Distribution and Dosing of Omega-3 Fatty Acids in Humans

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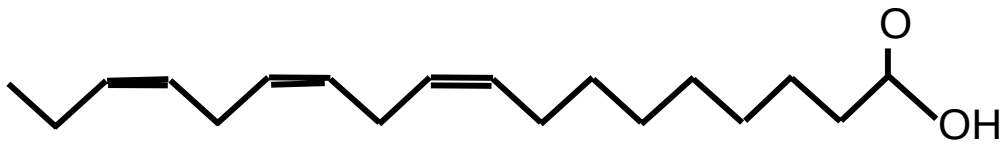
Overview

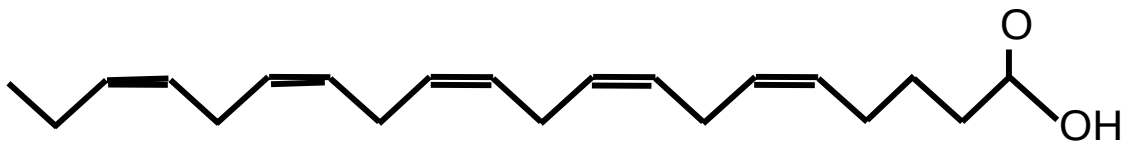
- Practical considerations for n-3 supplementation
  - fatty acid selection
  - dose levels
  - duration
- Discussion
  - tissue distribution
  - inter-conversion
  - dose effects on blood/tissues

Principal Omega-3 Fatty Acids

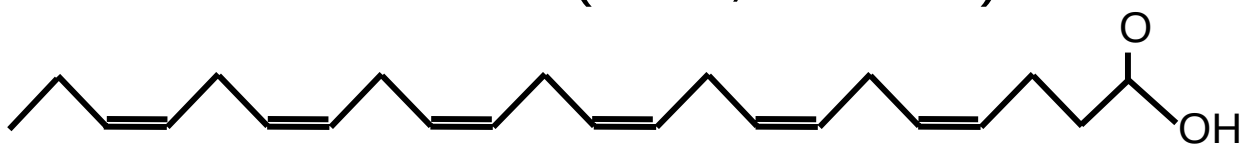
α-Linolenic Acid (ALA; 18:3n-3)



Eicosapentaenoic Acid (EPA; 20:5n-3)

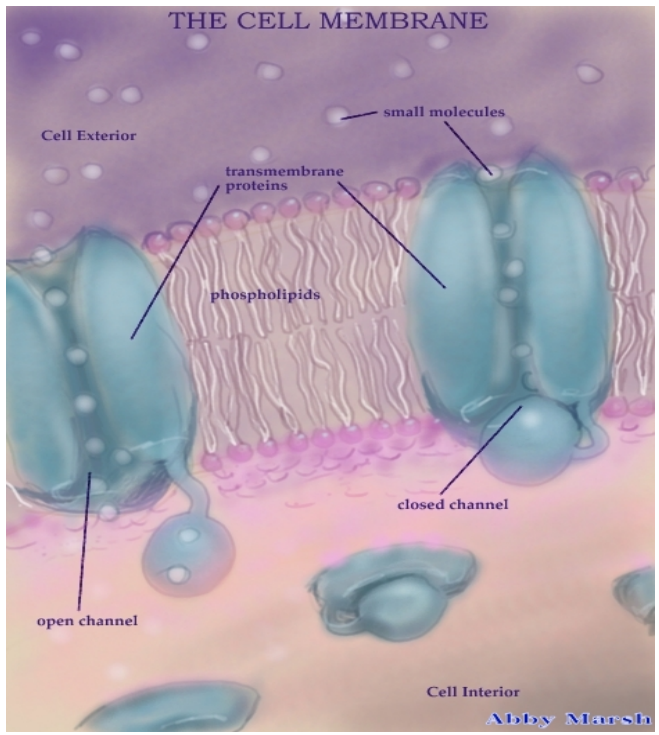


Docosahexanoic Acid (DHA; 22:6n-3)

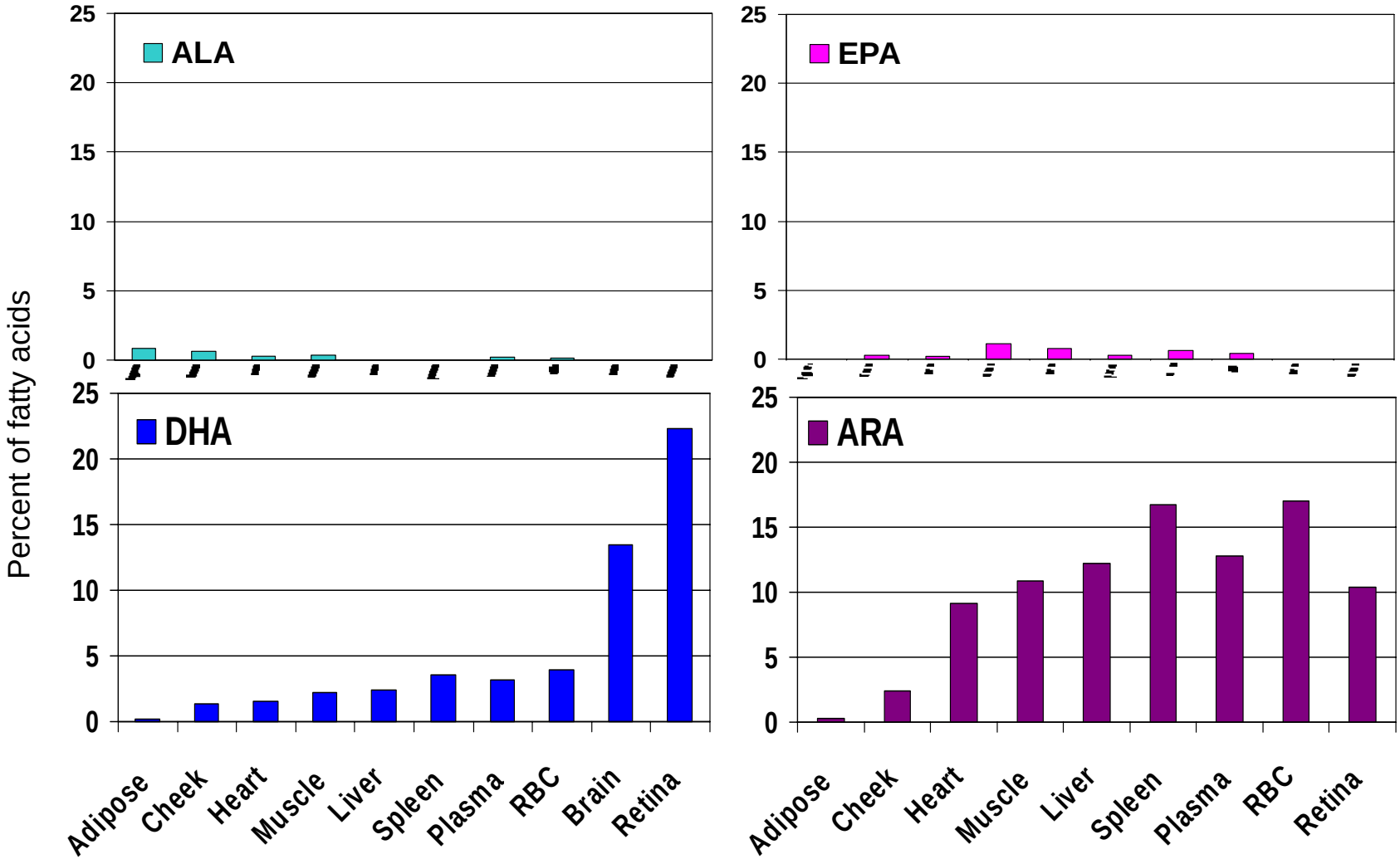


Physiological Roles of Fatty Acids

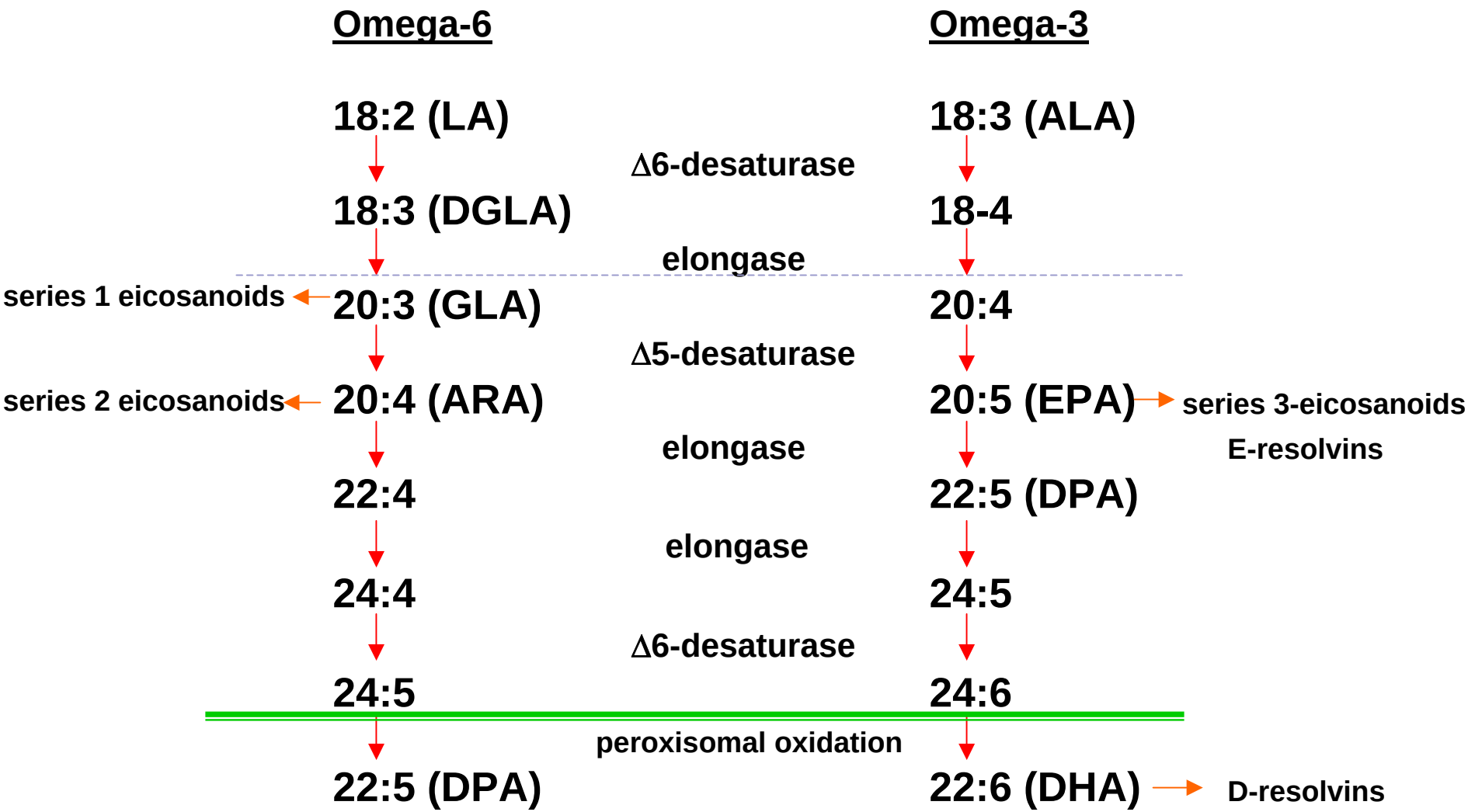
- Energy
- Structural components of membrane
  - Biophysical properties
  - Protein interactions
- Precursors to bioactives
  - Eicosanoids, resolvins
- Gene regulation
  - Ligands for nuclear receptors



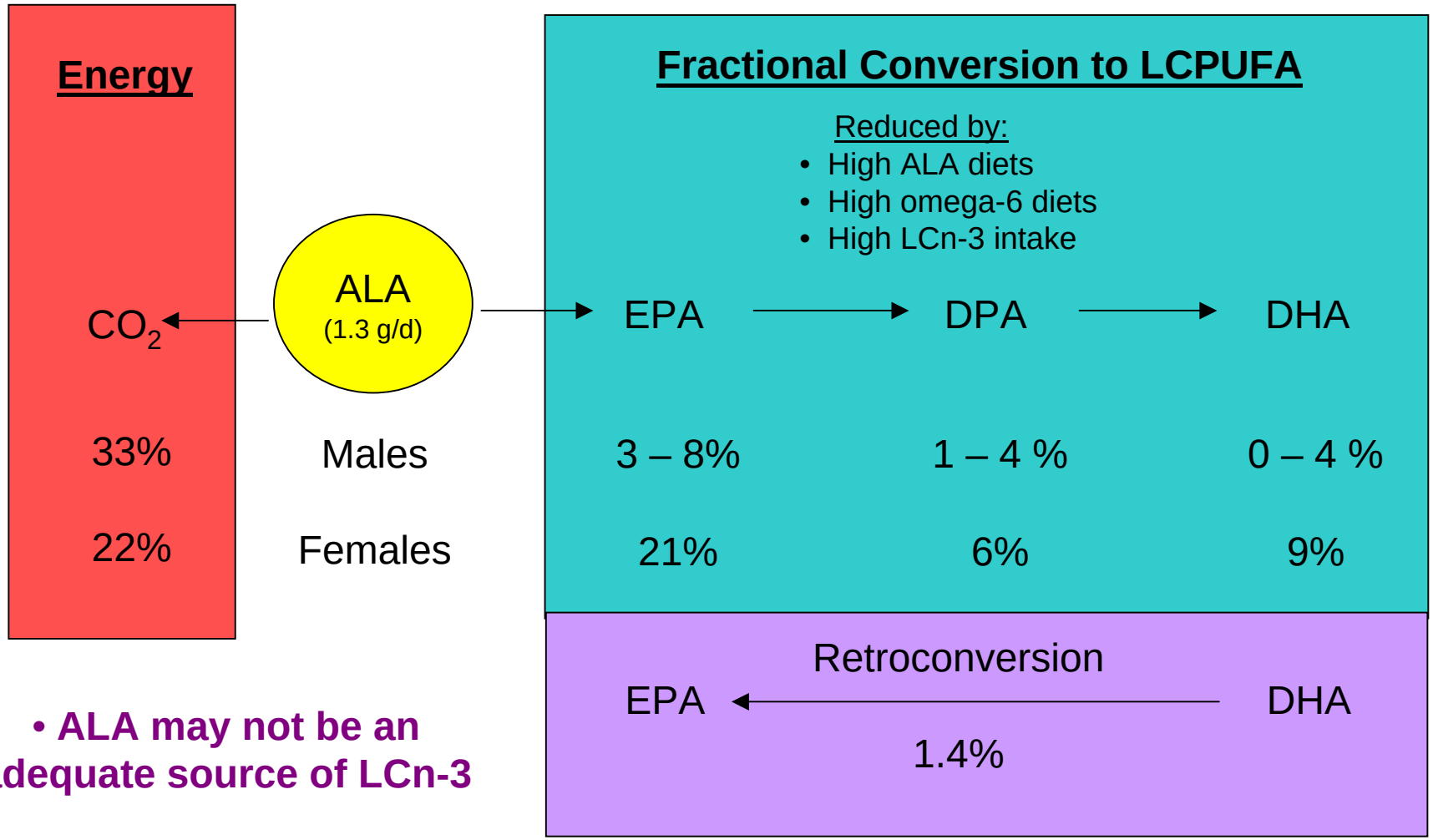
Tissue levels of LCPUFA in humans



Biochemical Pathway

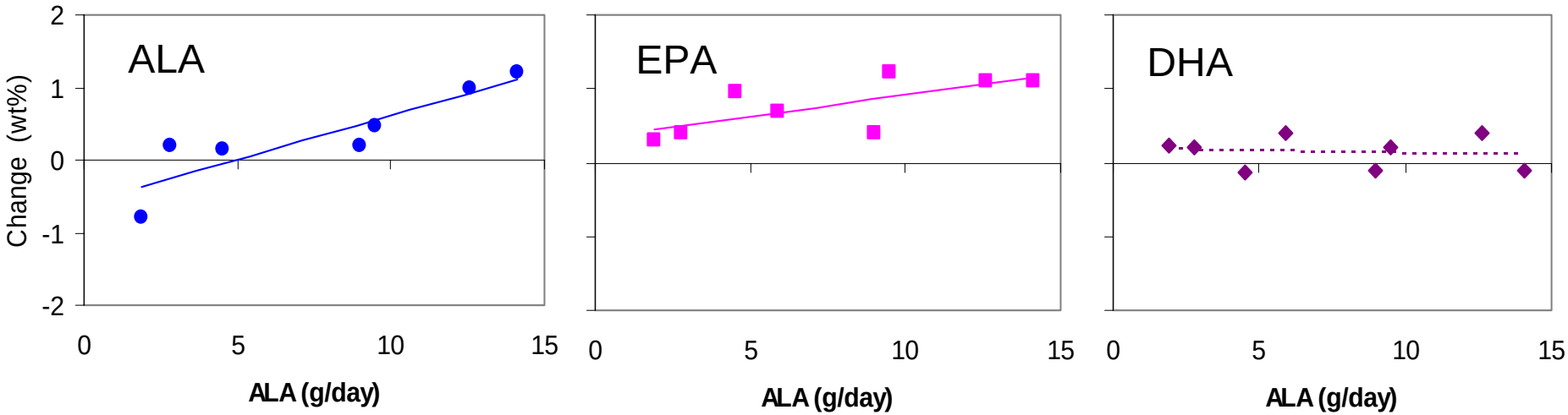


Inter-conversion of Omega-3 Fatty Acids
Stable Isotope Studies in Humans



• ALA may not be an adequate source of LCn-3

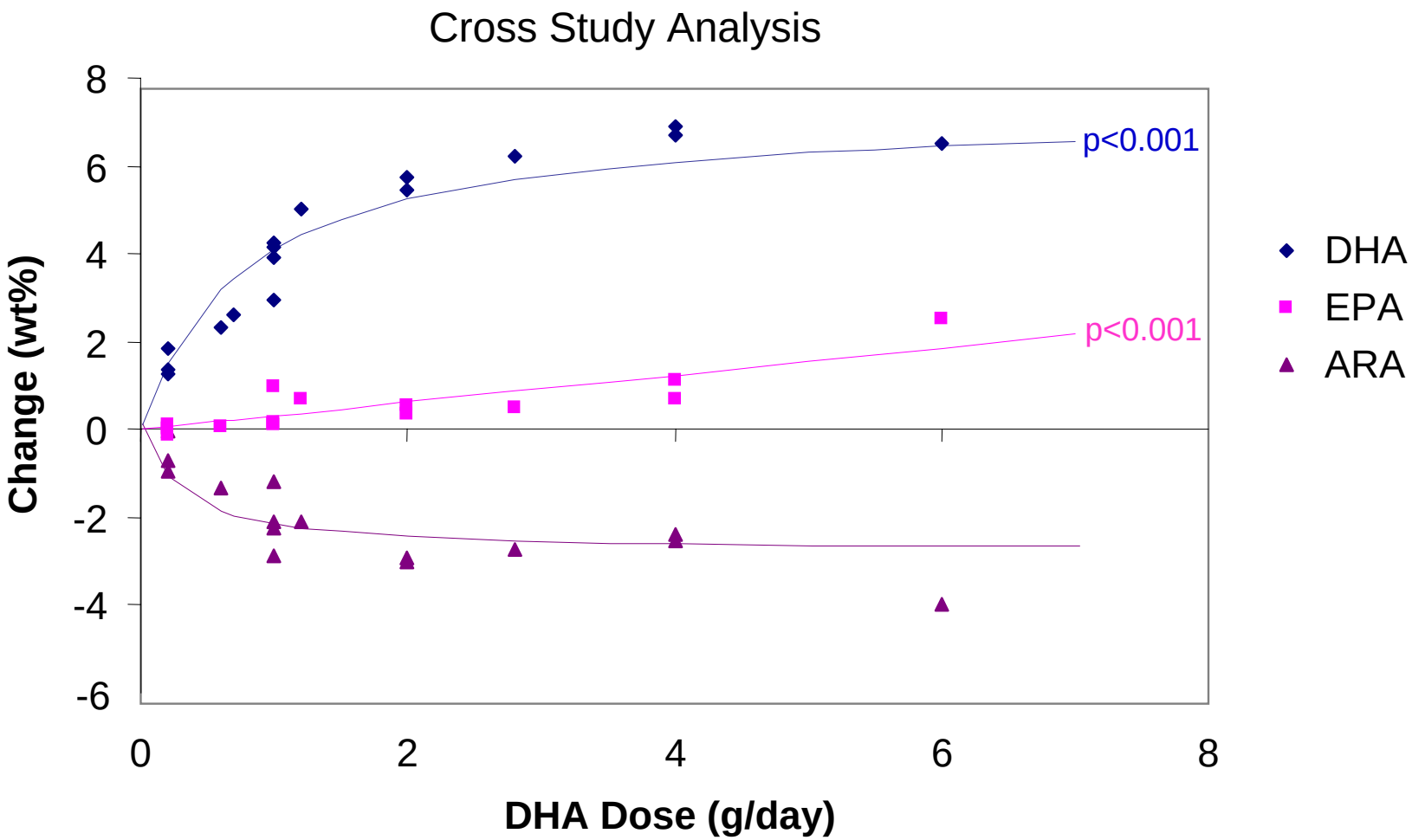
Effect of dietary ALA on plasma LCPUFA levels - Cross Study Analysis



r^2=0.79, p=0.008

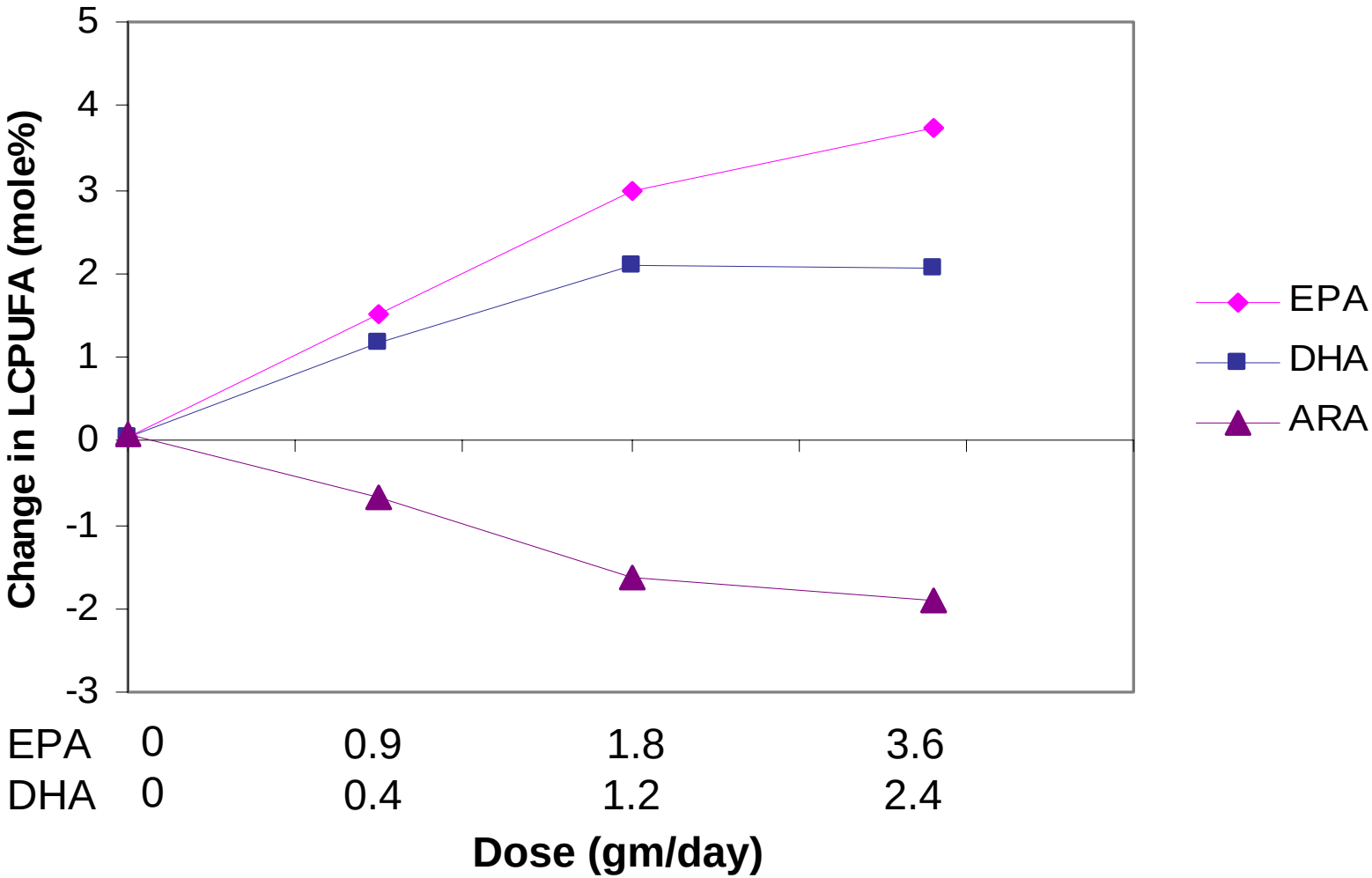
r^2=0.49, p=0.052

Effect of DHA supplementation on plasma LCPUFA levels



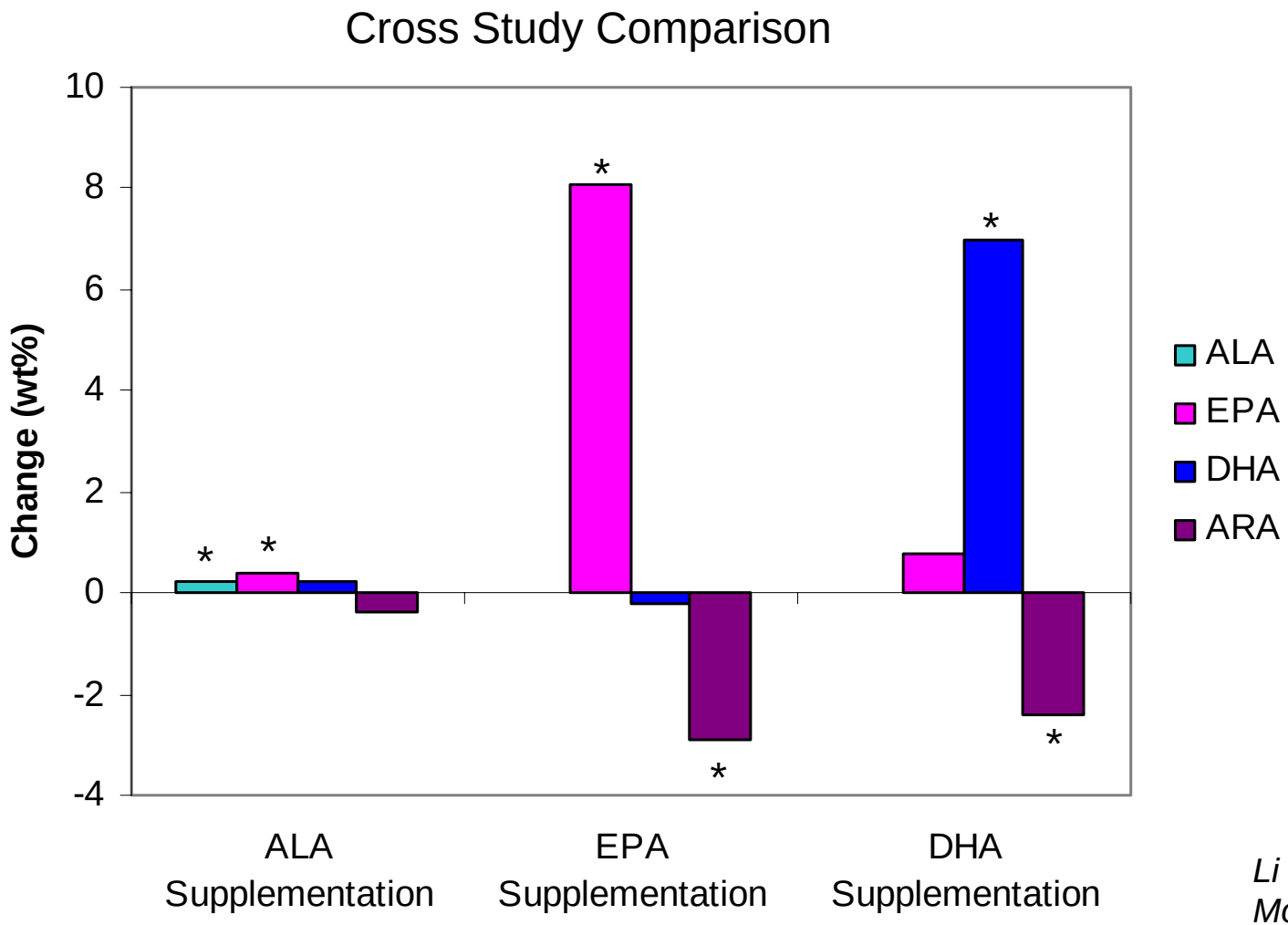
Mean baseline DHA ~3-3.5 wt%

Effect of DHA and EPA on Plasma LCPUFA Levels



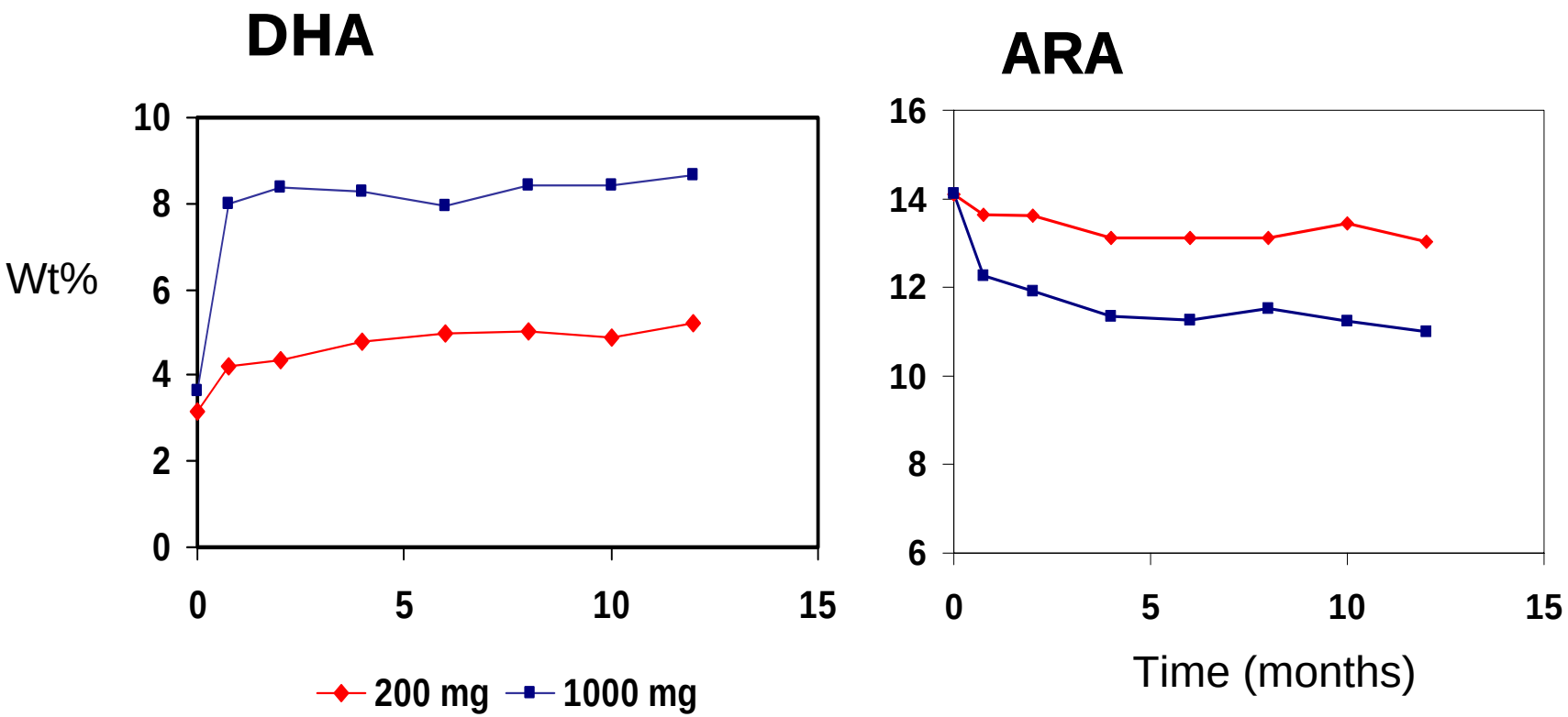
Blonk et al, 1990

Effects of omega-3 supplementation on plasma LCPUFA



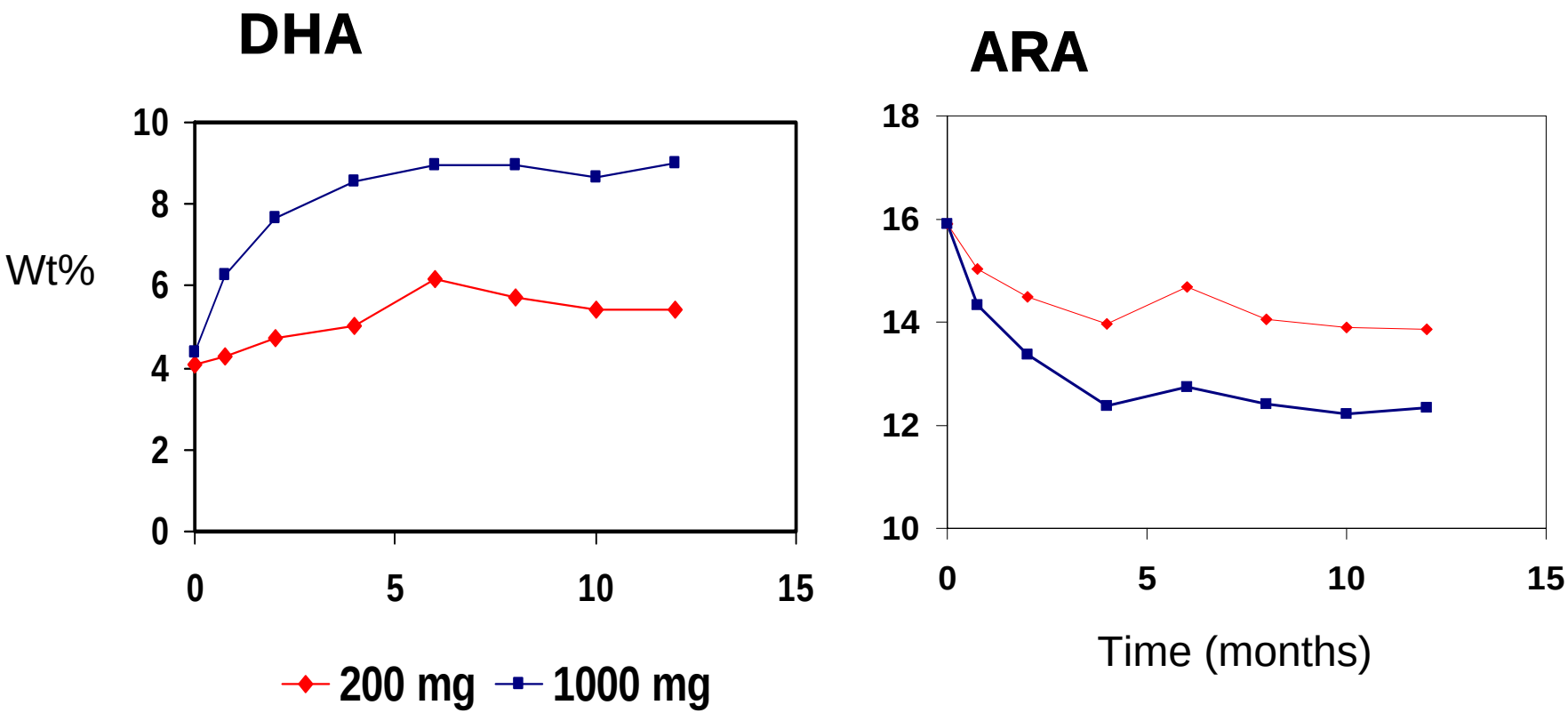
Li et al, 1999
Mori et al, 2000

DHA supplementation
Plasma PL kinetics



Martek data on file

DHA Supplementation
RBC kinetics



Martek data on file

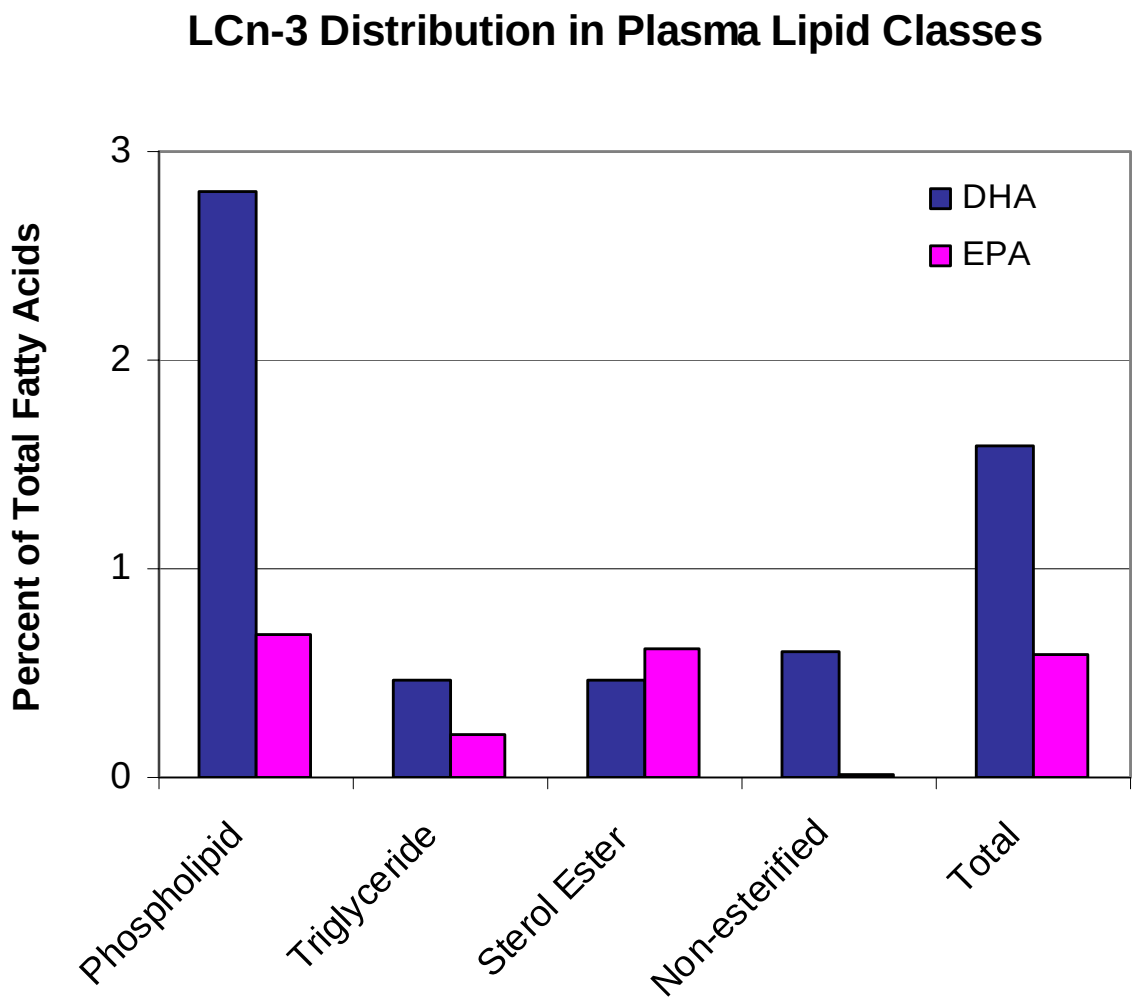
Comparison of DHA and EPA Kinetics

Whole Plasma – LCn-3 Supplementation

Fatty Acid	Time to reach steady state	Washout
EPA	14 days	~4 wks
DHA	21 days	>24wks

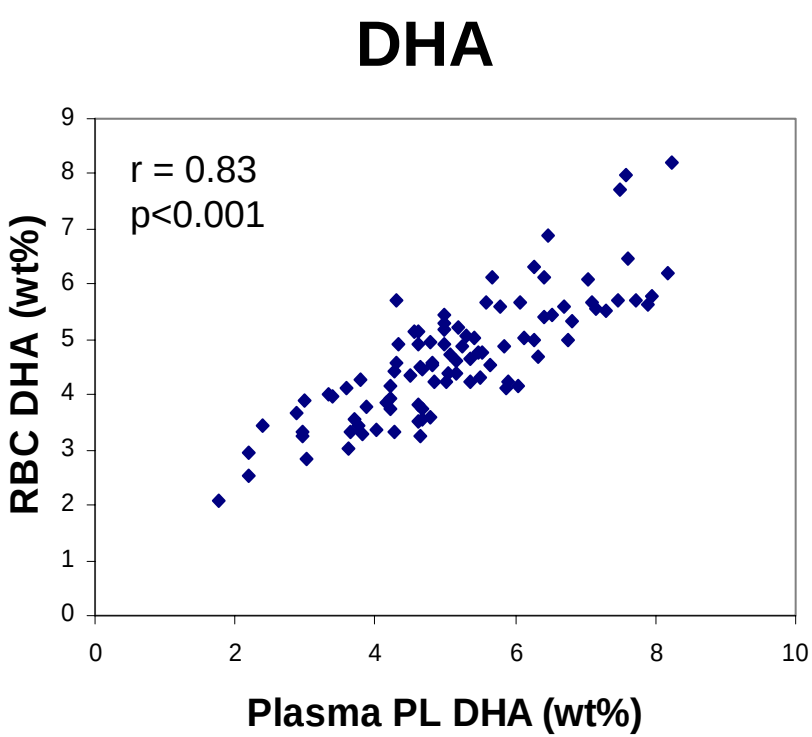
Subbaiah et al, 1993 (3.5g EPA, 2.2 g DHA)
Marangoni et al, 1993 (1.4 g EPA, 0.8 g DHA)

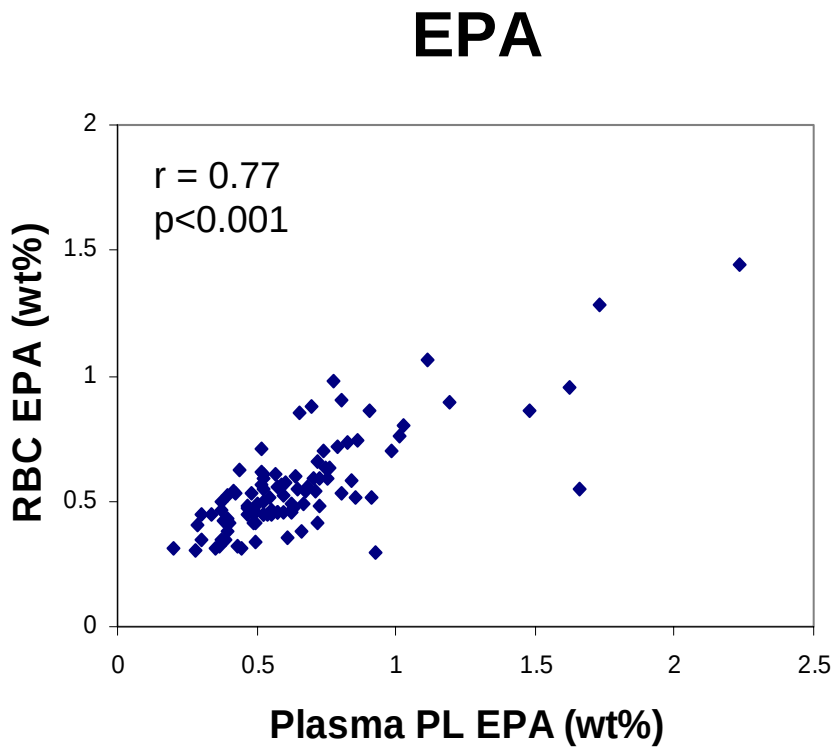
Distribution of DHA and EPA in Human Plasma



Source: Martek data on file

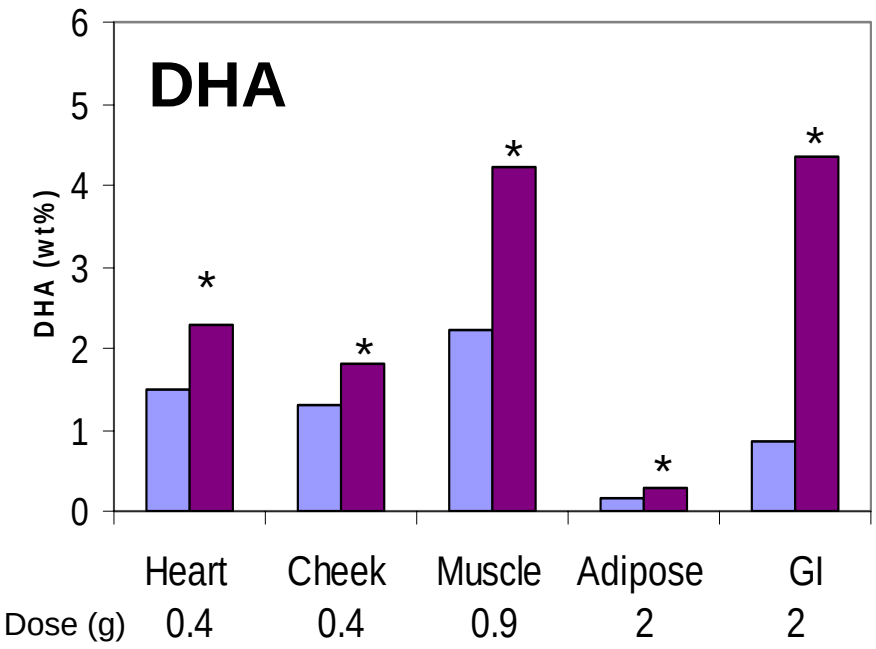
Plasma and RBC DHA and EPA levels are highly correlated

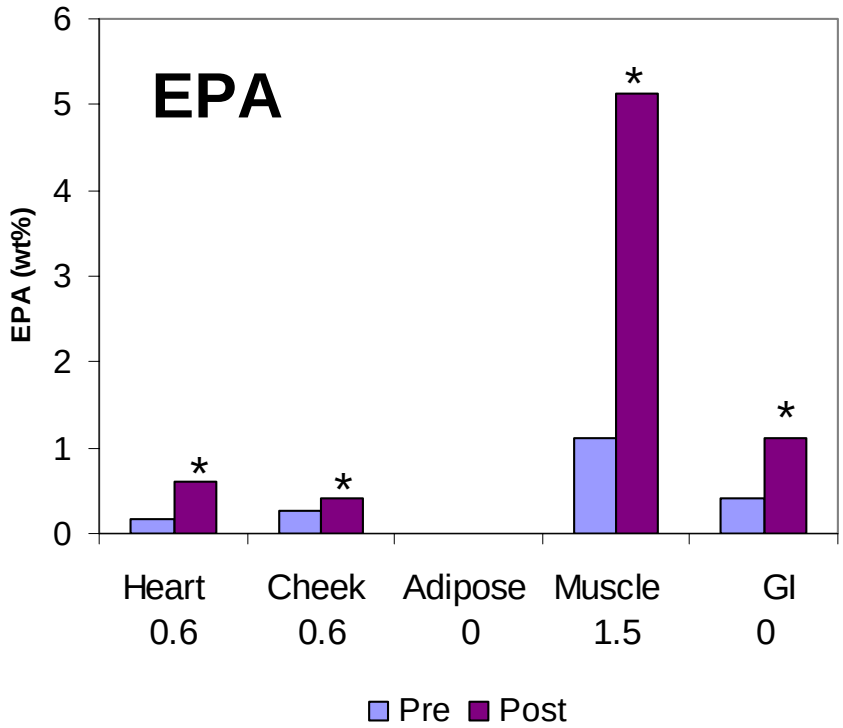




Source: Martek data on file

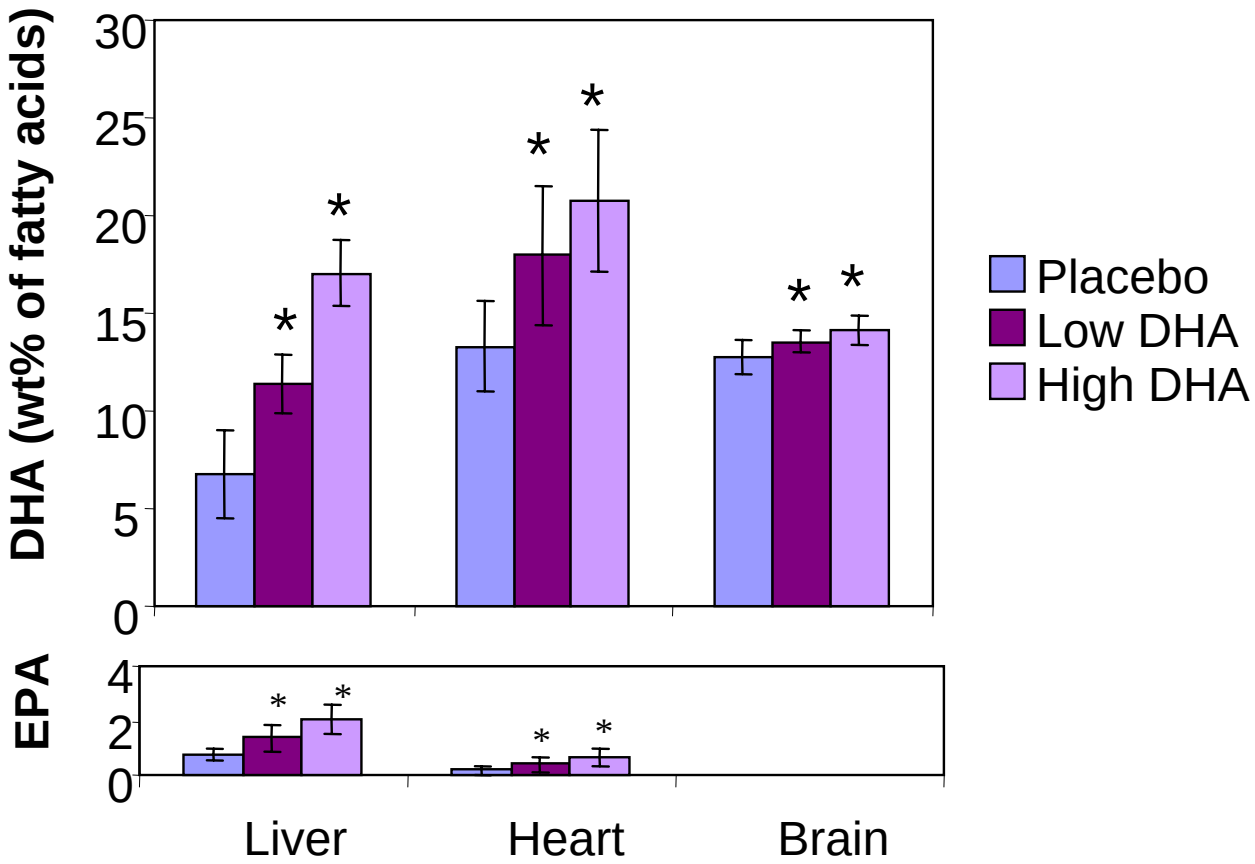
Human tissues are responsive to DHA and EPA supplementation





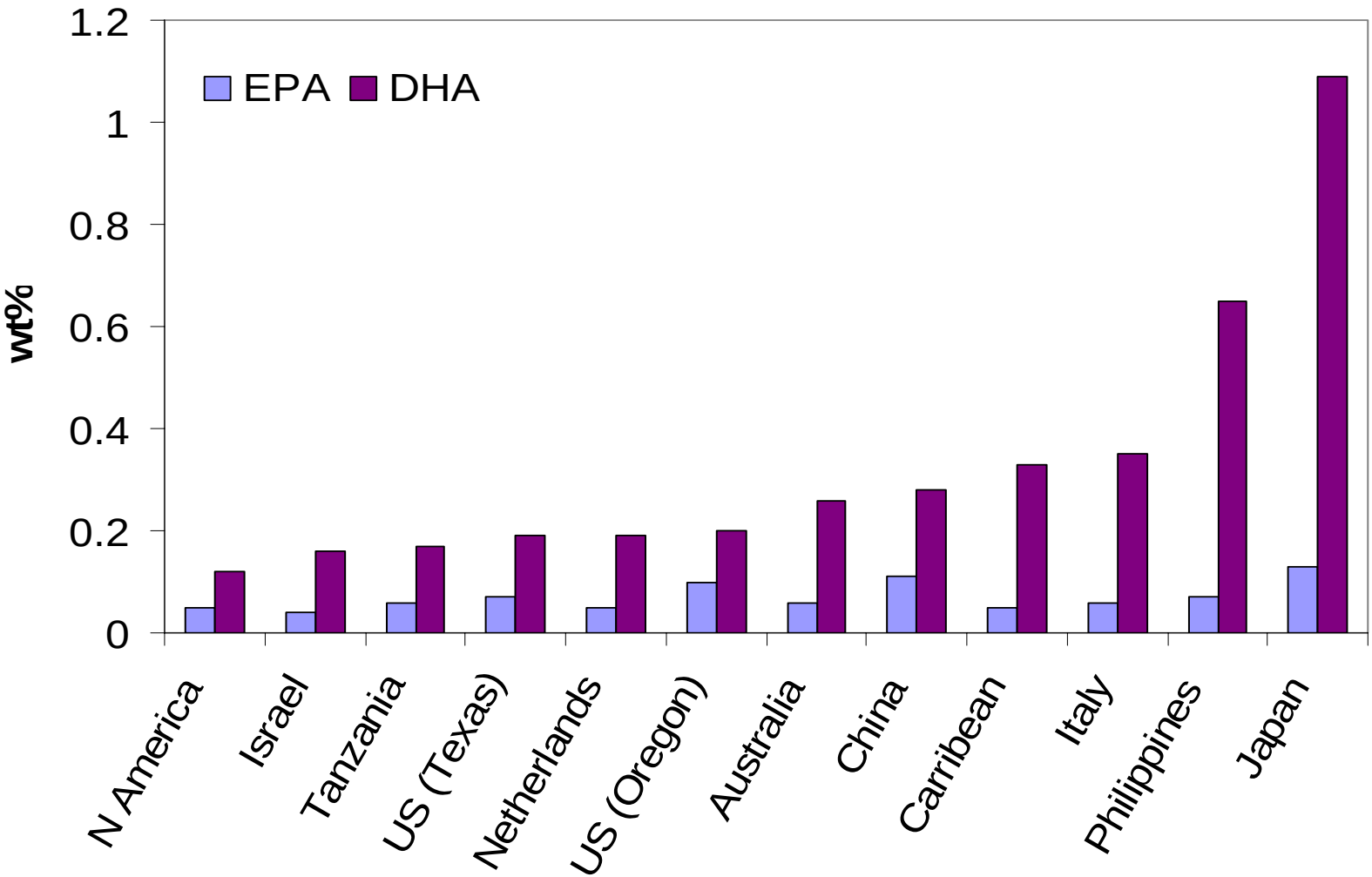
Harris et al, 2004
Breslow, unpublished
Andersson, 2002
Lloyd-Still, in press

Dietary DHA Increases Tissue Levels of DHA in Rats

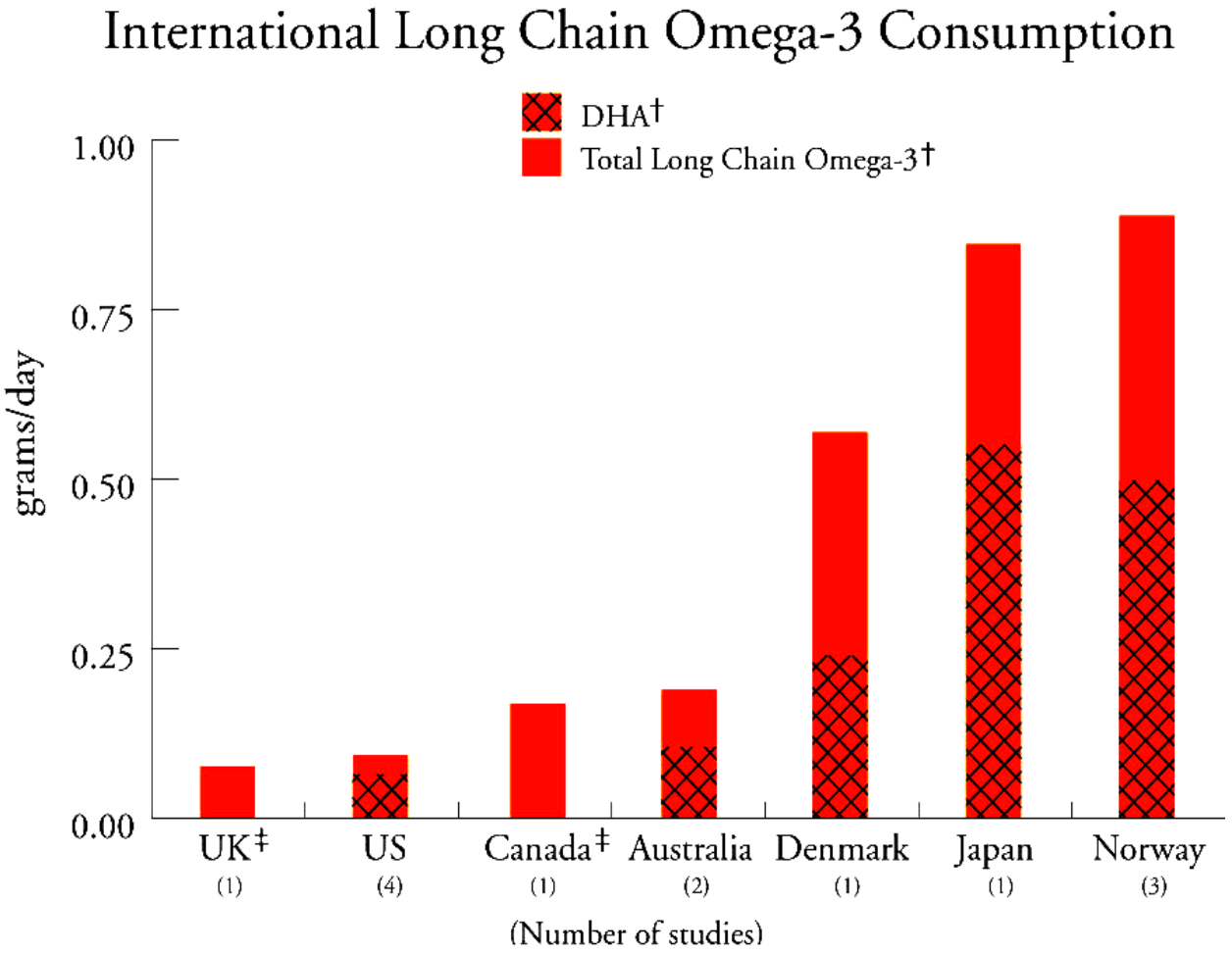


Arterburn et al, 2000

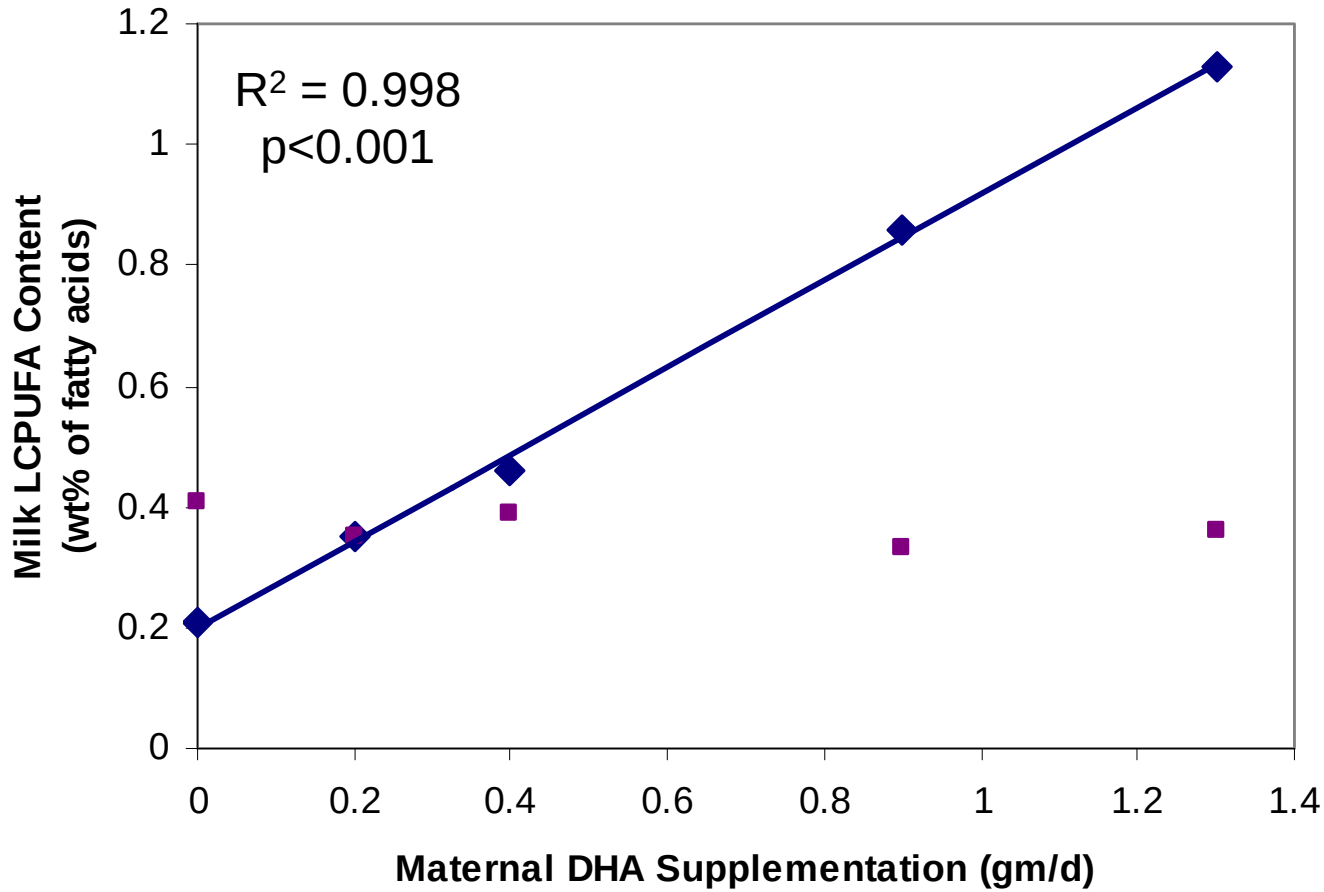
Recent reports of DHA and EPA levels in human milk



Long chain omega-3 consumption is low in US compared to other countries

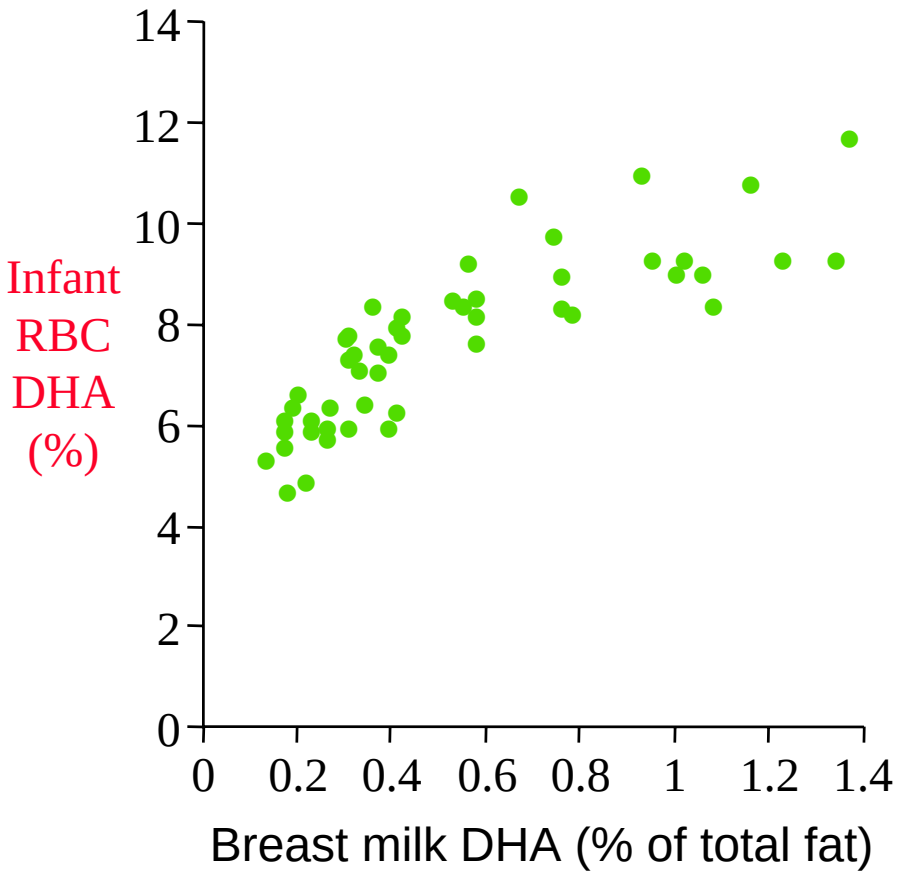


Maternal Intake of DHA Determines Breast Milk DHA Content



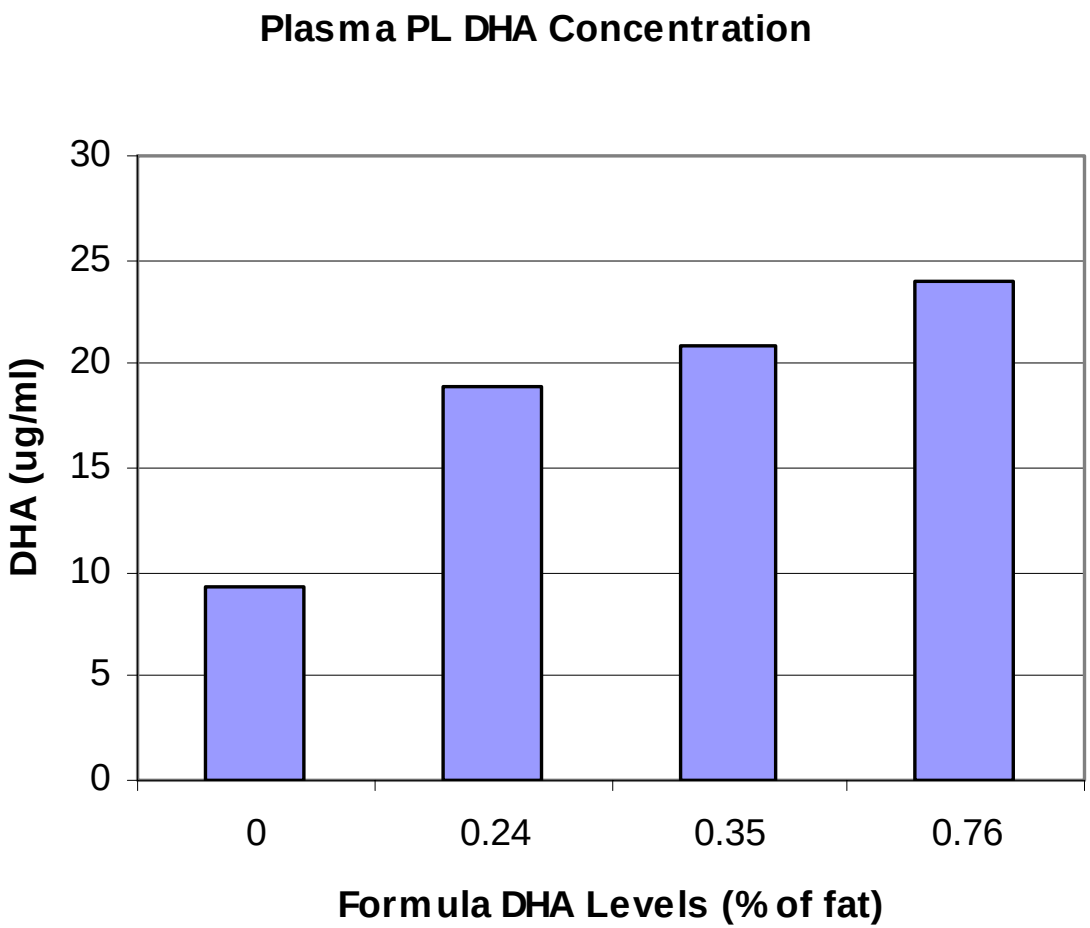
Adapted from Makrides *et al* (1996) Europ J Clin Nutr

Infant DHA status determined by breast milk DHA content



Makrides et al 1997

Infant DHA Levels Depend on DHA Levels in Formula



Clandinin et al, 1997

Conclusion

- Supplement with the fatty acid of interest using doses and durations appropriate to raise plasma and/or tissue levels
  - Which fatty acid? DHA and/or EPA
    (ALA is not a good source of LCn-3)
  - How much? 2g DHA saturates plasma
  - How long? 1 mo for plasma
    3-6 mo for tissues
    < wk for milk
    (FAs stay elevated during whole supplementation)

Summary

- DHA is principal n-3 fatty acid in tissues
- Limited inter-conversion of n-3 FAs
  - ALA not adequate source of LCn-3
- Plasma response to dietary intake
  - ALA does not accumulate appreciably
  - Dose dependent increases in EPA and DHA
  - Plasma levels equilibrate within 4 wks
  - 2 g DHA/day gives close to maximal DHA response
- Tissue levels LCn-3 increase with supplementation
- Milk DHA levels reflect maternal dietary intake
- Infant DHA levels determined by dietary intake