



## Structuring Food to Improve the Delivery of Bioactives

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# Portrait

## The National Institute for Agronomic Research

- Set up in 1946
- A public, scientific and technological establishment
- Under the joint authority of the Ministries of Agriculture and Research
- Staff of nearly 11000 and a budget of 700 M€
- Largest European organisation for agricultural research, 2<sup>nd</sup> largest in the world
- Working on Food, Nutrition, Agriculture and the Environment

DIET  
AGRICULTURE  
ENVIRONMENT

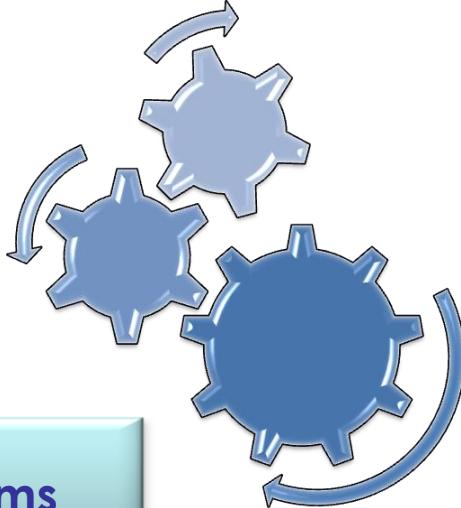
INRA

**140 people  
25 PhD students  
7 private companies**

## **Our disciplinary skills**

**Biochemistry  
Microbiology/ Mol Biology  
Process & technology**

**Model systems**



**Milk & Egg Science & Technology**

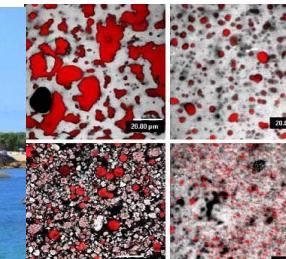


**In situ systems**

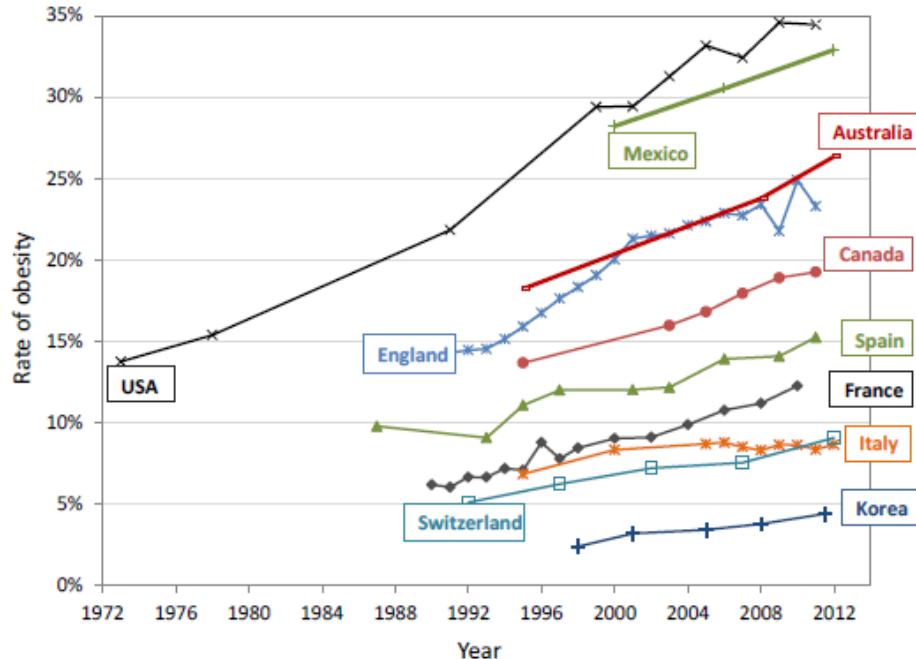
## **Our facilities**

**Mass spectrometry  
Confocal microscopy, AFM  
Quantitative PCR  
ITC, Biacore 3000**

**Technology platform, Spray-drying tower  
Biological Resource Centre**

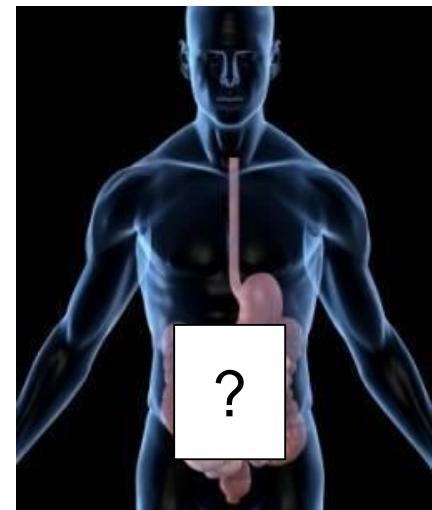


# Food and human health: the key role of the digestive process



Diet-related diseases ↑

→ Prevent these pathologies rather than cure them



Gut = interface between food and human body

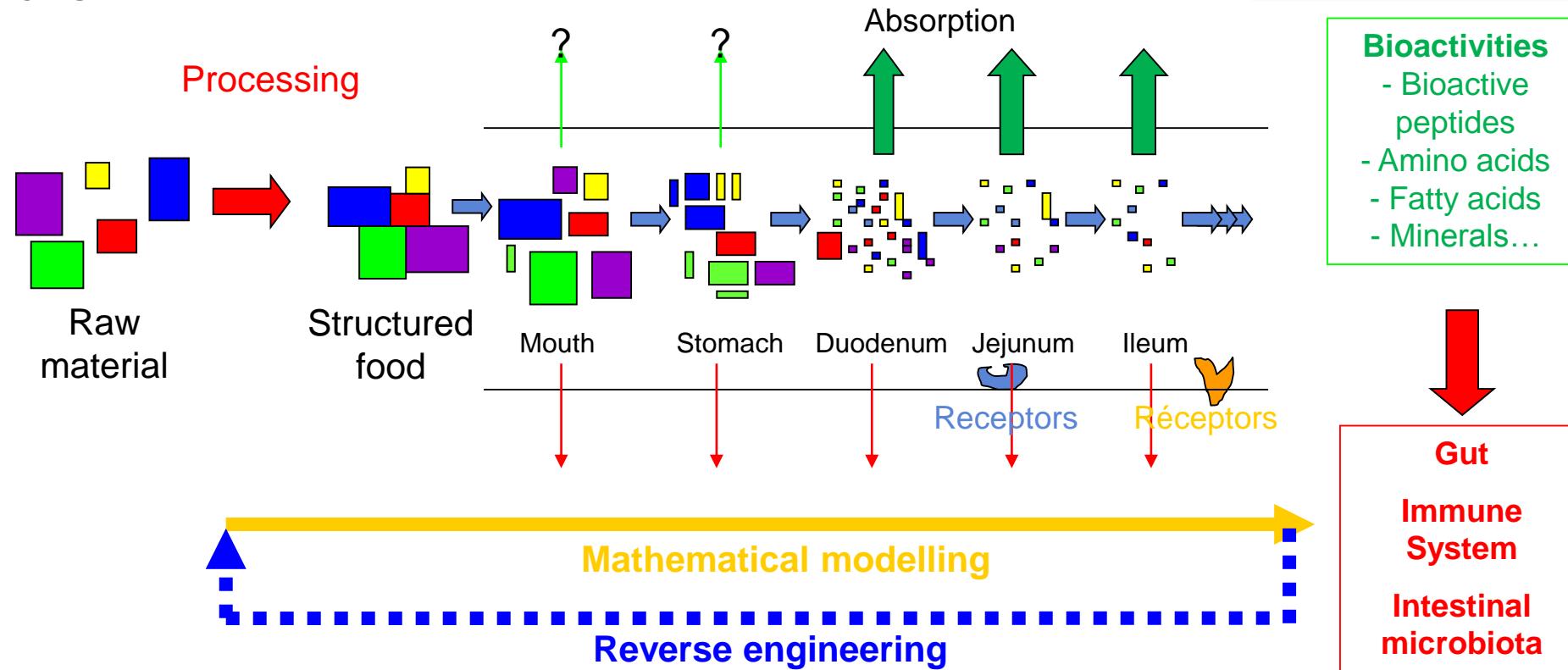
Digestion releases food components that can have a beneficial or a deleterious effect on human health

... but the mechanisms of food disintegration in the gastrointestinal tract remain unclear and the digestive process has been considered as a black box so far

**Increasing our knowledge on food digestion to increase our knowledge on the effect of food on human health**

# Our goals

Healthy Adult/ Neonate/ Elderly



- ☞ To understand the mechanisms of breakdown of food matrices and their constituents in the gut and identify the beneficial/deleterious food components released during digestion
- ☞ To determine the impact of the structure of food matrices on these mechanisms
- ☞ To model these phenomena in order to develop a reverse engineering approach

# Models available at INRA for simulating digestion

Dupont et al. 2010ab,  
Mol Nutr Food Res  
Minekus et al. 2014  
Food Funct

Menard et al. 2014,  
Food Chem  
Sanchez et al. 2015  
Food Res Int

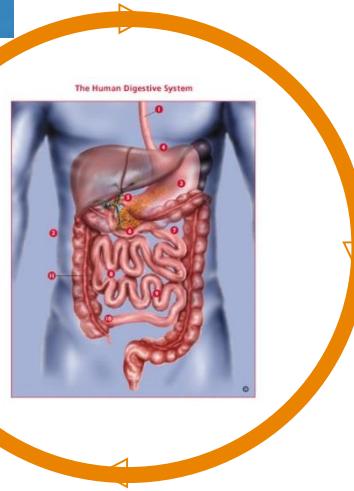
Le Feunteun et al. 2014  
Food Bioprocess Tech

$$\Phi_{12} = k_{12\text{whey}} \times (V_1 - m_{\text{caswpd1}} \times \alpha) + k_{12\text{aggr}} \times m_{\text{caswpd1}} \times \alpha$$

*In vitro static  
models  
(infant, adult)*



*In silico  
models*



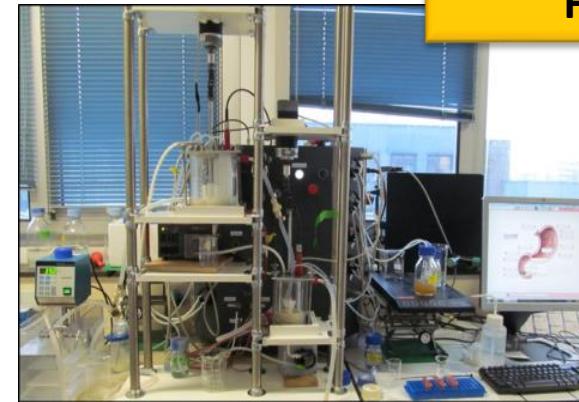
*Human  
models*

De Oliveira et al. 2016

Am J Clin Nutr

De Oliveira et al. 2017

Clin Nutr



*In vitro dynamic models  
(infant, adult, elderly)*



*Animal models*

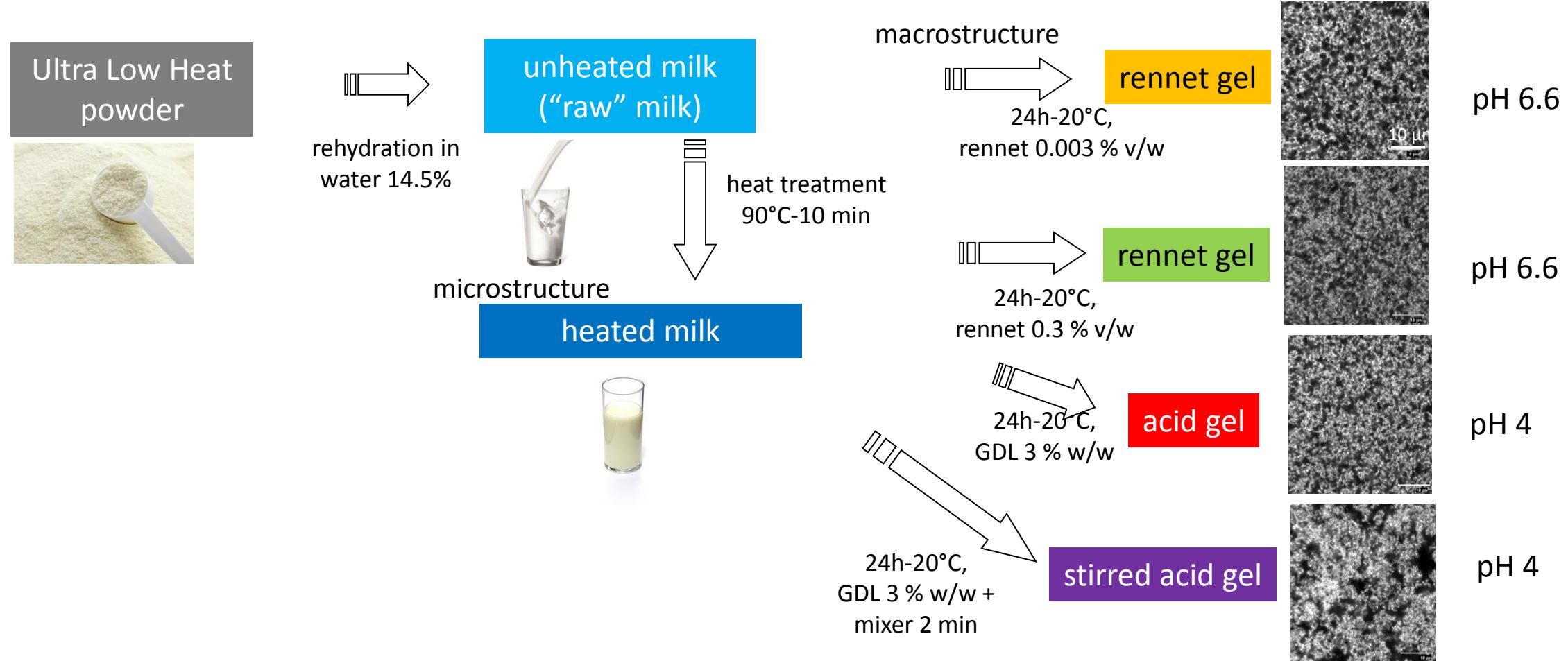


Barbé et al. 2013, 2014  
Food Chem  
Le Huerou-Luron et al.  
2016 Eur J Nutr

# Example 1

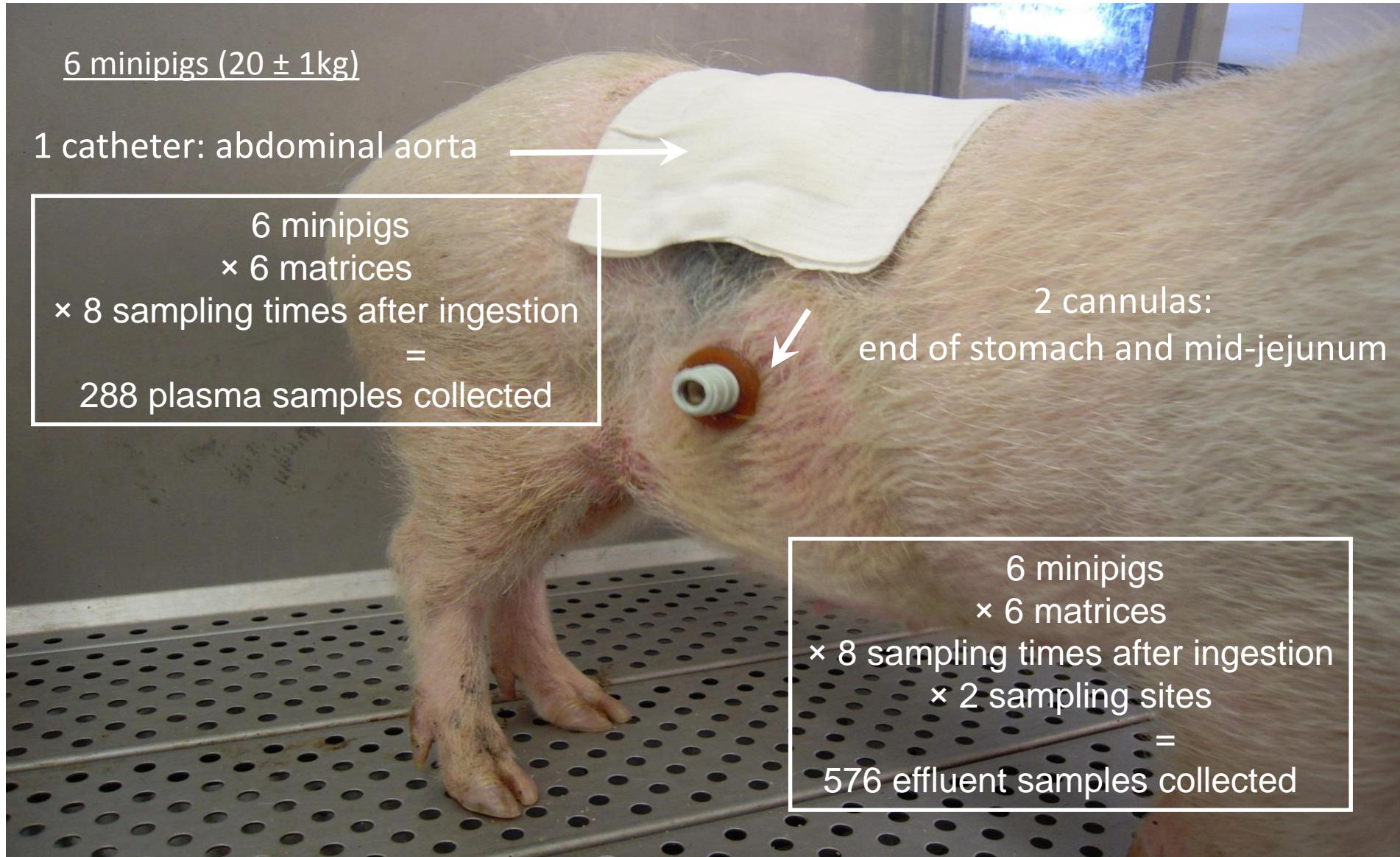
## Food structure and delivery of bioactive peptides

# The food matrices

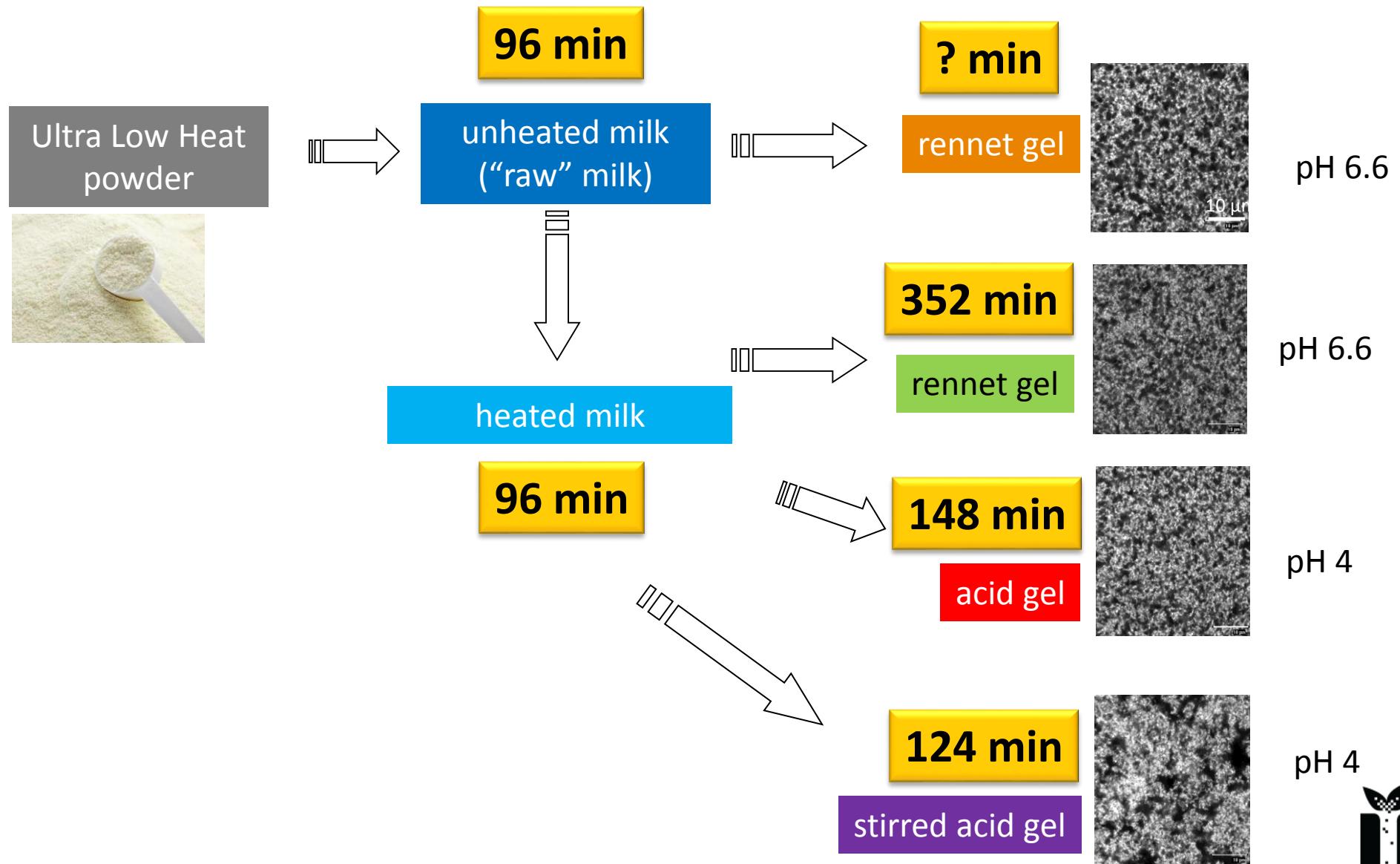


Fat-free matrices: 40 g/L caseins, 10 g/L whey proteins, 95 g/L lactose and minerals  
+ marker of the meal transit ( $\text{Cr}^{2+}$ -EDTA)  $\rightarrow$  Gastric emptying half-time

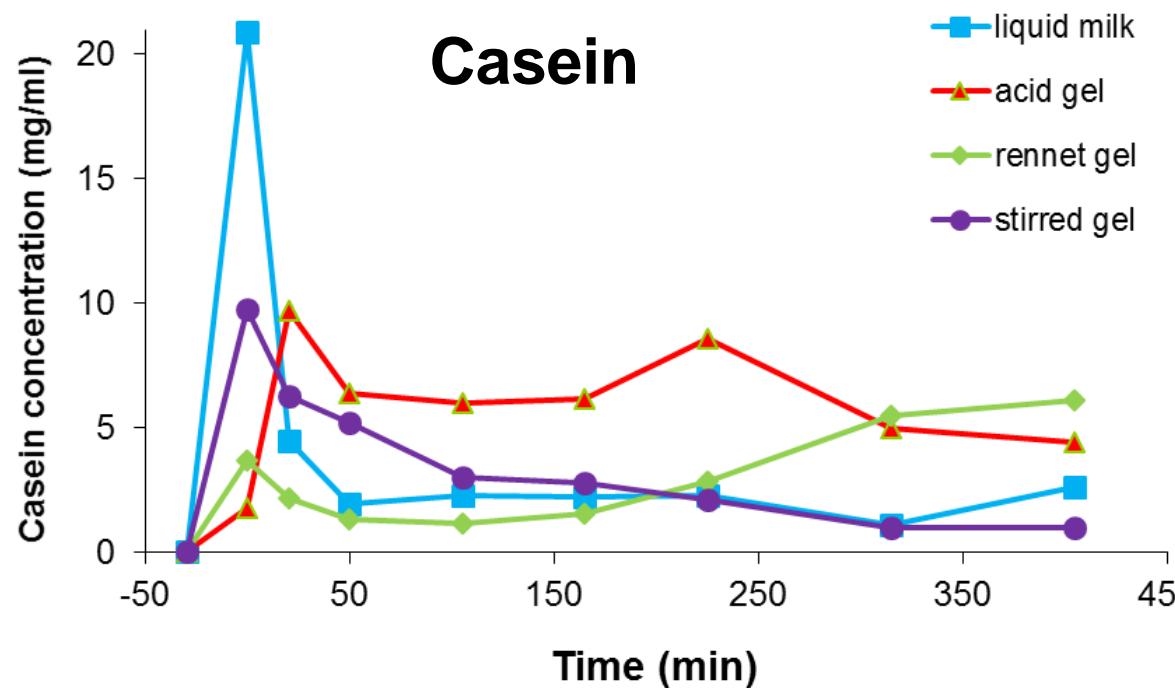
# The multi-canulated mini-pigs



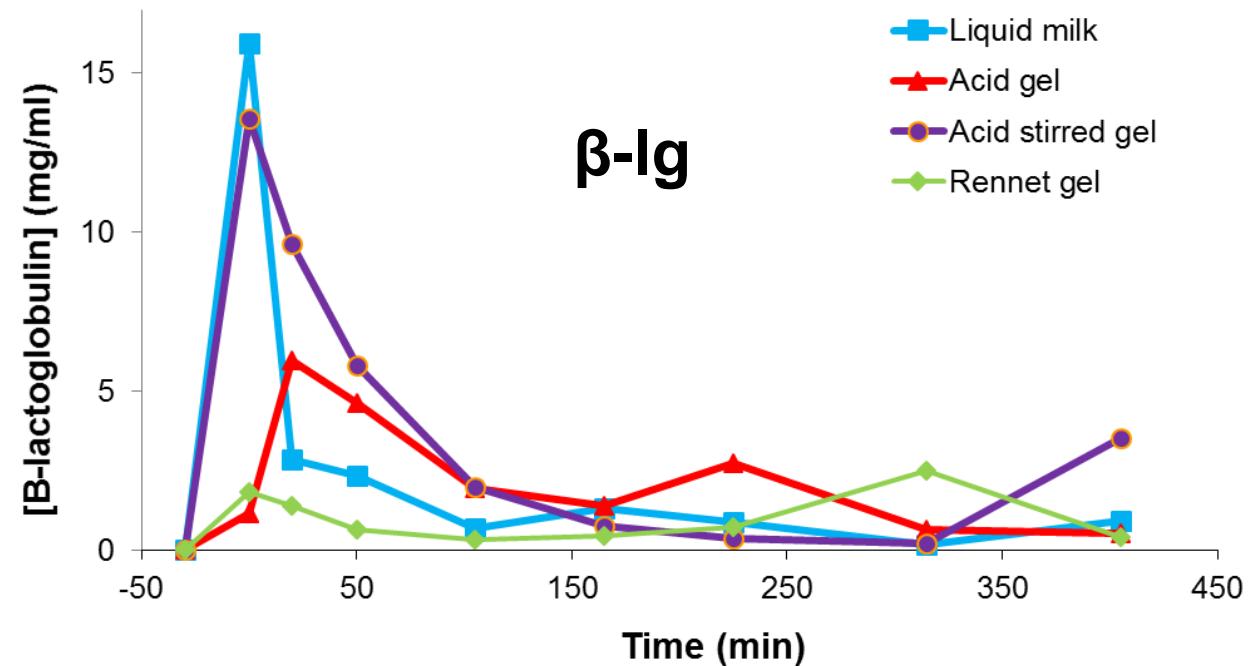
# Impact of food structure on gastric emptying half-time



# Milk proteins in the duodenum (ELISA)



- Intense and early peak with milk/ lower and delayed with gels
- Intermediate behaviour with stirred gel
- Low concentrations with rennet gel but casein release tends to increase over time

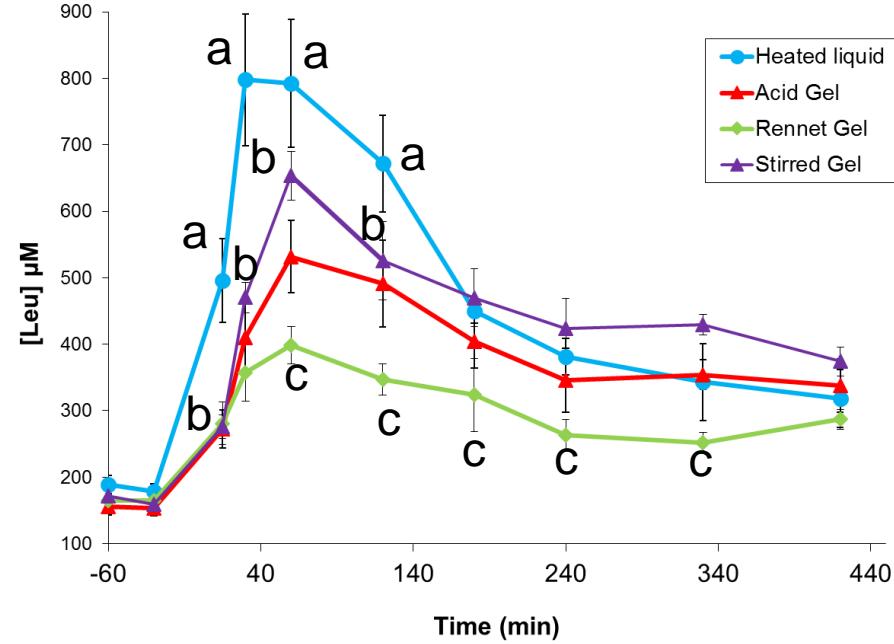


- Only traces of milk proteins found in the jejunum
- Dairy products remain highly digestible

Barbé et al. 2013, 2014  
Food Chem

# The liquid-gel transition

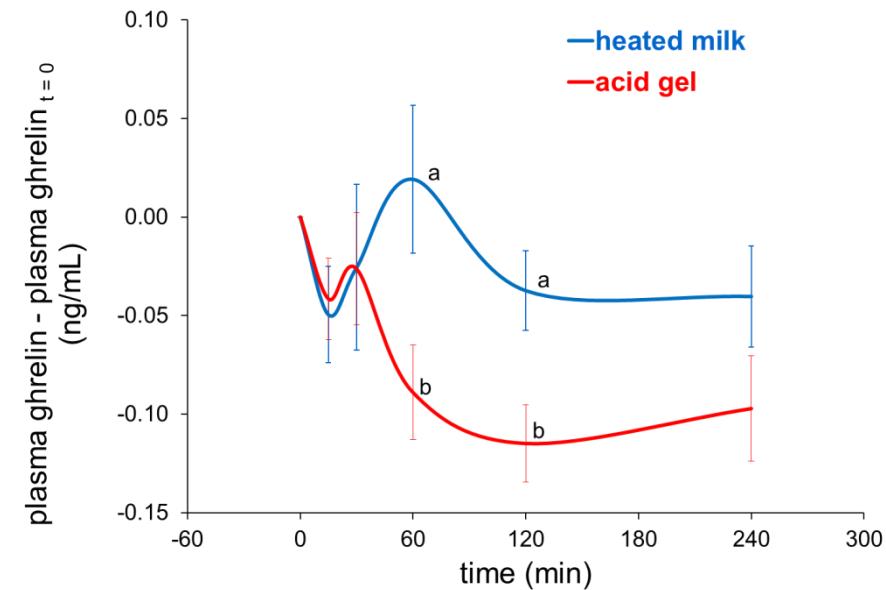
## 2) effect on absorption



milk gelation: → delayed proteins transit → delayed AA absorption  
→ maximal AA concentration in the plasma

## 3) potential effect on satiety

ghrelin (gastrointestinal hormone → appetite stimulation)



milk gelation: → postprandial ghrelin concentration =  
satiety ?

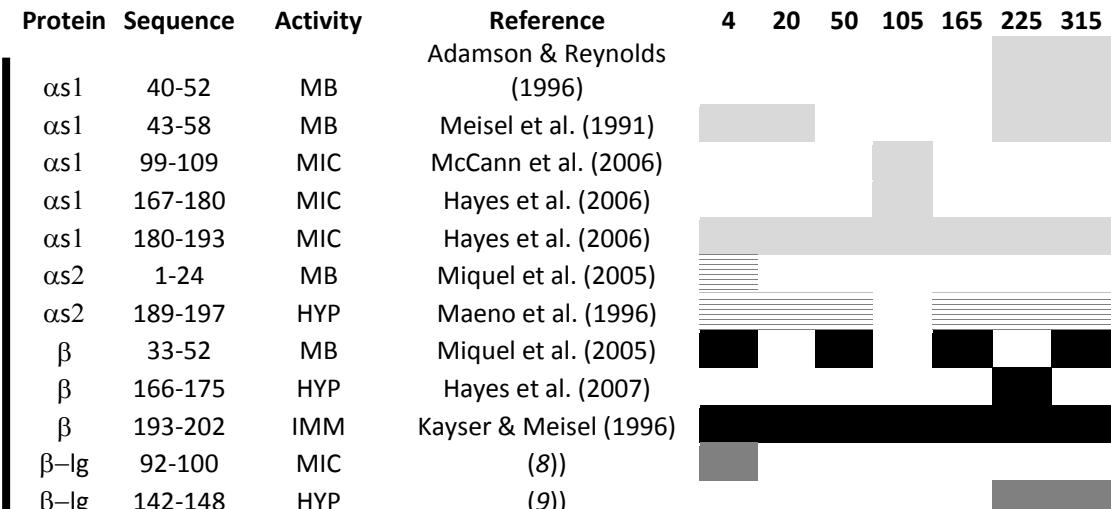
Kinetics of proteolysis and amino acid bioavailability are driven by gastric emptying

# Bioactive peptides released during digestion differ from one matrix to another

More than 16,000 milk peptides identified in the gastrointestinal tract of pigs

Protein	Sequence	Activity	Reference	4	20	50	105	165	225	315
αs1	1-23	EMUL	Shimizu et al. (1984)							
αs1	23-34	HYP	Maruyama & Suzuki (1982)							
αs1	30-45	MB	Meisel et al. (1991)							
αs1	40-52	MB	Adamson & Reynolds (1996)							
αs1	43-58	MB	Meisel et al. (1991)							
αs1	91-100	STRE	Miclo et al. (2001)							
αs1	99-109	MIC	McCann et al. (2006)							
αs1	167-180	MIC	Hayes et al. (2006)							
αs1	180-193	MIC	Hayes et al. (2006)							
αs2	1-24	MB	Miquel et al. (2005)							
αs2	124-146	MB	Miquel et al. (2005)							
αs2	183-206	TRAN	Kizawa et al. (1996)							
αs2	183-207	MIC	Recio & Visser (1999)							
αs2	189-197	HYP	Maeno et al. (1996)							
αs2	190-197	HYP	Maeno et al. (1996)							
β	1-24	MB	Bouhallab et al. (1999)							
β	33-52	MB	Miquel et al. (2005)							
β	60-80	OPI	Jinsmaa & Yoshikawa (1999)							
β	98-105	OXI	Rival et al. (2001)							
β	114-119	OPI	Jinsmaa & Yoshikawa (1999)							
β	132-140	HYP	Robert et al. (2004)							
β	192-209	IMM	Coste et al. (1992)							
β	193-202	IMM	Kayser & Meisel (1996)							
β	193-209	IMM	Coste et al. (1992)							
κ	18-24	HYP	Lopez-Exposito et al. (2007)							
κ	106-116	THR	Jolles et al. (1986)							
β-Ig	32-40	HYP	Pihlanto-Leppala et al. (2000)							
β-Ig	92-100	MIC	Pellegrini et al. (2001)							
β-Ig	142-148	HYP	Mullally et al. (1997)							

Acid Gel



Rennet Gel

- More bioactive peptides identified during digestion of acid gel than rennet gel
- Nature of peptides is identical (clearly defined by the digestive enzyme specificity)
  - Kinetics of release are different

Barbé et al. 2014  
Food Res Int

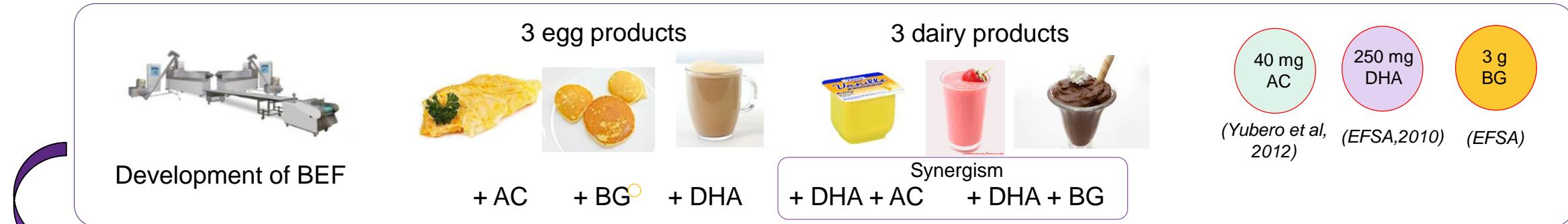
But identifying a bioactive peptide in the lumen does not prove that it will exert a biological action!

## Example 2

### Food structure and delivery of phytochemicals



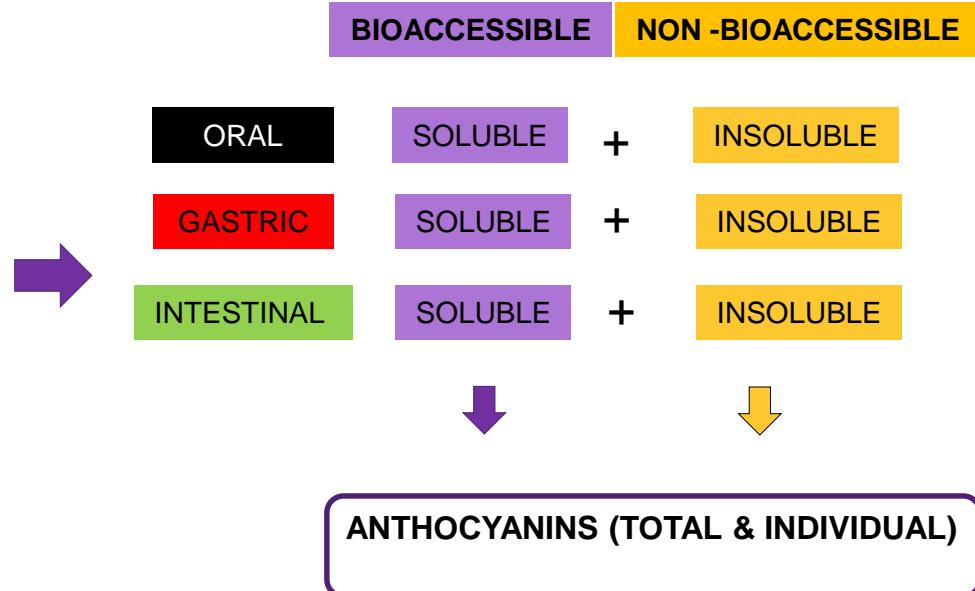
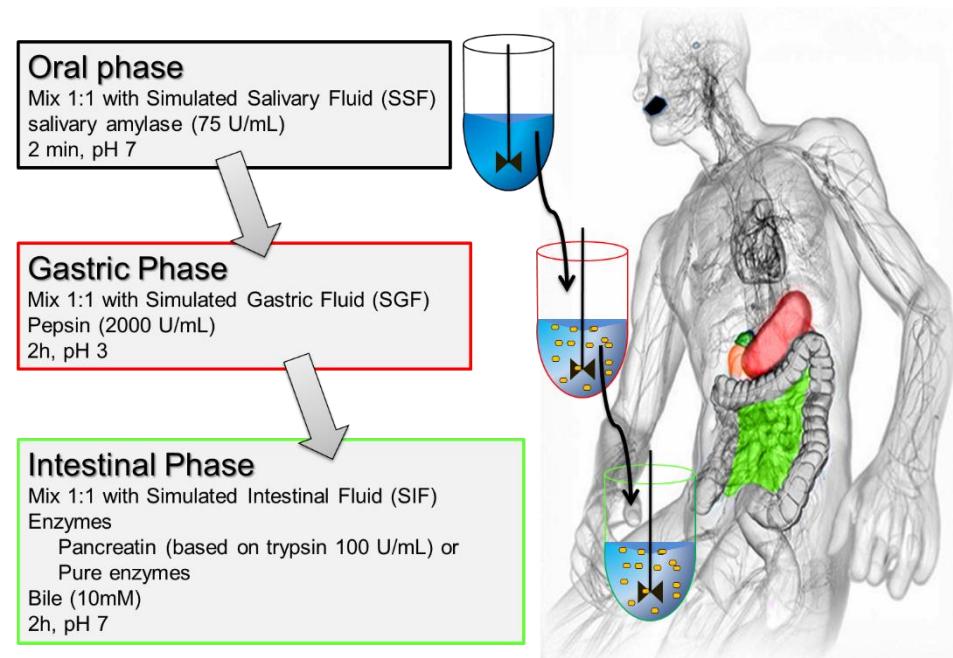
## Development of bioactive-enriched food to fight the risk of developing a metabolic syndrome



6 M€ European project  
2015-2019  
26 partners

## *In vitro* digestion to determine the effect of the food matrix on the delivery of anthocyanins

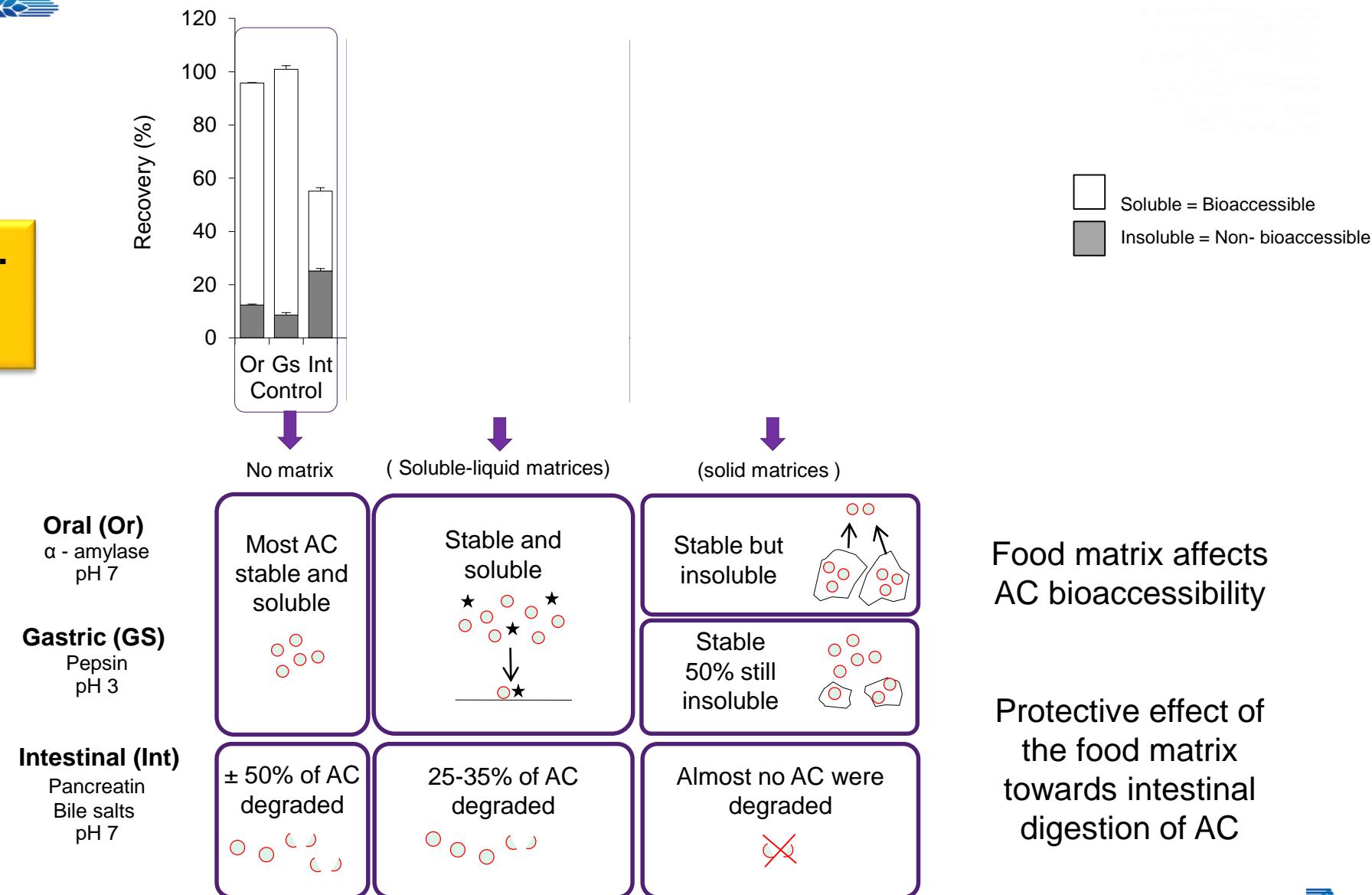
+AC Dairy and egg  
matrices  
**PATHWAY-27**  
+  
Control solution



Infogest consensus *in vitro* digestion model

## Total anthocyanins

Pineda-Vadillo et al.  
2015  
*Food Res Int*



## Example 3

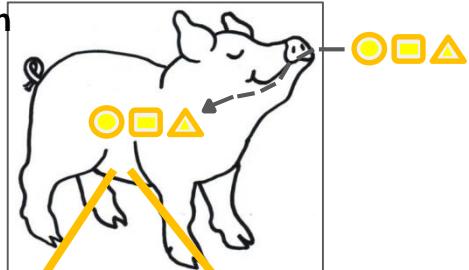
### Food structure and delivery of DHA

## STRATEGY

3 egg products with identical composition  
but different structure



In vivo digestion

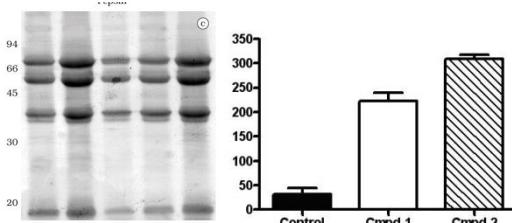
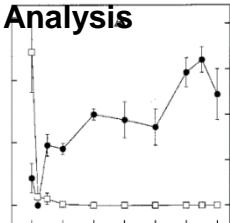


Sampling

Blood  
(Bioavailability)

Intestinal effluents  
(Bioaccessibility)

Analysis



## FOOD MATRICES

Same composition but different structure

**OMELETTE:** Egg yolk and egg white **MIXED** and **WELL COOKED**

**HARD-BOILED EGGS:** Egg yolk and egg white **NOT MIXED** and **WELL COOKED**

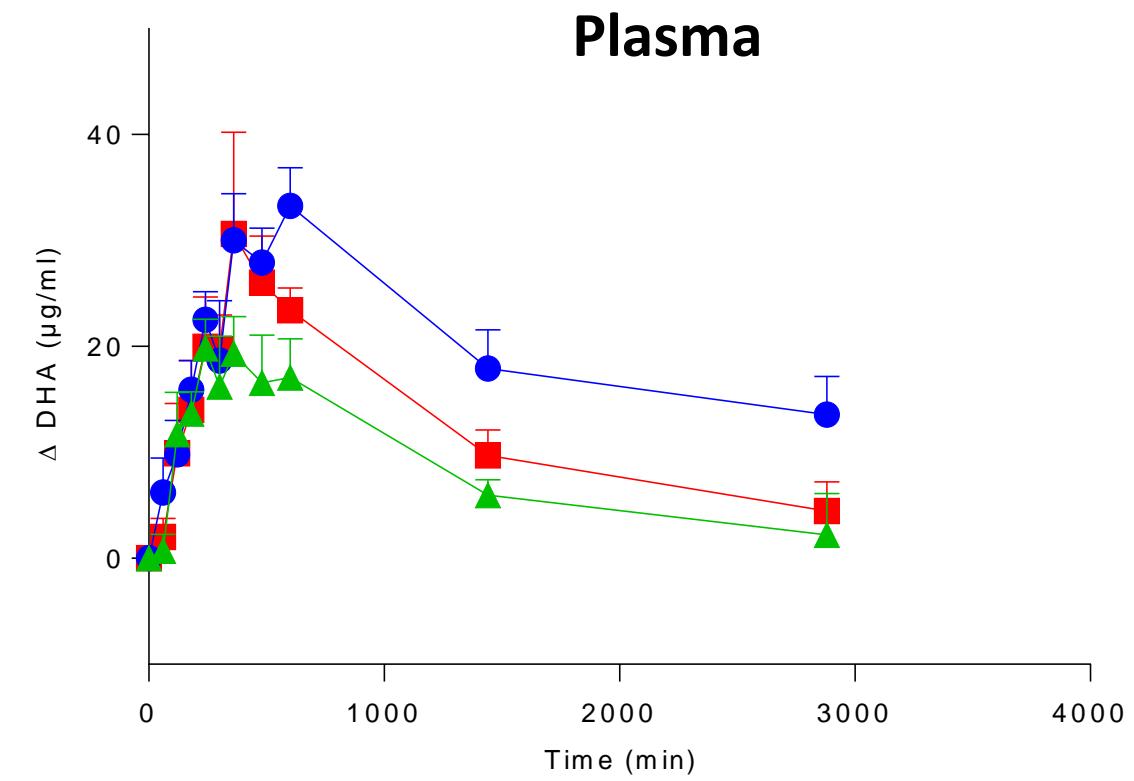
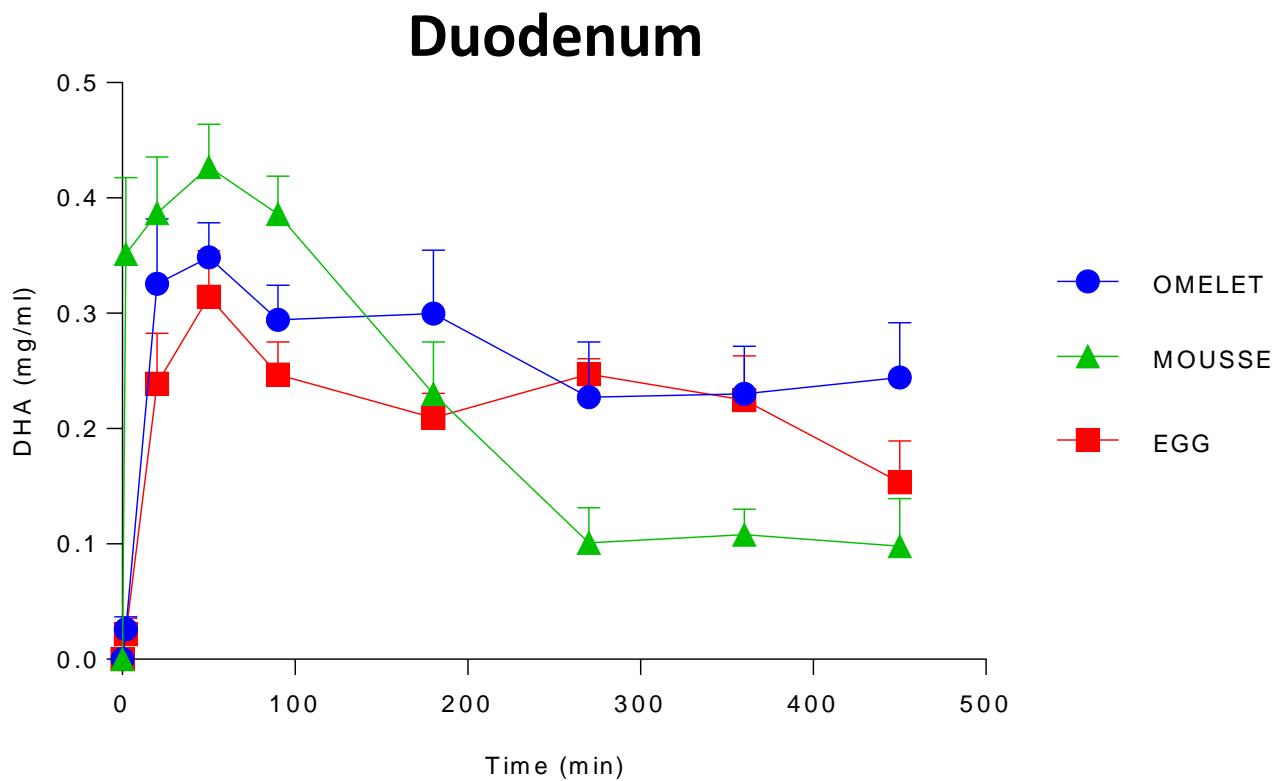
**MOUSSE:** FOAMED RAW Egg white + RAW egg yolk. **MIXED**



Egg yolk: egg white proportion as in real eggs  
500g /intake **1.74 g of DHA**

**Recovery DHA after cooking**  
Omelet (99.4%) Egg (104%) Mousse (91.7%)

# DHA bioaccessibility and bioavailability



DHA bioavailability (Area Under the Curve) : Mousse = Hard-boiled Eggs < Omelette ( $p<0.005$ )

The food matrix regulates DHA bioavailability

# Improving health properties of food by sharing our knowledge on the digestive process

International Network

Dr. Didier DUPONT, Senior Scientist, INRA, France



June 2011 – May 2021



# INFOGEST



## INFOGEST



Chair  
Didier Dupont - France



Vice-chair  
Alan Mackie - UK



*In vitro/in vivo*  
correlations  
**WG1**

*In vitro* semi-  
dynamic  
model of  
digestion  
**WG2**

Models for  
specific  
populations  
**WG3**

Digestive  
lipases and  
lipid digestion  
**WG4**

Digestive  
amylases and  
starch  
digestion  
**WG5**

*In silico*  
models of  
digestion  
**WG6**

The “Mind-  
the-Gap”  
group



Didier Dupont



Alan Mackie



Uri Lesmes



Myriam Grundy



Nadja Siegert



Choi-Hong Lai



Guy Vergeres



Frederic Carriere



Fred Warren



Steven Le Feunteun



We are pleased to announce the next  
**6<sup>th</sup> International Conference on Food Digestion**



**in Granada, Spain, April 2019**

# Key Takeaways

- ▶ Understanding the mechanisms of food digestion is a necessary step to strengthen our knowledge on the relationships between food and human health
- ▶ The effect of food structure on bioactive and nutrient bioavailability can only be demonstrated by comparing foods with identical composition (but different structure)
- ▶ Food structure drives the kinetics of nutrient/bioactive release in the GI tract and the bioavailability. Gastric emptying can be a key parameter.
- ▶ An international effort is needed to harmonize the digestion models used by the scientific community

# The Bioactivity & Nutrition team

## Head

Didier DUPONT - Senior Scientist

## Scientists

Rachel BOUTROU – *Junior Scientist*

Amélie DEGLAIRE – *Lecturer*

Juliane FLOURY – *Lecturer*

Catherine GUERIN - *Lecturer*

Joëlle LEONIL – *Senior Scientist*

Françoise NAU – *Professor*

Frédérique PEDRONO – *Lecturer*

Jonathan THEVENOT – *Post-doc*



## PhD students

Lucie LORIEAU (2016-2019)

Linda LEROUX (2016-2019)

Manon HIOLLE (2016-2019)

Yohan REYNAUD (2016-2019)

## Masters students

## Technicians

Gwenaële HENRY

Yann LE GOUAR

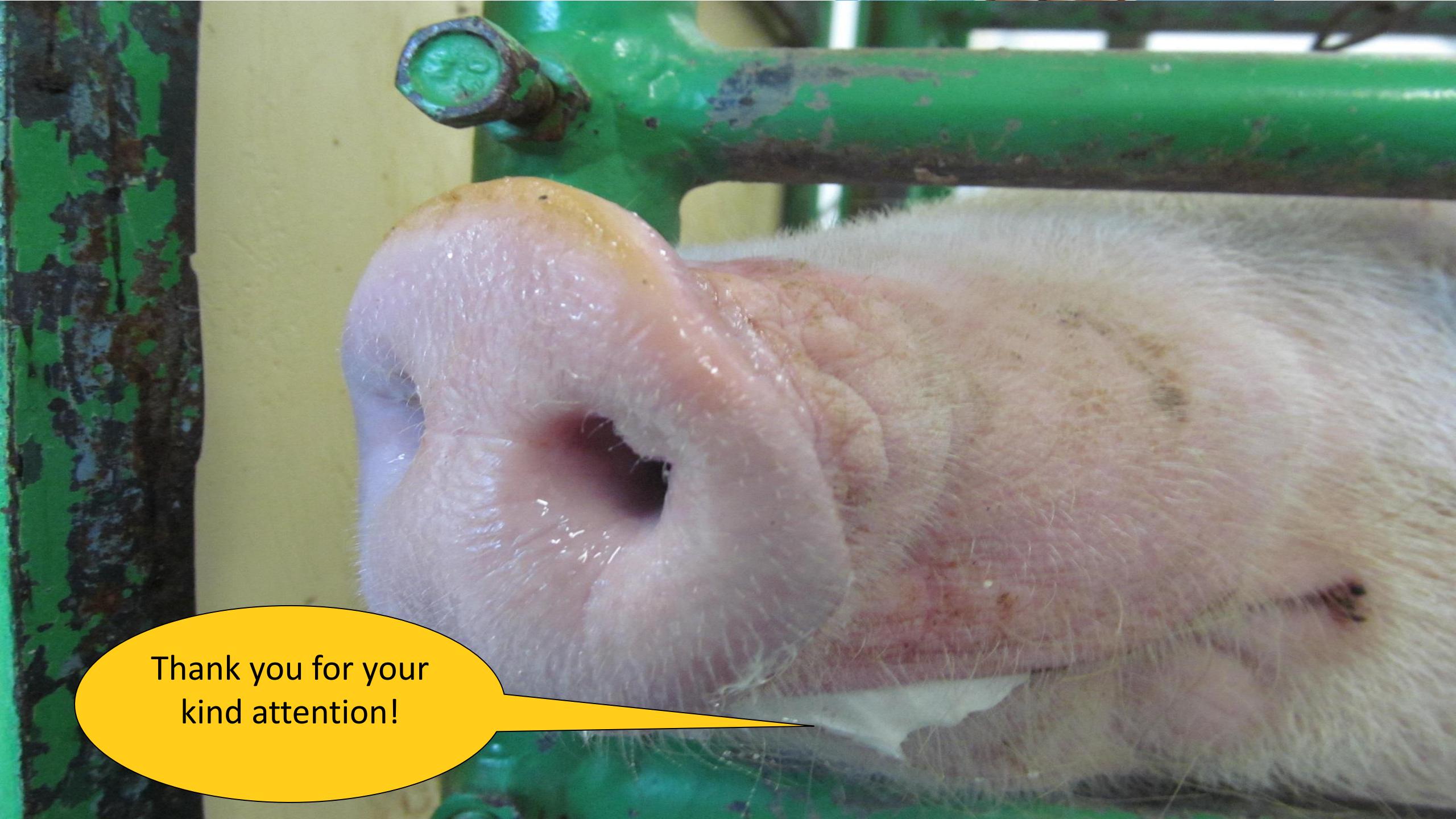
Nathalie MONTHEAN

## Engineers

Julien JARDIN

Olivia MENARD

Jordane OSSEMOND



Thank you for your  
kind attention!