



Omega-3 & Immune Health

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GC Rieber Oils, Norway



GC RIEBER

The GC RIEBER GROUP

- Privately-owned company founded in Bergen, Norway, 1879
- Provides long-term active ownership to a range of core businesses
- Business areas characterized by high competence within niches
- Operates on a local, as well as on a global scale, primarily in the business markets.

CORE BUSINESSES

- Industry
- Shipping
- Commercial Property

OWNERSHIP STRUCTURE

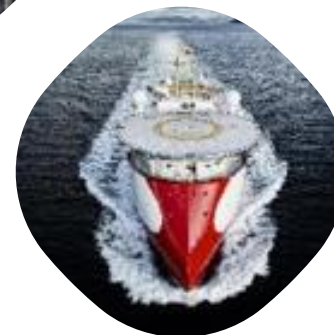
- Private holding companies: 50%
- Personal Shareholders: 30%
- Charitable Foundations: 20%

EMPLOYEES

- 500 employees

OPERATING REVENUE

- USD mill: 250



GC RIEBER

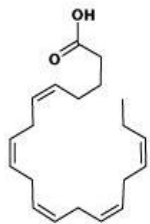
GC Rieber Oils - Norwegian producer of high omega-3 concentrates fish oil

- Established in 1965
- Part of the GC Rieber Group
- 70 employees
- Sales in excess of 30 million USD in 2019
- Two factories + pilot factory plant
- Laboratory, departments for quality assurance, logistics, sales, finance and R&D
- State-of-the-art technology
- Sales office and distributors around the world

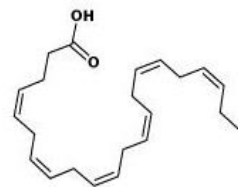


Omega-3s role in the immune system (intro)

- Factors that impact our immune system: sleep, stress, smoking, genes and diet.
- Malnutrition or unbalanced diet suppress our immune system which again increase the risk of infections and disease.
- A large body of scientific evidence indicates that EPA and DHA, the omega-3 essential fatty acids in fish oil, helps to support the immune response and regulate the internal repair systems that operate in response to inflammation
- EPA and DHA are converted into anti-inflammatory molecules



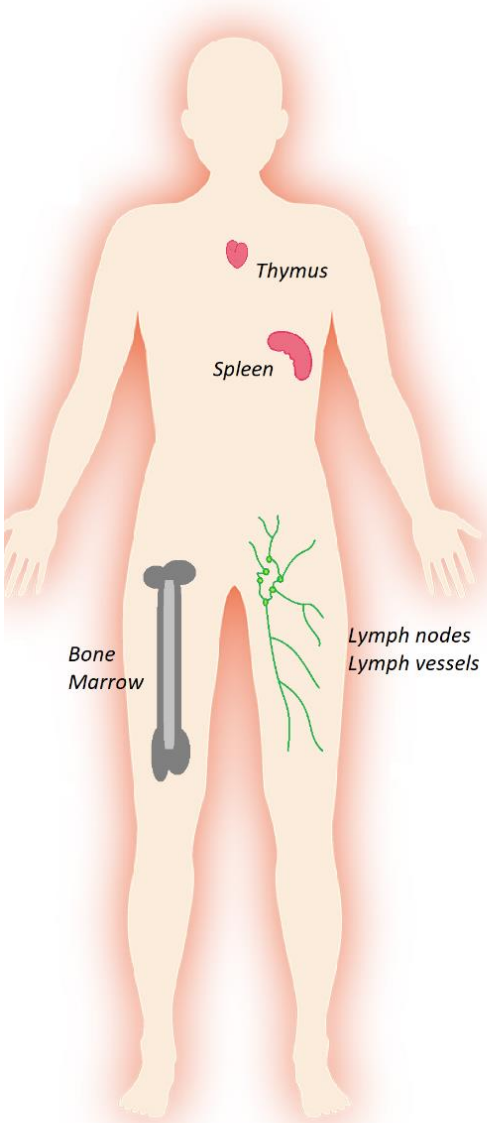
Eicosapentaenoic acid
EPA (20:5n-3)



Docosahexaenoic acid
DHA (22:6n-3)

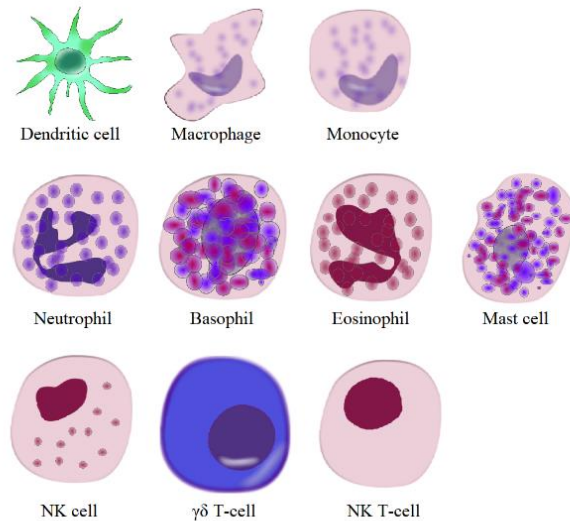


The immune system – our protection against infection and disease

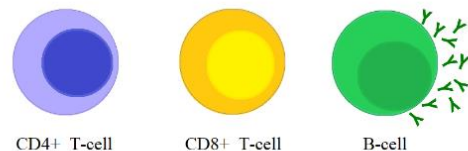


1) **Barriers** - Prevent entry
Skin and mucus membranes, stomach acid and digestive enzymes, beneficial bacteria that live in the colon, urine flow.

2) **Innate immunity** - General defence
WBCs called neutrophils and macrophages engulf and destroy foreign invaders and damaged cells



3) **Adaptive immunity** - Specific defence
WBCs called T-lymphocytes (T-cells) target and destroy infected cells; WBCs called lymphocytes (B-cells) and plasma cells produce antibodies that target and destroy infected cells.



- A complex system of organs, tissues, and white blood cells (or *leucocytes*).
- Recognizes foreign invaders (e.g. bacteria, viruses, parasites, fungi) and also abnormal cells such as cancer cells.

• 3 different layers of immunity defence:

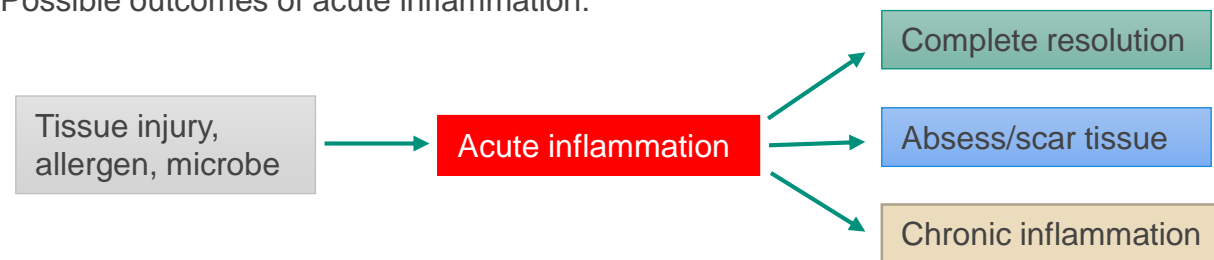
- Physical barriers
- Innate: fast, non-specific response; main role to recognize and destroy by *phagocytosis* or by the release of toxic chemicals
- Acquired: slower, highly specific, involves antigen presentation and antibody production to inactivate the antigen. Development of memory against pathogens

- Immune cells communicate with each other directly or by the help of cytokines

Inflammation – a key component of the immune system

- When the immune system is triggered—for example by injury, allergy, or infection — the immune system will mount an inflammatory response
 - Results in changes in blood flow, oedema, recruitment of immune cells, and lipid mediators that function to eliminate the infection and heal the injured cell and tissue.
 - Resolution of inflammation is necessary to bring the tissue back to homeostasis (“normal state”)
 - Prolonged inflammation can lead to tissue damage and the development of chronic inflammation and disease

Possible outcomes of acute inflammation:



(Modified from Kohli P. and Levy B. D. Br J Pharmacol. 2009;158(4):960-71).

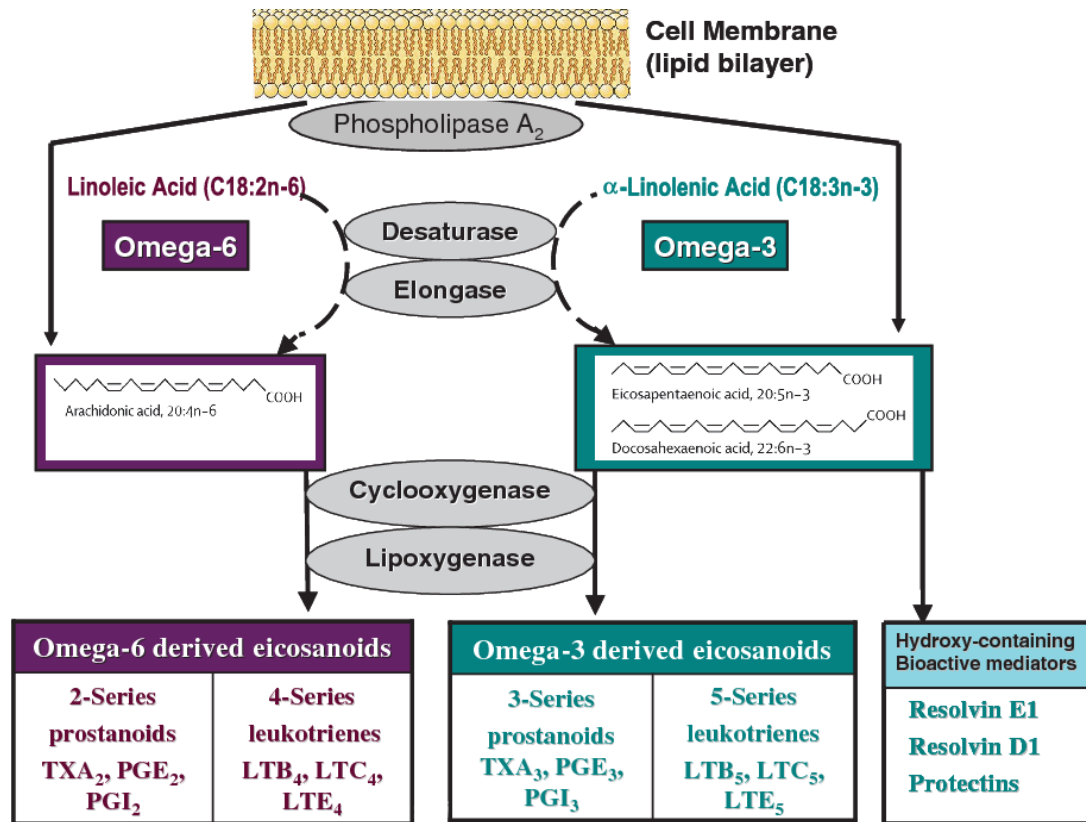


Omega-3 fatty acids – and their role in the immune system, cont'

- Omega-3 (EPA and DHA) and omega-6 (arachidonic acid) fatty acids form the framework of cell membranes that surrounds **ALL** cells in our body.
- As structural components of cells membranes, EPA and DHA, are especially important for brain & nervous system development, as well as eye and the immune system development.
- Growing evidence indicate that incorporated into immune cell membranes, omega-3s influence:
 - Cell membrane structure & fluidity
 - Function of receptors and enzymes
 - Immune functions mediated at the membrane level
 - Cytokine production
 - Activity of different immune cells



Omega-3s in inflammation



Essential fatty acid production and metabolism to form eicosanoids.

(Illustration borrowed from Kang J. X. 2008, *Subcell Biochem*,49:133-43)

- Omega-3s and omega-6s are both precursors of Eicosanoids which are important cell signalling molecules (lipid mediators).
- Generally, the eicosanoids produced from omega-3 fatty acids EPA and DHA are typically anti-inflammatory and those produced from the omega-6 fatty acid arachidonic acid (ARA) are inflammatory.
- EPA and DHA compete for the same enzymes (here in gray) as omega-6 fatty acids
- Higher concentrations of EPA and DHA in the body **tip the "eicosanoid balance" toward less inflammation**
 - Which reduces platelet aggregation, vasoconstriction, and immune cells chemotaxis and adherence properties
- Newer research has shown that EPA and DHA not only produces anti-inflammatory eicosanoids, **but also inflammation resolving compounds.**
- This "new" class of bioactive compounds are often termed specialized pro-resolving mediators (SPMs).



Omega-3 may be important for the immune system in early life

- Epidemiological studies have found that higher intake of fish (source of EPA and DHA) during pregnancy and infancy, is associated with preventing and reducing allergies and atopic disorders later on in the children's life
- Clinical supplementation studies:
 - Higher levels of DHA in the mothers milk, have been found to reduce allergies including food allergy during the baby's first year and eczema later on
 - High levels of omega-3s in milk from omega-3 was related to less atopic eczema in infancy
 - Fish oil consumption in pregnancy reduced persistent wheeze and asthma in the children at ages 3 to 5 years.



B-cell activity



- Main function of B-cells is to make antibodies against antigens to fight off pathogens
- Evidence indicate that the membrane microdomains, termed “lipid rafts”, have a role in B-cell activation as platforms for B-cell receptor signalling and they might also act in antigen trafficking
- Omega-3s, in particular DHA, have been shown to change the organization and size of these membrane microdomains, as well increase B cell function
- Immunomodulating effects related to increased B cell activity have also been shown in human



Immunity after exercise

- Physical exercise is known to alter the immune function and increase the risk of infectious agents to enter the body
- Fish oil supplementation may improve the immune function in the recovery period after exercise
- Omega-3 PUFA supplementation has shown (after exercise/recovery period after exercise):
 - Decrease pro-inflammatory cytokine production
 - Increase in IL-2 cytokine production (which triggers production of T-cells)
 - Increase in NK cytotoxic activity
 - Reduced number of symptom days of URTI



INFECTION & DISEASE

The immune system protects the body against infection and disease. EPA and DHA are essentially important for the immune system development

ANTI-INFLAMMATORY & INFLAMMATION RESOLVING

New research has discovered that EPA and DHA give rise to specialized pro-resolving mediators (SPMs) which are both anti-inflammatory and inflammation resolving

OIL RICH IN DHA & EPA

may in particular enhance the function of white blood cells known as immune B cells

Supplementation of omega-3 give rise to endogenous pro-resolving mediators

These pro-resolving mediators derived from EPA and DHA, have protective actions, not only by directing resolution of inflammation but may also by exerting direct antimicrobial and antiviral actions.

- Studies that have suggested protective effects in controlling infections (examples):
 - Better lung function in Cystic Fibrosis patients
 - Increased clearance (phagocytosis) of E. coli
 - Improved survival of influenza-virus-infected mice
- The production of inflammatory and pro-resolving lipid mediators can be altered by dietary and supplemental intake of omega-3s.
- Presence in human breast milk suggesting that omega-3s serve as precursors for these mediators already during early life





Omega-3s intake

- EPA and DHA are under consumed in the Western World; increased consumption of these fatty acids to decrease the omega-6 to omega-3 fatty acid ratio has potential health benefits for a range of inflammatory and autoimmune diseases.
- Recommend intakes for EPA + DHA (EFSA):
 - from 250 to 1000 mg/day for adults
 - 100 mg/day for infants older than six months and children up to 2 years
 - 100-250 mg/g for older children and adolescents
- Omega-3 fatty acids are GRAS approved, and safe up to 3 and 5 gram per day by FDA and EFSA, respectively.



Conclusions

- EPA and DHA: structural components of cells; have various immune-modulating effects, and are important mediators in regulating both inflammation and resolution
- More studies are needed to fully understand the immune-modulating mechanisms behind the potential clinical effects of omega-3 fatty acids, *the unique roles of EPA and DHA*, and the optimal dose.
- But safe to say that it is generally agreed that omega-3s should be part of a balanced diet together with other important nutrients (vitamins, minerals etc)?!

Fatty Acids and Immunity

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To conclude, we hope that we have shown in this review that immunology may have a place in fatty acid research. We only hope that, in making this point, we do not blind the reader to the reality that effects on immunity represent only one of many ways in which fatty acids might be relevant to disease.



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Thank you for your attention!!

