

# Fucoxanthin enhanced protein level of delta6-desaturase in the liver of mice

○Takayuki Tsukui, Masashi Hosokawa, Kazuo Miyashita  
(Faculty of Fisheries Science, Hokkaido University)



## Introduction



Wakame

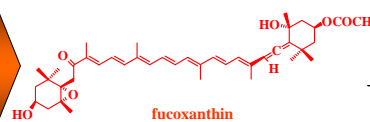
Extraction

### Composition of Wakame lipids

Glicolipid* (+Phospholipid)	68.3 (%)
Fucoxanthin	9.6 (%)
Fucoesterol	0.7 (%)
Others	21.7 (%)

\*MGDG:DGDG:SQDG=59:23:18 (w/w)

Purification



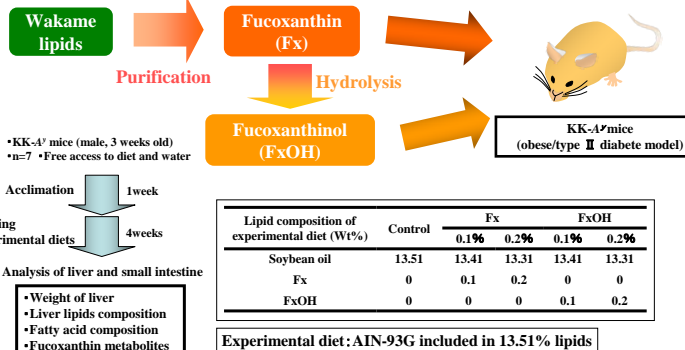
### Function of fucoxanthin

- Reduction of fat accumulation into WAT of mice  
*Biochem. Biophys. Res. Commun.* **332**, 392-397 (2005).
- Suppression of preadipocyte differentiation  
*Int. J. Mol. Med.* **18**, 147-52 (2006).
- Apoptosis induction activity  
*Food Sci. Technol. Res.* **5**, 243-246 (1999).
- Biochim. Biophys. Acta **1675**, 113-119, (2004).
- Anti-inflammatory effect  
*Exp. Eye Res.* **81**, 422-428 (2005).

(brown seaweed, *Undaria pinnatifida*)

Fucoxanthin (Fx) which is a characteristic marine carotenoid found in brown seaweeds such as *Undaria pinnatifida* and *Sargassum fulvellum* has an unique structure including an allenic bond and a 5,6-monoepoxide. Its structure is different from that of common carotenoids such as  $\beta$ -carotene and lycopene. In our recent study, we served enhancement of docosahexaenoic acid (DHA) levels in the liver of diabetic/obese KK-*A*<sup>y</sup> mice fed Fx diet. Delta6-desaturase (D6D) is the rate-limiting enzyme in the biosynthesis of n-3 and n-6 polyunsaturated fatty acids (PUFA) such as DHA and arachidonic acid from  $\alpha$ -linolenic and linoleic acid, respectively. In this study, we investigated the effect of dietary xanthophylls (Fx, fucoxanthin and astaxanthin) and phytol on fatty acid composition in the liver of C57BL/6J mice.

## Experiment I



### Fatty acid composition (mg/g) of small intestine and liver

Fatty acids	small intestine			liver				
	control	Fx 0.2%	FxOH 0.2%	control	Fx		FxOH	
					0.1%	0.2%		
16:0	11.6±2.8	7.4±2.5	6.1±1.0	10.4±2.6	9.9±2.3	10.3±1.7	7.5±0.8	9.1±1.5
18:0	4.9±0.7	4.2±0.7	3.8±0.2	4.6±1.0	5.5±0.5	5.3±0.4	5.1±0.4	5.2±0.4
18:1n-9	13.1±3.8	9.1±3.4	6.3±1.4	13.1±4.7	9.1±2.8**	8.2±1.6*	7.1±1.0*	8.1±2.0**
18:2n-6	14.5±3.3	13.3±4.5	9.3±1.5	11.9±2.7	10.9±2.5	13.4±2.2	8.3±0.4	10.8±2.3
18:3n-3	0.8±0.2	0.9±0.4	0.5±0.1	0.6±0.2	0.7±0.2	0.8±0.2	0.4±0.0	0.6±0.2
18:4n-3	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D
20:4n-6(AA)	1.9±0.3	2.2±0.3	1.9±0.1	3.8±0.9	4.5±0.3	4.2±0.5	4.7±0.4**	4.6±0.4**
20:5n-3(EPA)	N.D	0.1±0.0	0.1±0.0	0.1±0.0	0.1±0.0	0.1±0.0	0.2±0.0	0.1±0.0
22:5n-3(DPA)	0.1±0.0	0.1±0.0	0.1±0.0	0.1±0.2	0.2±0.0	0.2±0.0*	0.1±0.0	0.2±0.0
22:6n-3(DHA)	0.8±0.1	0.7±0.1	0.7±0.0	2.2±1.0	3.7±0.3*	4.2±0.6*	2.9±0.4*	3.9±0.3*

\*:p<0.01 vs control  
\*\*:p<0.05 vs control

- No changes were seen in the fatty acid composition of small intestine of KK-*A*<sup>y</sup> mice fed experimental diet.
- However, the amount of AA, DPA and DHA in the liver increased in mice fed experimental diet.

## Conclusion

◎ Fx enhances the amount of DHA in the liver. This effect was seen in C57BL/6J, normal mice, as well as KK-*A*<sup>y</sup>, obese/type II diabetic mice.

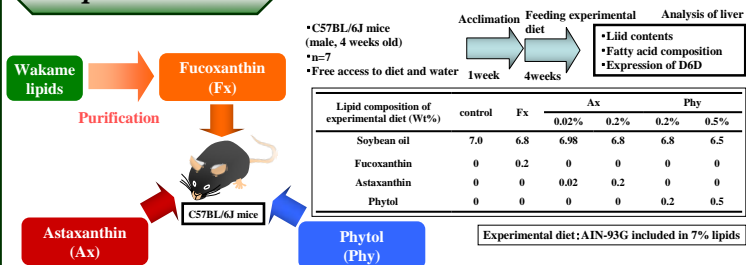
◎ Fx up-regulates delta6-desaturase in the liver of C57BL/6J mice.

◎ Ax and Phy don't change the amount of DHA, and down-regulate D6D in the liver of C57BL/6J mice.

### Acknowledgements

This work is supported by Grant-in-Aid for JSPS Fellows (08J00394).

## Experiment II



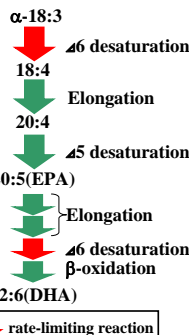
### Fatty acid composition (mg/g) of liver

Fatty acids	control	0.2% Fx	Astaxanthin		Phytol	
			0.02%	0.2%	0.2%	0.5%
			16:0	5.1±0.3	6.3±0.6	5.6±0.5
18:0	3.0±0.1	3.7±0.2*	2.9±0.1	3.2±0.1	3.0±0.1	3.4±0.2
18:1n-9	3.6±0.4	4.5±0.7	4.3±0.7	7.0±0.9**	4.0±0.6	3.3±0.4
18:1n-7	0.5±0.0	0.8±0.1	0.6±0.1	0.8±0.1	0.6±0.1	0.5±0.0
18:2n-6	5.0±0.3	7.2±0.8	5.3±0.4	8.1±1.0**	4.6±0.3	4.2±0.4
18:3n-3	0.1±0.0	0.2±0.0	0.2±0.0	0.3±0.1**	0.1±0.0	0.0±0.0
18:4n-3	N.D	N.D	N.D	N.D	N.D	N.D
20:4n-6(AA)	3.9±0.2	4.7±0.3	3.8±0.0	4.1±0.1	3.9±0.2	4.6±0.3*
20:5n-3(EPA)	0.1±0.0	N.D**	0.1±0.02	0.1±0.0**	0.1±0.0	N.D*
22:5n-3(DPA)	0.1±0.0	0.1±0.0	0.1±0.0	0.2±0.0**	0.1±0.0	0.1±0.0
22:6n-3(DHA)	2.1±0.2	2.8±0.2*	2.1±0.1	2.3±0.1	2.2±0.1	2.2±0.2

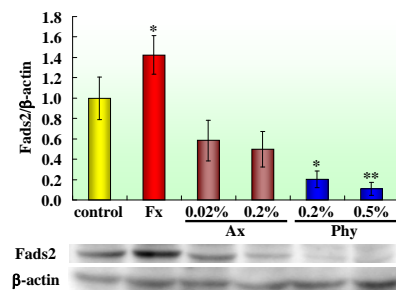
\*:p<0.05 vs control of C57BL/6J mice  
\*\*:p<0.01 vs control of C57BL/6J mice

•The amount of DHA in the liver of mice fed Fx diet was significantly increased.  
•On the other hand, the amount of DHA in the liver fed Ax and Phy diet was not changed.

### n-3 PUFA synthetic pathway



### Expression level of delta6-desaturase



- Delta6-desaturase expression level in the liver of mice fed Fx diet was up-regulated.
- On the other hand, D6D expression level in the liver of mice fed Ax and Phy was down-regulated.