

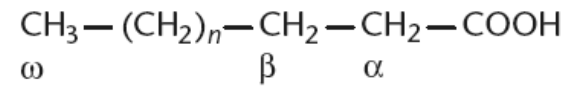
FRM2041 10.05.2006



Essensielle fettsyrer (omega-3 og omega-6)

Arild Chr. Rustan

Nomenclature for fatty acids



hydrophobic

hydrophilic

Rustan and Dreven, Encyclopedia of life sciences 2005

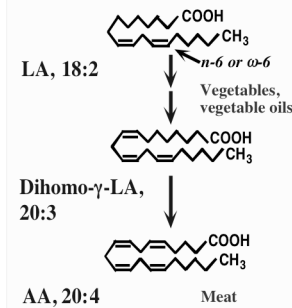
Structure of different fatty acids

ω -characteristics	Methyl end	Carboxyl end	Saturation	Δ -characteristics
Stearic 18:0		COOH	Saturate	18:0
Oleic 18:1, ω -9		COOH	Monoene	18:1 Δ 9
Linoleic 18:2, ω -6		COOH	Polyene	18:2 Δ 9,12
α -Linolenic 18:3, ω -3		COOH	Polyene	18:3 Δ 9,12,15
EPA 20:5, ω -3		COOH	Polyene	20:5 Δ 5,8,11,14,17
DHA 22:6, ω -3		COOH	Polyene	20:6 Δ 4,7,10,13,16,19

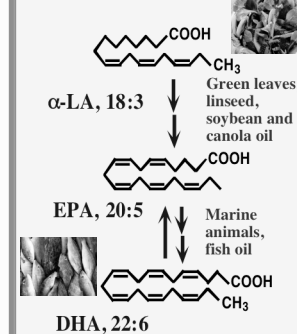
Rustan and Dreven, Encyclopedia of life sciences 2005

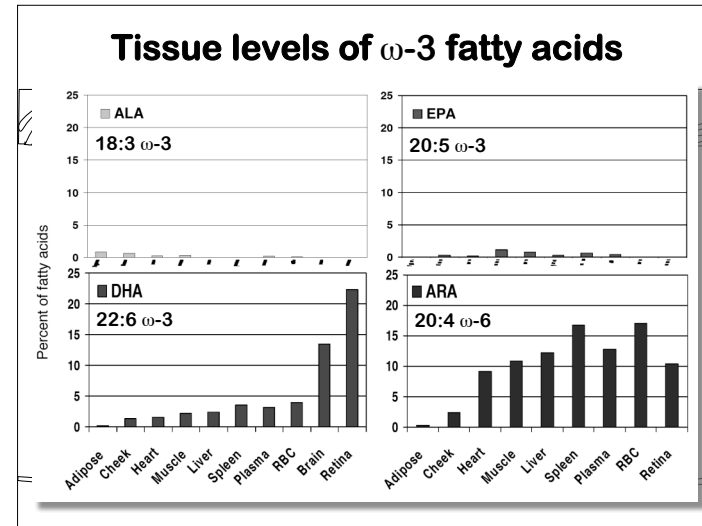
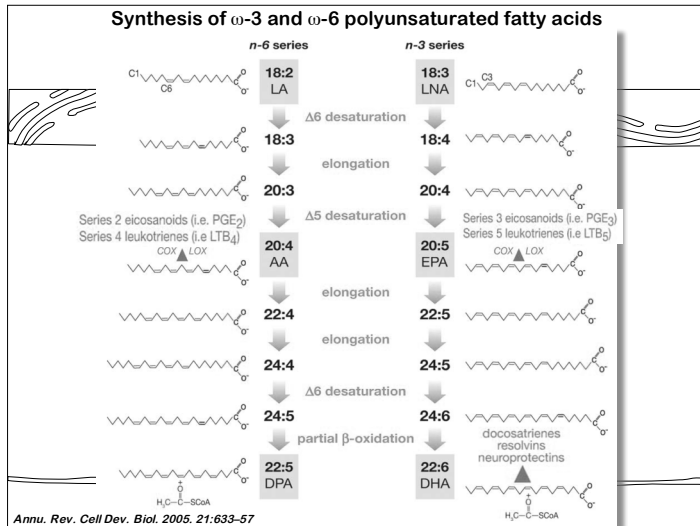
Polyunsaturated fatty acids (PUFAs)

Omega-6 (n-6)



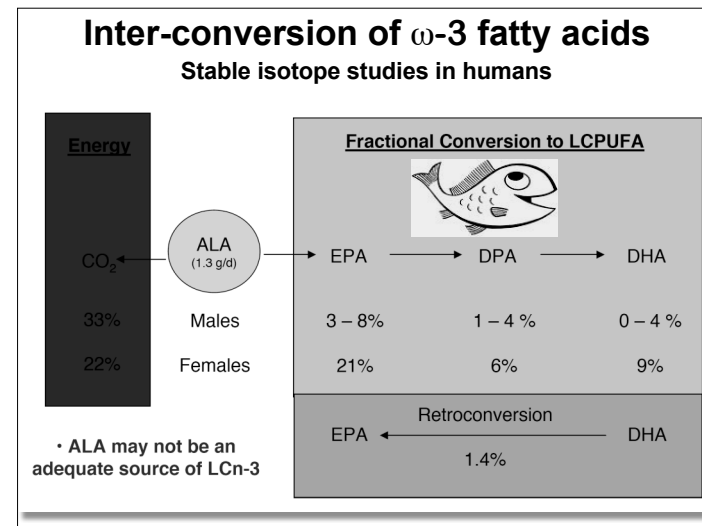
Omega-3 (n-3)

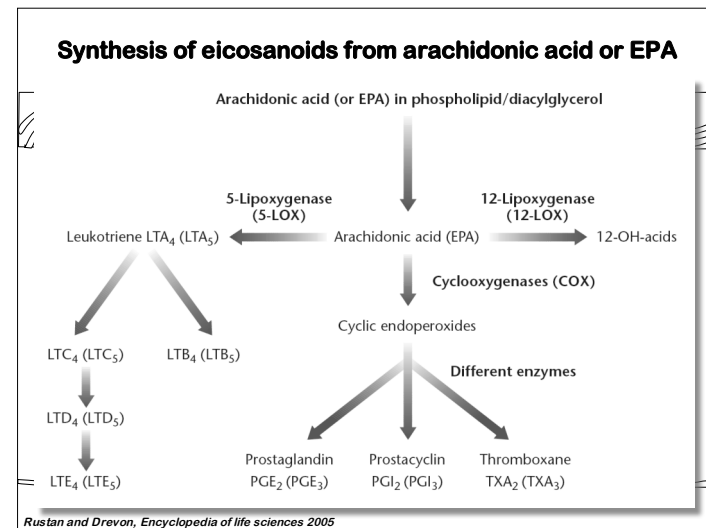
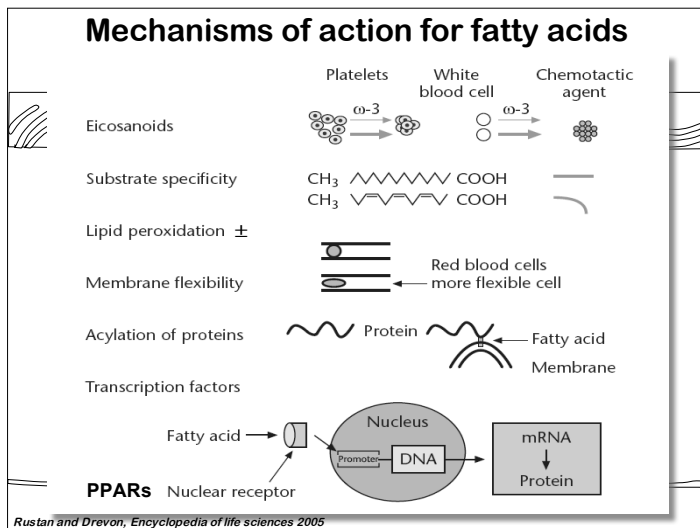
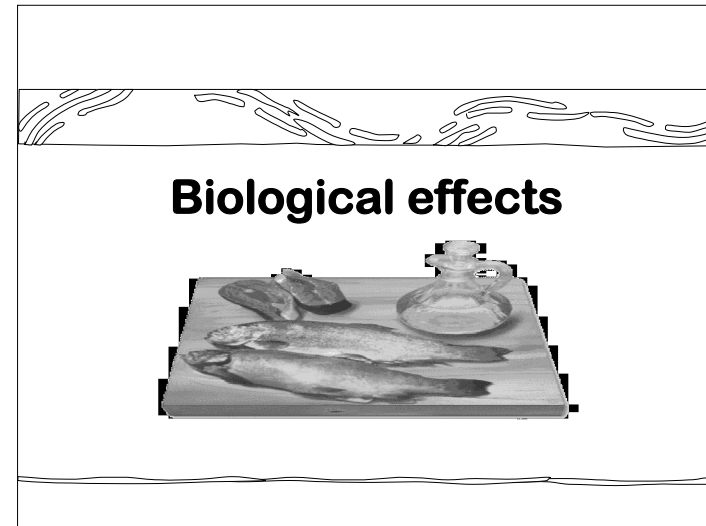
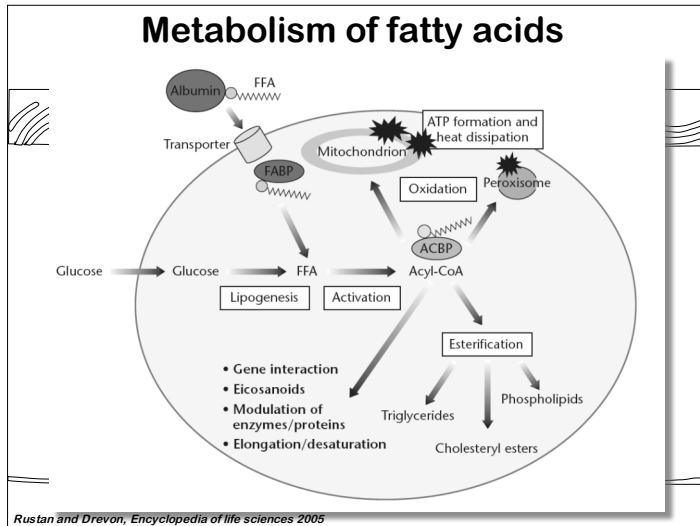


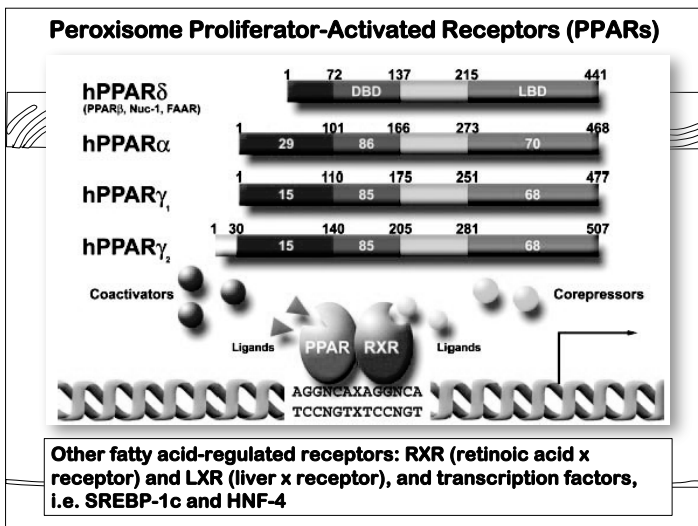
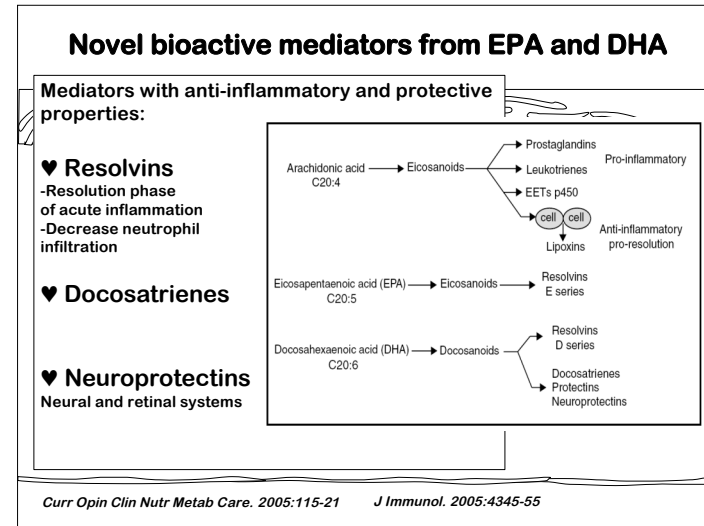
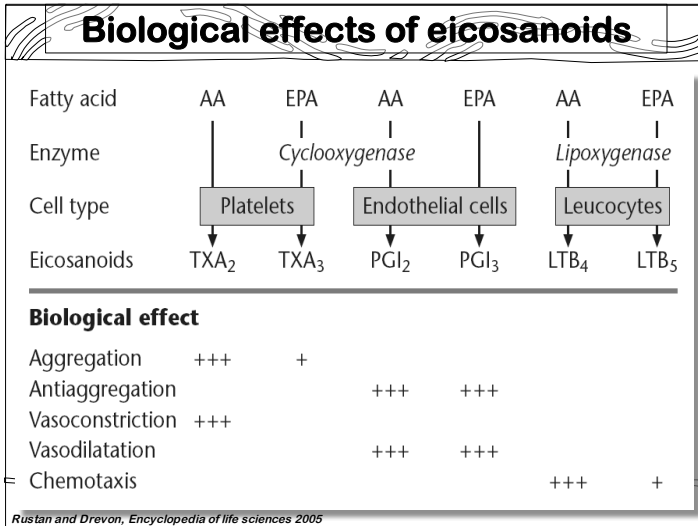


Functions of fatty acids

- ♥Energy
high per gram (37 kJ/g fat)
- ♥Transportable form of energy
blood lipids (triacylglycerol in lipoproteins)
- ♥Storage of energy
adipose tissue (obesity) and skeletal muscle
- ♥Structural components of cell membranes
phospholipids
- ♥Insulation
thermal, electrical and mechanical
- ♥Signaling molecules
eicosanoids, docosanoids, resolvins, protectins
ligands for nuclear receptors





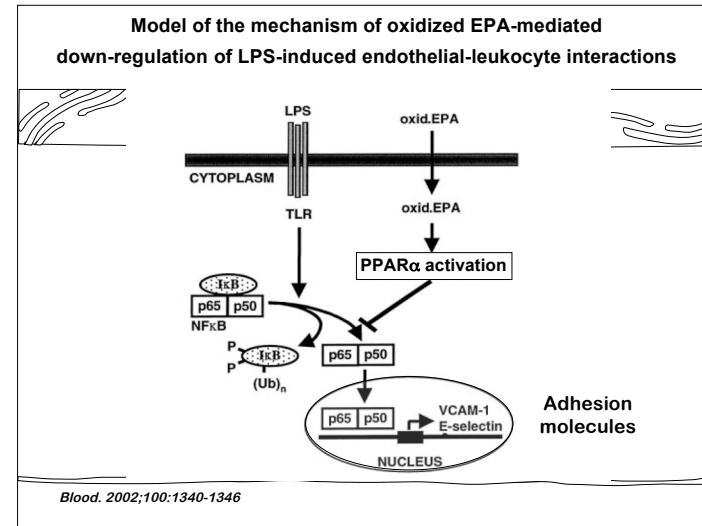
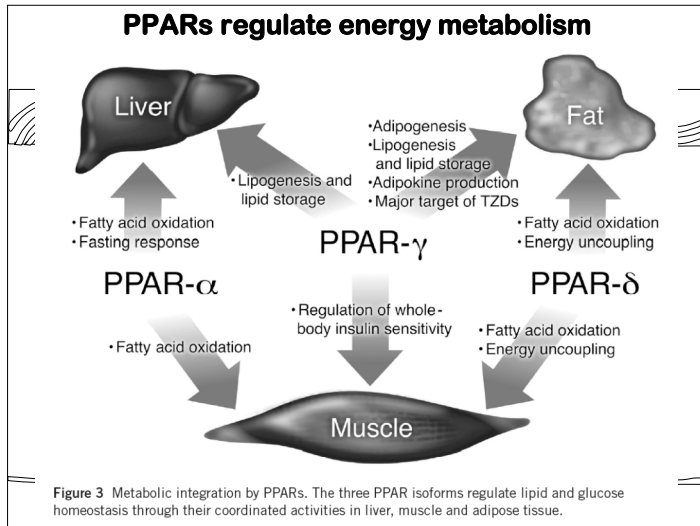


PPARs bind fatty acids

Endogenous ligands	Biological effect		
PPAR-α	PPAR-δ	PPAR-γ	
Palmitic acid	Fatty acids	Linoleic acid	Lipid and glucose metabolism
Stearic acid		Arachidonic acid	
Palmitoleic acid		15d-PGJ2	
Oleic acid		9-HODE	
Linoleic acid		13-HODE	
Arachidonic acid		15-HETE	
Eicosapentaenoic		Eicosapentaenoic acid	

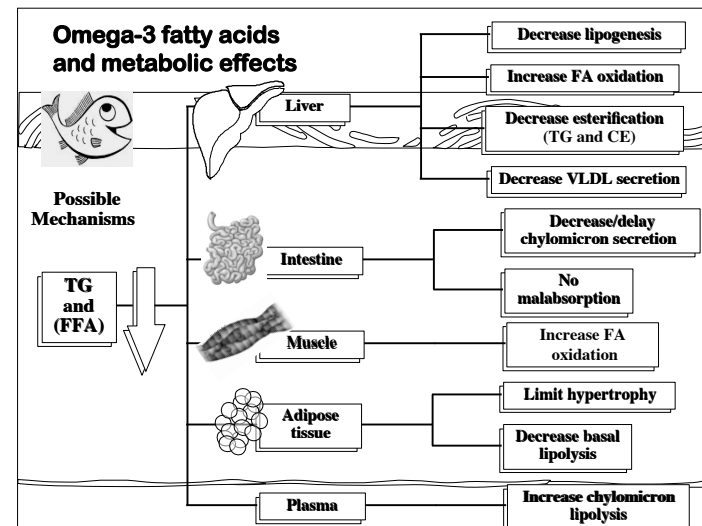
Pharmacological agonists:

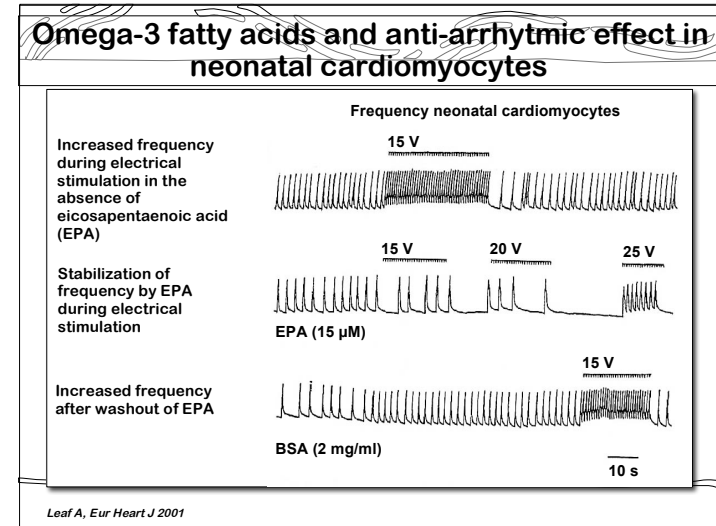
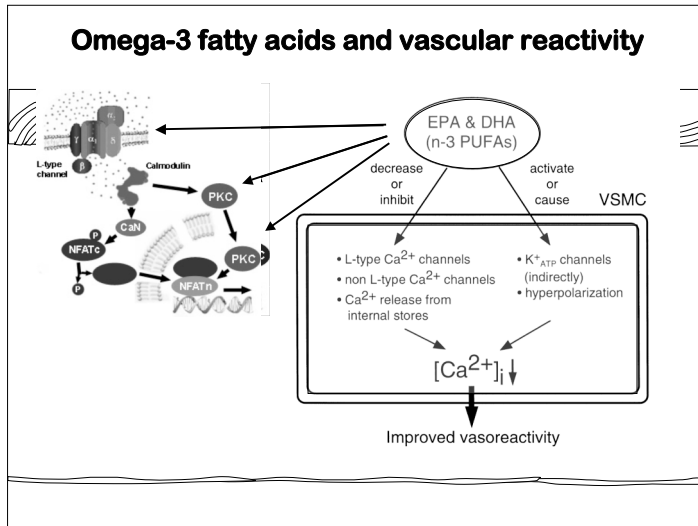
- PPAR-α- fibrates, i.e. gemfibrozil, treat hyperlipidemia
- PPAR-δ - lipophilic carboxylic acids, i.e. GW501516
- PPAR-γ - glitazones, i.e. rosiglitazone, treat insulin resistance



Effects of dietary fatty acids on lipoprotein metabolism

	Saturated (14:0 & 16:0)	Monoenes (18:1 n-9, cis)	Omega-6 (18:2 n-6)	Omega-3 EPA & DHA
Chylomicron				
VLDL production	↑	→	↓	↓
VLDL			?	↓
LDL production	↑	→	↓	↓
LDL				?
LDL clearance	↓	↑	↑	→
LDL-receptor activity	↓	↑	↑	→
HDL	↑	?	→	?
Hepatic cholesterol excretion	↓	↑	↑	↑





ω -3 fatty acids have positive influence on metabolic and cardiovascular events

	Negative influence	Positive influence
Coronary artery disease	Saturated	ω -3 PUFA and monoenes
Stroke	Saturated	?
Blood pressure	Saturated	ω -3 PUFA
Insulin resistance/ type 2 diabetes	Saturated	ω -3 PUFA (ω -6 PUFA)
Blood clotting and fibrinolysis	?	ω -3 PUFA (?) and ω -6 PUFA (?)
Function of platelets	?	ω -3 PUFA and ω -6 PUFA (?)
Hyperlipidemia	Saturated	ω -3 PUFA, ω -6 PUFA and monoenes
Oxidation of LDL	ω -6 PUFA (?)	Monoenes
Atherogenesis (leukocyte reactivity, immunological functions)	Saturated	ω -3 PUFA and ω -6 PUFA
Endothelial dysfunction	?	ω -3 PUFA (?)
Cardiac arrhythmias	Saturated	ω -3 PUFA (DHA) and ω -6 PUFA
Inflammation (rheumatoid arthritis)	Saturated	ω -3 PUFA

Rustan and Drevon, Encyclopedia of life sciences 2005

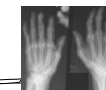
- ### ω -3 fatty acids and the metabolic syndrome
- ↘ Fasting, and postprandial TAG and FFA ↘
 - ↘ Platelet and leucocyte reactivity ↘
 - ↘ Blood pressure ↘
 - ↗ Insulin sensitivity ↗
 - ↘ Positive influence on vessel wall characteristics and blood rheology
 - ↘ Cardiac arrhythmias
 - ↘ Coagulation and fibrinolysis ↘
 - ↘ Atherogenesis ↘

Omega 3 fatty acids and side effects

- ♥ common: nausea, fishy belching and looseness of the stools (higher dosage fish oil preparations)
- ♥ do not appear to have clinically significant effects on bleeding time (caution: high dosage and patients with pre-existing haemorrhagic disorders or those on anticoagulant treatment)
- ♥ worsen glycemic control in diabetic subjects? (meta-analysis show no effect)
- ♥ increased lipid peroxidation? (vit E added)

Omega-3 in health and disease

- ♥ Cardiovascular
 - ♥ vascular function, hypertension, atherosclerosis, myocardial infarction
- ♥ Type 2 diabetes - obesity
 - ♥ metabolic syndrome, blood lipids, insulin resistance
- ♥ Cancer (?)
 - ♥ breast, prostate, colorectal
 - ♥ cachexia
- ♥ Neurological development (childhood) and degeneration (?)
 - ♥ nervous tissue and retina, learning and memory
 - ♥ brain ischemia, Alzheimer's disease, amyotrophic lateral sclerosis (ALS)
 - ♥ depression, schizophrenia
- ♥ Inflammatory/immunological (?)
 - ♥ rheumatoid arthritis, inflammatory bowel disease, asthma, IgA nephropathy



Suggested intake of PUFA

	ω -3 (% of energy)	ω -6 (% of energy)	ω -3 (mg/day)	ω -6 (mg/day)
Minimum	0.2-0.3	1-3	400-600	2400-7200
Optimum	1-2	3-7.5*	2400-4800	7200-18000

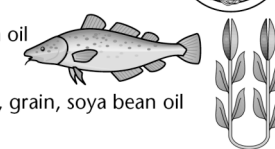
*Pregnant and breast feeding women. The numbers are based on data from patients with essential fatty acid deficiency and on estimation of required and optimal intake in healthy, normal individuals with energy intake of 2200 kcal/d (9.2 MJ/d).

We suggest: 1-2 g/day of EPA + DHA

Rustan and Drevon, Encyclopedia of life sciences 2005

Advice for dietary lipids

- ↓ Intake of saturates
 - milk- and meat-products, hard margarine
- ↓ Intake of *trans* fatty acids
 - margarine with PHFO, milk products
- ↑ ω -3 fatty acids
 - fatty fish, cod liver oil, fish oil
- ↑ Vitamins D and E
 - fatty fish, cod liver/fish oil, grain, soya bean oil



Rustan, A.C., and C.A. Drevon

Fatty acids: structures and properties

Encyclopedia of Life Sciences, 2001,
Revised version September 2005

electronic publication at <http://www.els.net/>