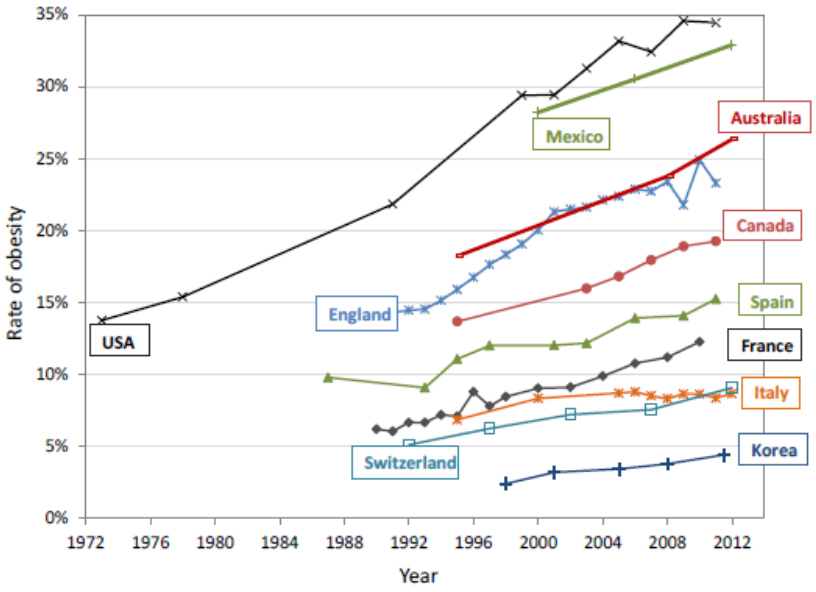
Understanding the mechanisms of dairy products digestion in infant and elderly

Didier Dupont

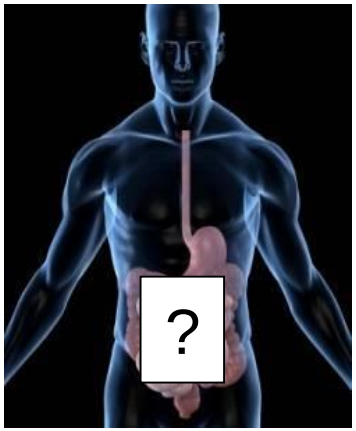
Understanding the mechanisms of dairy products digestion in infant and elderly

Dr Didier DUPONT, INRAE, STLO, Rennes, France

Food and human health: the key role of digestion



Diet-related diseases ↑
Prevent these pathologies rather than cure them



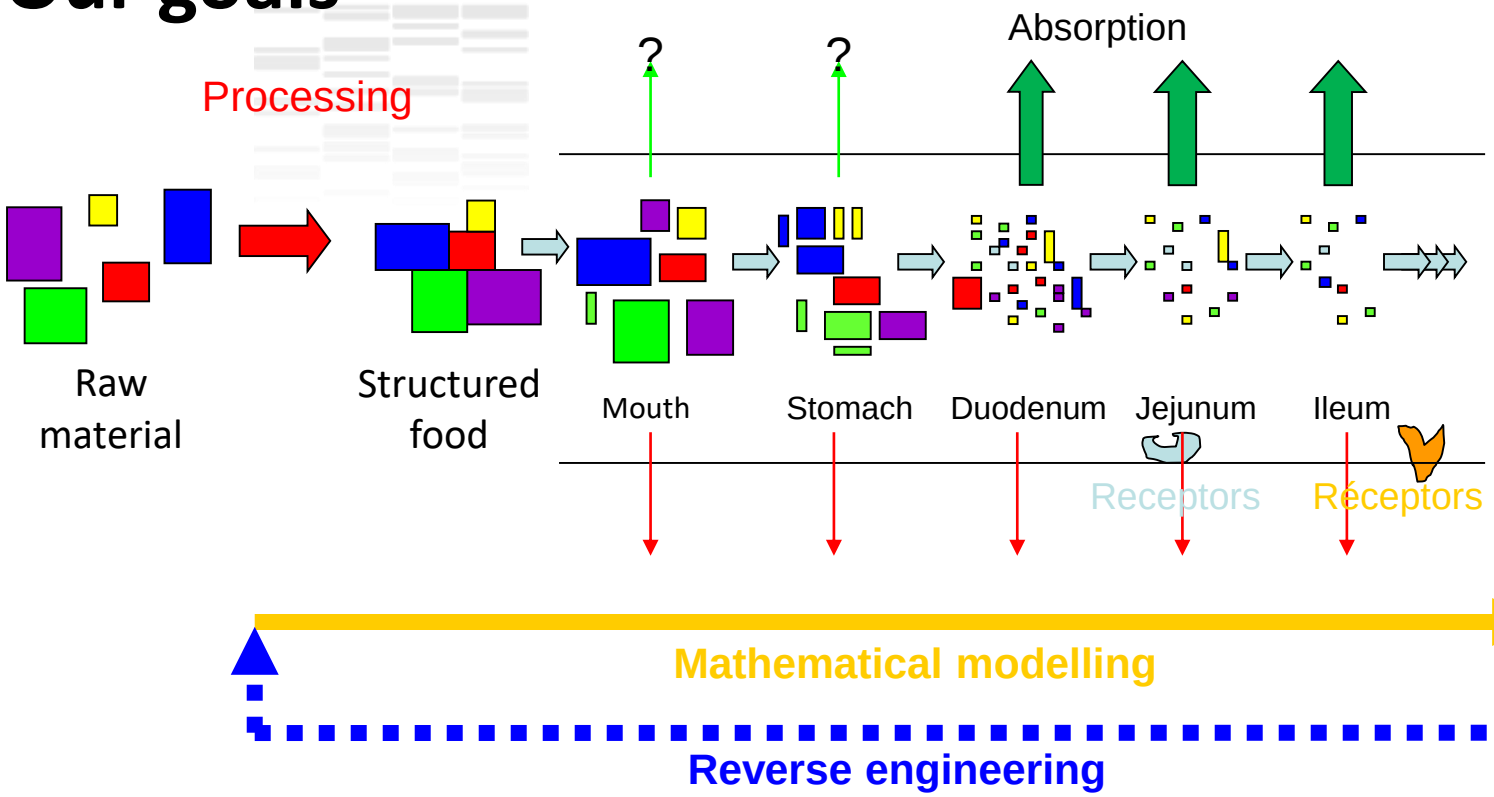
Gut = interface between food and human body
Digestion releases food components that can have a beneficial or a deleterious effect on human health

… 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

By increasing our knowledge on food digestion, we will increase our knowledge on the effect of food on human health

Our goals

Healthy Adult/ Infant/ Elderly



Bioactivities
- Bioactive peptides
- Amino acids
- Fatty acids
- Minerals…

Gut

Immune System

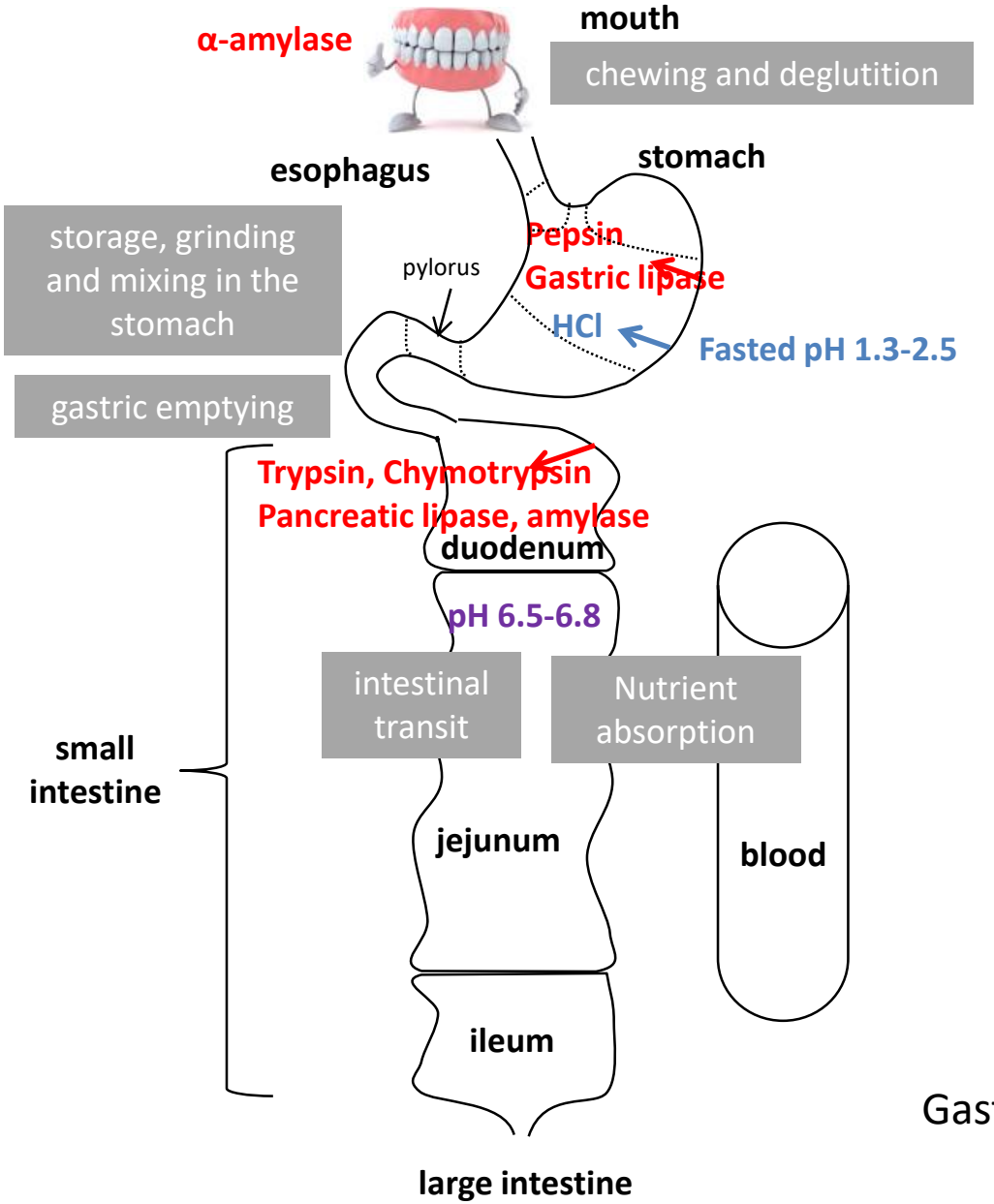
Intestinal microbiota

☞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

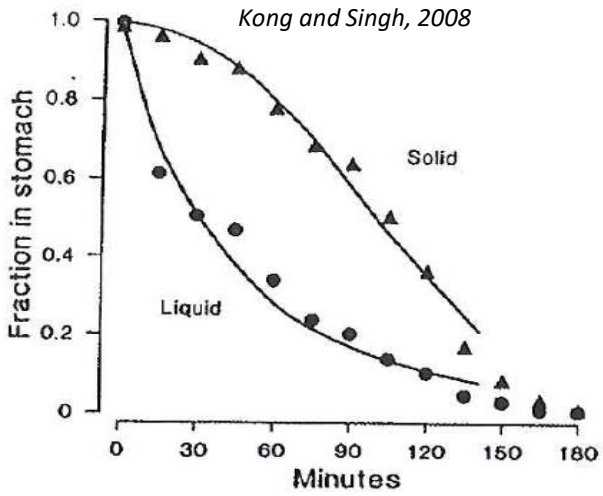
☞To determine the impact of the structure of food matrices on nutrient bioavailability

☞To model these phenomena in order to develop a reverse engineering approach

The digestive process



From Roger Lentle, Massey Univ. NZ



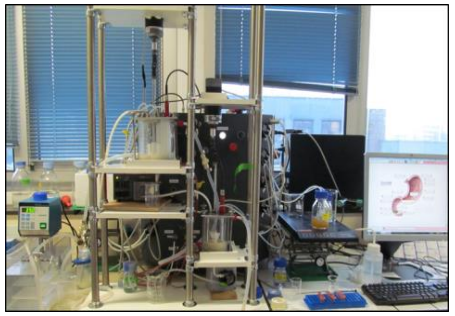
Gastric phase = a very complex but crucial step for the whole digestion process

Models available at INRAE for simulating digestion

Dupont et al. 2010ab, Mol Nutr Food Res

In vitro static models (infant, adult)

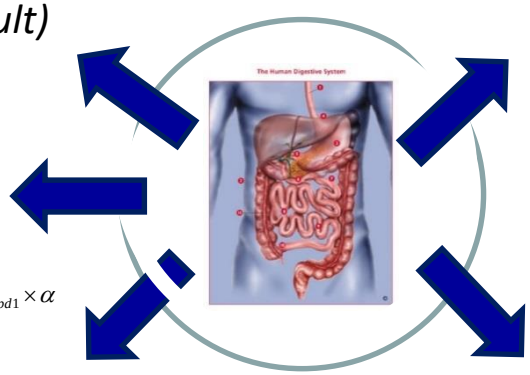
Menard et al. 2014, Food Chem
Sanchez et al. 2015 Food Res Int



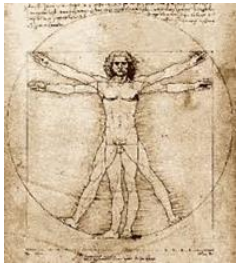
In vitro dynamic models (infant, adult, elderly)

Le Feunteun et al. 2014 Food Bioprocess Tech

In silico models



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



Human models

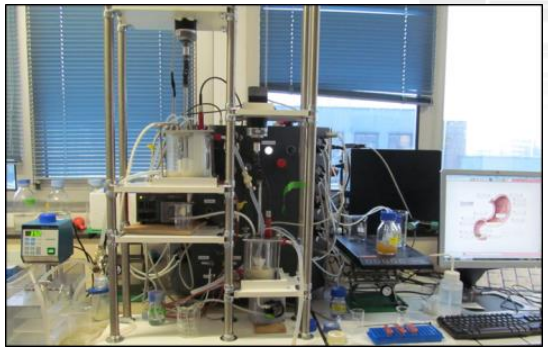
Animal models

De Oliveira et al. 2016 Am J Clin Nutr
De Oliveira et al. 2017 Clin Nutr

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

STLO

Validation of the dynamic *in vitro* digestion system



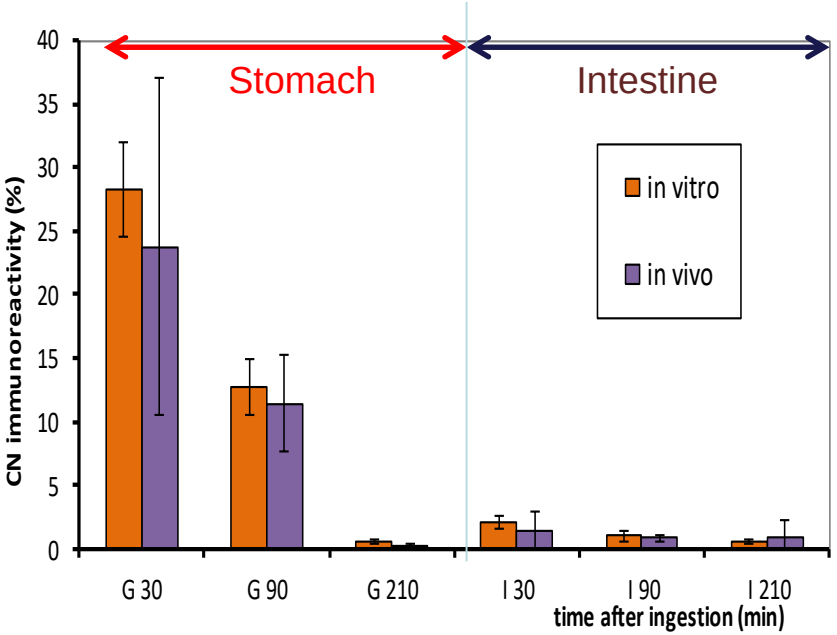
Infant Formula

In vitro

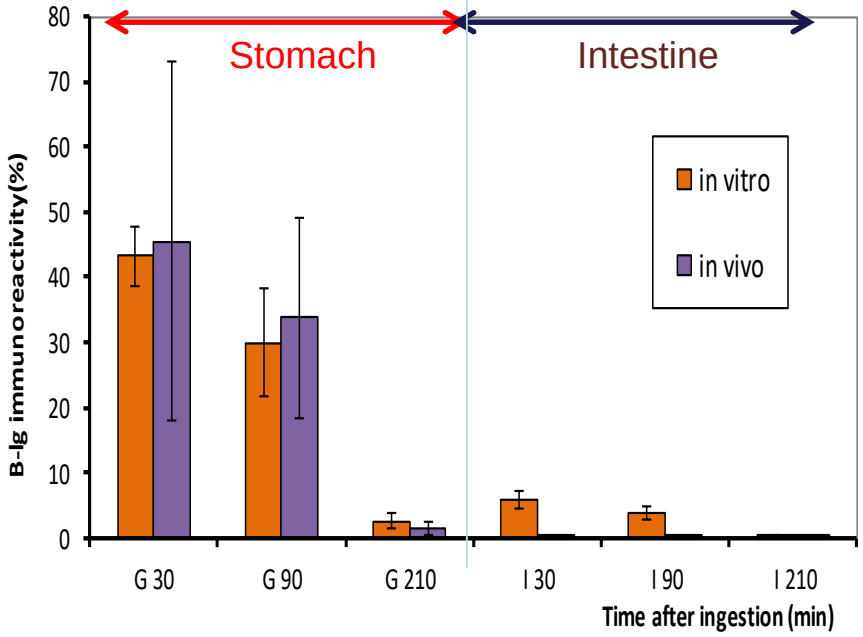
N=3

In vivo

18 piglets



Caseins



β-lactoglobulin

Menard et al. 2014 Food Chem

Understanding human milk digestion to design new infant formulas that will have the same behaviour in the GI tract

Deglaire A., Menard O., De Oliveira S., Bourlieu C. & Dupont D.

INRA, Rennes, France

Human/ bovine milk / Infant Formula

Protein structures

Human milk

Bovine milk

Infant Formula

(Turck *et al*, 2010)

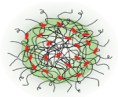
Ø = 64 nm

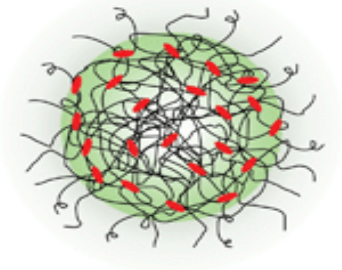
(β, κ-casein)

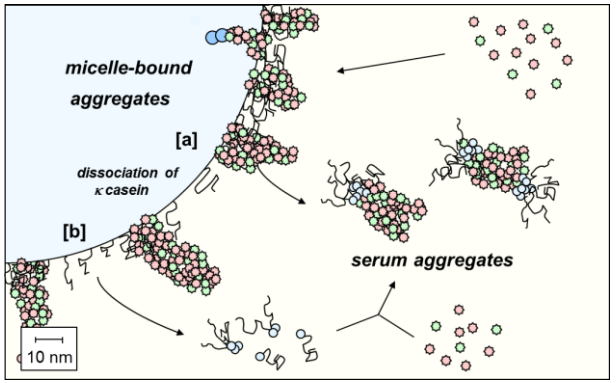
ø = 182 nm

(αs1, β-casein)

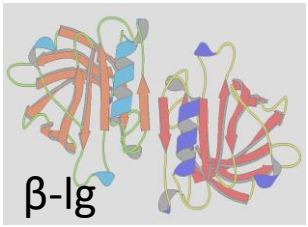
Casein micelle







Whey Proteins



Human/ bovine milk / Infant Formula

Lipid globule structure

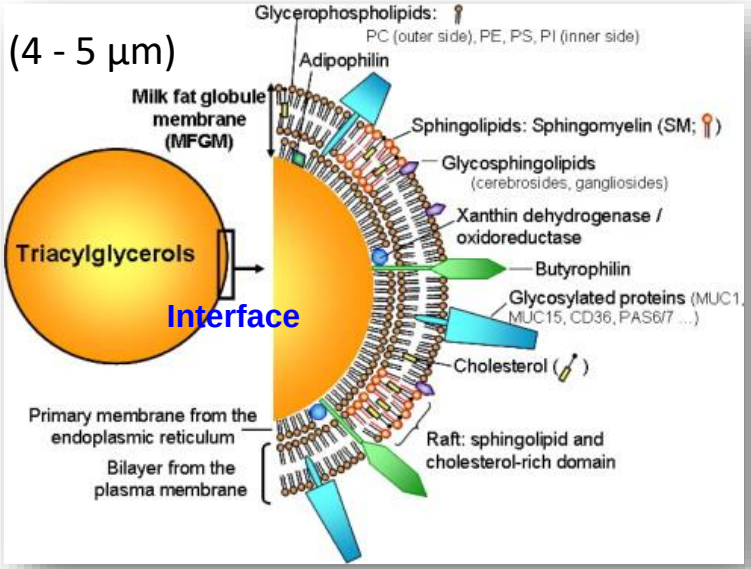
Human milk

Bovine milk

Infant Formula

Native milk fat globule

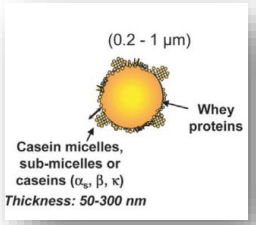
(4 - 5 µm)



(Lopez, 2010)

Lipid droplets

Triacylglycerols



(0,2 - 1 µm)

(Lopez and Briard-Bion, 2007)

In vivo study in the preterm infant

ClinincalTrials.gov Identifier: NCT02112331
ARCHILACT

Preterm hospitalized infants
Feeding nasogastric tube
Fed every 3 hours

Aim: to compare meals with similar composition but different structure

Human milk from their **own mother**

Human milk from **anonymous donor**

GROUP A

GROUP B

Raw human milk

Pasteurized human milk

Pasteurized human milk

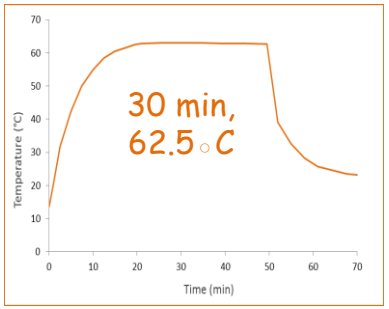
Pasteurized-homogenized human milk

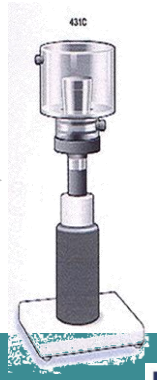
24h before feeding (4°C)

Stored at -20°C (bank milk)

Stored at -20°C (bank milk)

Bank milk





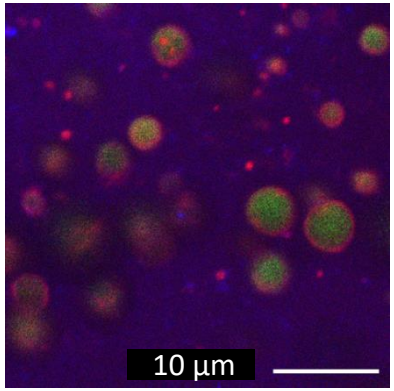
Homogenization by sonication

Pasteurization affected the initial structure and the emulsion disintegration of HM

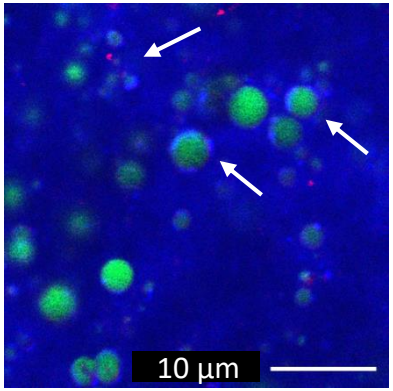
(n = 6 infants)

Initial structure

Raw HM



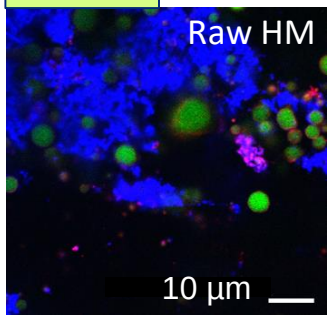
Past HM

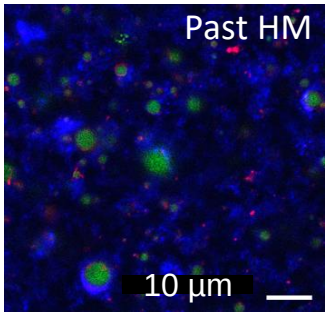


→ Protein heat-induced aggregation

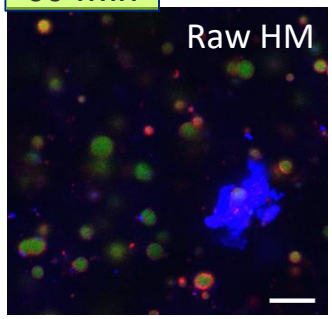
Gastric disintegration

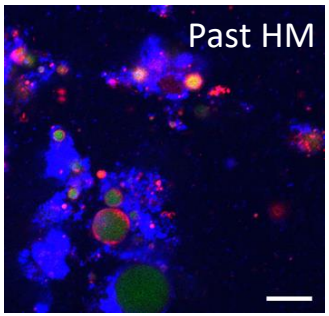
35 min



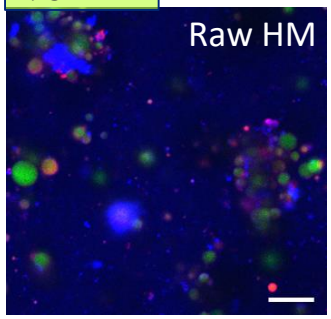


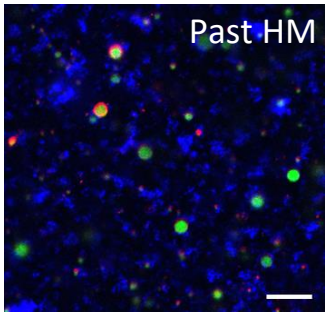
60 min

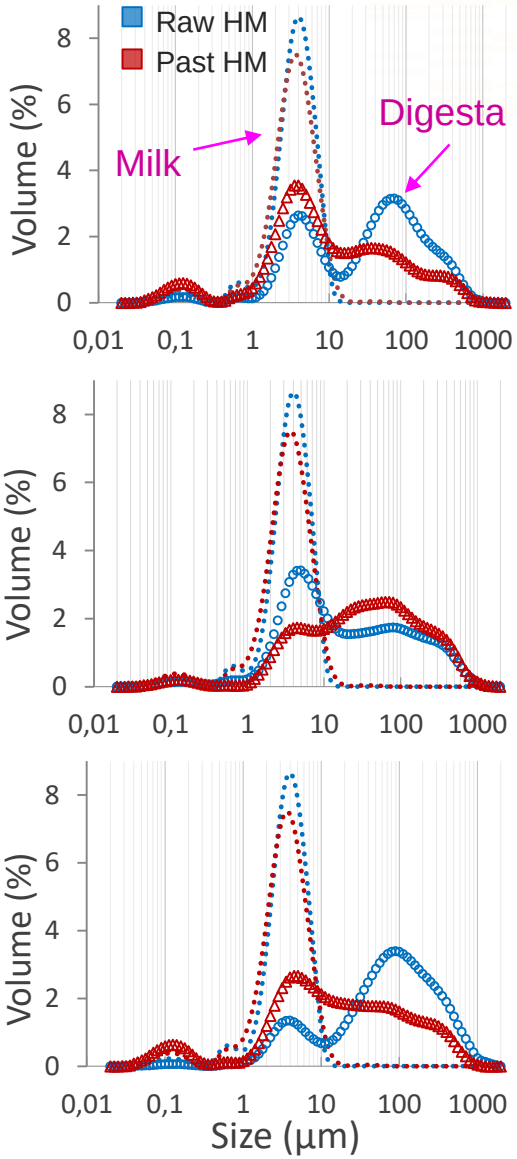




90 min

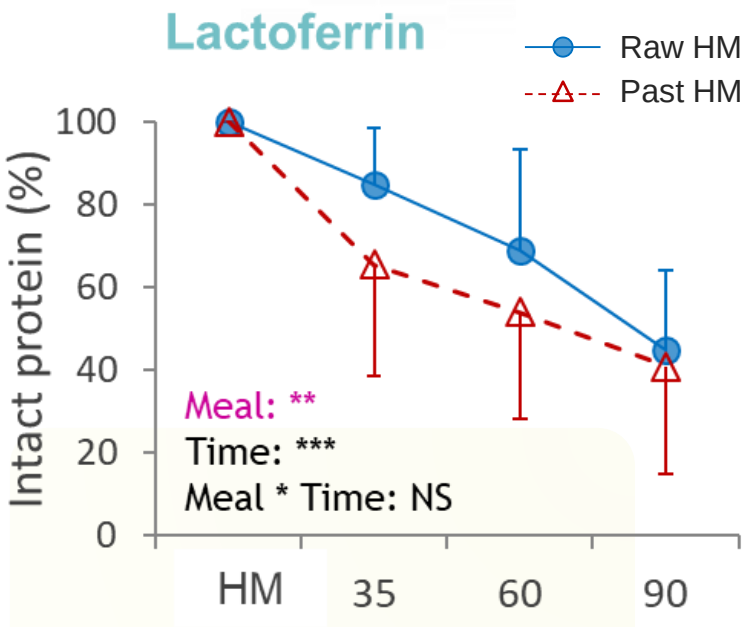






Apolar lipids | Amphiphiles | Proteins

Pasteurization impact Lf hydrolysis

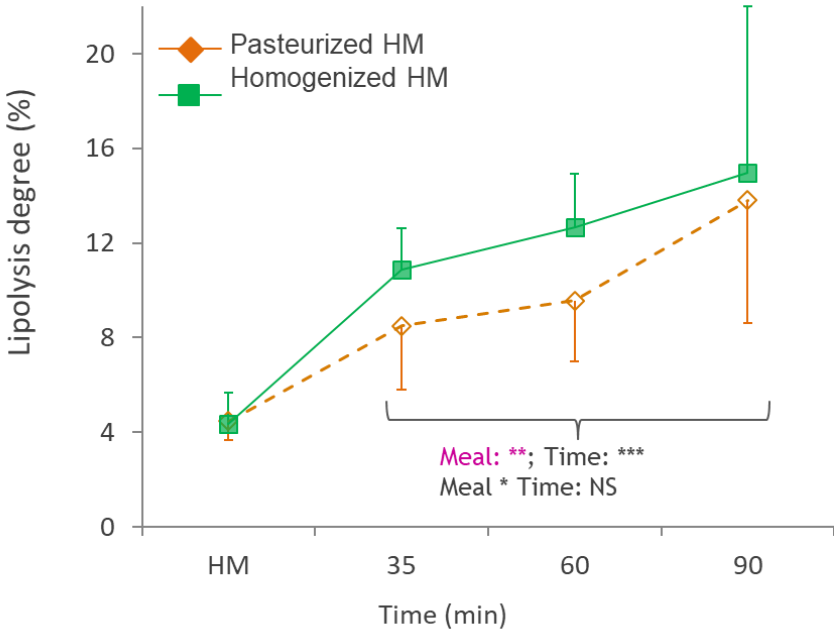


→Faster decrease of lactoferrin in Past HM

Impact on protective qualities of the native lactoferrin?

De Oliveira et al., Am J Clin Nutr 2017

Homogenization accelerates gastric lipolysis



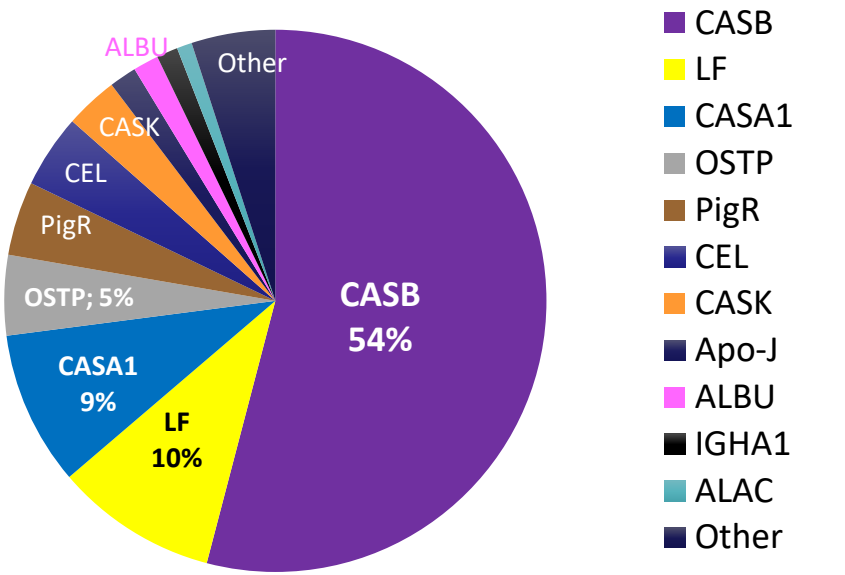
↗ Increase of specific surface of droplets facilitating HGL adsorption

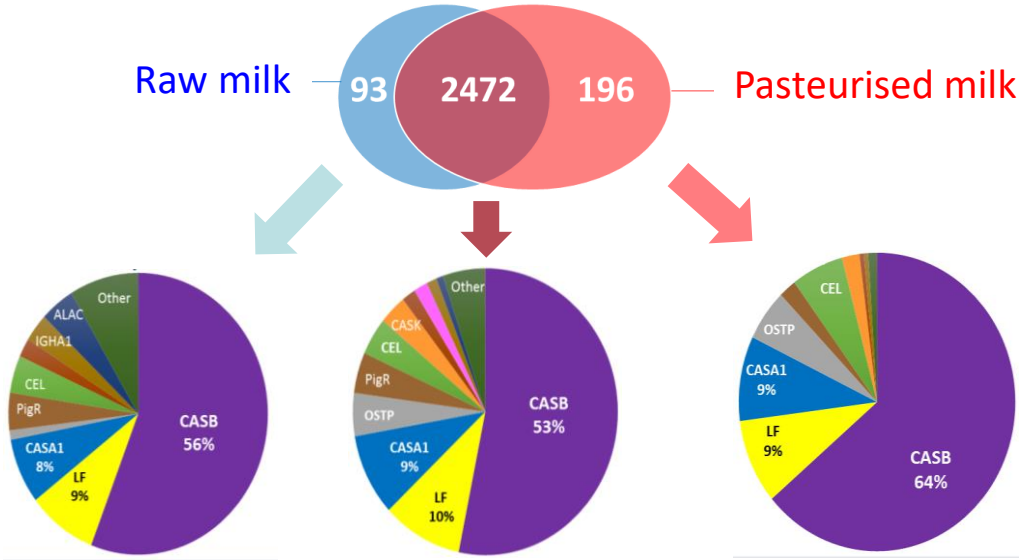
De Oliveira et al., Clin Nutr 2017

Effect of pasteurisation on gastric peptidome

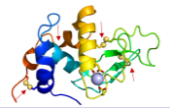
→ **2761 peptides in milk and digestas**

Originating from 18 proteins
with 7 proteins contributing
to less than 1% of the peptides





- Peptides essentially come from β-casein
- α-lactalbumin (ALAC) : 1% of peptides
  - → Resistant to gastric digestion
  - → 4 disulphide bridges



- More peptides specific of pasteurised milk

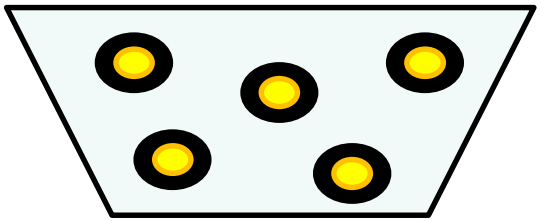
INRA
SCIENCE & IMPACT

Can we design new generation of infant formula that would be biomimetic of human milk?

INSTITUT CARNOT QUALIMENT

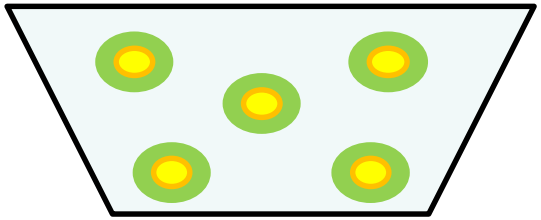
Infant formulas: can we create lipid structures biomimetic on the native fat globule?

Formula T1



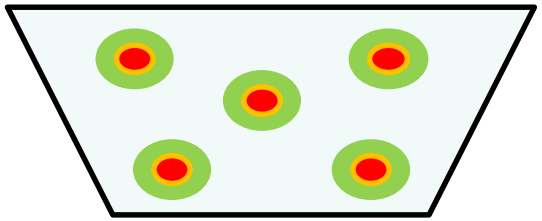
Interface 100 % Proteins
100% vegetable oil

Formula T2

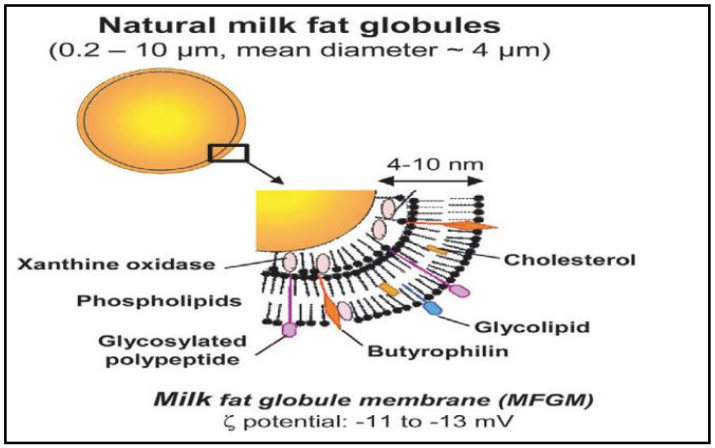


Interface 100 % phospholipids
100% vegetable oil

Formula T3

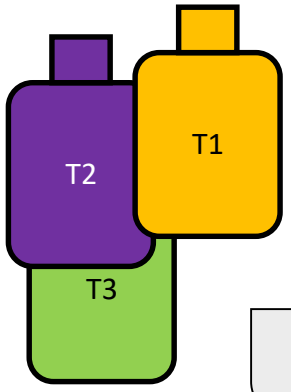


Interface 100 % phospholipides
40% vegetable oil + 60% milk fat



Lopez, (2007)

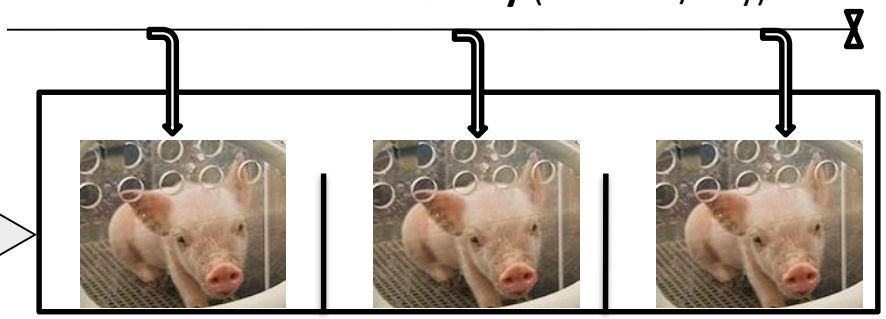
Can the composition of infant formula modulate the physiological response of the neonate?



Veg
Veg + PL
Dairy Fat + PL

Rehydration at 20%

Automatic meal delivery (10 meals/ day)



\+

Mother-fed piglets (MF = + control)

Slaughtering after

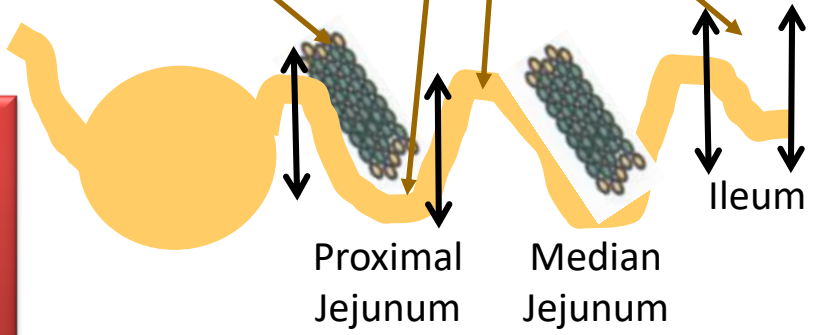
7 days

28 days

(90 min postprandial)

Mesenteric Lymph Nodes (MLN)

Collect of effluents and tissues

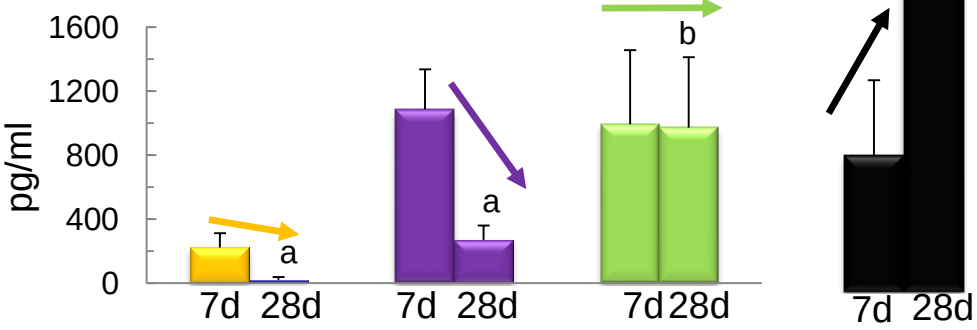


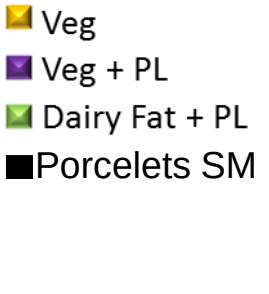
Effluents:
-SDS-PAGE
-Elisa

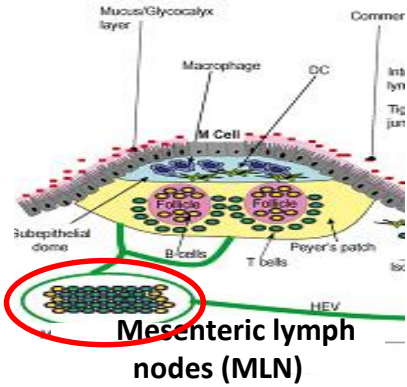
Tissues:
-Morphometry
-Enzyme Activities
-Intestinal Permeability
-Local immune response
-Microbiota

Secretory activity of MLN

Interferon-g (Th1 pro-inflammatory)

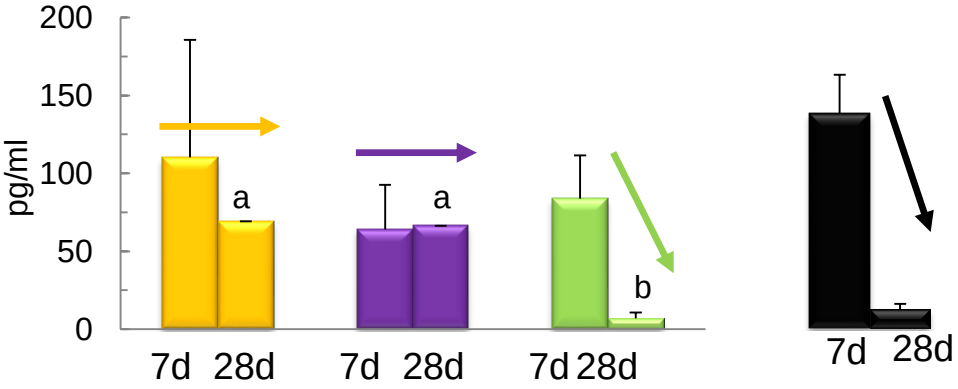






Mesenteric lymph nodes (MLN)

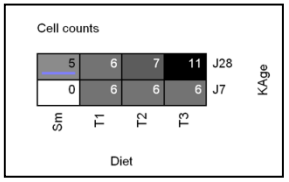
Interleukine-10 (Th2 anti-inflammatory)



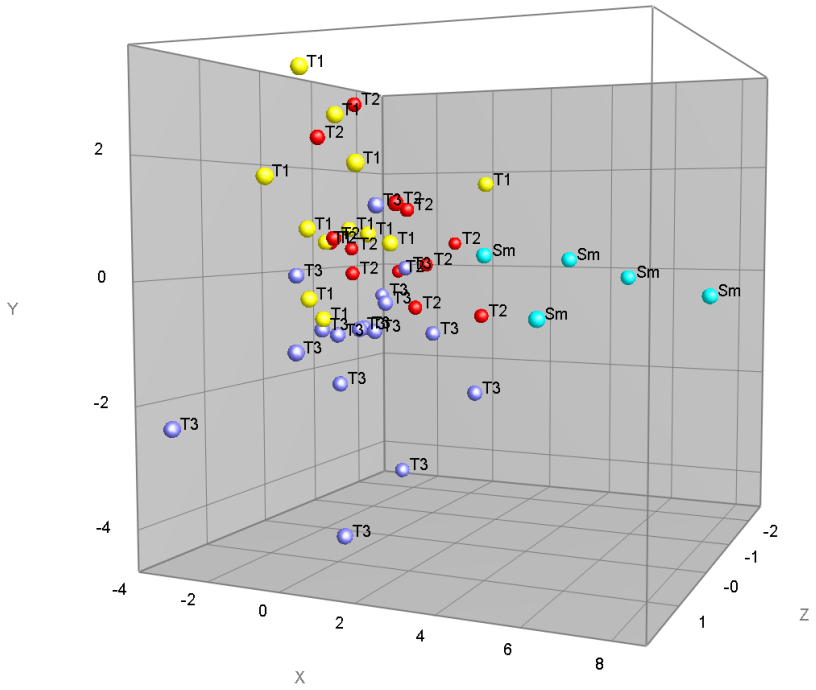
Milk lipids ➔ maturation of the piglet's immune system more similar than with sow's milk

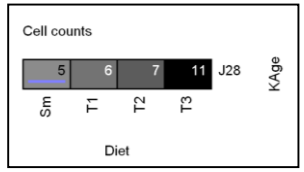
Le Huerou et al.
Eur J Nutr 2017

Microbiota by DHPLC

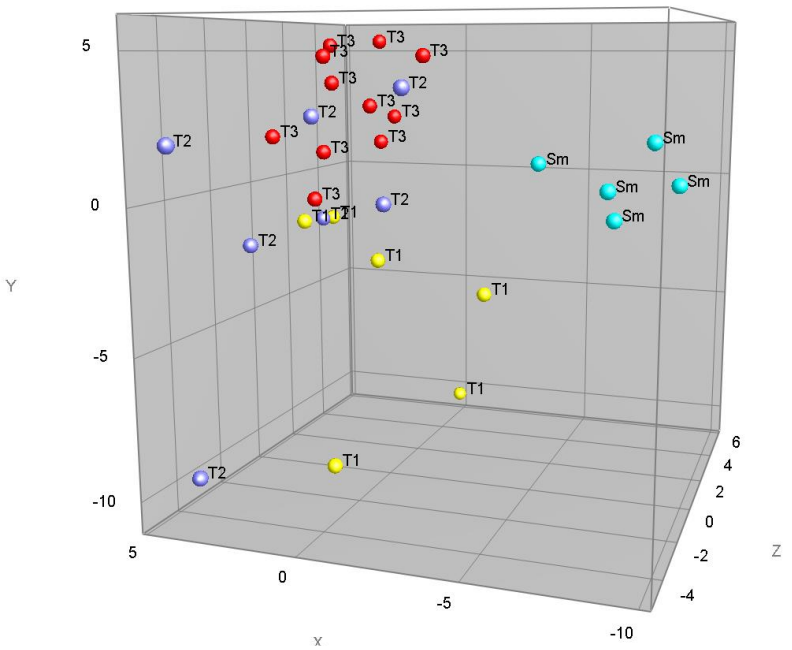


D7 & D28



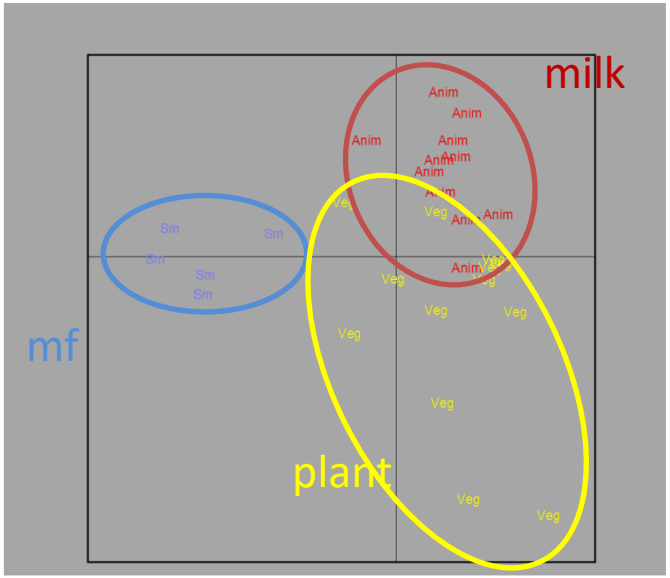


D28



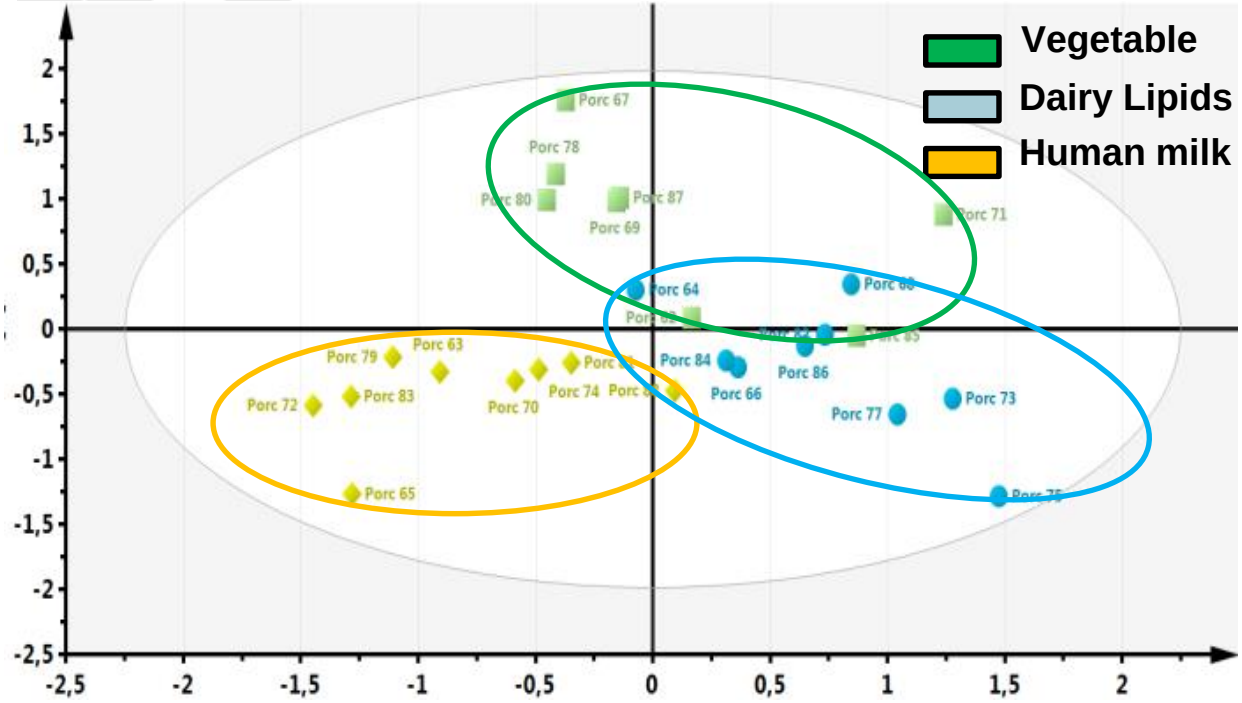
The composition/structure of the infant formula « orientates » the microbiota

More Proteobacteria with milk fat /
More Firmicutes with plant oil



Bourlieu et al. Eur J Lipid Sci Technol 2016

What happens when they become older (140 d)?



Some differences remain in:

* the microbiota composition
* the metabolome with 5 discriminating metabolites (including propionate)
* the immune system with a reduced susceptibility to inflammation with milk lipids (lower TNFα and IL8 with dairy lipids)

The production of an infant formula with a minimally processed route impacts its nutritional, physiological and sensorial qualities

Amélie Deglaire[1], Anne Blais[2], Juliane Calvez[2], Géraldine Lucchi[3,4], Karine Gourrat[3,4], Nadine Leconte[1], Romain Jeantet[1], Didier Dupont[1], Sophie Nicklaus[3] & Anne-Marie Davila[2]

[1] **STLO**, INRAE, Institut Agro, Rennes, France
[2] **PNCA**, INRAE, AgroParisTech, Université Paris-Saclay, Paris, France
[3] **CSGA**, AgroSup Dijon, CNRS, INRAE, Université Bourgogne Franche-Comté, Dijon, France
[4] **ChemoSens Platform**, CSGA, Dijon, France

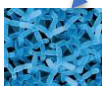
Infant formula production

Yu et al. J Dairy Sci 2021

0.8 µm microfiltration efficiency

(Fauquant et al., 2009, 2014; Tomasula et al., 2011 ; Trouvé et al., 1991; Madec et al., 1992)

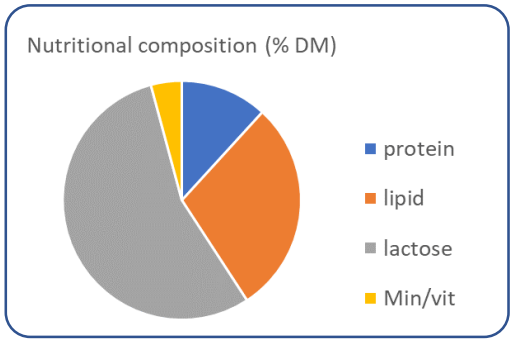
Cronobacter spp.

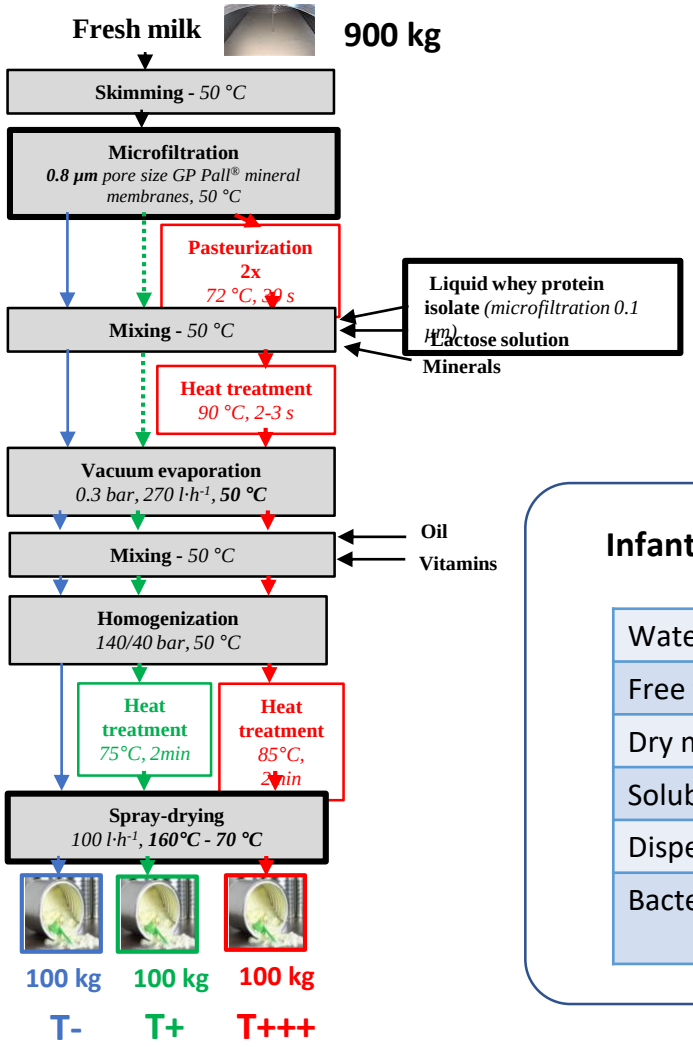


Lactobacillus casei

Propionibacterium Freudenreichii

→ reduction of 4-5 log





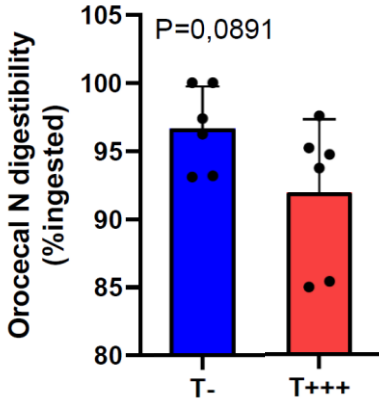
Infant formula powder properties

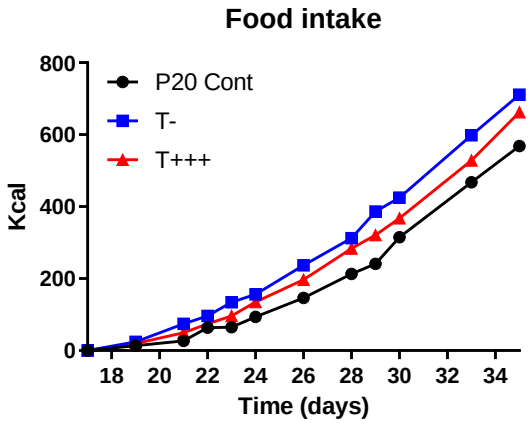
Water activity	0.2 ± 0.0
Free fat	2.9 ± 0.1 % of total fat
Dry matter	97.8 ± 0.1%
Solubility	> 99%
Dispersibility	98.5 ± 0.6%
Bacteriology	≤ 10^3 cfu/ g no pathogen

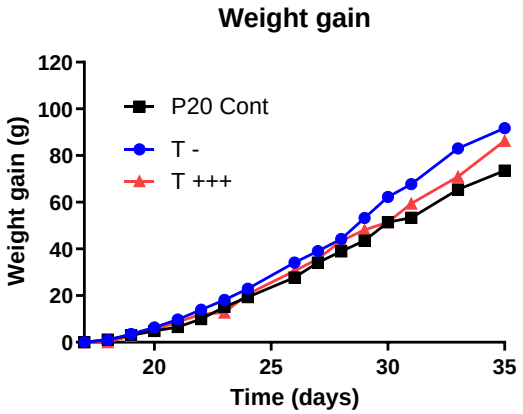
Production of a good quality and bacteriologically safe infant formula powder

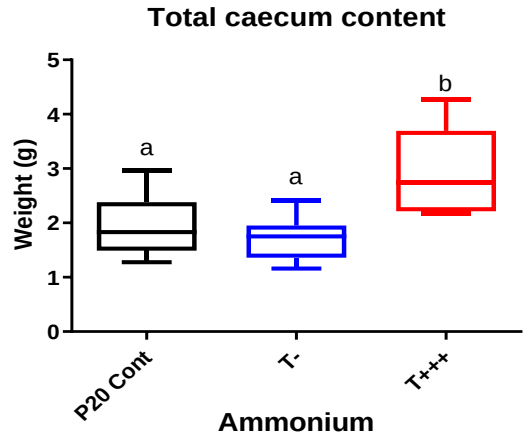
Nutritional properpties

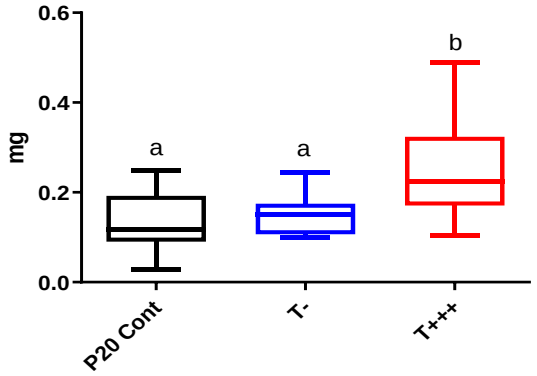
For more info, please contact
amelie.deglaire@agrocampus-ouest.fr











Tendency towards an **increased N and AA digestibility for T-** compared to T+++

Transiently, increased food intake and weight gain for T-

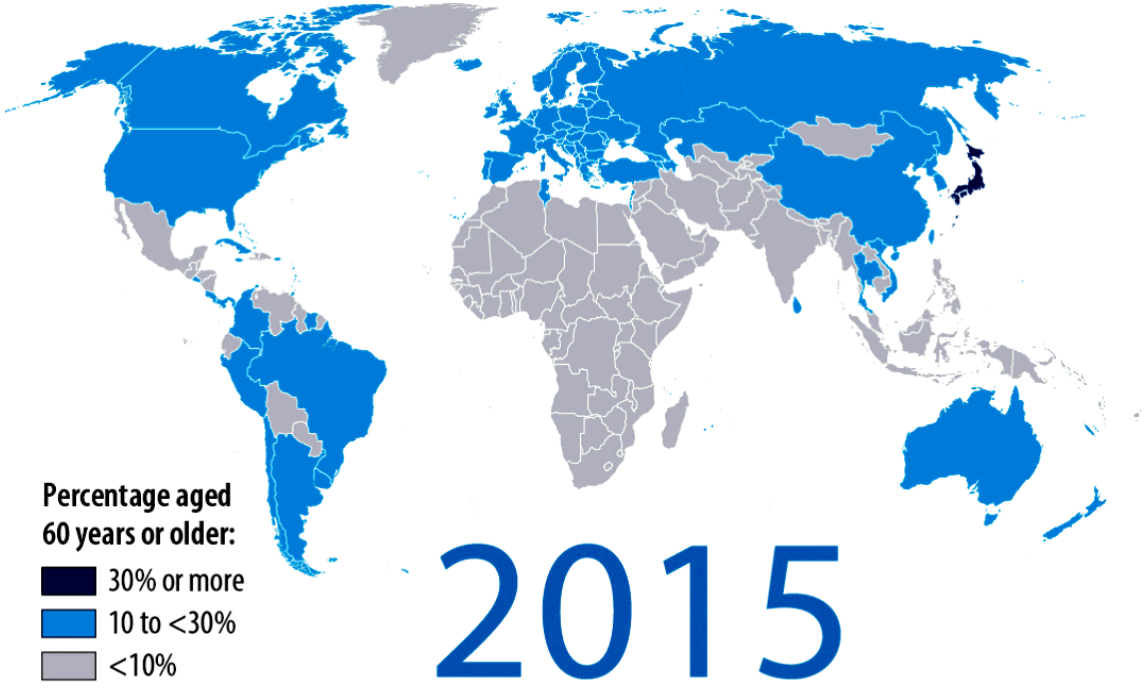
Decreased caecum content, ammonia and total bacteria quantity for T-
Less sulfate reducing and acetogenic bacteria for T-

AGEING = a world problem…

The EU population over 65

2015 : **1/5** of the population

2050 : **1/3** of the population

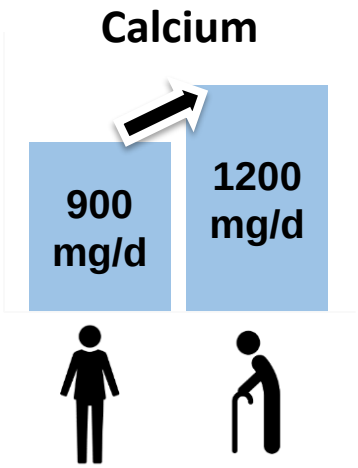


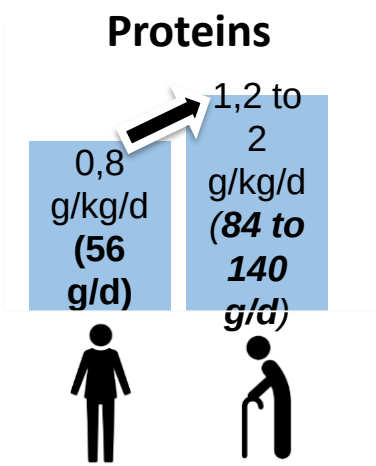
Challenge : healthy ageing

=

- Keeping people autonomy
- Offering them physical and social activities
- Preventing the development of pathologies
- **Offering them an adequate diet**

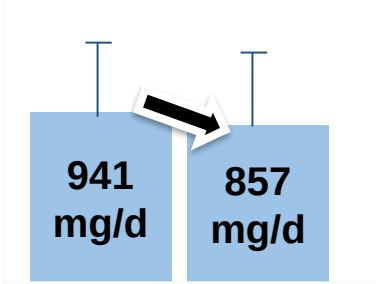
The nutritional needs of elderly people



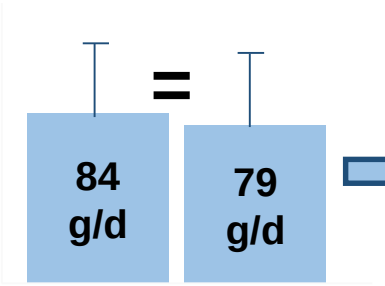


(Baum et al. 2017)

Mean daily intake



Osteoporosis



Sarcopenia

(INCA 3, 2017)

Objectives of AlimaSSenS

To **design a range of cheeses** with identical composition (n=4):

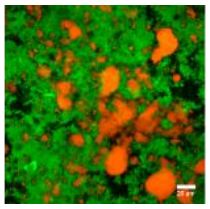
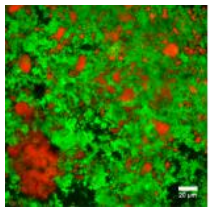
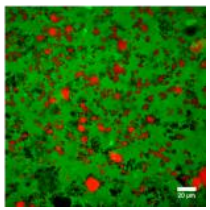
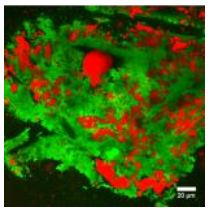
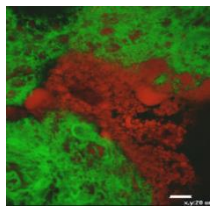
☞ exclusively made of whey proteins to provide 10 g of protein/portion and a high intake of Leucine

☞ enriched in calcium to provide 280 mg of calcium (25% of the daily intake)

To **assess the sensory perception of these cheeses** by elderly people with impaired or intact dental health (n=76)

To **assess the calcium and amino acid bioavailability** in conventional pigs

Design of the cheeses

	Liquid (24%)	Soft	Processe	Hard	Whipped	Mozzarell
Texture perception		Soft and melting	Sticky and pasty	Firm and slightly dry	Dry and granular	Elastic
pH	**6.4** *±0.05*	**6.4** *±0.05*	**6.0** *±0.05*	**6.4** *±0.05*	**5.6** *±0.05*	**5.3** *± 0.05*
Hardness		**16** *±8*	**9** *±4*	**108** *±20*	**6** *±1*	**95** *± 1*
Type of protein	Whey proteins					Caseins
[Leucine] g/kg	**4.70** *±0.41*					**3.61** *±0.01*
Microstructure confocale x60 scale: 20 µm						

Proteins
Lipids

Which textures of cheeses are comfortable for older people with or without oral health impairment?

76 volunteers + 65 y.o
(Dentition and Flow saliva)
x
4 cheese models

Perception

Food comfortability
Questionnaire
(Vandenberghe-Descamps *et al,* 2017)

Q1. Comfort
Q2. Bolus formation
Q3. Pain
Q4. Product texture
Q5. Flavor

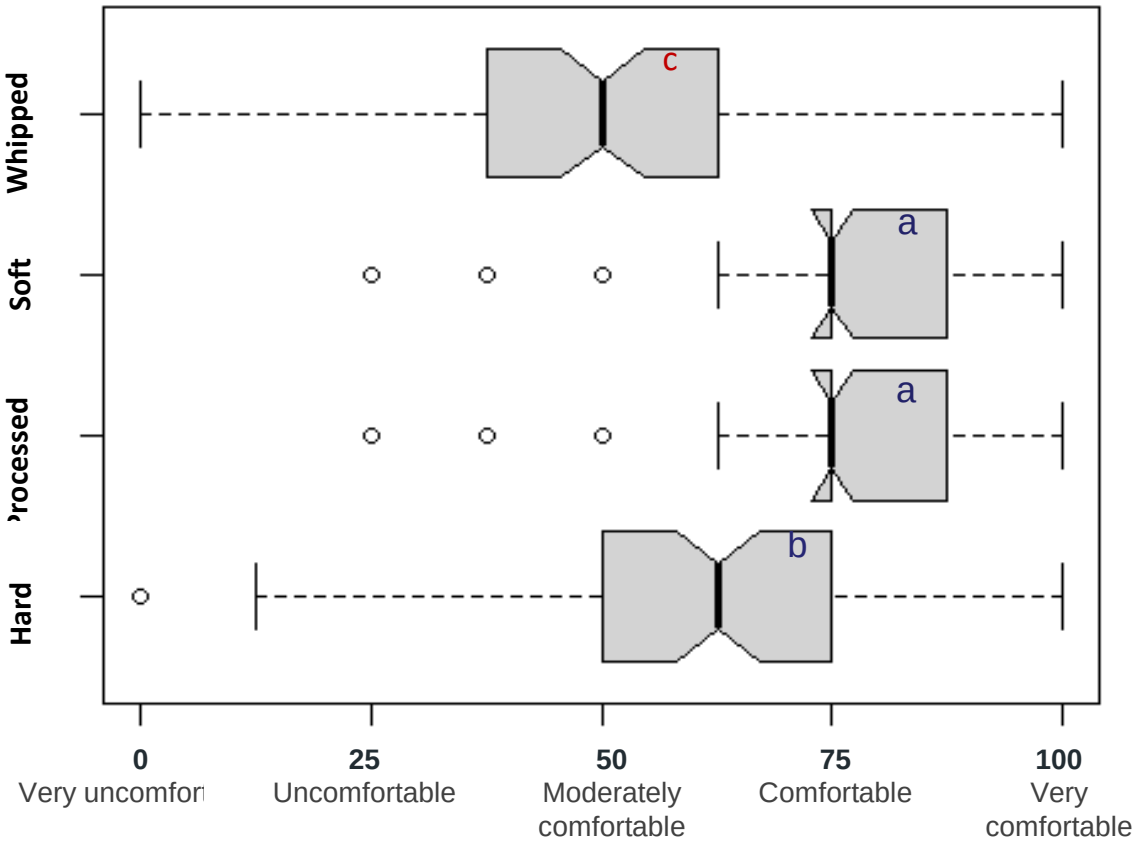
Bolus formation

- **Chewing behavior** :
  Video
  Cycle number
  Chewing time

- **Food bolus**

Rheology - *Compression*
Quantity of saliva– *Dry extract*
(Drago *et al,* 2011)

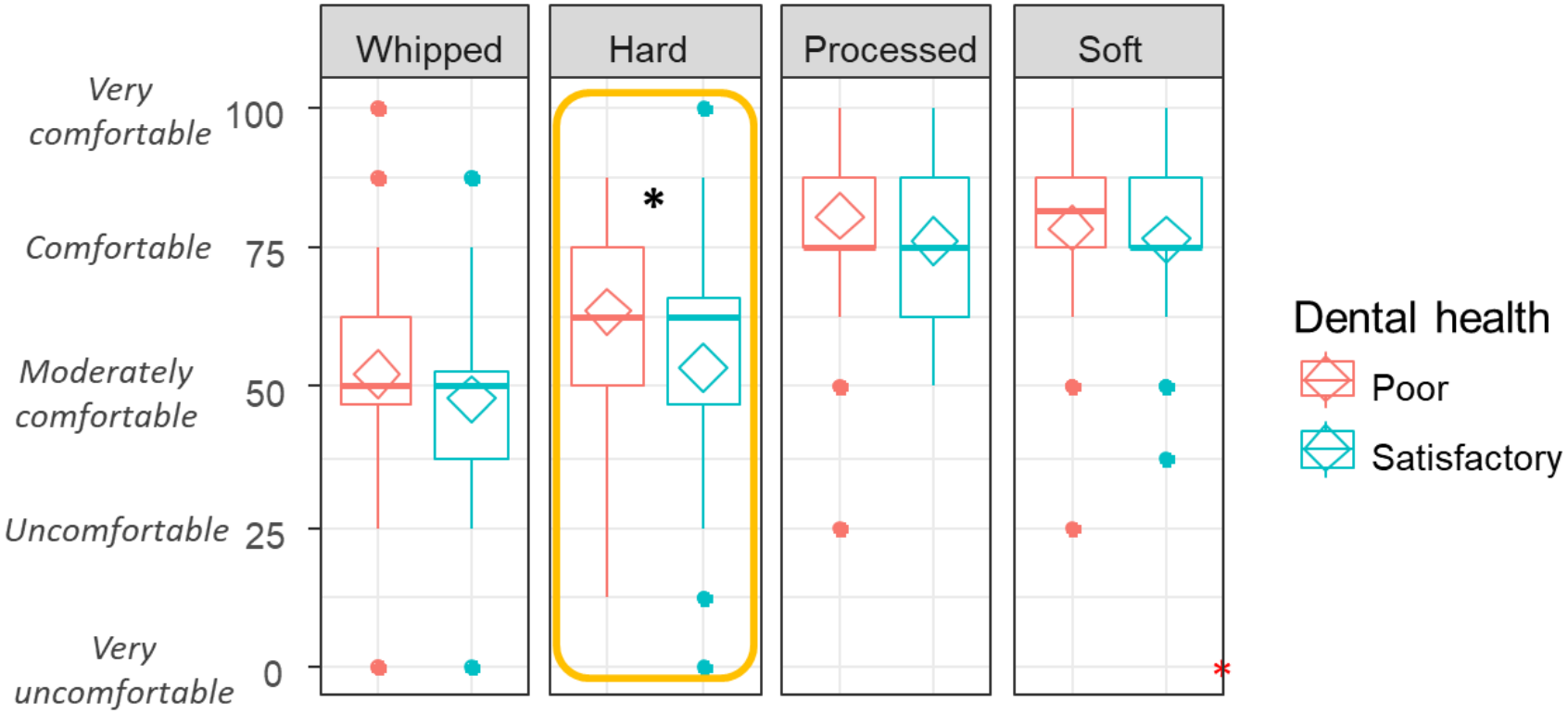
The food comfortability is mainly impacted by the type of product consumed



ANCOVA : Variable~ Product + Error(Subject)

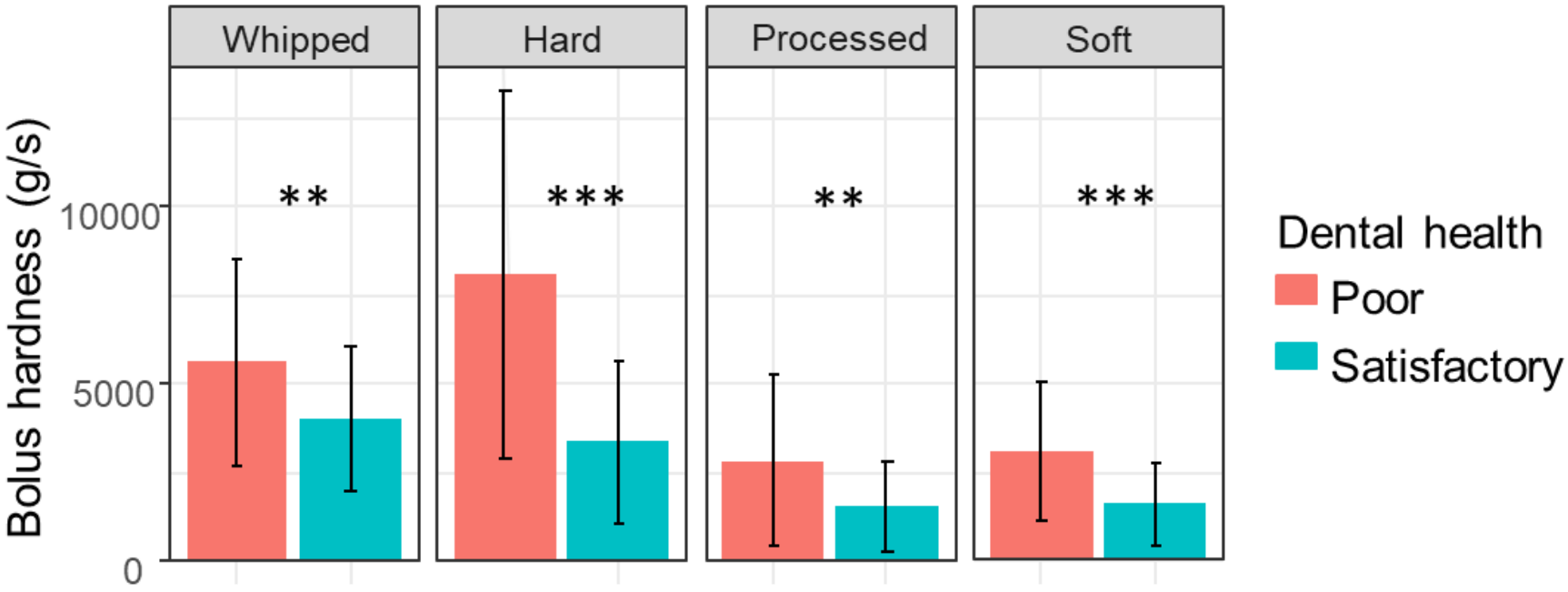
The most comfortable products are the Soft and Processed products

The food comfortability is not negatively impacted by the dental health



Elderly people with a poor dental health considered the Hard product more comfortable than elderly people with a satisfactory dentition

Elderly persons with a poor dental health made harder bolus than elderly persons with a satisfactory one



Decrease in food bolus disintegration by denture wearers observed by Mishellany-Dutour *et al.* (2008), Woda *et al.* (2006), Yven *et al.* (2006)

In vivo digestion

Whey-based Soft cheese $CaCO_3$

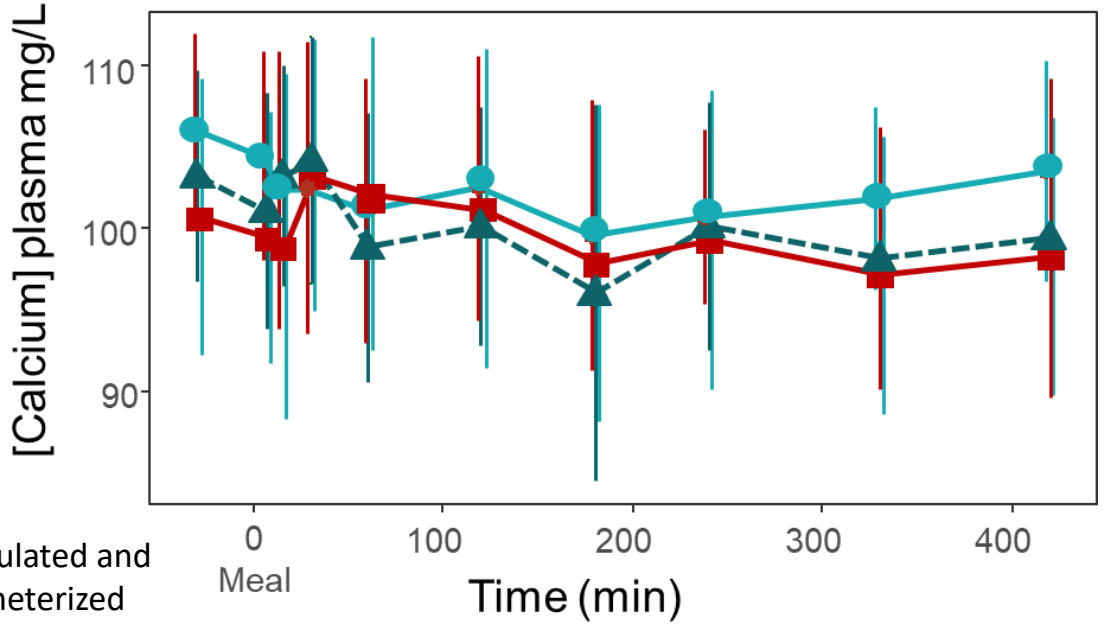
Mozzarella Milk Calcium

Whey-based Soft cheese CaP

Iso-calcium : 0,7%
Isocaloric ≈
280 kcal /100g

Test meals

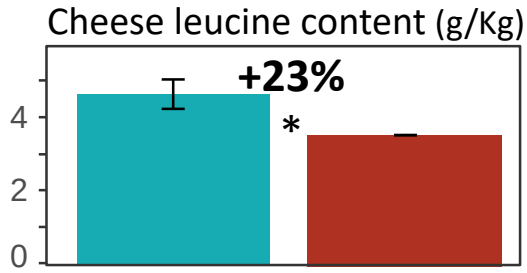
Blood samples
from 30 min before to 7h after meal ingestion

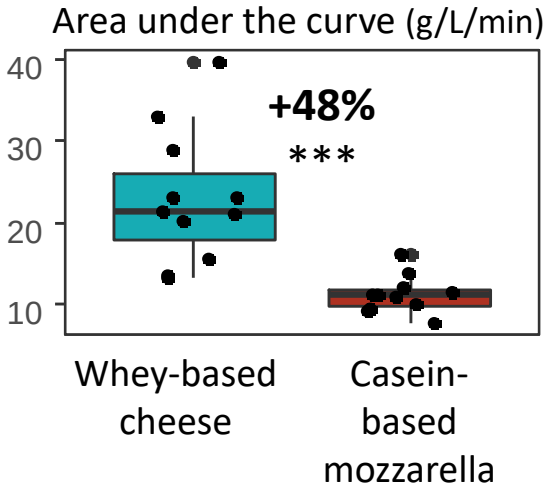


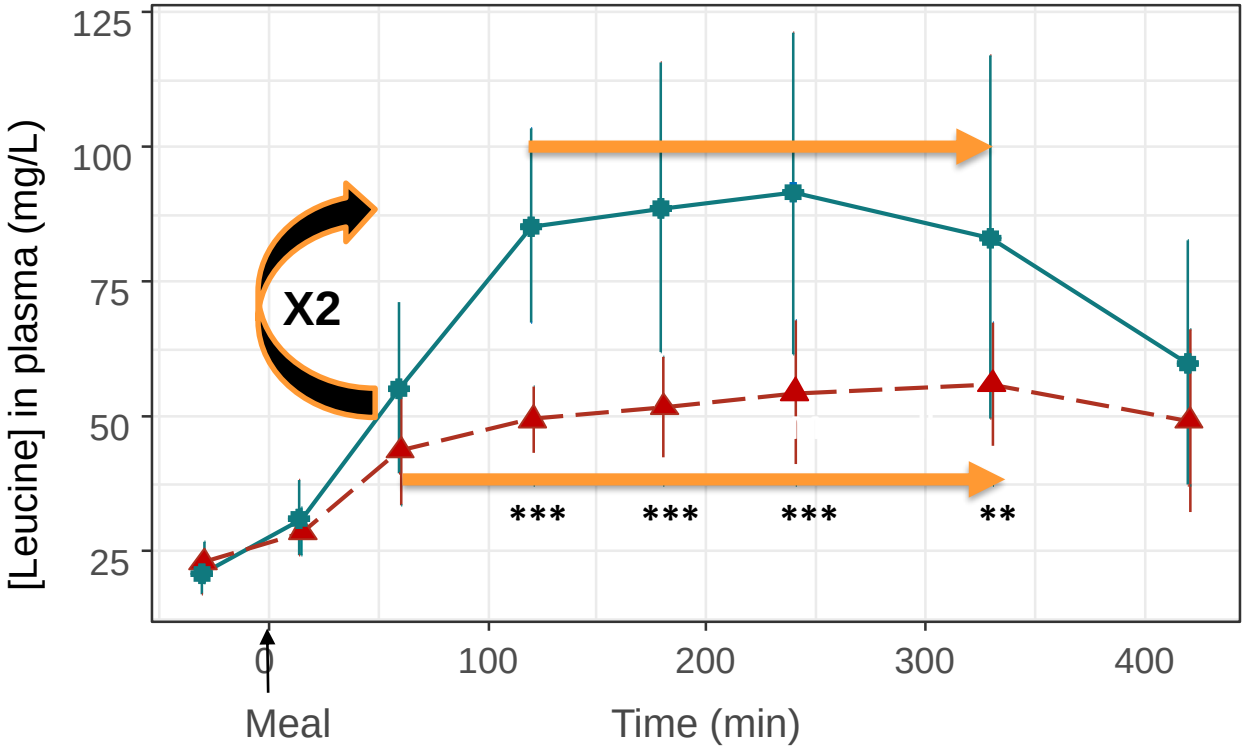
6 canulated and catheterized pigs

[Calcium] in plasma is highly stable
Both calcium sources allow to provide bioavailable calcium
Needs long-term studies for possible consequences on bone health

Plasma concentration of Leucine



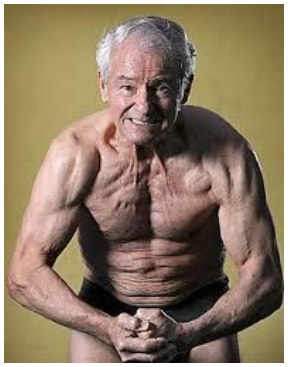


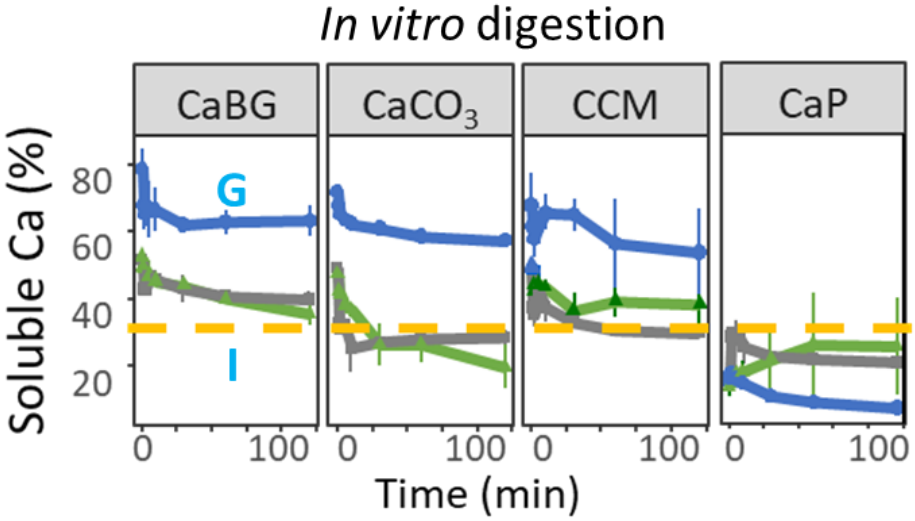


Leucine in bloodstream

Whey-based cheese > Casein-based Mozzarella

Conclusion & perspectives





No differences in blood [Ca] were seen during the *in vivo* study on pigs

Whey-based cheeses allowed to increase the [Leu] in plasma

The differences between casein and whey-based cheeses could be due differences in kinetics of digestion. This could result in the selective sequestration of some AA by the splanchnic area ? Or be due to oxidation of some AA before and after absorption???

In the future, we would like to determine:

if other sources of calcium can increase its bioavailability

how the hardness and humidity of the bolus will affect digestion in elderly

if the whey-based cheeses really allow to restore muscle synthesis in elderly

EAT4AGE

The Bioactivity & Nutrition Team

20-25 people, 14 permanent staff

8 INRAE

6 L'INSTITUT agro Rennes Angers

2015-2021 : 12 PhD, 7 post-docs, 5 international visiting scientists

Head

Didier DUPONT – *DR*

Scientists

Françoise NAU – *PR*
Amélie DEGLAIRE – *MC*
Juliane FLOURY – *MC*
Catherine GUERIN – *MC*
Frédérique PEDRONO – *MC*
Steven LE FEUNTEUN – *CR*
Martine MORZEL – *CR*

PhDs

Elise CHARTON *(2019-2022)*
Lucile CHAUVET *(2020-2023)*
Ousmane SUWAREH *(2019-2022)*
Jiajun FENG *(2020-2023)*
Rozenn LE FOLL *(2020-2023)*

Post-docs

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Stefano NEBBIA *(2020-2022)*
Imen JEBALIA *(2021-2023)*

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Gwénaële HENRY – *AI*
Julien JARDIN – *IE*
Olivia MENARD – *IE*
Jordane OSSEMOND – *IE*
Marie-Françoise COCHET – *IE*

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

International Network

Dr. Didier DUPONT, Senior Scientist, INRAE, France

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Industry involvement

☞ ~ 60 private companies are following INFOGEST

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Alan Mackie - UK

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In vitro models of digestion WG1

Isidra Recio

Food interaction – meal digestion WG2

Pasquale Ferranti

Absorption models WG3

Linda Giblin

Digestive lipases and lipid digestion WG4

Myriam Grundy

Digestive amylases and starch digestion WG5

Nadja Siegert

In silico models of digestion WG6

Choi-Hong Lai

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International Conference
Porto, Portugal
2024

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8th International Conference on Food Digestion

in Porto, Portugal, April 2024