balance can influence cellular inflammation and cardiovascular risk factors. 	<ul style="list-style-type: none"> Elevated levels are generally favorable. Index of Omega-3 can be used in conjunction with cardiometabolic and inflammatory labs to optimize treatment. Higher levels are associated with lower all-cause mortality and dementia.^{20,28} Evaluate diet, omega-3 supplementation, and overall fatty acid composition of the diet. <ul style="list-style-type: none"> » If just EPA & DHA are excessive, reduce intake or supplementation as needed. If several fatty acids are elevated, consider lowering total fat intake. 	<ul style="list-style-type: none"> A lower Index of Omega-3 has been associated with lower scores for visual memory, executive function, and abstract thinking in some studies.²⁰ Consider omega-3 supplementation. Increase omega-3 rich food sources. Check omega-6/omega-3 ratio. 	

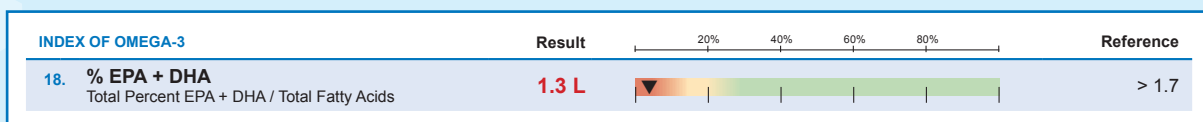


Figure 3. The Index of Omega-3 is a one-tailed test, and only low values are of concern clinically. Very low EPA + DHA levels are associated with negative health impacts. The results list the bottom 20% as borderline (yellow) and the bottom 5% as low (red).

OMEGA-6 MARKERS

OMEGA-6 POLYUNSATURATED FATTY ACIDS

While omega-6 fatty acids are required in the diet and are important for cellular energy, they can compete with omega-3 fatty acids for desaturation and elongation enzymes and drive the production of pro-inflammatory biological mediators. Eight omega-6 fatty acids are tested and six are reported on FAp.

MARKER & DESCRIPTION	IF HIGH	IF LOW	FOOD SOURCES ^{4-5,23}
<p>Total Omega-6 Fatty Acids</p> <ul style="list-style-type: none"> Total of all omega-6 fatty acids measured. Western diets tend to be high in omega-6 fatty acids largely due to intake of processed foods and seed oils. Soybean oil is a major contributor of Western intake.³⁴ 	<ul style="list-style-type: none"> Evaluate dietary sources and reduce accordingly. Monitor with cardiometabolic, inflammatory, and gut health biomarkers. Examine supplement sources. Evaluate the omega-6/omega-3 ratio. 	<ul style="list-style-type: none"> Examine total dietary fat intake and evaluate the omega-6/omega-3 ratio. 	<ul style="list-style-type: none"> Evaluate all omega-6 food sources.
<p>Linolenic (LA) 18:2n6</p> <ul style="list-style-type: none"> The second essential polyunsaturated fatty acid required for normal growth and development.³³ The primary dietary omega-6 fatty acid, widely available in plant-based foods, especially nuts, oils, and seeds. LA is the precursor of many bioactive molecules, including proinflammatory eicosanoids and anti-inflammatory molecules. LA converts to GLA via the delta-6-desaturase enzyme and cofactors: zinc, B2, B3, B6, vitamin C, Mg. This enzyme can compete with ALA conversion to EPA in the omega-3 pathway. 	<ul style="list-style-type: none"> Negative outcomes with high levels. Elevated levels may be beneficial for cardiovascular disease prevention, as LA appears to reduce inflammation and lower CVD risk.^{35,36} The relationship between LA and CVD outcomes are mixed in literature.²² Decrease intake from diet or supplements. High LA with low GLA can signal decreased delta-6-desaturase activity. 	<ul style="list-style-type: none"> Examine total dietary fat intake. Check omega-6/omega-3 ratio. Low LA with high GLA can signal fast/increased delta-6-desaturase activity. 	<ul style="list-style-type: none"> Seed oils <ul style="list-style-type: none"> » Safflower, corn, soybean, cottonseed Nuts and seeds <ul style="list-style-type: none"> » Walnuts, pine nuts, Brazil nuts, sunflower seeds, sesame seeds Peanuts/peanut oil Olive oil Poultry fat Egg yolks



MARKER & DESCRIPTION	IF HIGH	IF LOW	FOOD SOURCES ^{4-5,23}
<p>Gamma-Linolenic (GLA) γ-linolenic acid 18:3n6</p> <ul style="list-style-type: none"> GLA is rapidly elongated to DGLA via ELOVL5. Exerts anti-inflammatory and anti-proliferative and can lower the levels of blood lipids and CVD markers.⁹ 	<ul style="list-style-type: none"> Higher levels of GLA with lower LA can signal increased delta-6-desaturase. Higher levels of GLA with lower levels of DGLA can mean the elongase enzyme (ELOVL5) needs to be supported with cofactors: B3, B5, B6, biotin, vitamin C. 	<ul style="list-style-type: none"> Check LA above. Check delta-6-desaturase enzyme function and cofactors. Decreased enzyme activity can lead to lower levels of GLA, especially if LA is elevated. Low GLA associated with increased atopic dermatitis; increased intake of GLA or GLA-rich oils may improve atopic dermatitis.³⁷ 	<ul style="list-style-type: none"> GLA is rare in foods Best sources are borage oil, evening primrose oil, black currant seed oil, safflower oil
<p>Eicosadienoic (EDA) 20:2n6</p> <ul style="list-style-type: none"> EDA is a weaker pro-inflammatory agent than LA. 	<ul style="list-style-type: none"> Monitor for excess dietary intake of partially hydrogenated vegetable oil. 	<ul style="list-style-type: none"> Rapidly metabolized to DGLA & AA. May increase with intake of animal products. 	<ul style="list-style-type: none"> Partially hydrogenated vegetable oils
<p>Dihomo-gamma-linolenic (DGLA) 20:3n6</p> <ul style="list-style-type: none"> Increased DGLA can be converted to AA by delta-5-desaturase + B2, B3, B6, vitamin C, Mg, zinc. Conversion is limited. 	<ul style="list-style-type: none"> Plasma DGLA levels have been directly associated with several inflammatory markers, such as high-sensitivity C-reactive protein and cytokines.³⁷ The beneficial effects of DGLA presumably result from both the anti-inflammatory properties of its derivatives and the ability to compete with and reduce AA.³⁷ Elevated concentrations of DGLA have been seen in liver disease. 	<ul style="list-style-type: none"> Only a small fraction of DGLA is converted to AA. Lower DGLA and an increased LA/DGLA ratio have been noted in a lower dietary zinc intake and plasma zinc levels. Patients with atopic dermatitis may have lower circulating GLA and DGLA levels, which may be due to impaired delta-6-desaturase activities.³⁷ 	<ul style="list-style-type: none"> Borage, black currant, evening primrose, safflower oil Organ meats (liver and kidney) Trace amount in human milk and animal fats



OMEGA-6 POLYUNSATURATED FATTY ACIDS

MARKER & DESCRIPTION	IF HIGH	IF LOW	FOOD SOURCES ^{4-5,23}
<p>Arachidonic (AA) 20:4n6</p> <ul style="list-style-type: none"> Major omega-6 fatty acid and a crucial component of cell membranes throughout the body. It is a precursor to important lipid mediators like prostaglandins, thromboxanes, and leukotrienes. It plays a role in inflammation, blood platelet aggregation, and cardiovascular function. Measuring AA levels with EPA and DHA omega-3s can help determine the balance of these fatty acids and proinflammatory vs. anti-inflammatory pathways. 	<ul style="list-style-type: none"> Can be obtained from the diet or synthesized from the metabolism of linoleic acid (LA). Elevated levels are precursors to pro-inflammatory and pro-aggregatory mediators and are thus inflammatory disease modulators.³⁸ 	<ul style="list-style-type: none"> Evaluate levels of LA, as AA is produced from LA. Lower LA levels can lead to reduced AA levels. Conversion from AA to LA is dependent on elongase + B3, B5, B6, biotin, vitamin C. Evaluate these cofactors with lower levels. Evaluate omega-3 supplementation level. Low levels may impact sleep and lipid levels. 	<ul style="list-style-type: none"> Egg yolks Poultry (chicken and turkey) Organ meats Small amounts in fish, shellfish, beef, pork
<p>Docosatetraenoic (DTA) 22:4n6</p> <ul style="list-style-type: none"> Metabolism is dependent on delta-4-desaturase. 	<ul style="list-style-type: none"> Examine dietary sources. 	<ul style="list-style-type: none"> Examine dietary sources and total caloric intake. 	<ul style="list-style-type: none"> Sardines Black sea bream Beef, pork



MARKER & DESCRIPTION	IF HIGH	IF LOW	FOOD SOURCES ^{4-5,23}
<p>Omega-6/Omega-3 Ratio</p> <ul style="list-style-type: none"> • Omega-6/omega-3 ratio reflects the balance of these fatty acids in circulation. The ratio of these fatty acids can influence the balance between pro- and anti-inflammatory signaling. • The ratio reflects diet and supplement intake and also provides insight into fatty acid metabolism. • This ratio can be used along with other cardiometabolic, inflammatory, and gut health biomarkers to determine risk assessment. • Historically and prior to Westernized diets, the ratio was ~ 4:1. In recent decades, excess LA in the food supply has shifted the omega-6/omega-3 ratio from 4:1-20:1.³⁴ 	<ul style="list-style-type: none"> • Elevated levels are often correlated with high dietary intake of LA. People consuming Western diets tend to have higher ratios due to high consumption of seed oils and processed foods.³³ • Increases the risk of oxidized linoleic acid metabolites. The half-life of LA is ~2 years.¹⁵ • Reduce intake of omega-6 fatty acids, specifically LA and/or supplementation. 	<ul style="list-style-type: none"> • Optimal dietary intakes of the omega-6/omega-3 ratio have been proposed as 1-4:1. • Evidence suggests that a lower omega-6/omega-3 ratio is linked to reduced chronic inflammation, lower risk of heart disease, better brain function, and healthier immunometabolism.³⁹ 	

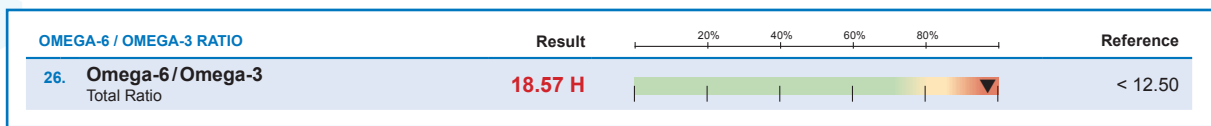


Figure 4. The omega-6/omega-3 ratio is a one-tailed test, and only high values are of concern clinically. An excess of omega-6 is associated with negative health impacts. The results list the top 20% as borderline (yellow) and the top 5% as high (red).



DESATURASE ENZYMES

Elongase and desaturase enzymes play critical roles in regulating the length and degree of unsaturation of fatty acids. The main desaturase enzymes include delta-6, delta-5, and delta-9.

By measuring concentrations and ratios of individual fatty acids, metabolic activities of these enzymes are calculated on the FAp Fatty Acids Profile. Recent evidence reveals that changes in the activity of delta-6 (D6D) and delta-5 (D5D) enzymes and altered blood and tissues concentrations of polyunsaturated FAs downstream of enzyme activity could be involved in the pathophysiology of development of insulin resistance.⁴⁰

Higher enzyme activity increases the rate of the reaction, while inhibitors can slow the reaction.

There are several factors that can influence enzyme activity:

- **Increases in the amount of starting fatty acid.**
- **Enzyme inhibitors: inadequate cofactors, interfering substances such as toxins or hormones, disease conditions.**
- **Genetics can influence functionality of enzymes and there are known SNPs that can impact the activity of certain desaturases—specifically D5D and D6D.**
- **Micronutrient deficiencies can also influence enzyme activity, and specific nutrients such as folate, vitamin B12, vitamin A, trace minerals (iron, zinc), and polyphenols (resveratrol, isoflavones) are relevant to desaturase enzyme activities.**

When assessing enzyme activity:

- **Higher number = increased enzyme activity**
- **Lower number = reduced enzyme activity**



DELTA-6-DESATURASE ENZYME (D6D)

Rate-limiting enzyme that catalyzes the desaturation of linolenic acid (LA) to gamma-linolenic acid (GLA) in the omega-6 pathway. This enzyme is also responsible for the desaturation of alpha-linolenic acid (ALA) to eicosapentaenoic acid (EPA) in the omega-3 pathway. Thus, there can be competition for this enzyme.

Delta-6-desaturase enzyme uses the **cofactors B2, B3, B6, vitamin C, Mg, and zinc.**⁴¹ Insufficient bodily levels of cofactors can result in decreased enzyme activity.

D6D activity can be impaired by viral infection, aging, high blood pressure, high alcohol intake, high cholesterol, stress-related hormones, radiation, nutritional factors (deficiencies of Zn⁺, Mg⁺, vitamins C, B3, B5, B6, and a high level of trans fatty acid), diabetes, and genetic SNPs.⁴² It can be upregulated by estrogen.⁴³

D6D is a 2-tailed test and there are risk factors associated with both increased and decreased enzyme activity.

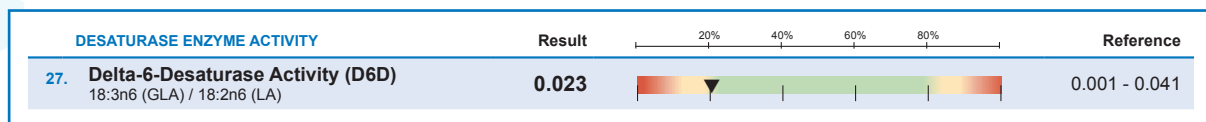


Figure 5. D6D enzyme activity is evaluated: 18:3n6 (GLA)/18:2n6 (LA)

See Table of D6D Activity on the following page...



DELTA-6 DESATURASE (D6D) ACTIVITY

MARKER & REPORT FINDINGS	INTERVENTIONS	ASSOCIATIONS AND RISK FACTORS
<p>INCREASED Delta-6 Desaturase (D6D) Activity</p> <p>LA → D6D → GLA High Ratio: 18:3n6 (GLA)/18:2n6 (LA)</p> <ul style="list-style-type: none"> • A ratio above the 80th percentile indicates increased enzyme activity. • Lower LA and higher GLA. More LA is converting to GLA and omega-6 pathway predominates. 	<ul style="list-style-type: none"> • Assess individual fatty acid levels—specifically, decreased LA and ALA, and increased GLA and EPA. • Balance total omega-6 and omega-6/omega-3 ratio; excessive intake of LA can interfere with ALA conversion. • Test for D6D (FADS2) genetic SNPs. • Check methionine levels and evaluate dietary intake. • Evaluate hormone levels; evaluate beta-glucuronidase on the GI-MAP. • Manage metabolic conditions — diabetes, IR, obesity, etc. • Exercise may help normalize activity. 	<ul style="list-style-type: none"> • Increased D6D associated with increased risk of chronic inflammation and associated conditions—diabetes, CVD, Alzheimer’s, MS, cancer. • Increase in autoimmune and inflammatory disease, diabetes, CVD, MS, cancer.⁴² • Higher in menopause.⁴¹ • Higher systolic and diastolic blood pressure, BMI, insulin, worsening of hyperglycemia, triglycerides and worse homeostatic model assessment (HOMA) score (n=1842).⁴⁴ • Omega-3 deficiency and omega-6 excess. • High protein diets/extra protein intake stimulated desaturase activity in animal studies. Supplementation with L-cysteine, L-glycine, and L-methionine increased delta-6 activity.⁴²
<p>DECREASED Delta-6 Desaturase (D6D) Activity</p> <p>LA → D6D → GLA Low Ratio: 18:3n6 (GLA)/18:2n6 (LA)</p> <ul style="list-style-type: none"> • A ratio below the 20th percentile indicates less enzyme activity. • Identifies reduced conversion of LA to GLA, leading to increased LA and reduced GLA. 	<ul style="list-style-type: none"> • Assess individual fatty acid levels—specifically, increased LA and ALA, and decreased GLA and EPA. • Check & balance omega-6/omega-3 ratio. • Support EPA, DHA, and GLA. • Ensure adequate cofactors: B2, B3, B6, vitamin C, Mg, and zinc. • Avoid or reduce alcohol, tobacco, and stress. • Test for D6D (FADS2) genetic SNPs. 	<ul style="list-style-type: none"> • Reduced D6D activity may be associated with aging. • Reduced D6D activity may reduce downstream fatty acids and subsequent synthesis anti-inflammatory eicosanoids and prostaglandins.⁴² • Diets rich in saturated fats and cholesterol have shown to suppress activities of desaturases.⁴² • Linked to lower basal insulin, atopic eczema.⁴⁵



DELTA-5-DESATURASE ENZYME (D5D)

Rate-limiting enzyme that converts dihomo- γ -linolenic acid (DGLA) to arachidonic acid (AA) in the omega-6 pathway. This enzyme is also responsible for producing eicosapentaenoic acid (EPA) in the omega-3 pathway; thus, there can be enzyme competition depending on the availability of omega-6 and omega-3 substrates respectively.

Delta-5-desaturase enzyme uses the same cofactors as delta-6-desaturase: B2, B3, B6, vitamin C, Mg, and zinc.⁴¹

Increased D5D activity has been associated with better health outcomes, while DECREASED activity has been associated with poor health outcomes.⁴⁴

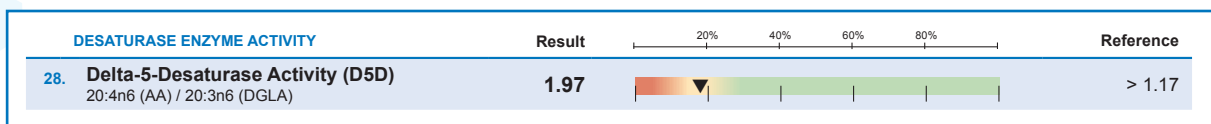


Figure 6. D5D enzyme activity is evaluated: 20:4n6 (AA)/20:3n6 (DGLA)

DELTA-5 DESATURASE (D5D) ACTIVITY

MARKER & REPORT FINDINGS	INTERVENTIONS	ASSOCIATIONS AND RISK FACTORS
<p>DECREASED Delta-5 Desaturase (D5D) Activity</p> <p>LA → D6D → GLA Low Ratio: 20:4n6 (AA)/20:3n6 (DGLA)</p> <ul style="list-style-type: none"> • A ratio below the 20th percentile indicates reduced enzyme activity. • High DGLA with low AA. • Reduced production of EPA and AA with reduced enzyme activity. 	<ul style="list-style-type: none"> • Evaluate all other fatty acid levels—especially AA, DGLA, ALA, and EPA. <ul style="list-style-type: none"> » Expect higher DGLA and lower AA. • Ensure adequate cofactors: B2, B3, B6, vitamin C, Mg, and zinc. • Sesame and curcumin can inhibit delta-5-desaturase.⁴⁶ • Exercise, phytochemicals, and weight loss may support D5D function.⁴⁷ • Test for D5D (FADS1) genetic SNP. 	<ul style="list-style-type: none"> • Decreased D5D activity has been associated with negative health outcomes. Research has noted associations of decreased activity with hepatic steatosis, increased ApoB, and increased protein-energy malnutrition in children.³⁷



DELTA-9-DESATURASE ENZYME (D9D)

Delta-9 desaturase (D9D) enzyme, also known as stearoyl-CoA desaturase 1 (SCD1), is the rate-limiting, iron-containing enzyme that catalyzes the conversion of **saturated 18:0** to **monounsaturated 18:1** fatty acid by adding a single double bond between C9 and C10 of long-chain fatty acids. It ‘desaturates’ saturated fats to monounsaturated fat and governs the production of triglycerides, composition of cell membranes, and lipoprotein metabolism.

INCREASED activity is linked to metabolic disorders. Decreased activity reduces fat production and increases fatty acid oxidation, and inhibition of this enzyme has been studied as a potential therapeutic target for improving metabolic syndromes.

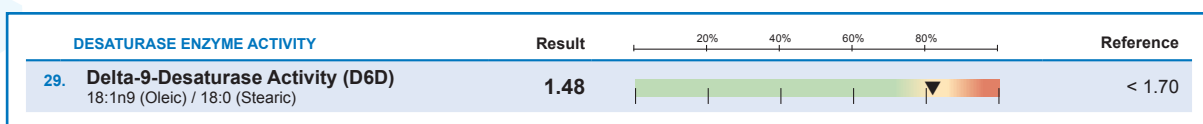


Figure 7. Delta-9 activity assessment: oleic acid (C18:1n-9) / stearic acid (C18:0)

DELTA-9 DESATURASE (D9D) ACTIVITY

MARKER & REPORT FINDINGS	INTERVENTIONS	ASSOCIATIONS AND RISK FACTORS
<p>INCREASED Delta-9 Desaturase (D9D) Activity</p> <p>Stearic → D9D → Oleic</p> <p>Oleic acid (C18:1n-9) / stearic acid (C18:0)</p> <ul style="list-style-type: none"> Ratio over 80th percentile. More stearic acid is converted to oleic acid. 	<ul style="list-style-type: none"> Monitor levels of saturated fatty acids and reduce dietary intake accordingly. Reduce saturated fatty acids—in particular palmitic acid (C16:0) and stearic acid (C18:0), as they may cause upregulation of delta-9-desaturase.⁴⁸ MUFA and omega-3 lower D9D, while SFA and sugar intake may increase.⁴⁹ Exercise may reduce D9D activity.⁴⁷ Phytochemicals downregulate D9D expression.⁴⁹ 	<ul style="list-style-type: none"> Increased D9D activity is correlated with obesity, insulin resistance and certain cancers. There are decreased rates of fatty acid oxidation with increased enzyme activity, leading to increased deposition of lipids into peripheral tissues. This leads to insulin resistance in muscle and liver.^{12,50-52} Associated with increased circulating SFAs and inflammatory markers.⁴⁸ D9D activity is positively correlated with the kynurenine/tryptophan ratio (K/T ratio) and thus “inflammaging.”⁴⁸ Delta-9-desaturase activity is heritable and is associated with the dyslipidemia observed in familial combined hyperlipidemia (n=400).⁵³



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