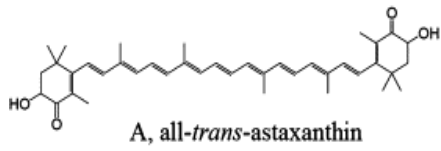


HYPOLIPEMIC ACTIVITY OF ASTAXANTHIN SUPPLEMENTATION IN MICE

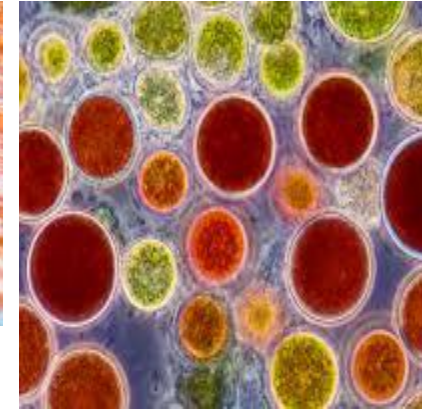
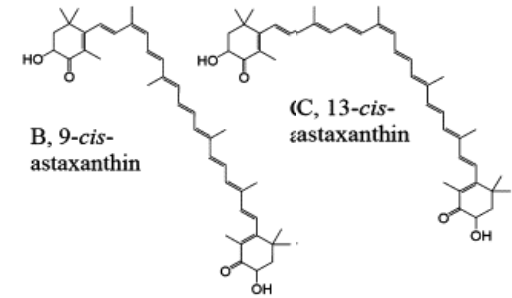
Flore Depeint

Myriam Benarroch, Justine Lallement, Larbi Rhazi, Camille Boroch,
Cindy Hugot, Claude-Narcisse Niamba, Hassan Younes





Astaxanthin

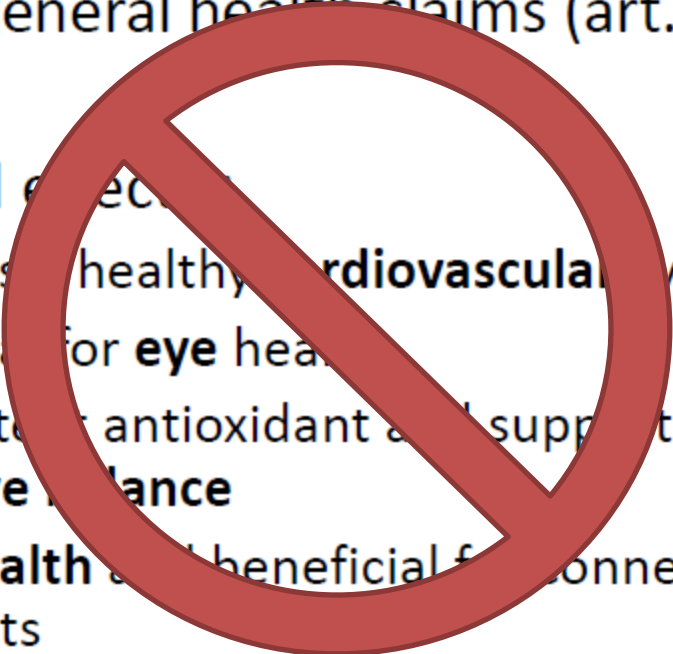


Astaxanthine dans différentes sources									
Source	Concentration (ppm)	isomères optiques (%)			isomères géométriques (%)		dérivation (%)		
		3R,3'R	3R,3'S	3S,3'S	al-E (trans)	cis	libre	mono-ester	di-ester
plankton	60								
krill	120	9~55	7~21	38~70	75	25	4~5	31~35	61~64
crevettes	1200						~5	~8	~91
Paracoccus bacteria	20 000						~5	~8	~91
Phaffia rhodozyma	6 000-10 000	-98	-	-2	70-90	10-30	100	-	-
Haematococcus pluvialis	10 000~40 000	~4	~8	~88	70	30	~5	~85	~15
synthétique	100 000	25	50	25	65~75	25~30	100		
Poissons		Isomères optiques (%)			isomères géométriques (%)		dérivation (%)		
		3R,3'R	3R,3'S	3S,3'S	al-E (trans)	cis	libre	mono-ester	di-ester
élevage	5~30	25	50	25					
sauvage	25~5	12~17	2~6	78~85					

Objectives of the APhaR project

- To develop astaxanthin extract from *Phaffia rhodozyma* yeast fermentation for human consumption
- To validate health benefits

Astaxanthin health benefits

- Under general health claims (art. 13.1)
 - Claimed effects
 - Supports a healthy **cardiovascular** system
 - Beneficial for **eye** health
 - High potent antioxidant and supports a healthy **oxidative balance**
 - **Joint health** and beneficial for connective tissue and joints
- 

Risks of cardiovascular disorders

> 45% of the population is overweight or obese

> 15% of the population is treated for dyslipidemia

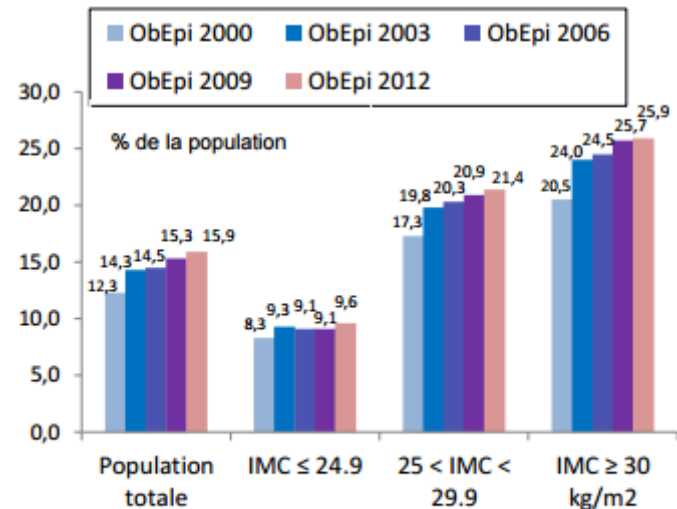
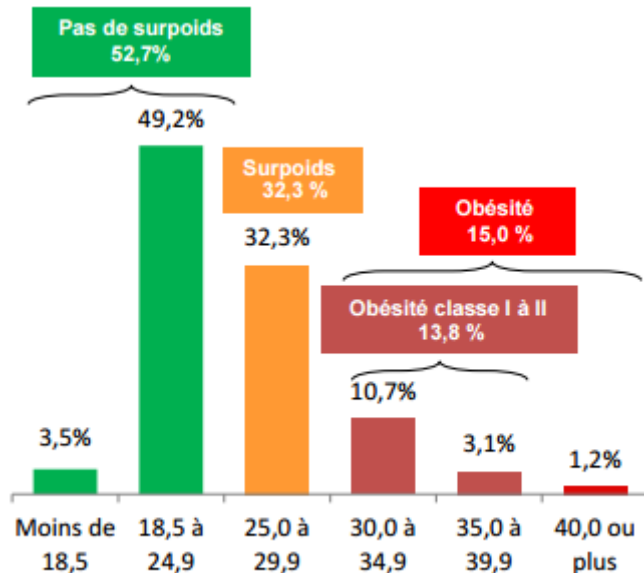
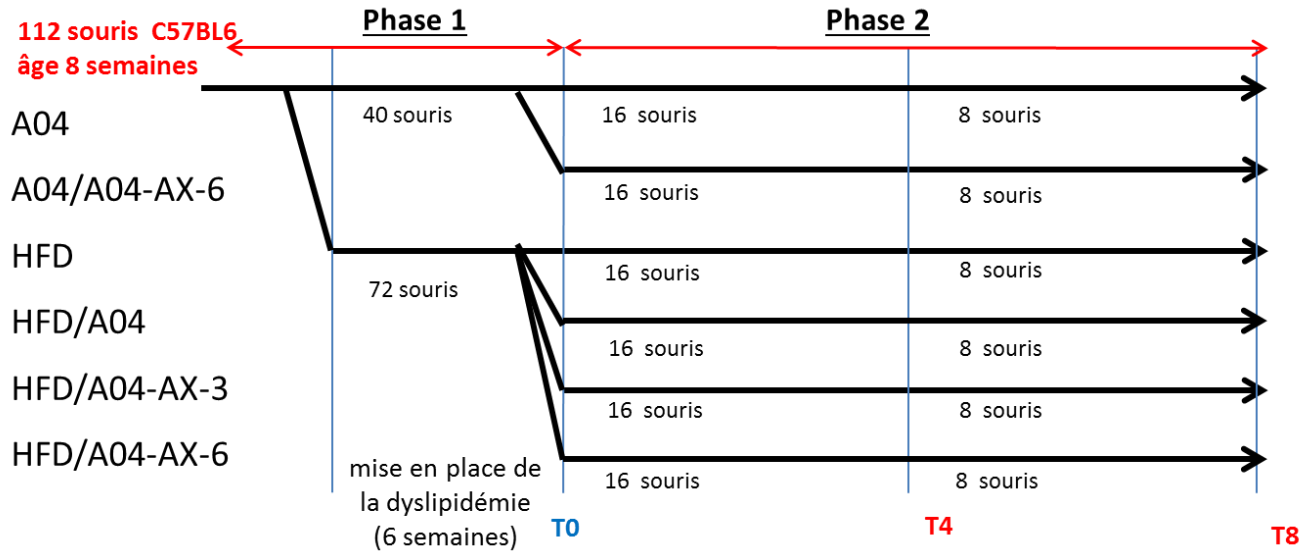


Figure 37 : Prévalence des dyslipidémies traitées déclarées en fonction de l'IMC depuis 2000

The risk of dyslipidemia is twice for overweight or obese people

A preclinical study



Composition	Régime standard A04	Régime hyper-gras HFD
Protéine (%)	16.1	20
Carbohydate (%)	60	44,5
	45.8	13
- amidon	2	24.3
- saccharose	/	2,2
- maltodextrin	3.9	5
- cellulose		
Lipides (%)	3.1	27,5

Astaxanthin at 0,03%
or 0,06% in the pellets

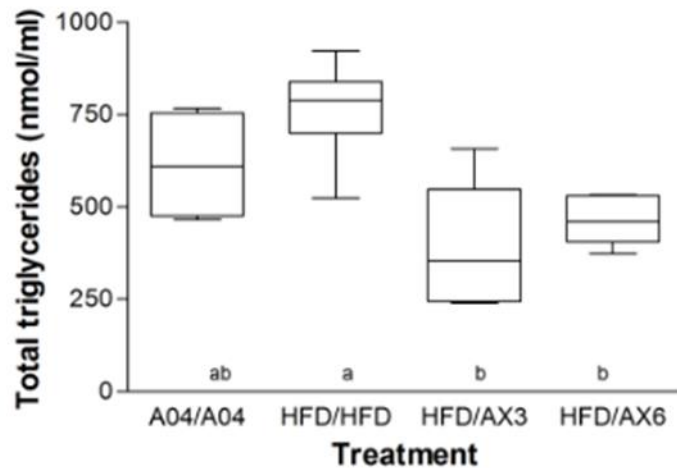
Phenotypic data at 8 weeks

- Animal weight
 - STD 27,6g (25,8-28,5); HFD 31,2g (24,8-38,4)
 - No astaxanthin effect

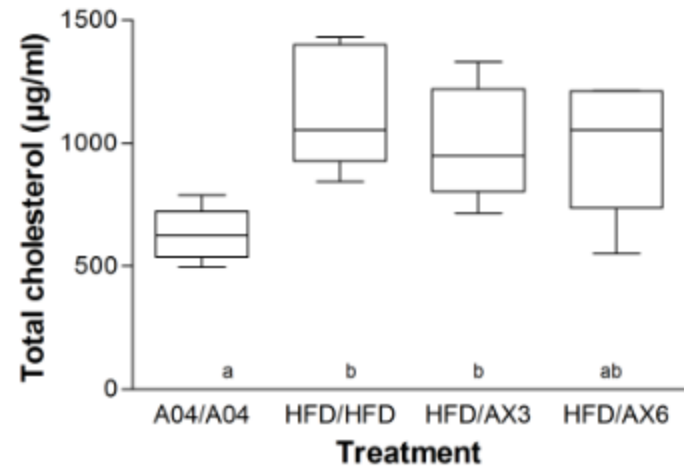
- Organs weight
 - Increase in adipose tissue with HFD
 - Decrease in cecum and colon with HFD
 - No astaxanthin effect

Modulation of dyslipidemia

- Triglycerides



- Total cholesterol



- AX reduce TG
- Not dose-dependent

- No beneficial effect

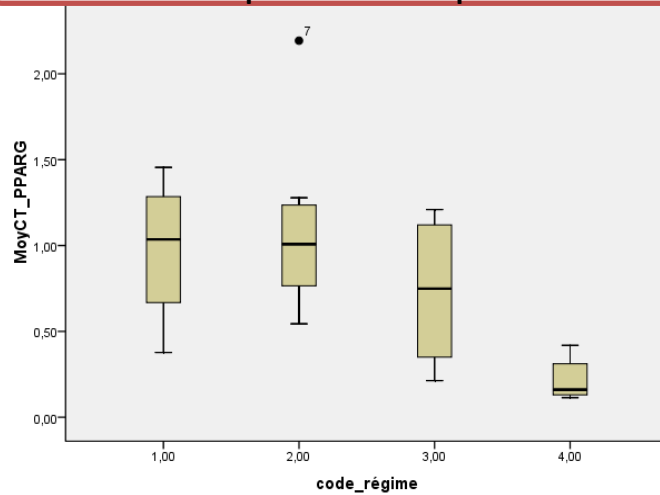
Similar to published data using Haematococcus astaxanthin

Figuring out mechanisms of action

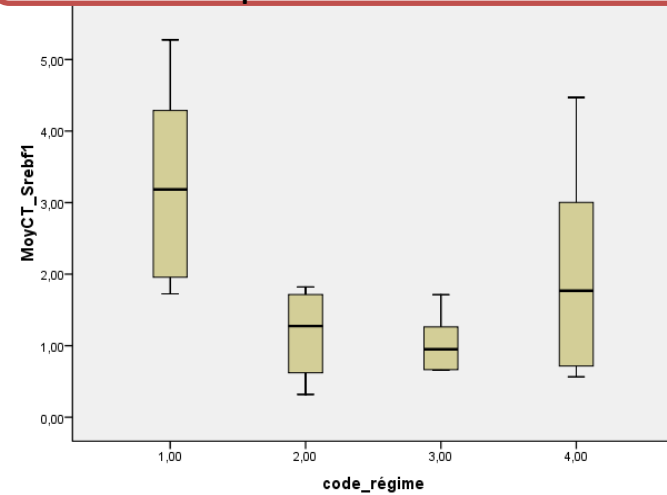
- Reduced circulating triglycerides
 - Increased hepatic or adipose cellular uptake?
 - Lower intestinal absorption?
 - Modulation of lipid metabolism?
- Gene expression studies in liver, adipose and intestinal tissue samples.

Some results

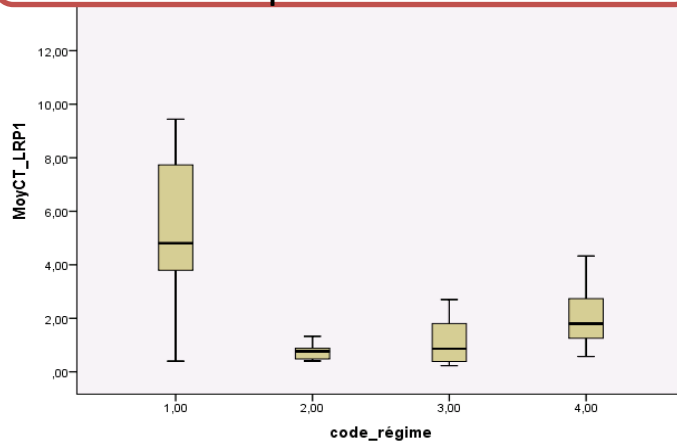
Dose-dependent inhibition of hepatic PPAR γ



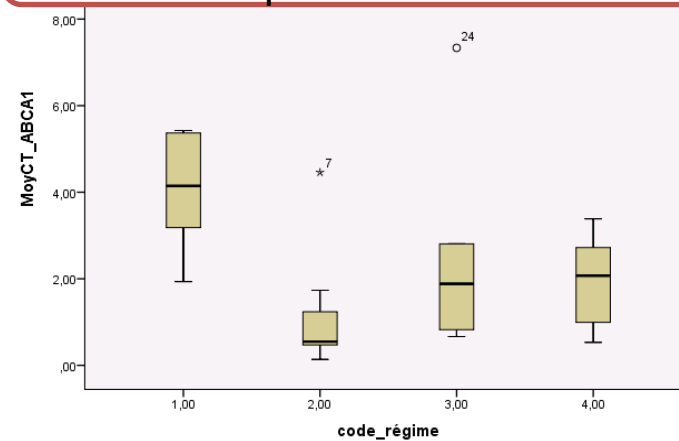
Dose-dependent recovery of hepatic SREBF1



Dose-dependent recovery of hepatic LRP1



Dose-dependent recovery of adipose ABCA1



« Astaxanthin activated ABCA1 promoters in an LXR-independent manner » *Ilizuka et Al, 2011*

« ASTX enhanced insulin-stimulated GLUT4 translocation to the plasma membrane » *Ishiki et Al, 2013.*

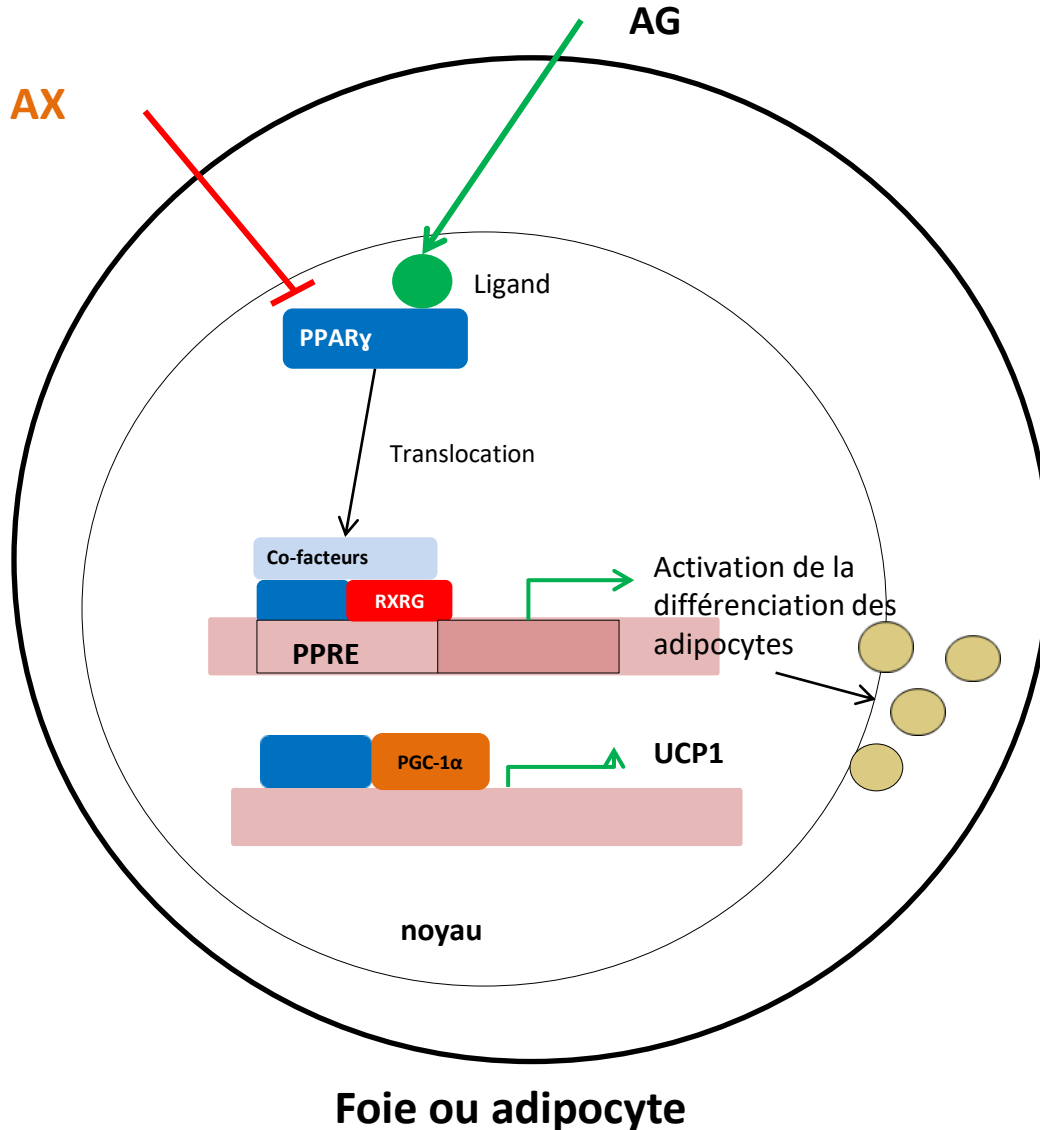
« AX is a moderate agonist for PPAR- α but an antagonist for PPAR- γ » *Yaoyao et Al., 2012*

Summary of RT-qPCR data

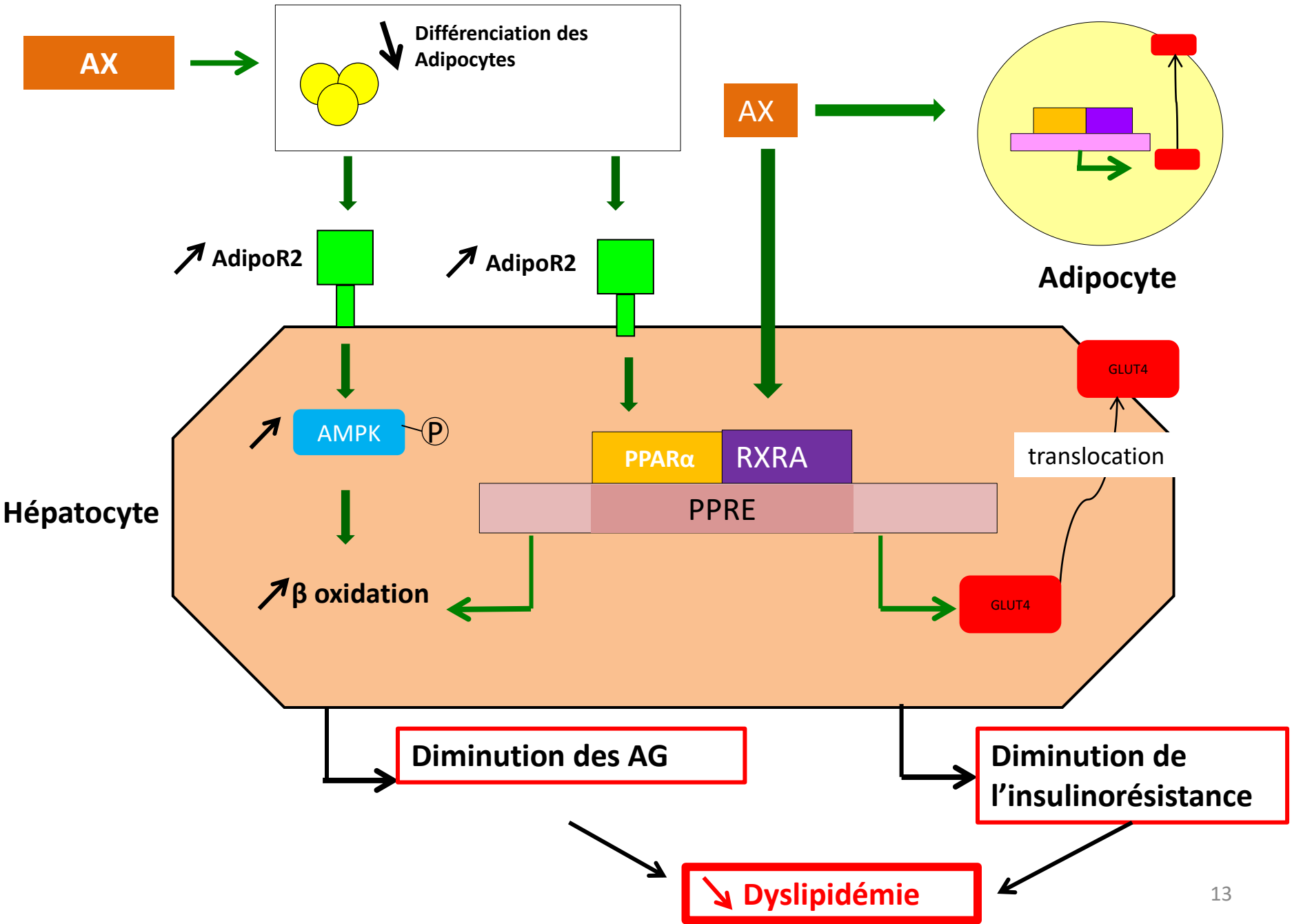
	Astaxanthine 0,03%		Astaxanthine 0,06%	
	Gènes exprimés dans le foie.	Gènes exprimés dans le tissu adipeux.	Gènes exprimés dans le foie.	Gènes exprimés dans le tissu adipeux.
Variation d'expression par rapport au régime standard (A04/A04)			↘ PPARγ	↗ GLUT4
Variation d'expression par rapport au régime hyper-gras (HFD/HFD) – tendance à la correction par rapport au régime standard.		↗ Abca1 ↗ AdipoR2	↗ SrebF1 ↗ Acat2 ↗ Lrp1	↗ Abca1 ↗ Rxra

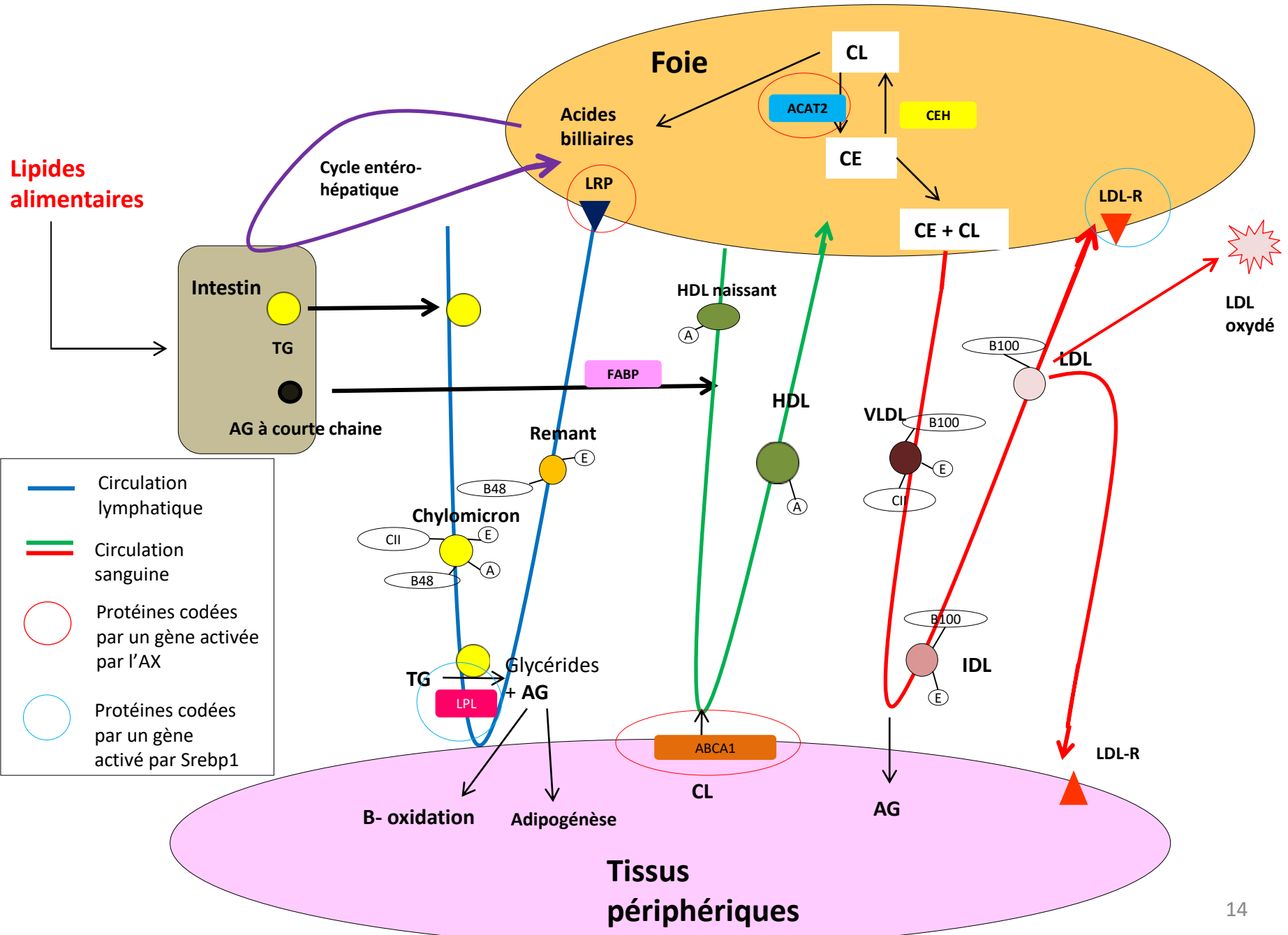
■ Métabolism
 ■ Storage
 ■ Transport

Astaxanthin is involved in lipid regulation



→ AX inhibe la différenciation des adipocytes.





Conclusions

- Sum of information is difficult to process
- Insufficient controls to validate the role of astaxanthin

- BUT proposed mechanisms seem to back up the observed phenotype (reduced TG)

Thank you for your attention

