Intestinal absorption of fat-soluble vitamins

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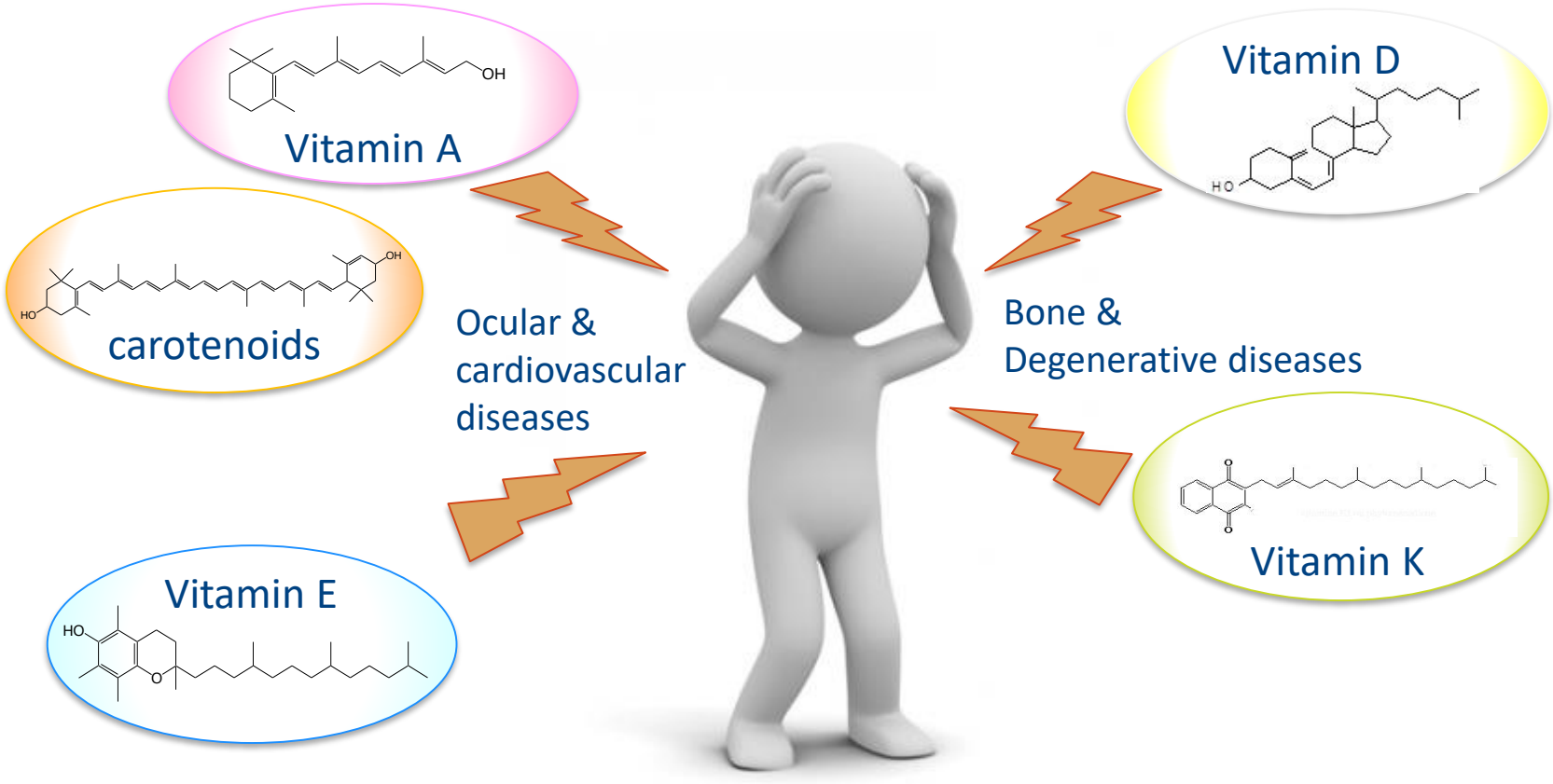
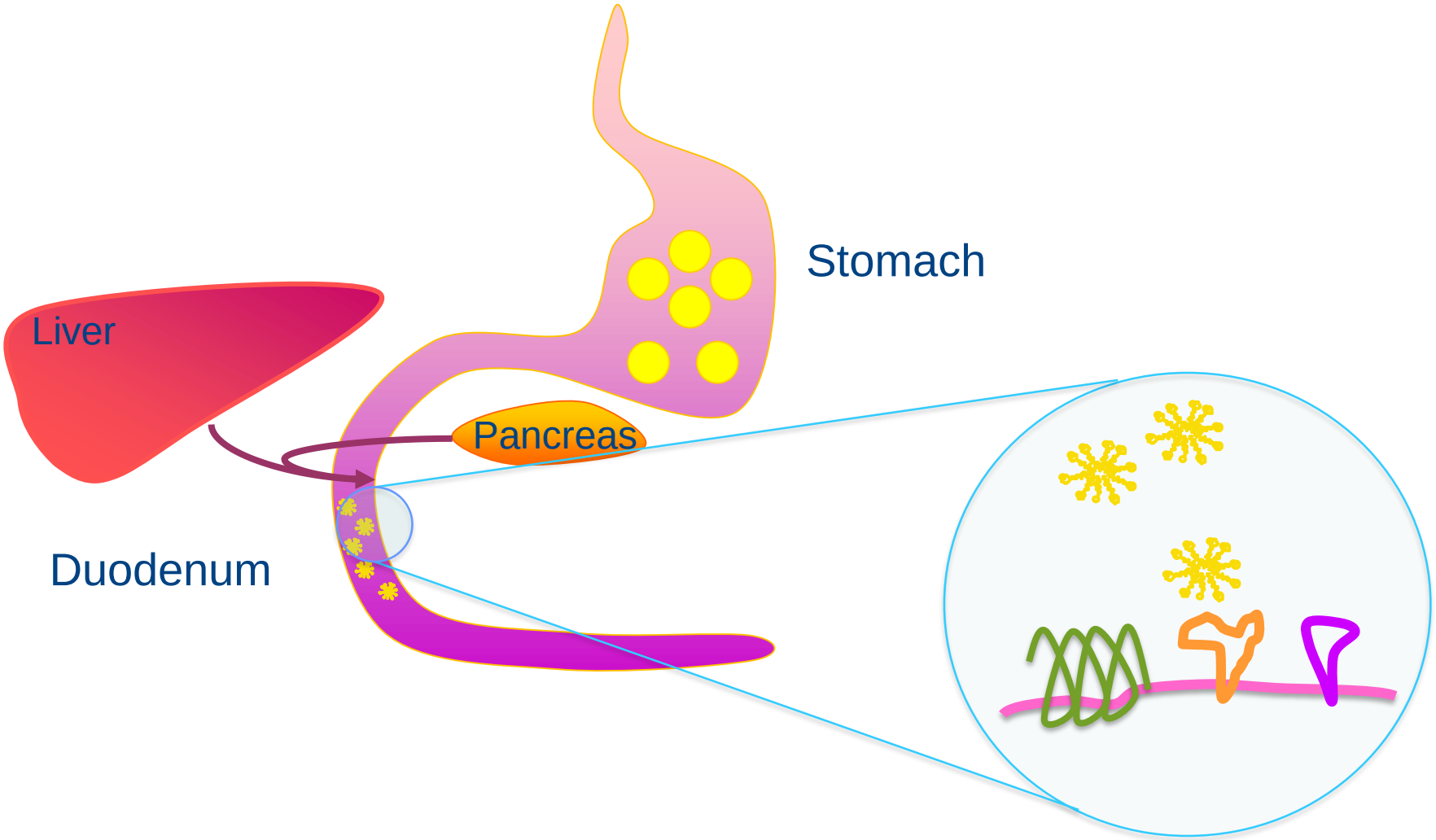
The lipid micronutrients

- 🕮 Vitamins are non-energetic molecules present in small amounts in our diet (< 1g/d), necessary for our development and health. 4 fat-soluble vitamins: A, D, E, K.
- 🕮 Carotenoids: not essential yet.

◆ Sub-deficiencies are very common



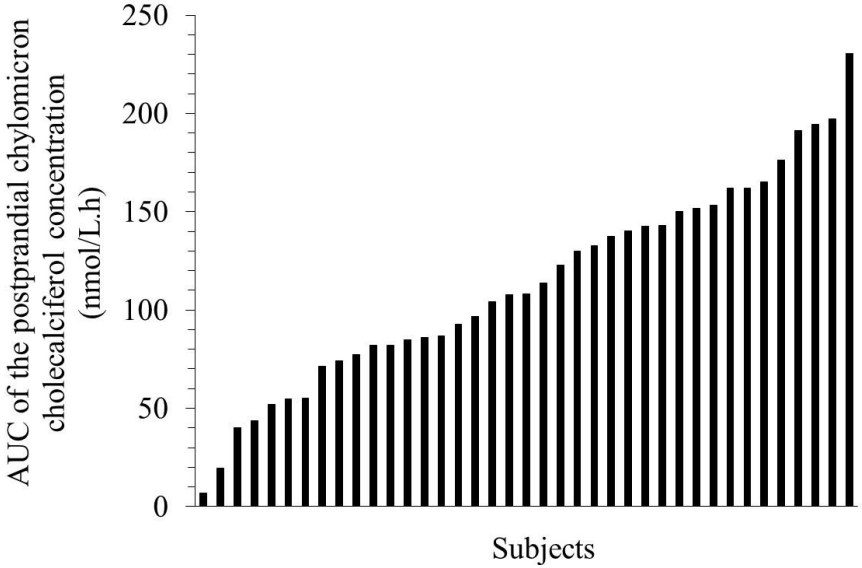
Digestion of lipid micronutrients



Absorption by the enterocyte

- Absorption mechanisms initially defined by Hollander et al. in the 70s
  - → Passive diffusion for vitamin D, E and carotenoids
  - → Active process for vitamin A and K

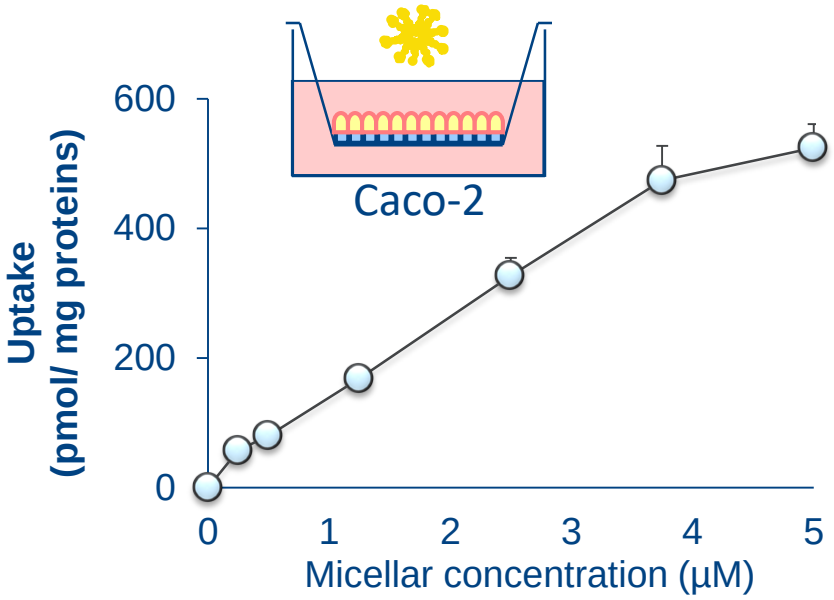
- Inconsistent data
  - → Competition for absorption
  - → **Very high** interindividual variability

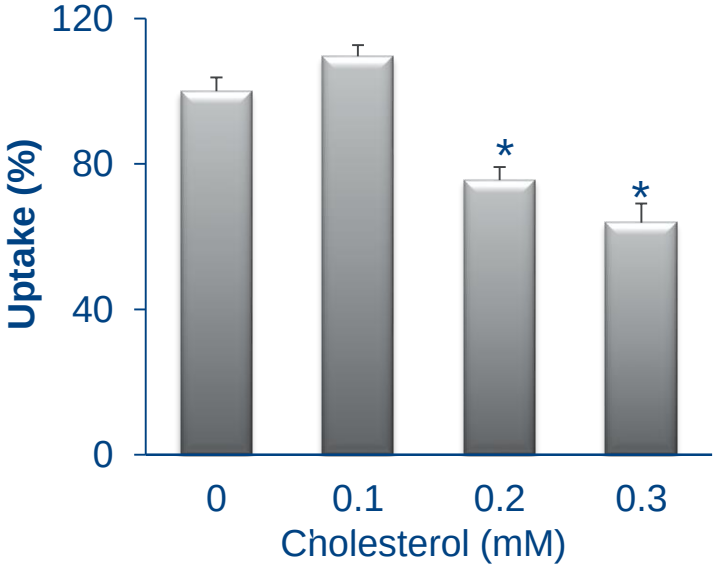


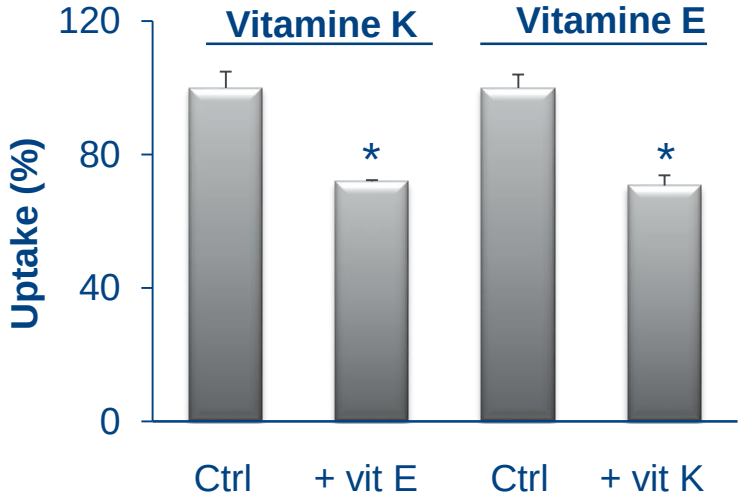
→Reinvestigation of lipid micronutrient absorption since 2002

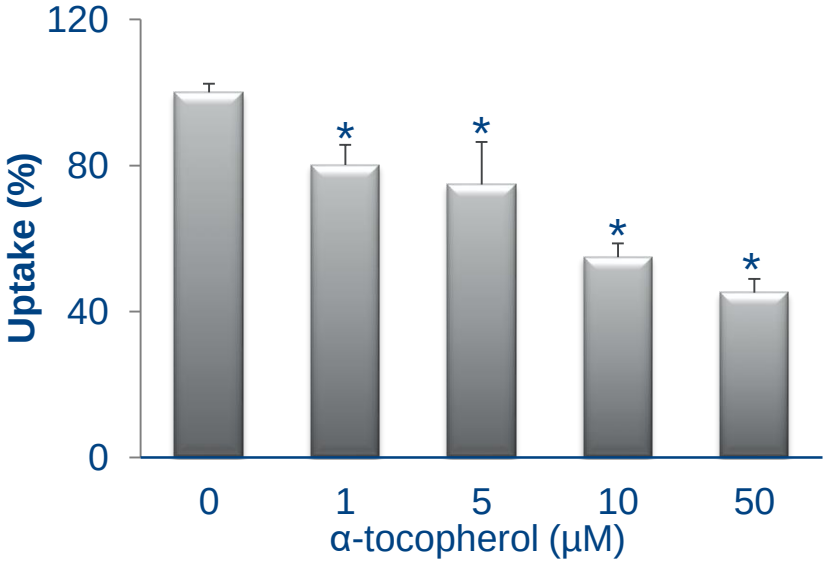
Desmarchelier et al. J Nutr 2016

Vitamin K absorption



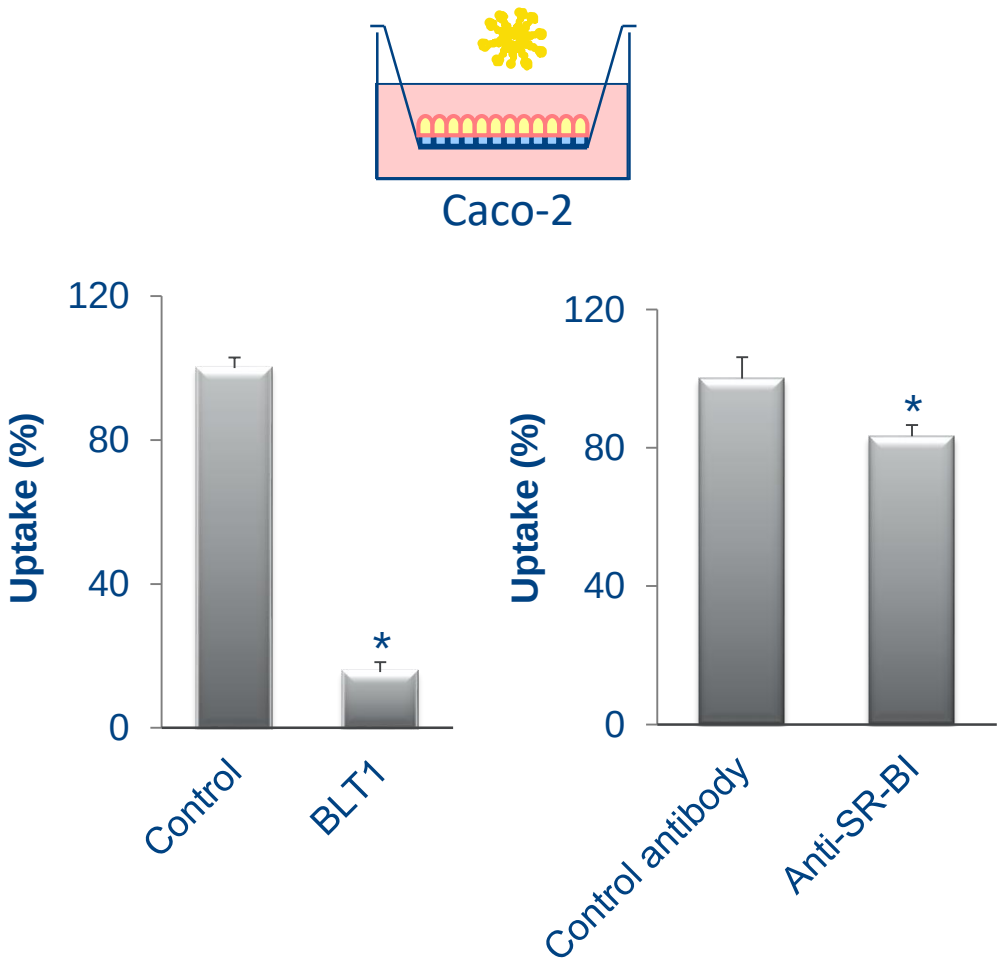






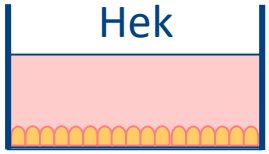
Goncalves et al. JBC 2014

Vit K and SR-BI in Caco-2 cells

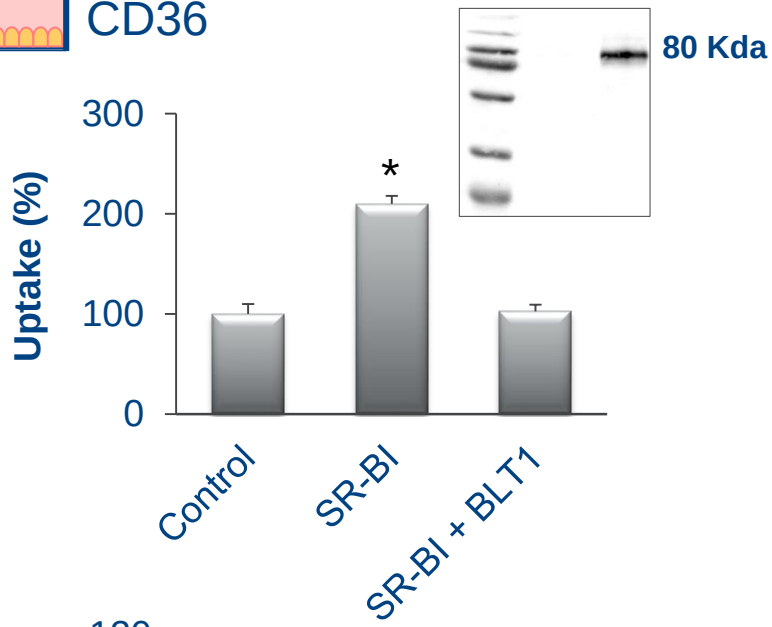


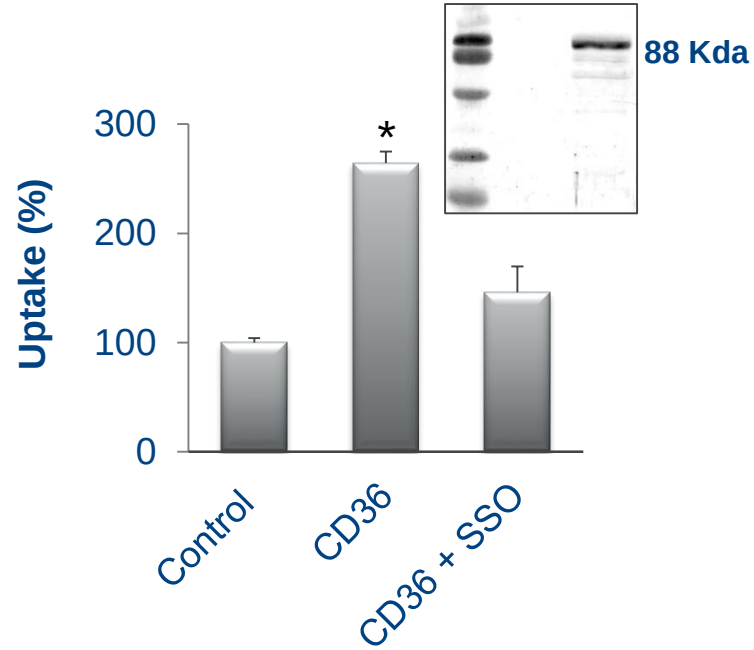
Goncalves et al. JBC 2014

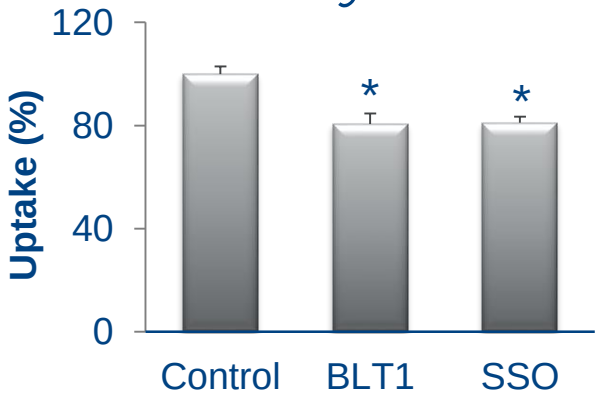
Vit K & scavengers in transfected HEK cells and mouse intestinal explants

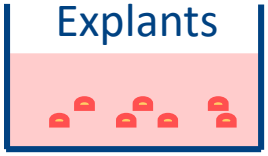


SR-BI
CD36



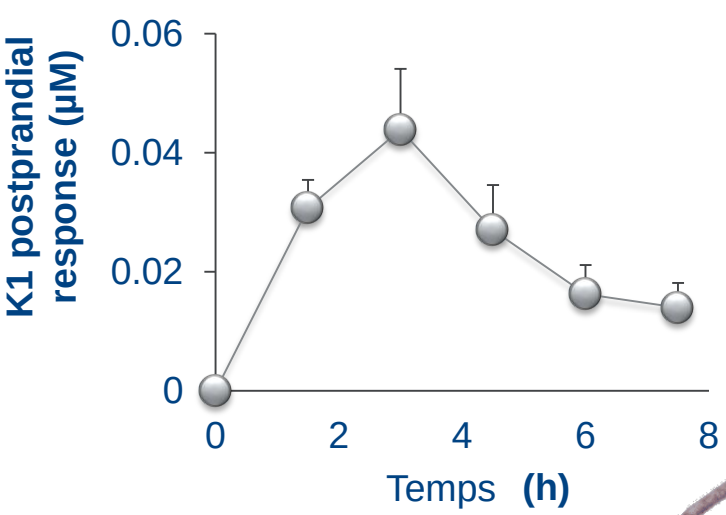


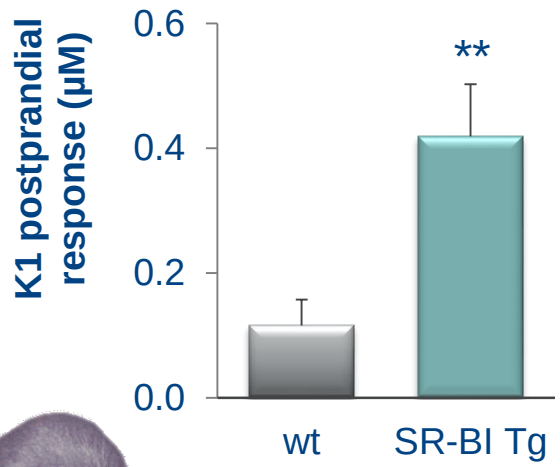


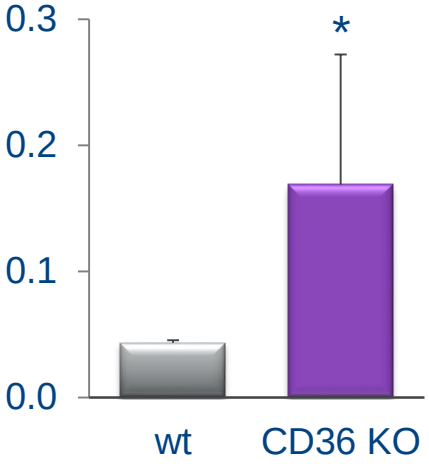


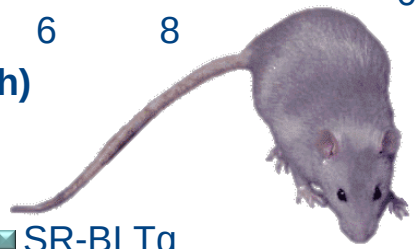
Goncalves et al. JBC 2014

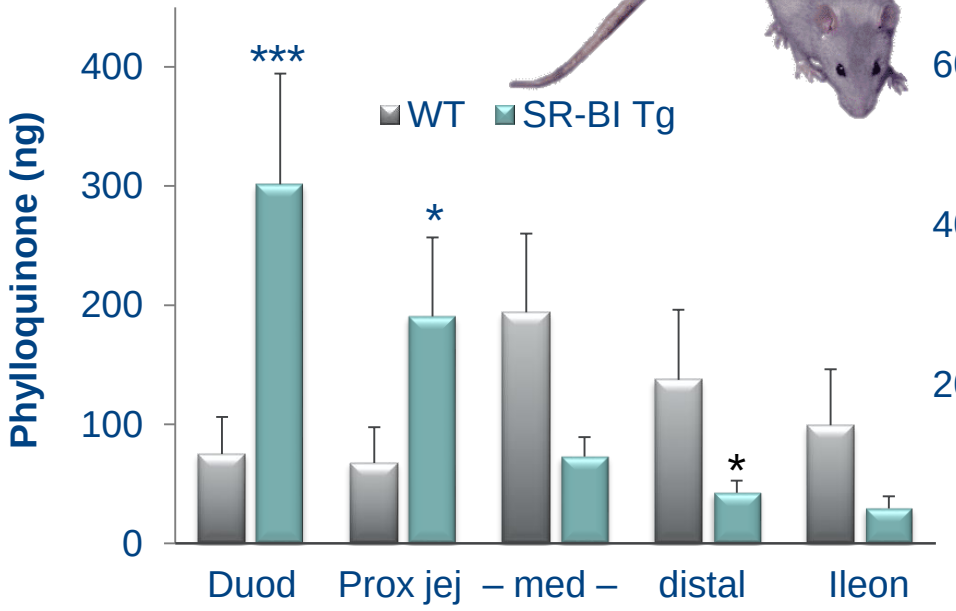
Vit K postprandial response in mice

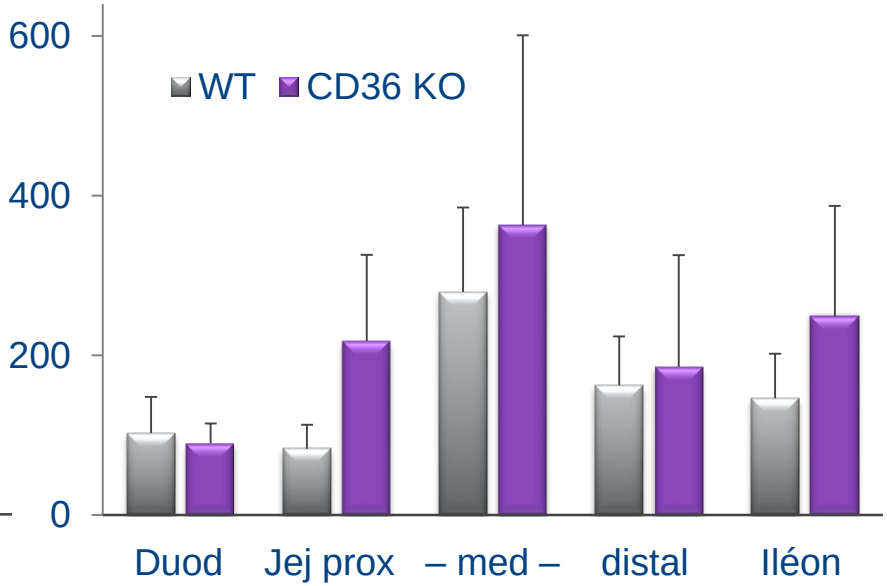






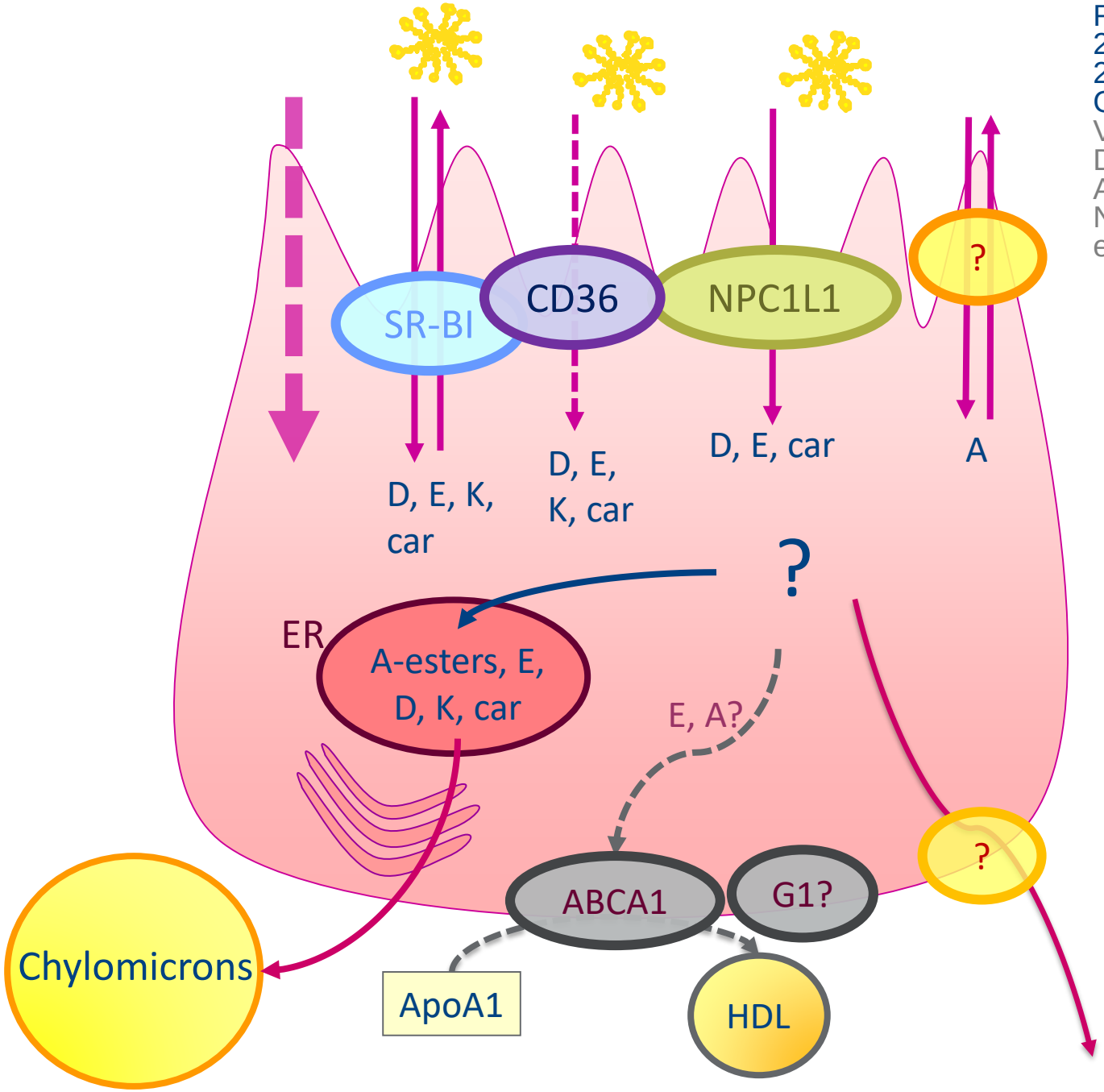






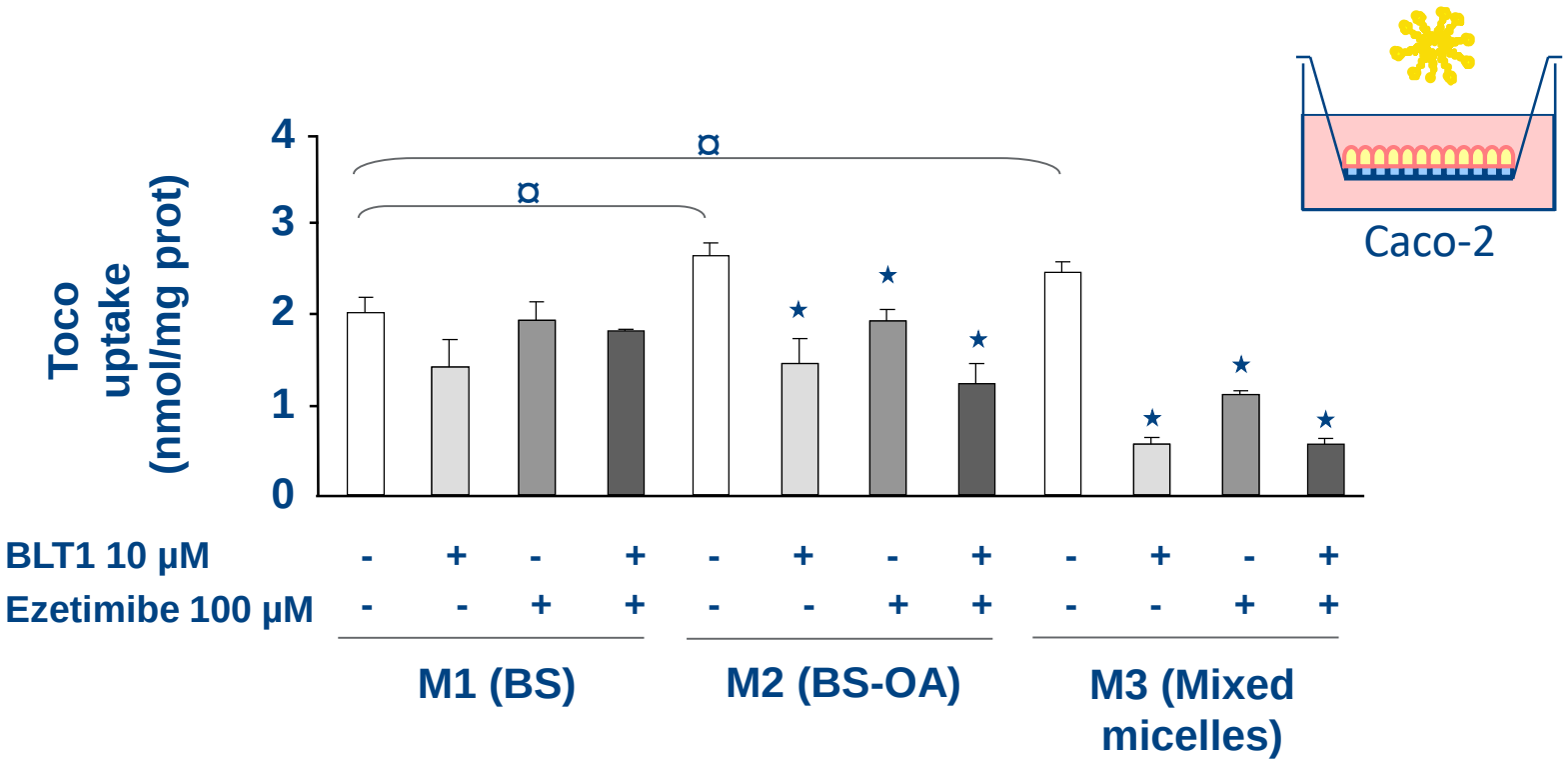
Goncalves et al. JBC 2014

Reboul et al. 2005, 2006, 2009, 2011; Moussa et al. 2008; Borel et al. 2013; Goncalves et al. 2014 a, b.
Van Benneckum et al. 2005; During et al. 2005, 2007; Anwar et al. 2006, 2007; Narushima et al. 2008; Nicod et al. 2013.



Adapted from Reboul et al. Progr Lipid Res 2011

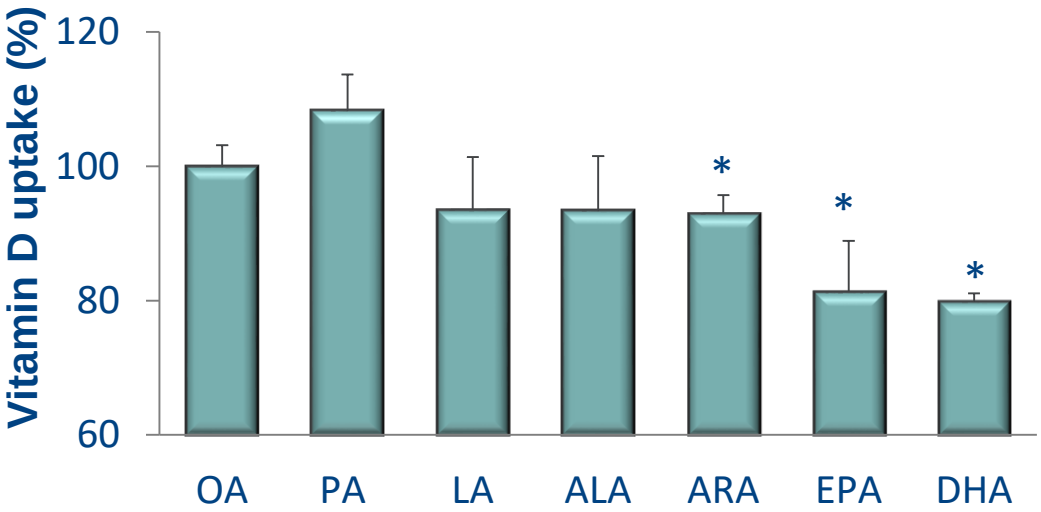
Importance of the vehicle

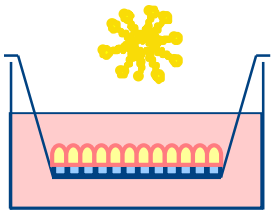


- Presence of bile salts + fatty acids required for a transporter-dependent uptake

Reboul et al. Brit J Nutr 2012

Importance of the vehicle





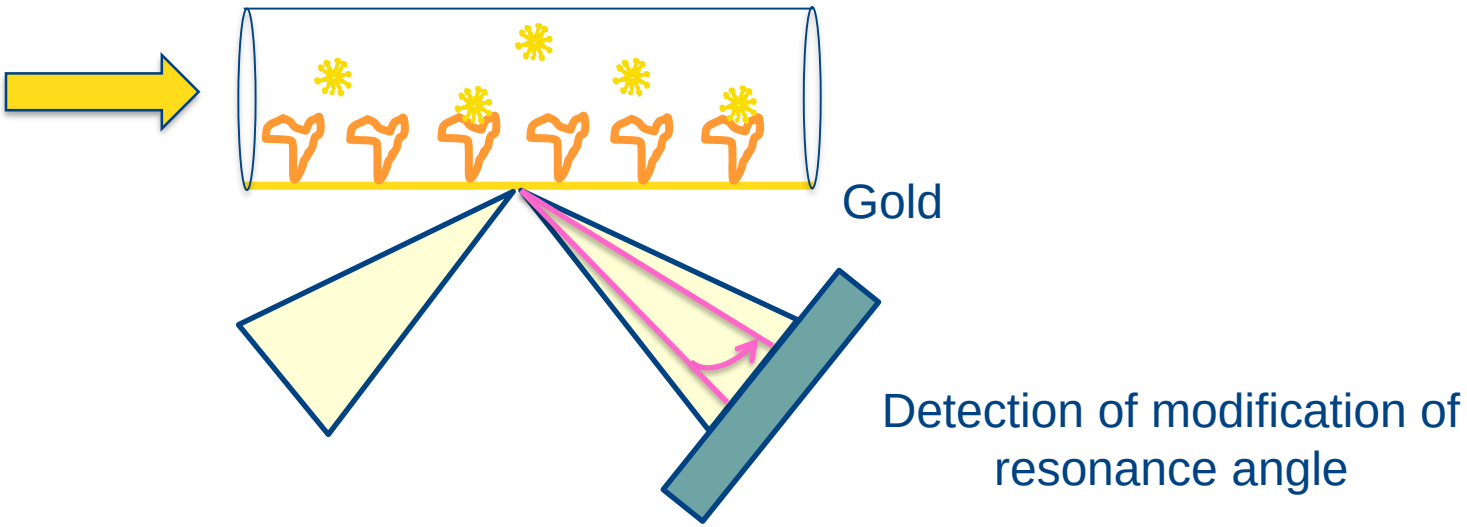
	OA	PA	LA	ALA	ARA	EPA	DHA
Zeta (mV)	-30,3 ± 2,4	-22,7* ±3,9	-34,5* ±2,7	-32,3* ±3,9	-31,0* ±1,9	-36,9* ±3,4	-38,8* ±3,9
Taille (r. nm)	5,4 ±0,2	5,1* ±0,4	3,6* ±0,6	3,5* ±0,5	3,4* ±0,1	3,5* ±0,2	3,6* ±0,1

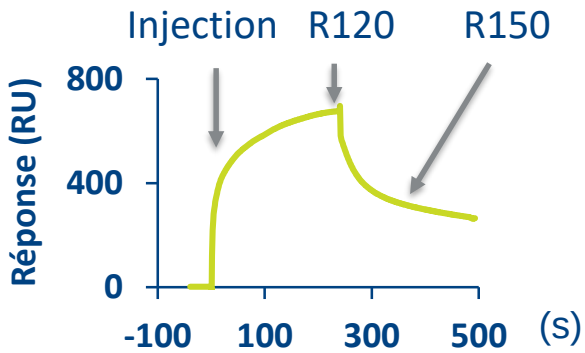
- Modification of micellar affinity with transporters?

Goncalves et al. J Nutr Biochem 2013

Intestinal scavenger receptor functioning

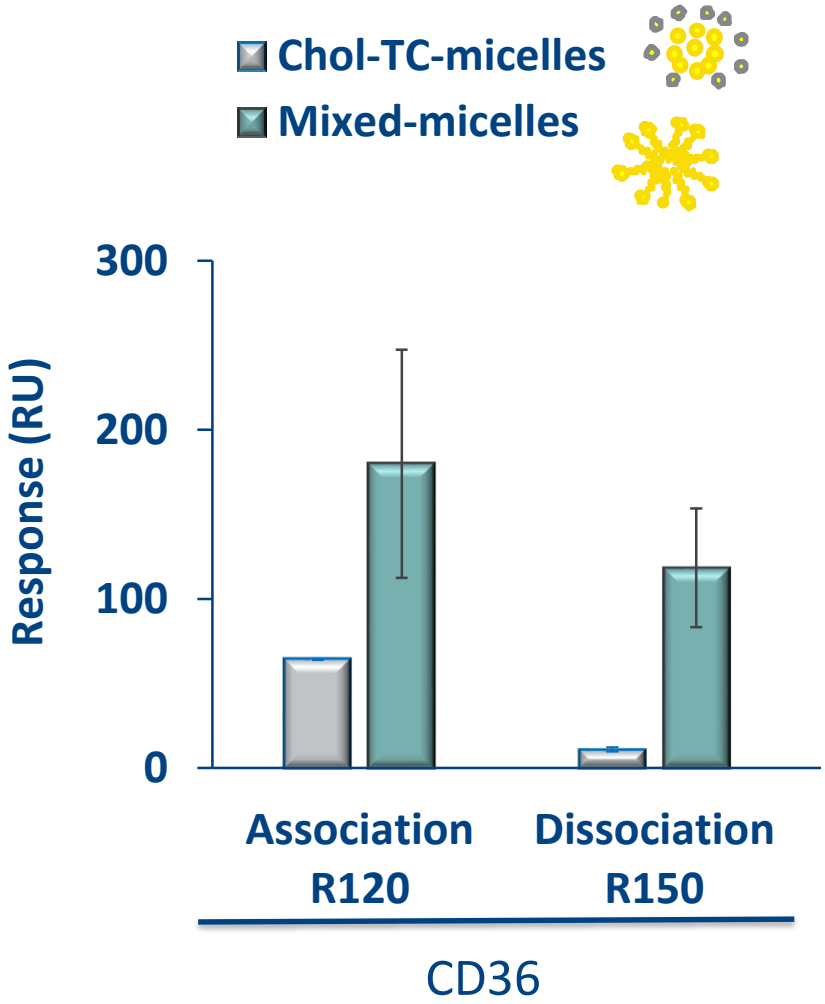
- Real-time analysis of protein-micelles interactions with Surface Plasmon Resonance
- Extracellular loop of SR-BI and CD36
- Synthetic mixed micelles





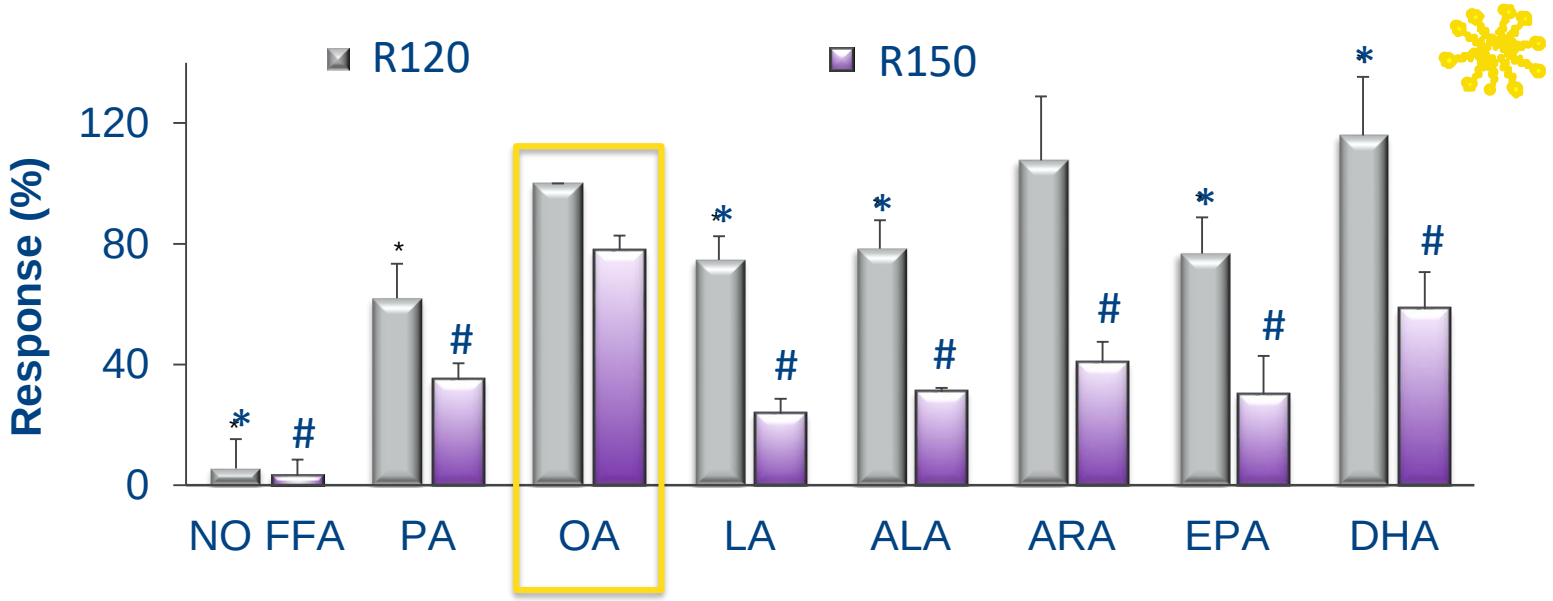
Goncalves et al. JLR 2015

Importance of micelle type



Goncalves et al. JLR 2015

Effect of micellar fatty acids

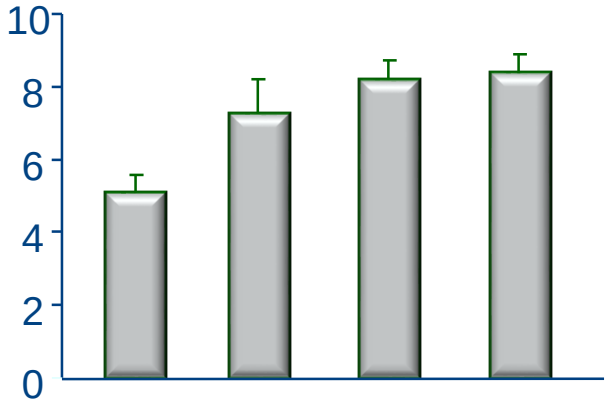


- Among the different micellar components (chol, PC), fatty acids are the most important regarding micelle-scavenger interactions

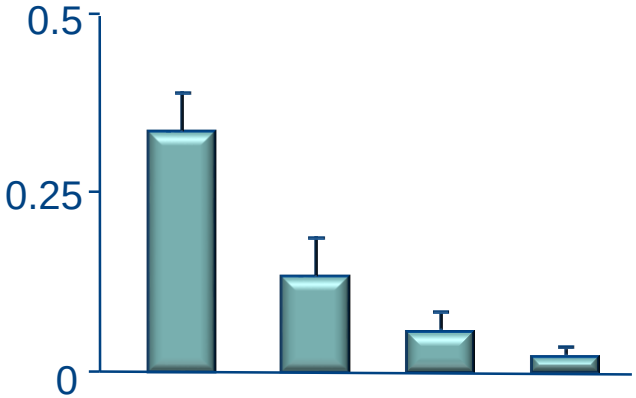
Goncalves et al. JLR 2015

Absorption sites of lipid micronutrients

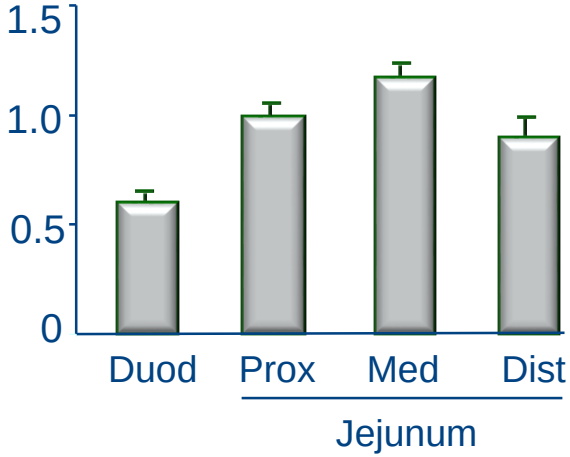
mRNA expression (NPC1L1/cyclophilin)



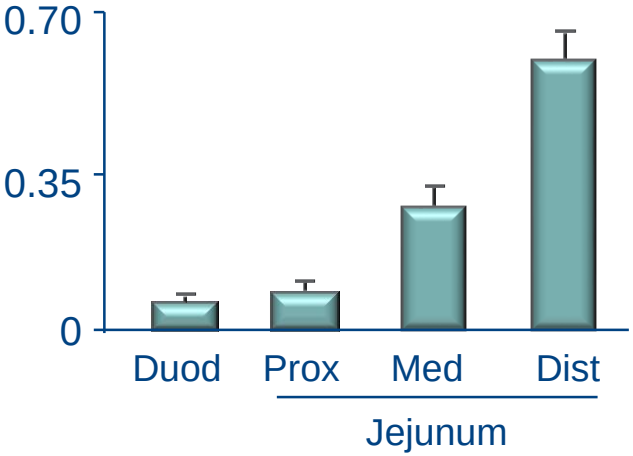
mRNA expression (SR-B1/cyclophilin)



[H3]-cholesterol (10^2 dpm/cm)



Tocopherol (µmol/cm)



Reboul et al. Brit J Nutr 2012

Take away messages

- **Vitamin D, E, K and carotenoids share similar absorption pathways but are not absorbed at the same level of the intestine.**
- **Lipid micronutrient uptake through transporters require an adequate vehicle.**
- **The specificity of the interaction lipid micronutrient - transporter is not known yet.**

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Center for CardioVascular and Nutrition research

✓ Laboratory

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Marielle Margier (PhD)
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Charlotte Halimi (RT)
Gabriel Masset (Postdoc)

MS-Nutrition (Start-up)

✓ Collaborations

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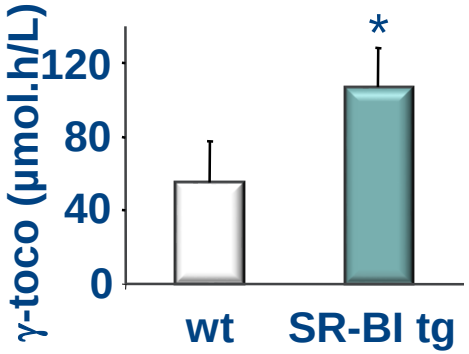
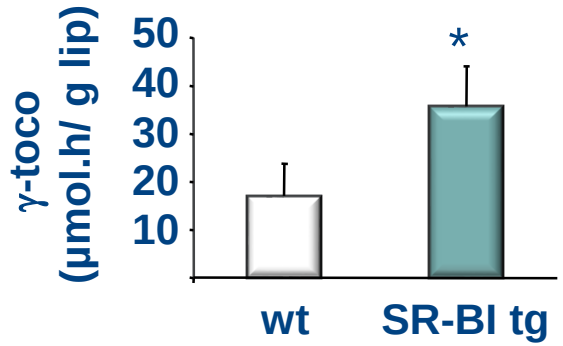
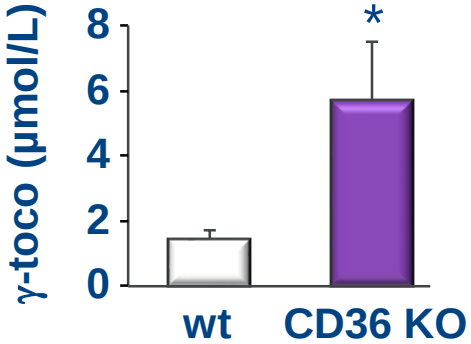
Catherine Caris (SQPOV, Avignon)
Isabelle Niot (Inserm 866, Dijon)
Xavier Collet (UMR 1048, Toulouse)
Wilfried le Goff (UPMC, Paris)
Anne Lespine (INRA, Toulouse)

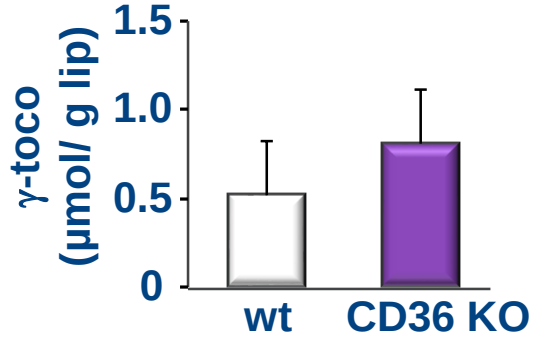
Direct of indirect transport?



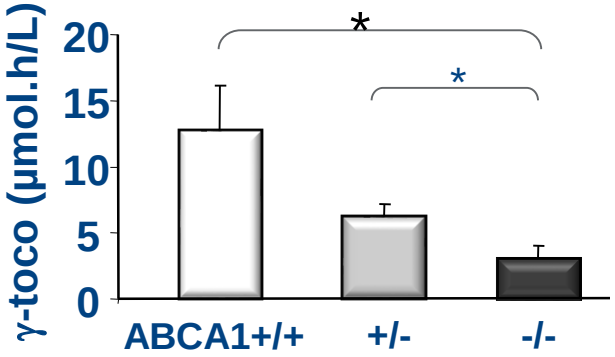


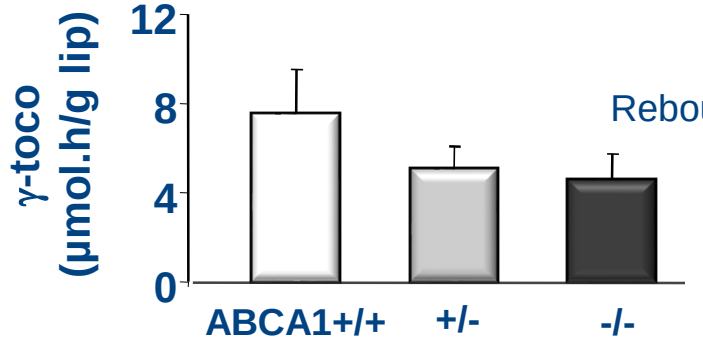
Reboul et al. JBC 2006





Goncalves et al. MNFR 2014

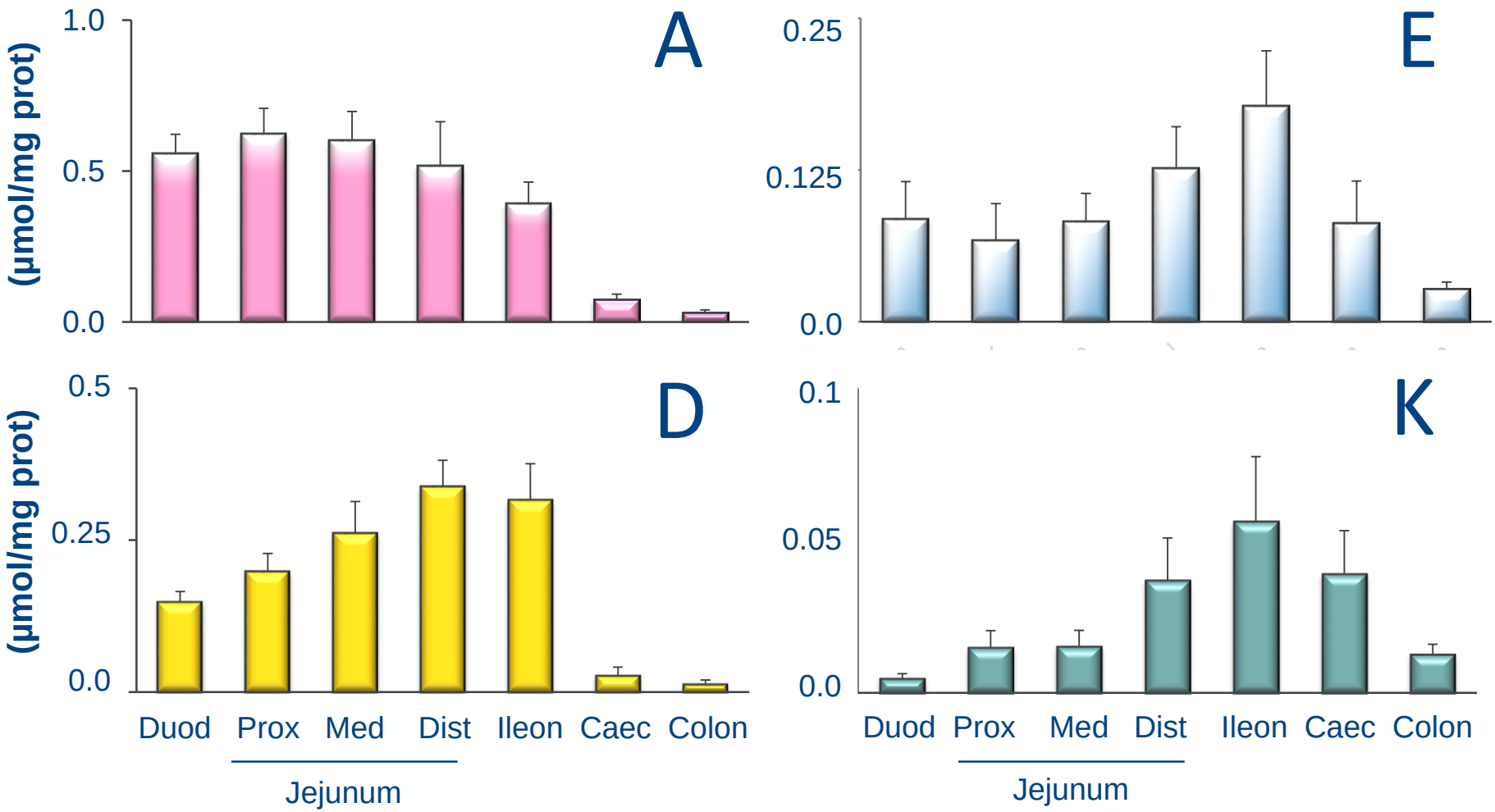




Reboul et al. Am J Clin Nutr 2009

- **Direct: SR-BI?**
- **Indirect: CD36, ABCA1?**

Absorption sites of lipid micronutrients



- Different absorption sites → different absorption mechanisms?

Goncalves et al. Food Chem 2015