The effect of dietary α-linolenic acid levels on regulation of omega-3 lipid synthesis in rat

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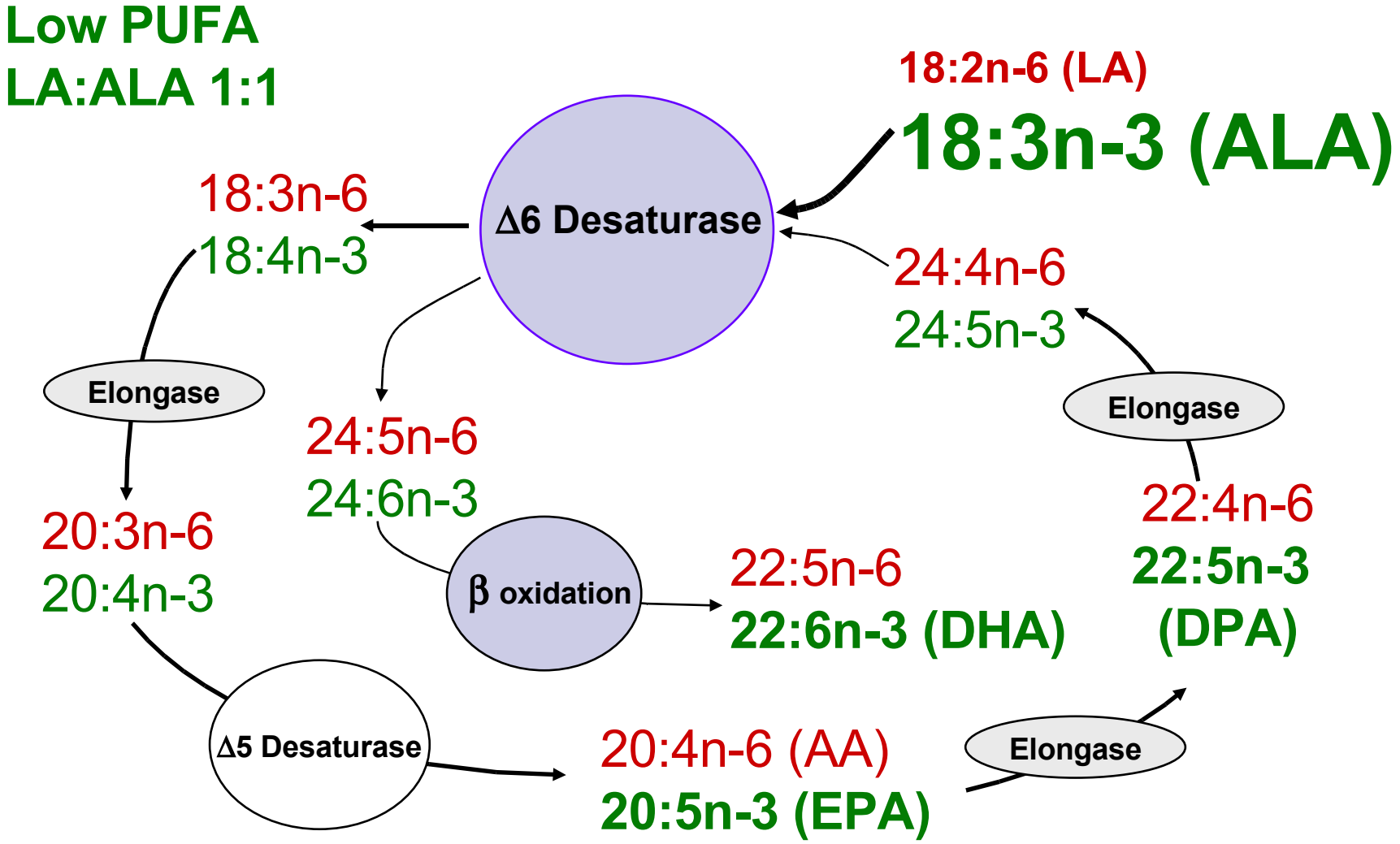
Conversion of PUFA to LCPUFA

	Omega 3		Omega 6
PUFA	18:3n-3 ALA		18:2n-6 LA
	↓ Δ6D	desaturation	↓ Δ6D
	↓	elongation	↓
	↓ Δ5D	desaturation	↓ Δ5D
LCPUFA	20:5n-3 EPA		20:4n-6 AA
	↓	elongation	↓
	22:5n-3 DPA		22:4n-6 DTA
	↓	elongation	↓
	24:5n-3		24:4n-6
	↓ Δ6D	desaturation	↓ Δ6D
	24:6n-3		24:5n-6
	↓	β oxidation	↓
	22:6n-3 DHA		22:5n-6

Dietary ALA increase



- **Increased DHA levels in the body of humans and animals have been achieved by**

- ***increasing the amount of dietary ALA*** ***(Goyens, P. L. et al, Am J Clin Nutr 2006; Arbuckle, L. D. et al, J Nutr 1994)*** ***or***

- ***lowering the LA to ALA ratio in the diets*** ***(Blank, C. M. et al, J Lipid Res 2002; Makrides, M. et al, Am J Clin Nutr 2000)***

- Hepatic D-6 desaturase activity is induced by diets low in essential fatty acids and suppressed by diets rich in vegetable or fish oils *(Melin, T., and Nilsson, A., Prostaglandins Leukot Essent Fatty Acids 1997; Peluffo, R. O. et al, Biochim. Biophys. Acta 1976)*

- High in dietary n-3 and n-6 PUFA status decrease D5D/D6D mRNA levels and activities *(Cho, H. P. et al, J Bio Chem 1999)*

Dietary PUFA ↑

Fads, Elovl gene expression

Desaturase, elongase activities

Fads1*: *delta 5 desaturase gene

Fads2*: *delta 6 desaturase gene

Elovl2: elongase2 gene

Elovl5: elongase 5 gene

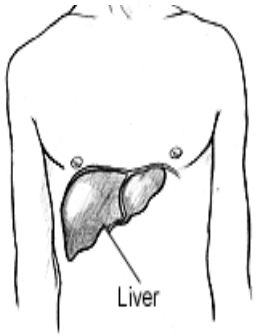
Aims

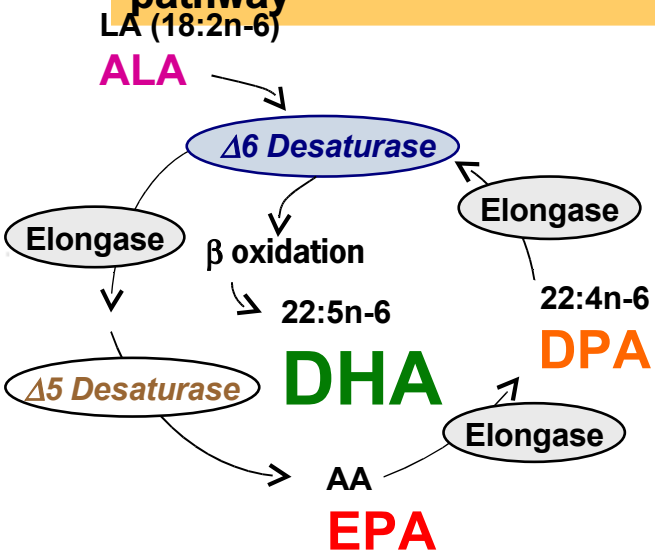
Omega-3 rich Vegetable oils

Cheap, Stable, Sustainable

With an optimised ALA level

Fatty acid synthetic pathway





High level n-3 LCPUFA accumulation in tissues

To evaluate whether…

- **Increased n-3 LCPUFA conversion can be achieved by optimizing dietary LA:ALA ratio & PUFA levels**
- **Desaturases and elongases gene can be affected by dietary PUFA resluted in n-3 LCPUFA conversion**

Dietary Design

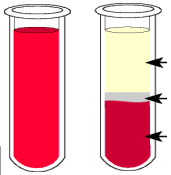
- A range of ALA levels were tested while the level of other competing PUFA (LA) were held constant at 1%en

Three week-old Hooded Wistar

Diet	Maca oil	Soy oil	Exp.1	Exp. 2	Exp. 3	Exp. 4	Exp. 5
LA %e	0.4	5	1	1	1	1	1
ALA %e	0.03	0.5	0.2	0.5	1.0	1.9	2.9

All diets 5% fat, 20% protein

3 weeks



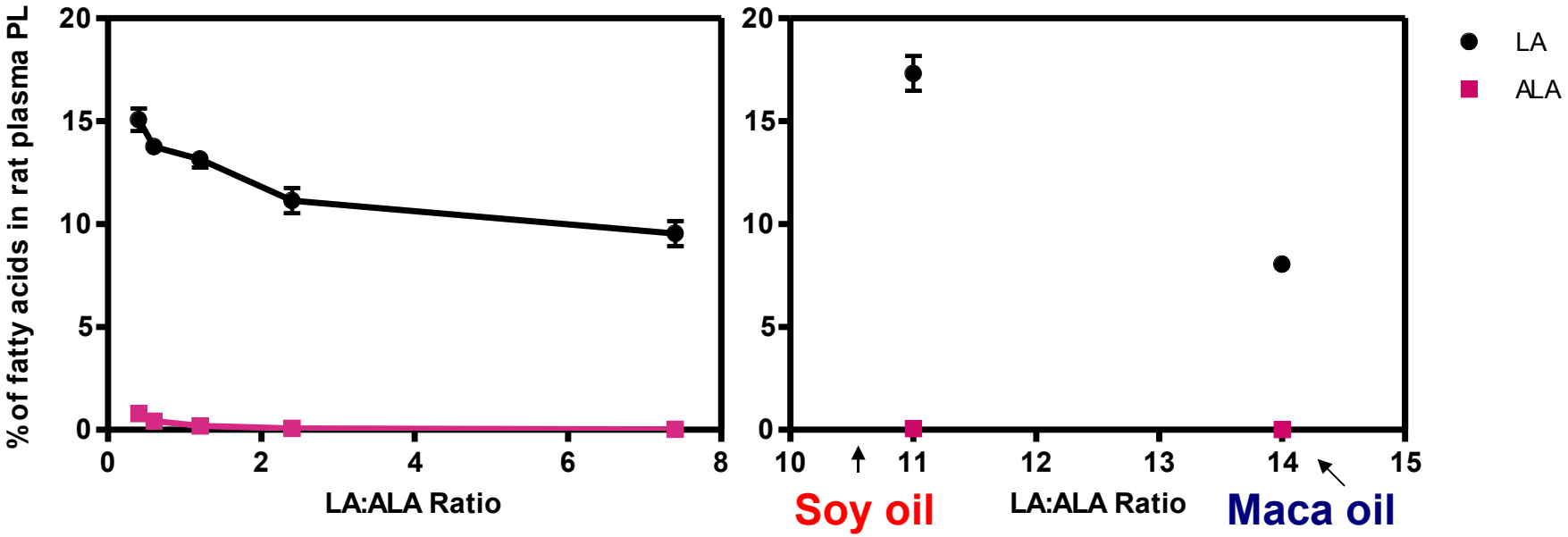
blood

liver

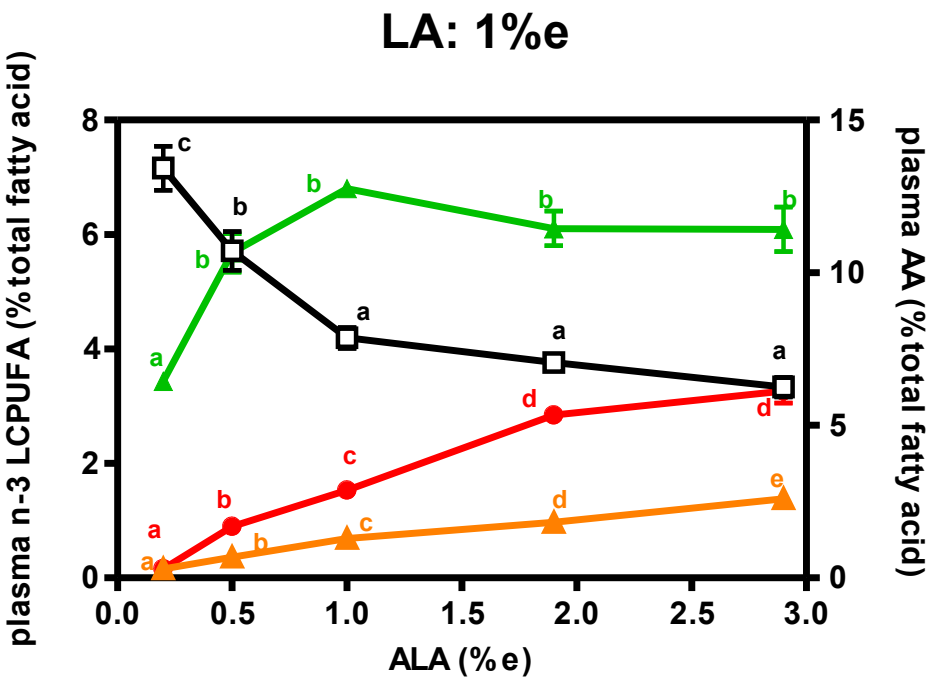
Fatty Acid Extraction

RNA Extraction & qRT-PCR Analysis

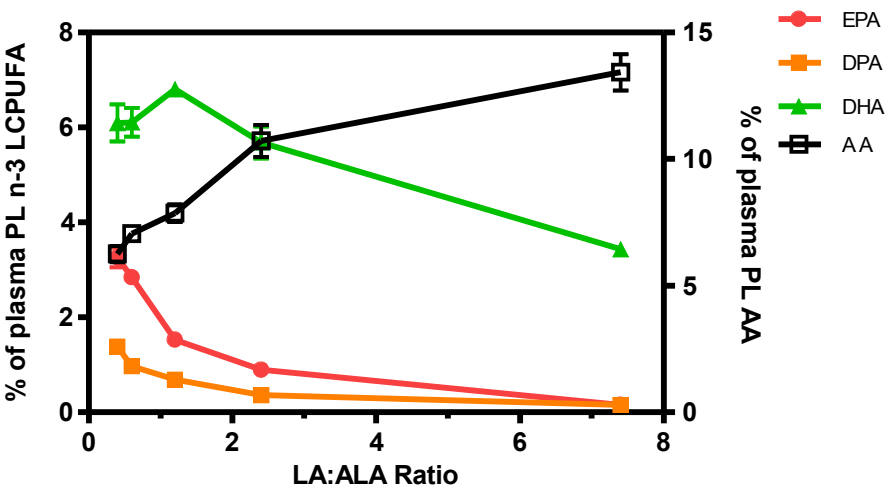
LA and ALA in plasma PL



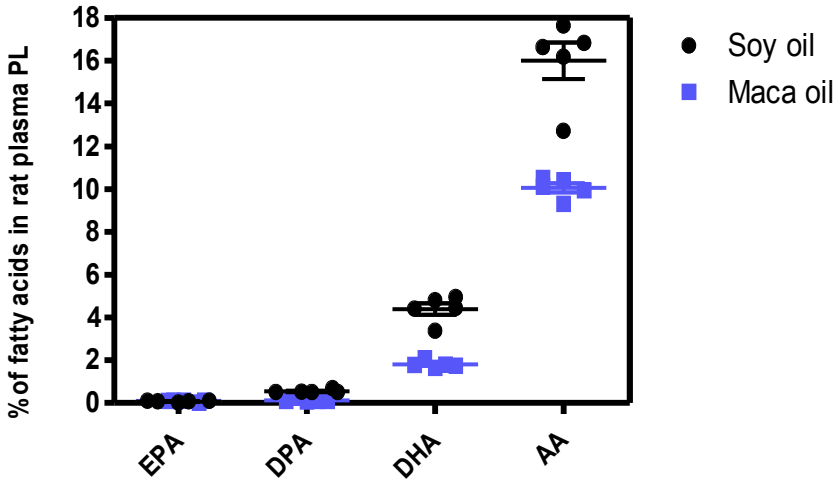
Diet	Exp.1	Exp. 2	Exp. 3	Exp. 4	Exp. 5	Maca oil	Soy oil
LA %e	1	1	1	1	1	0.4	5
ALA %e	0.2	0.5	1.0	1.9	2.9	0.03	0.5
LA:ALA	7.4	2.4	1.2	0.6	0.4	14	11

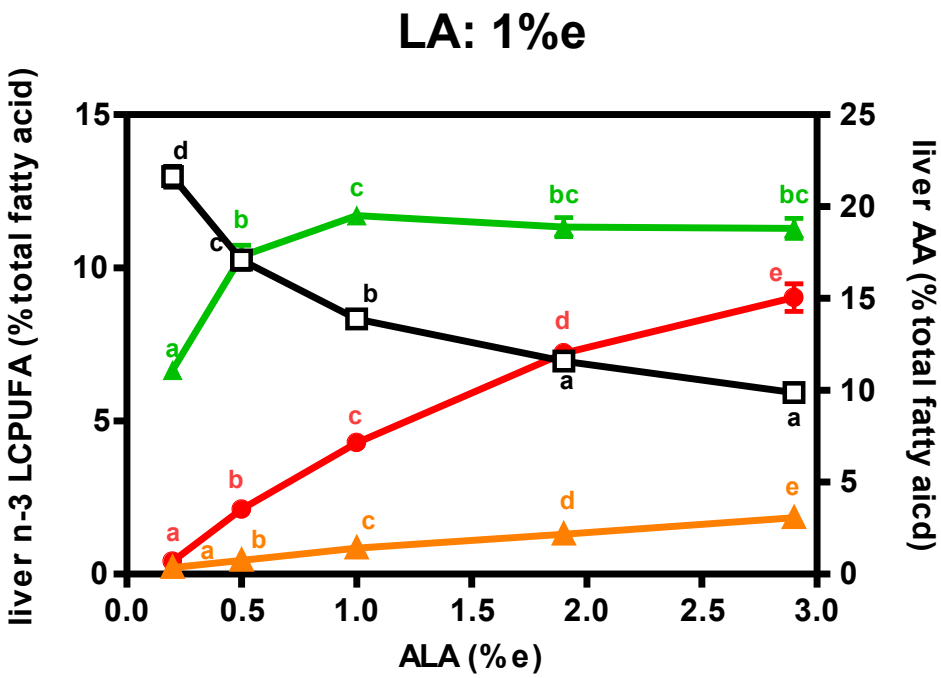


Plasma PL

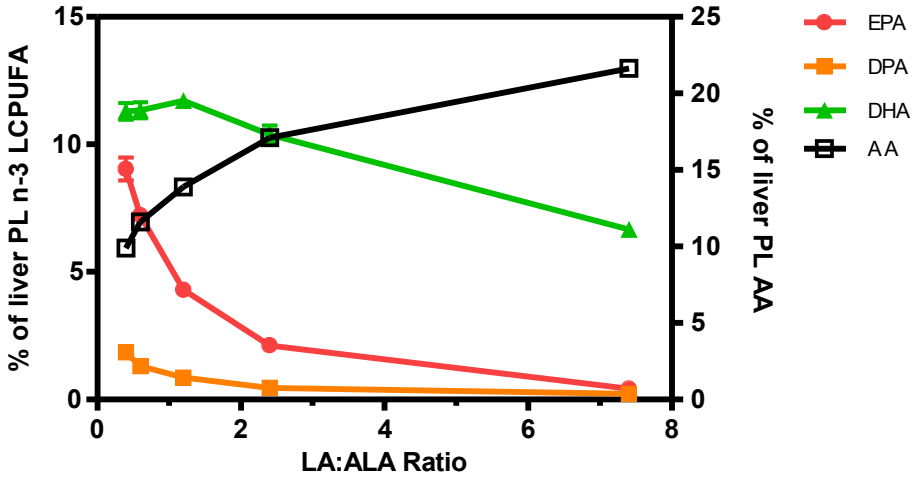


Maca oil	Soy oil
LA%en 0.4	LA%en 5
ALA%en 0.03	ALA%en 0.5





Liver PL



Maca oil	Soy oil
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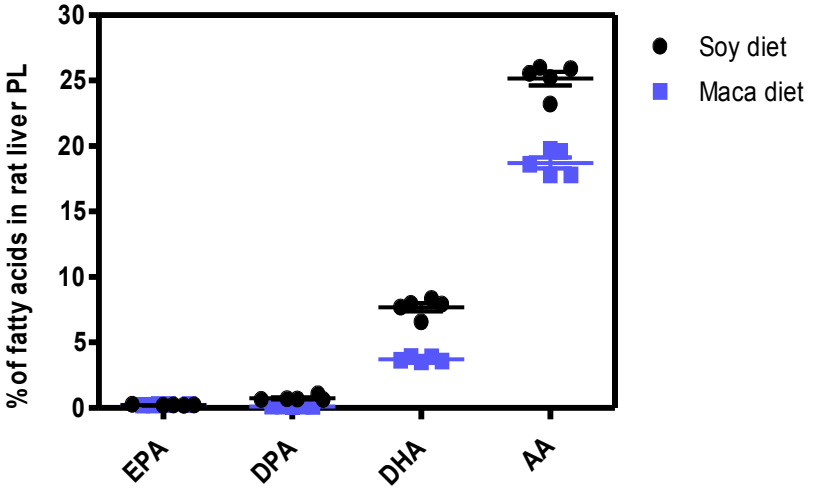
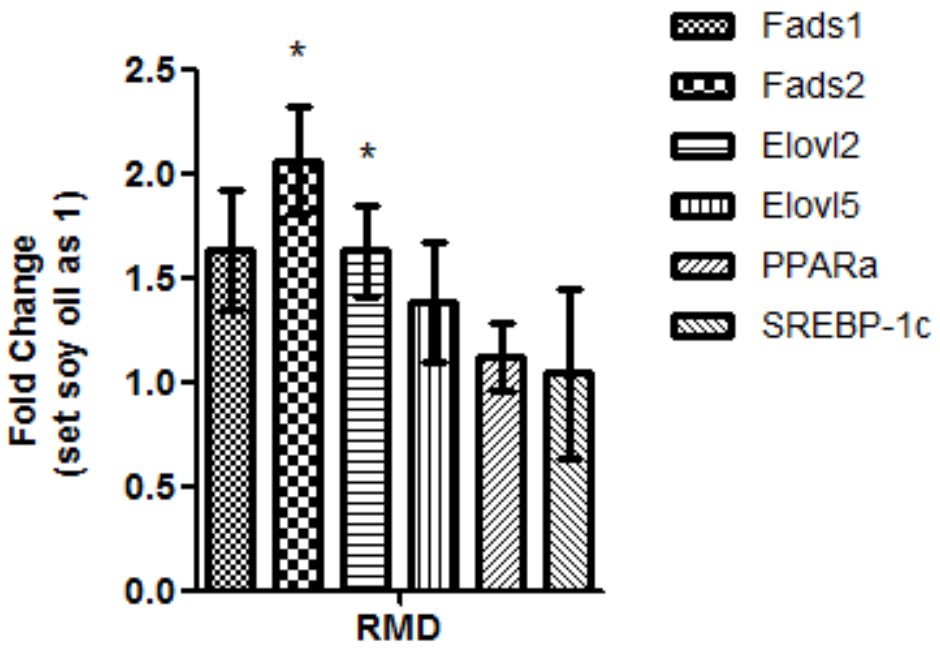


Summary

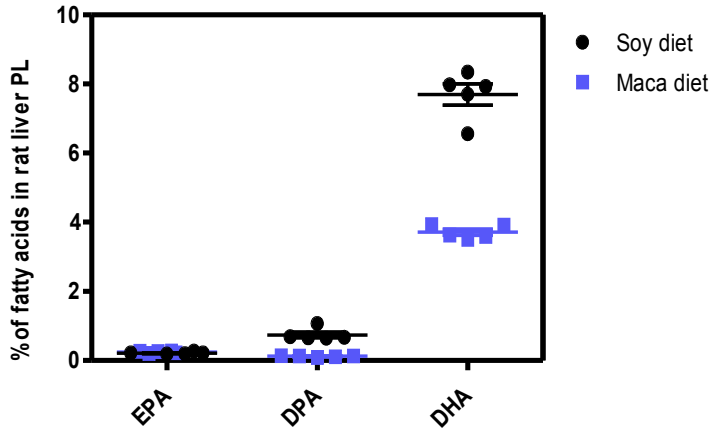
- Fatty acid in plasma reflected dietary PUFA levels
- A significant increase in EPA matched by an decrease of plasma AA in plasma and liver
- Low dietary ratio of LA to ALA and high energy level of ALA resulted in high n-3 LCPUFAs in plasma and liver
- EPA and DPA levels in plasma and liver increased in a dose dependent manner

What happen to the gene expression of key enzymes in the n-3 LCPUFA conversion pathway?

Hepatic gene expression level

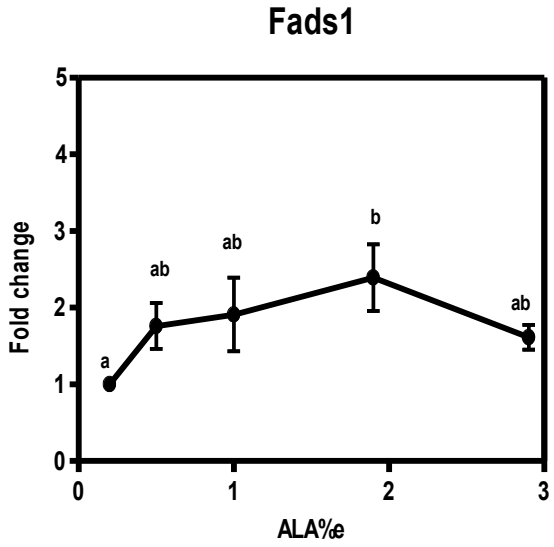


Fatty acid level in liver PL

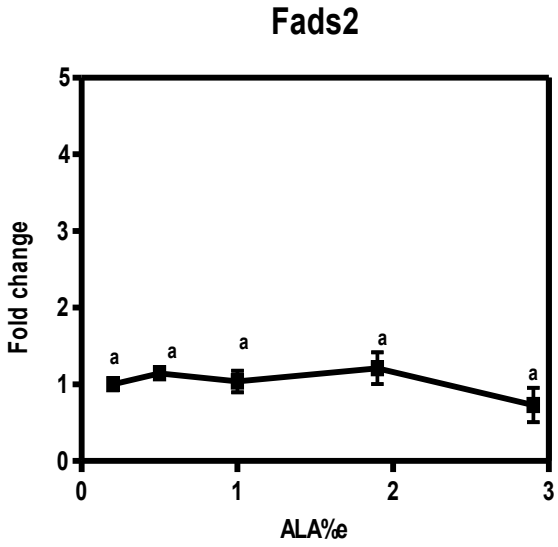


Gene expression level

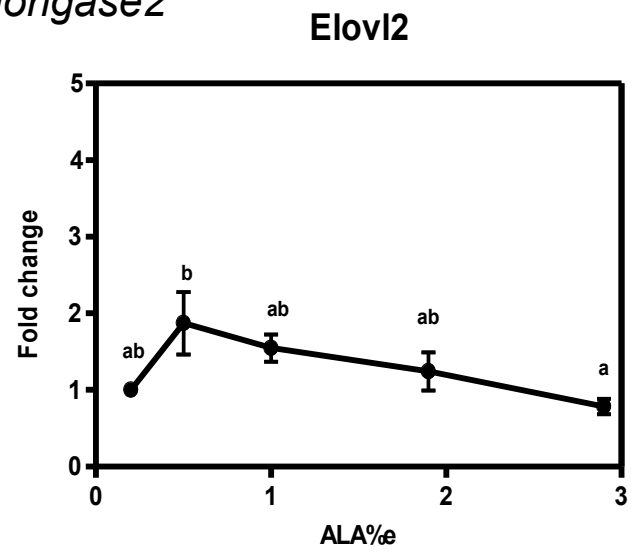
Delta-5 desaturase



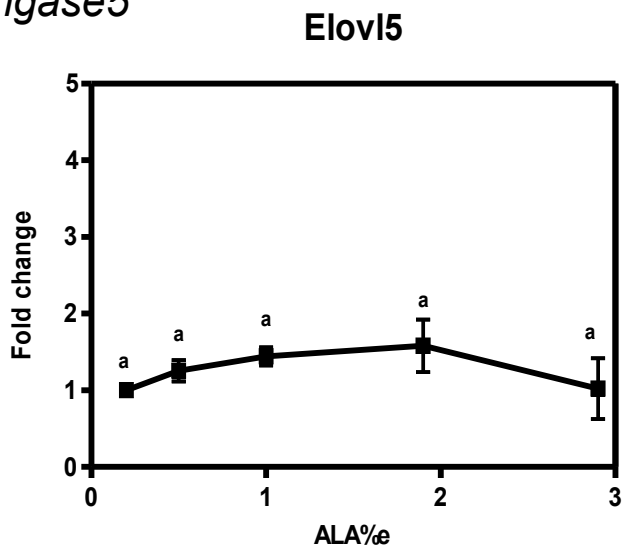
Delta-6 desaturase

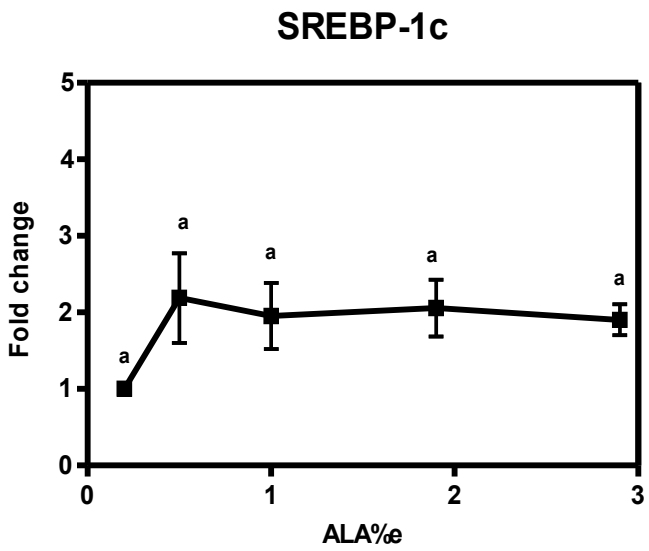


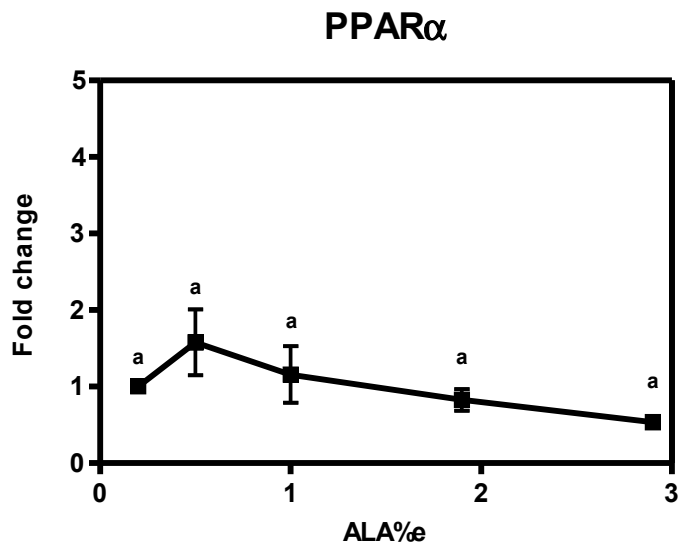
Elongase2



Elongase5







Sterol regulatory element binding proteins (SREBP) are membrane bound transcription factors. Liver express predominantly SREBP-1c that activates genes of fatty acid synthesis.

Peroxisome proliferator activated receptors (PPAR) are single polypeptides nuclear receptors. Liver express PPARαthat activates transcription of genes involve in in fatty acid βoxidation.

Conclusions

- Dietary PUFA with lower LA:ALA ratio and higher ALA %en results in significant incorporations of DPA and EPA plasma and liver phospholipids

- Enzyme competition effects may be stronger than gene expression on driving n-3 LCPUFA conversion

Acknowledgements

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