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How does the structure of dairy products affect their digestion mechanisms? Consequences on human health

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How does the structure of dairy products affect their digestion mechanisms?

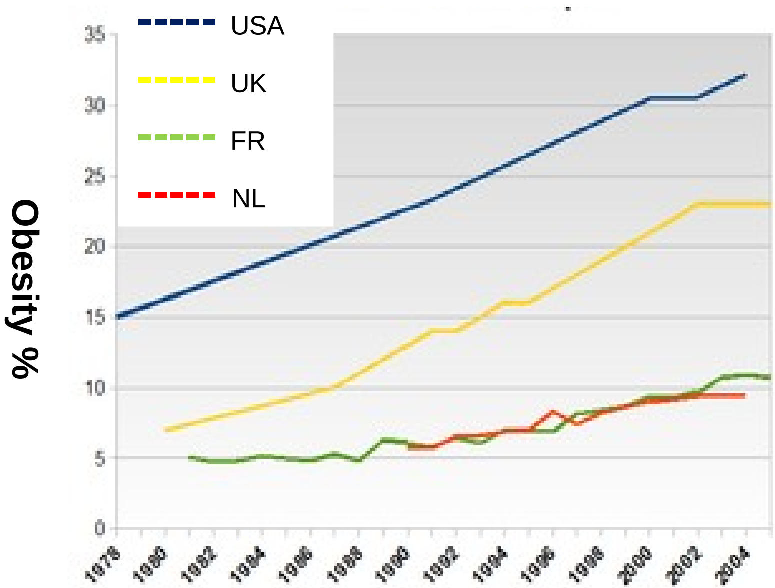
Consequences on human health

Dupont D

INRA Agrocampus Ouest – Milk and Egg Science & Technology
Rennes FRANCE

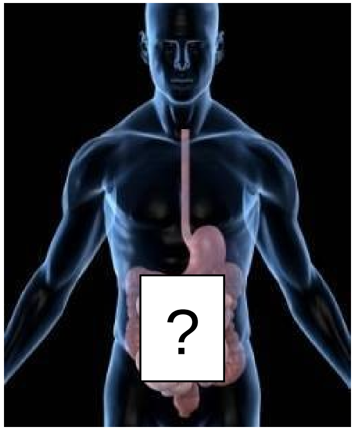
HEALTH PROMOTION AND DISEASE PREVENTION OF FUNCTIONAL FOODS, NUTRACEUTCALS, AND NATURAL HEALTH PRODUCTS
TÜBİTAK TÜSSİDE, Gebze/Kocaeli, Turkey

Scientific Context



Diet-related diseases ↑

□ Prevent these pathologies rather than cure them

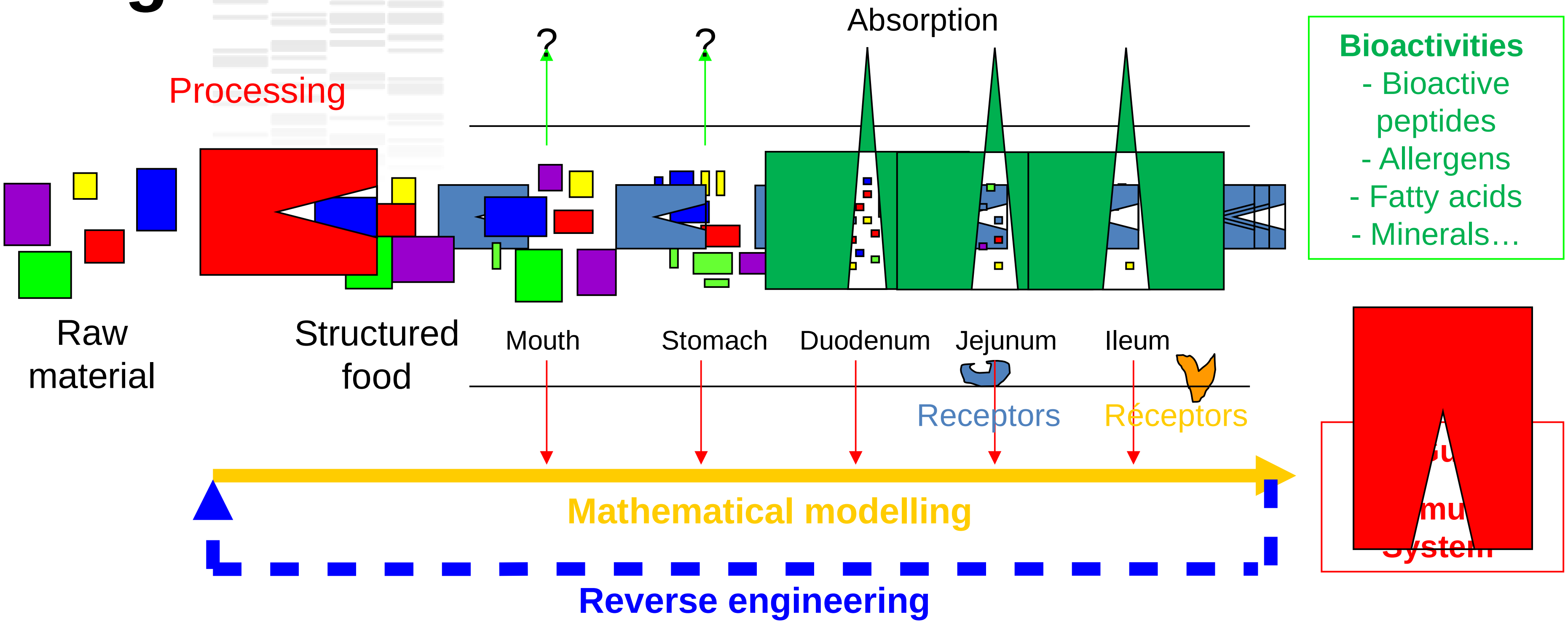


Gut = interface between food and human body
Digestion releases food components that can have a beneficial or a deleterious effect on human health

… 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

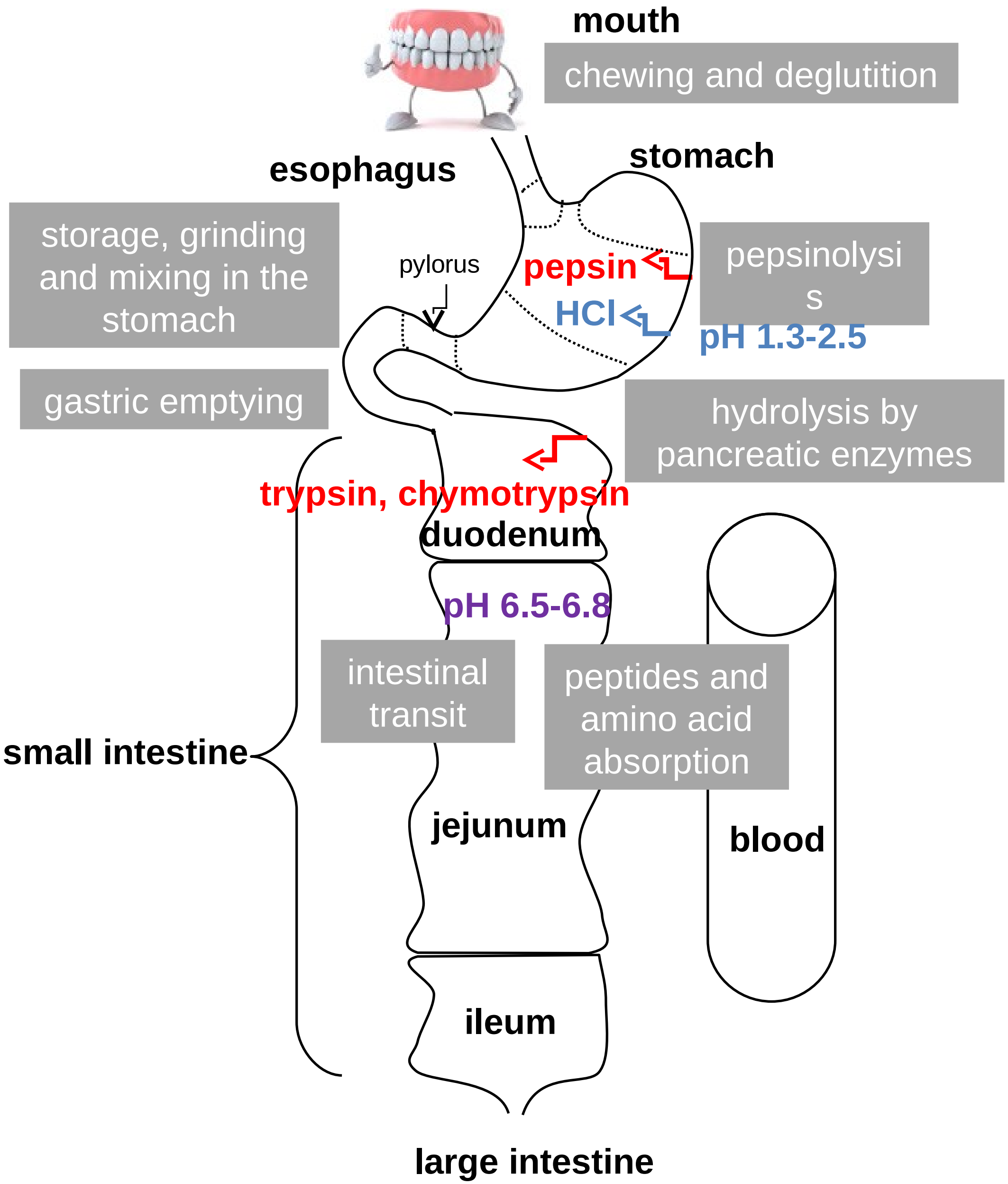
By increasing our knowledge on food digestion, we will increase our knowledge on the effect of food on human health

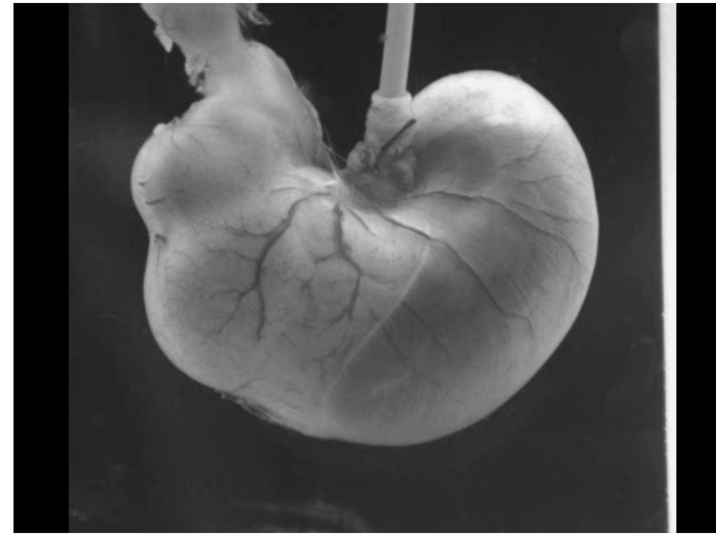
Our goals

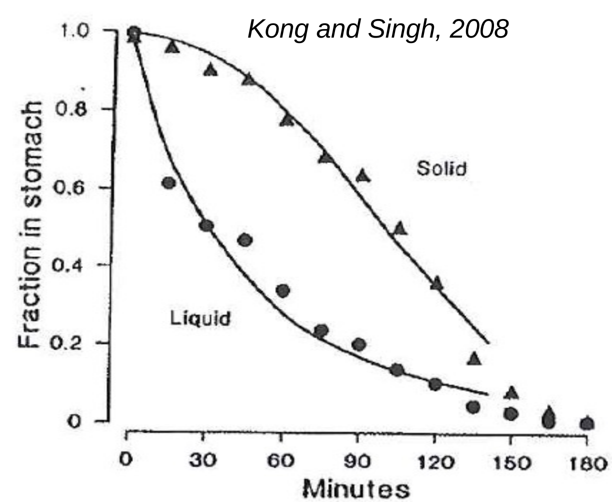


- To understand the mechanisms of breakdown of food matrices and their constituents in the gut and identify the beneficial/deleterious food components released during digestion
- To determine the impact of the structure of food matrices on these mechanisms
- To model these phenomena in order to develop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

The digestive process

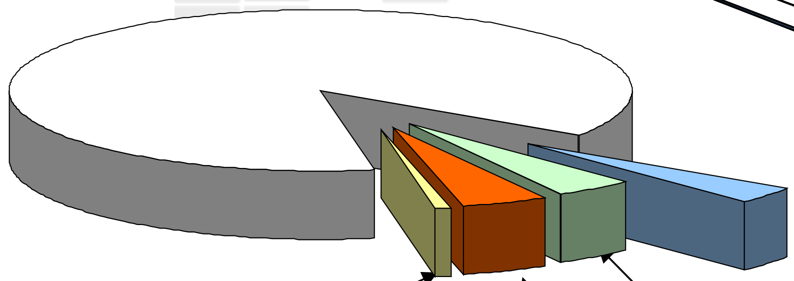






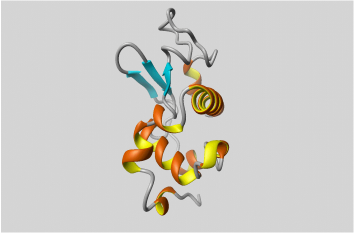
→ Gastric phase = key step for the whole digestion process

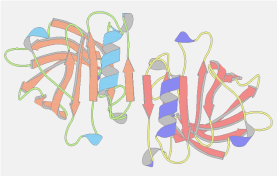
Milk



Caseins (80%) αs1, αs2, β, κ

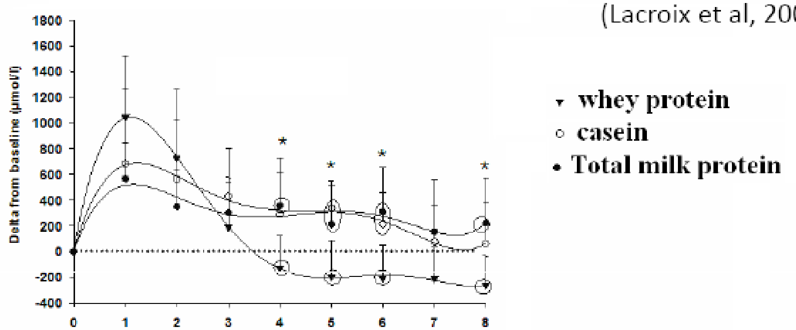
Whey Proteins (20%) α-la, β-lg





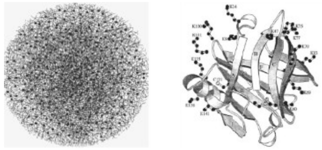
Caseins and whey proteins are:

- Structurally opposite (globular/flexible)
- Differently metabolized (fast/ slow proteins)
- Highly digestible (>95%)
- Excellent sources of essential amino acids
- Milk can be transformed into several dairy products (liquids, gels, solids) of similar composition but different structure



(Lacroix et al, 2006)

Does the food matrix regulate protein digestion and aa bioavailability?



milk proteins
(caseins, β-lactoglobulin)
↓
peptides
↓
amino acids

Understanding and modeling milk proteins digestion in the gastrointestinal tract of mini-pigs in relation with the dairy matrix ingested

How does the milk product structure influence:

1) Transit and proteolysis in the gastrointestinal tract ?
2) Appearance of (bioactive) peptides in the lumen?
3) Release of amino acids in the blood compartment ?

Experimental strategy

dynamic modeling of milk proteins transit and absorption (+ hydrolysis)

6 dairy matrices manufacturing

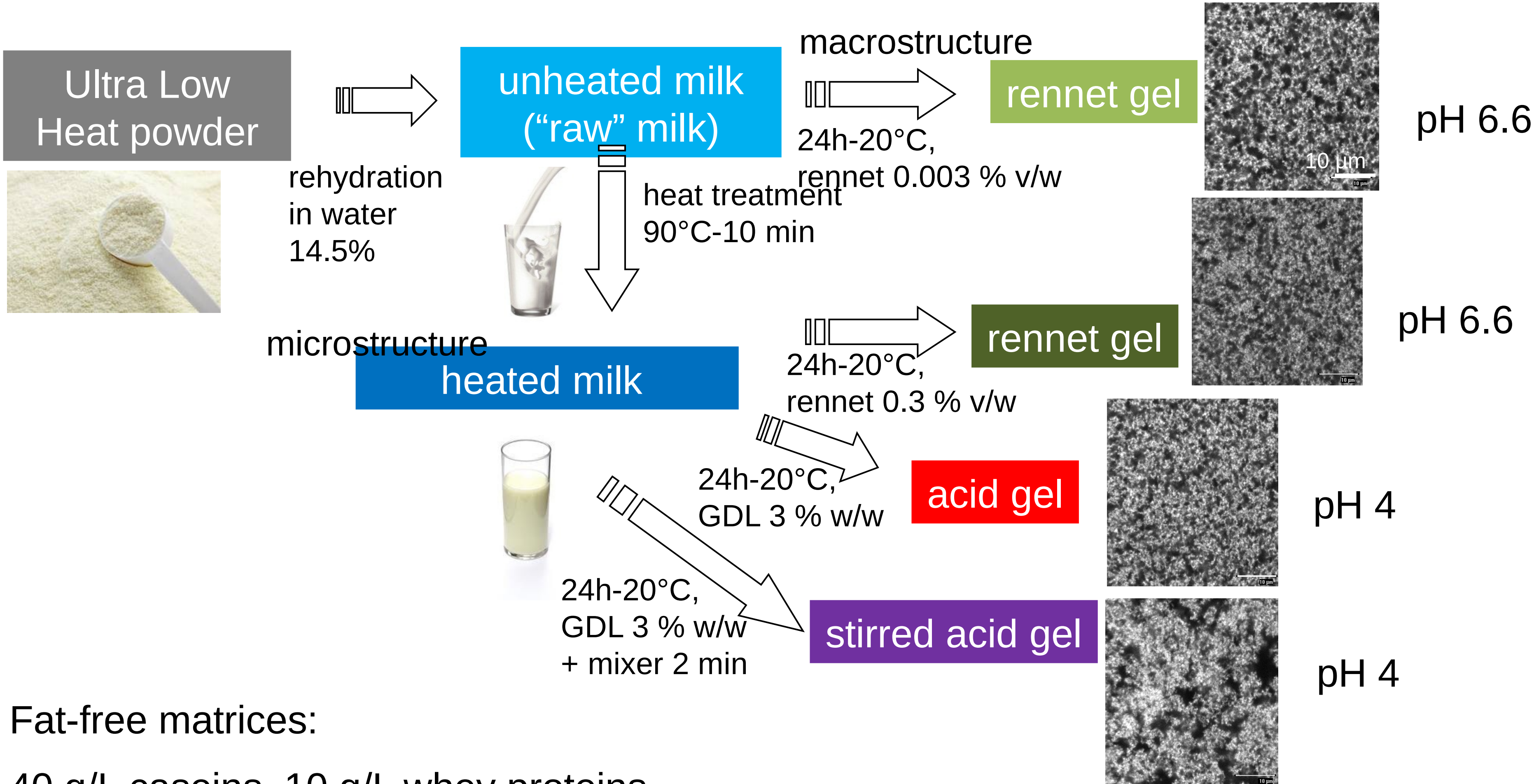
in vivo digestion by 6 mini-pigs

protein digestion products (end of stomach and jejunum)
+ amino acids (plasma)

effect of the structure of the dairy matrix on the kinetics of milk proteins digestion (gastric emptying, hydrolysis and absorption)

INRA
SCIENCE & IMPACT

The food matrices

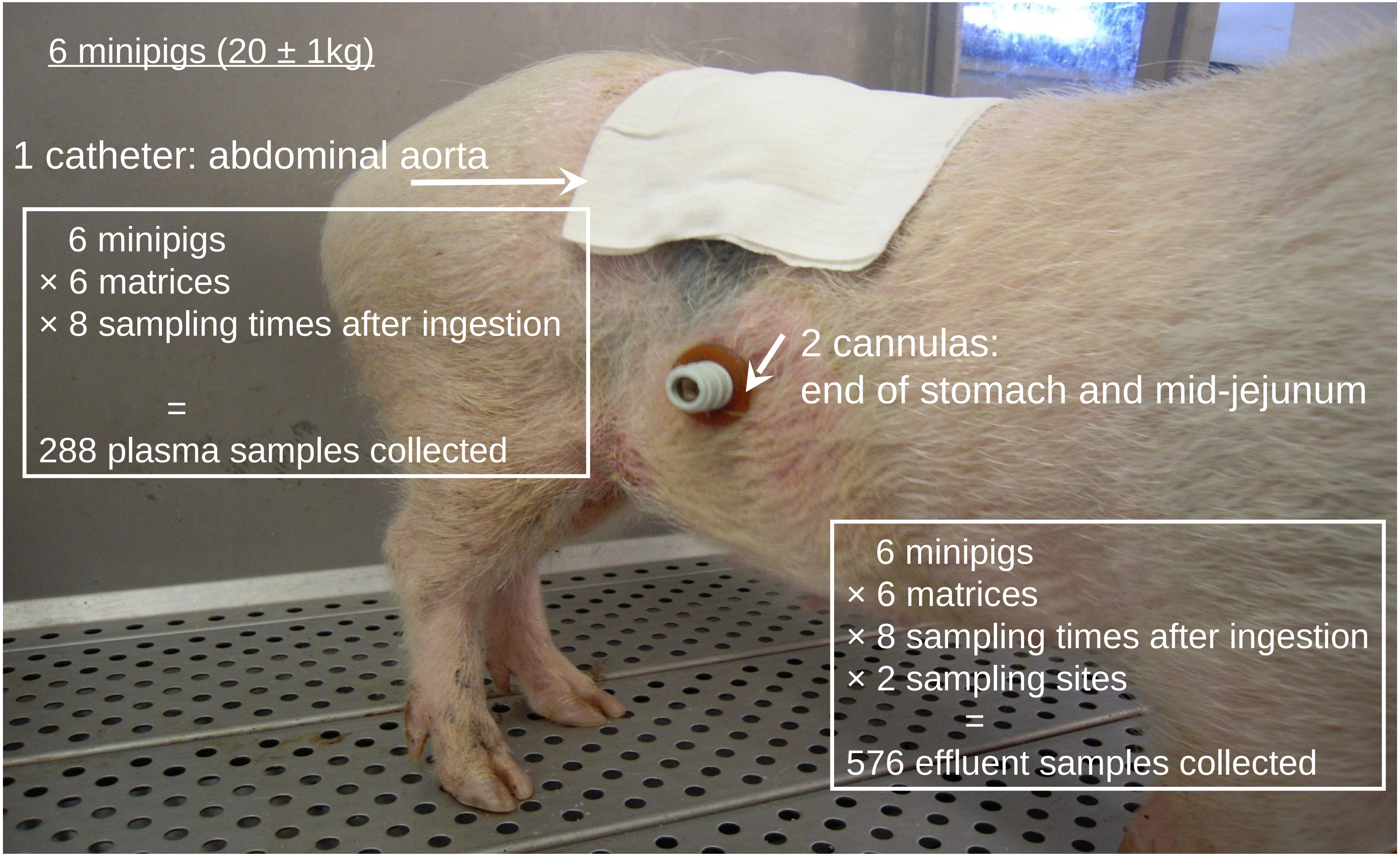


Fat-free matrices:

40 g/L caseins, 10 g/L whey proteins,
95 g/L lactose and minerals

+ marker of the meal transit (Cr2+-EDTA) □ Mean Retention Time in the stomach

The multi-canulated mini-pigs



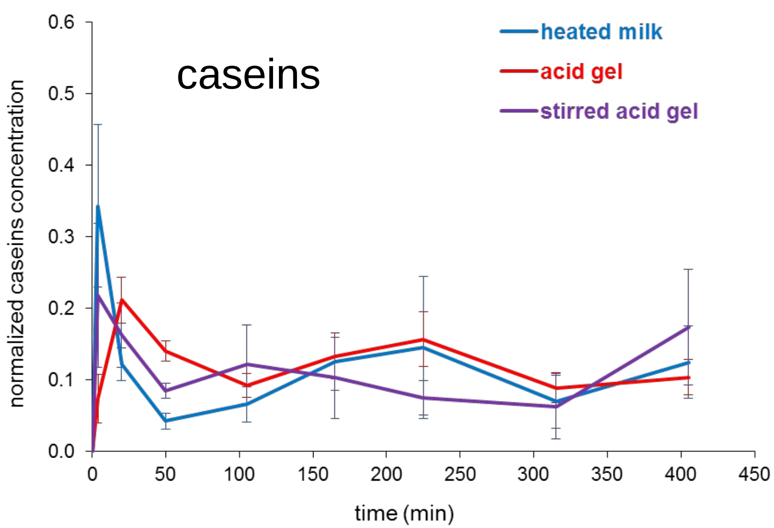
The liquid-gel transition

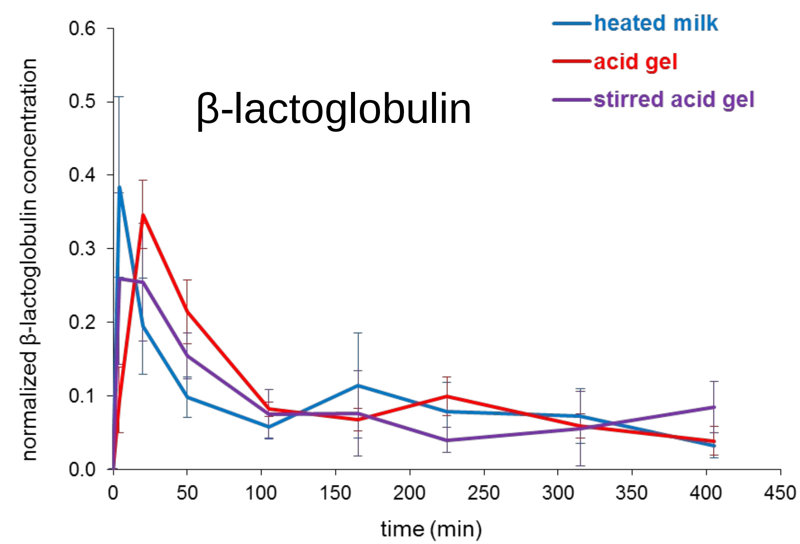
heated milk → acid gel → stirred acid gel

acid gelation stirring

1) effect on transit

Mean Retention Time in the stomach (min)	96.9 ± 14.3	→ acid gelation	148.0 ± 8.9	→ stirring	124.0 ± 14.2



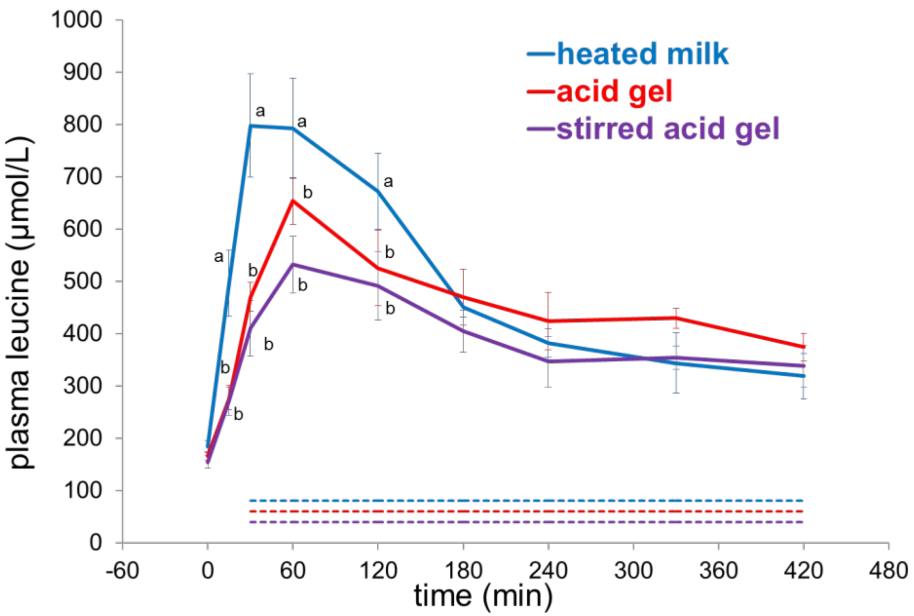


intermediate structure (stirring) □ similar digestion kinetics liquid milk/stirred acid gel

Barbé et al, Food Chem. 2013, 2014; Le Feunteun et al. 2013

The liquid-gel transition

2) effect on absorption



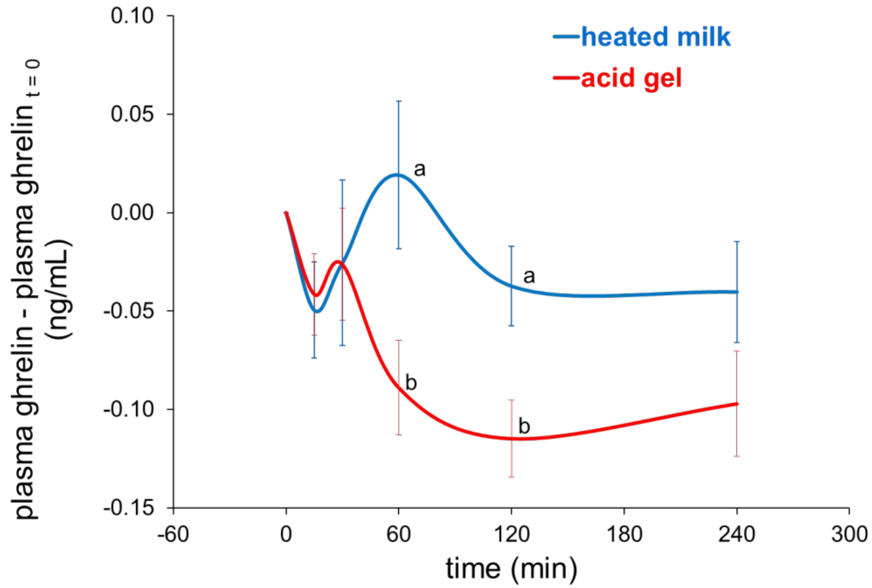
milk gelation:

□ 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 ?

any bioactive peptides are released in the gut during digestion

More than 16000 peptides identified in the lumen

Barbé et al. 2014 Food Res Int

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–lg	32-40	HYP	Pihlanto-Leppala et al. (2000)							
β–lg	92-100	MIC	Pellegrini et al. (2001)							
β–lg	142-148	HYP	Mullally et al. (1997)							

Impact of skim milk powder processing on casein digestion by an *in vitro* infant model

Hoarau B, Boutrou R, Jardin J, Molle D, Tanguy G, Gaucheron F, Schuck P, Léonil J, Haab B* & Dupont D

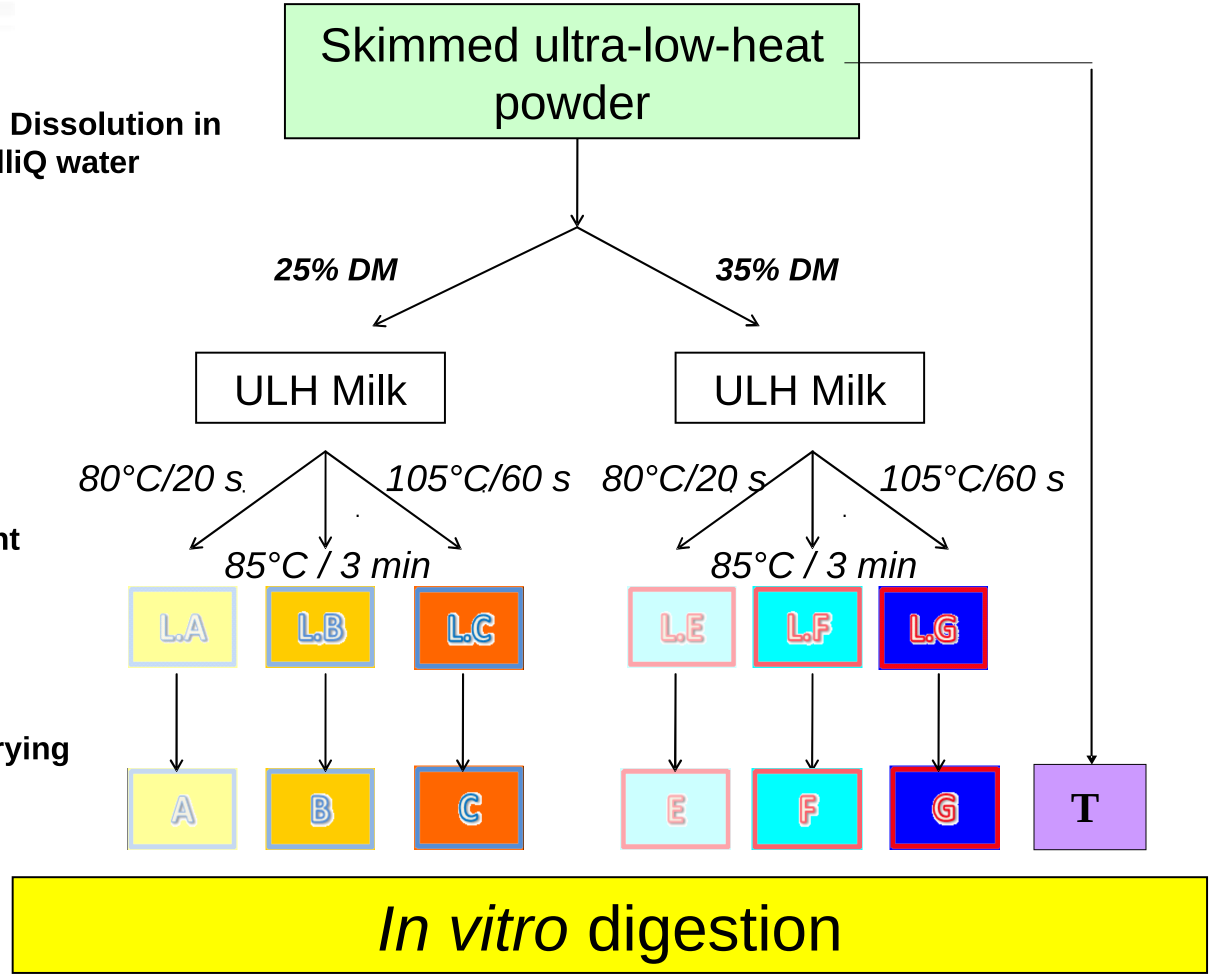
INRA – Agrocampus Ouest, UMR STLO, 65 rue de St Brieuc 35042 Rennes France
* VAN ANDEL Institute, 333 Bostwick NE, Grand Rapids, MI 49503, USA

Objective: Determine if heat treatment affects casein digestion

Step 1 : Dissolution in milliQ water

Step 2 : Heat treatment

Step 3 : Spray drying



Infant gut Model

Milk powders

Gastric phase

60 min
pH 3.0
+ pepsin
+ PC

Aliquots taken after 0, 1, 2, 5, 10, 20, 40 and 60 min digestion

Duodenal phase

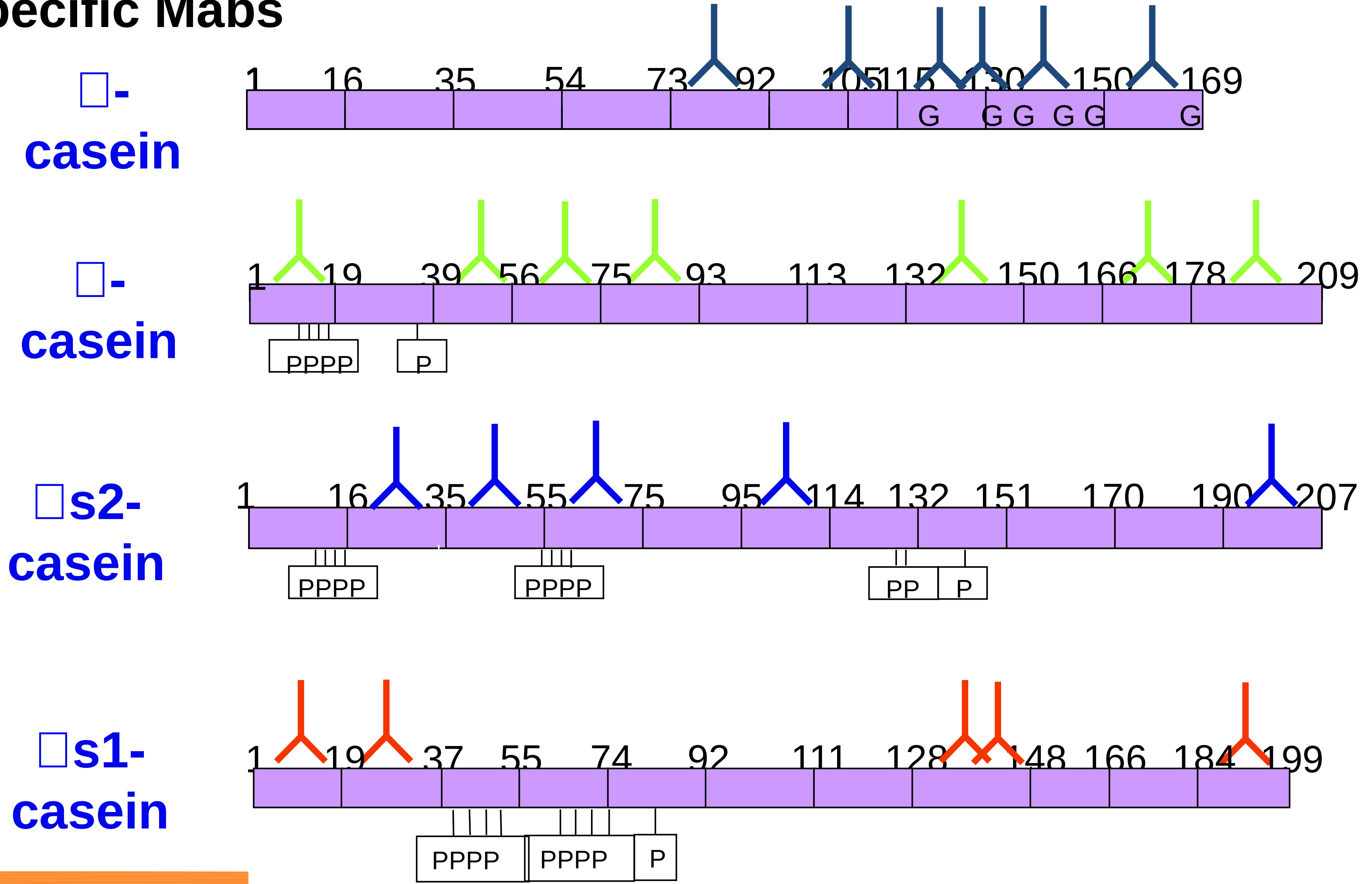
30 min
pH 6.5
+ trypsin
+ chymotrypsin
+ bile salts

Aliquots taken after 0, 1, 2, 5, 10, 15 and 30 min digestion

Dupont et al. 2010 Mol Nutr Food Res

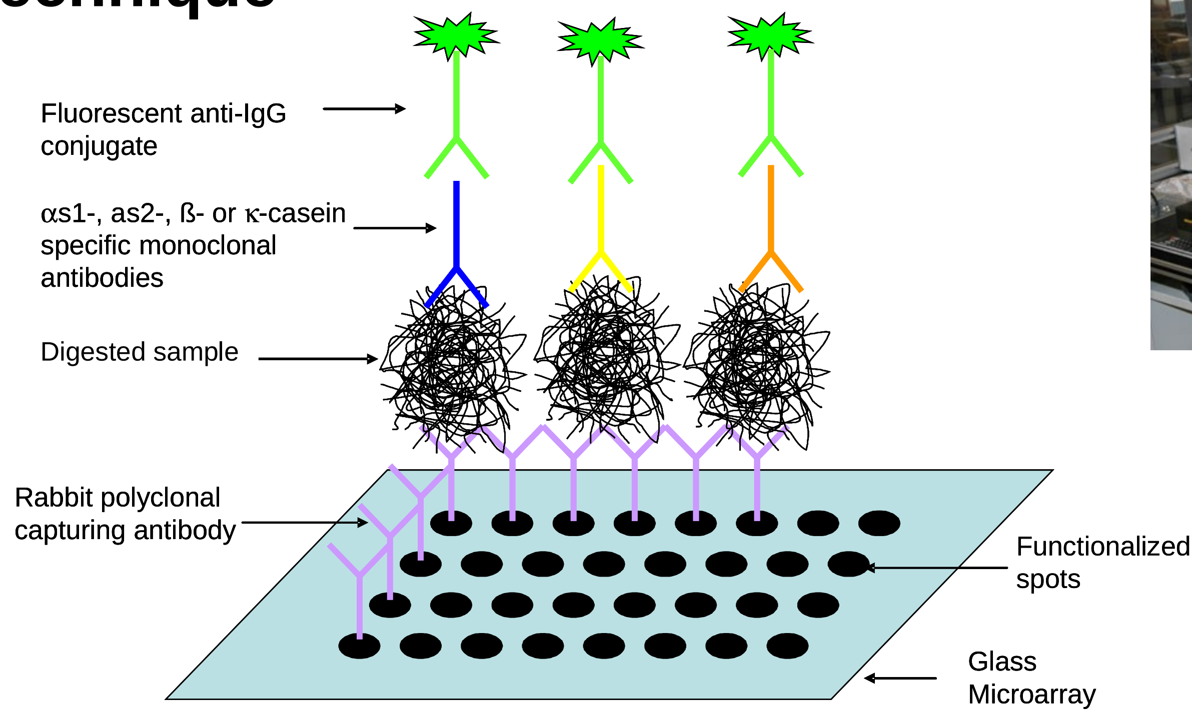
Biochemical characterisation

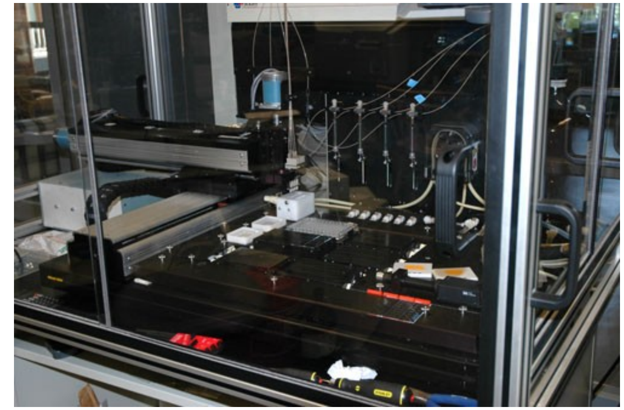
Identification of epitopes resistant to digestion using specific Mabs



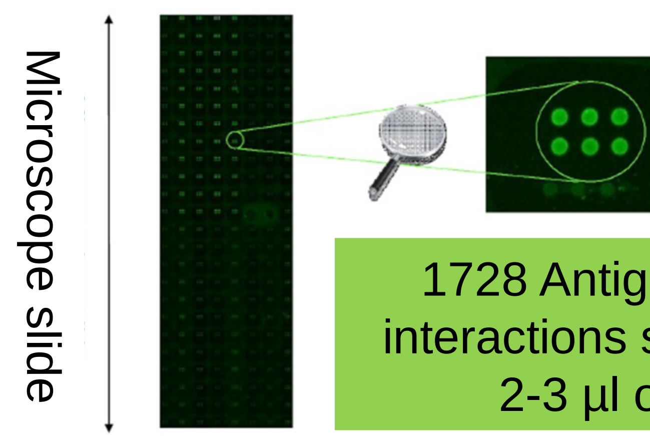
Johansson et al. 2009 Mol Immunol

Principle of the technique





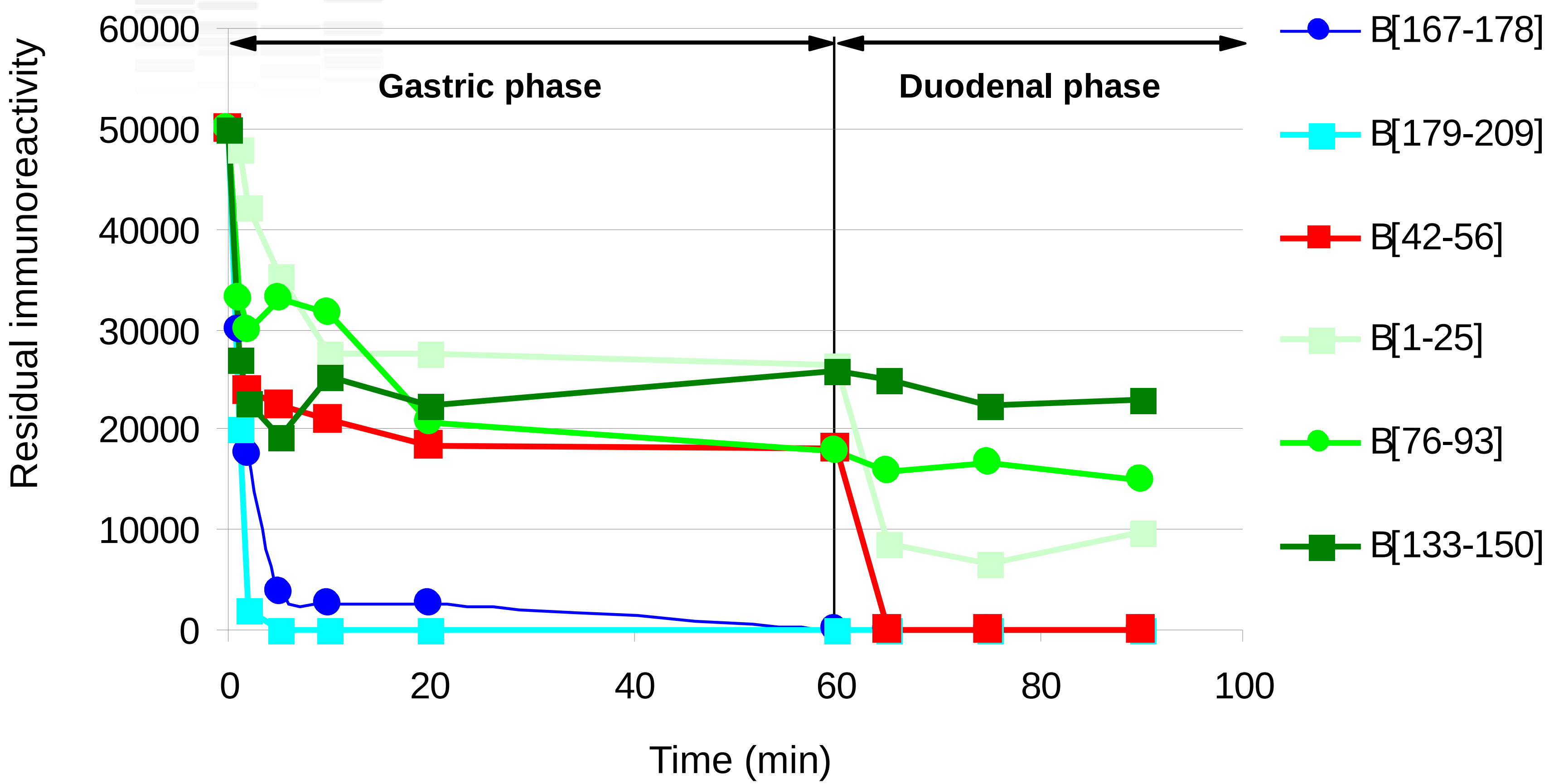
Dupont et al. 2010 Food Dig



Van Andel Inst.

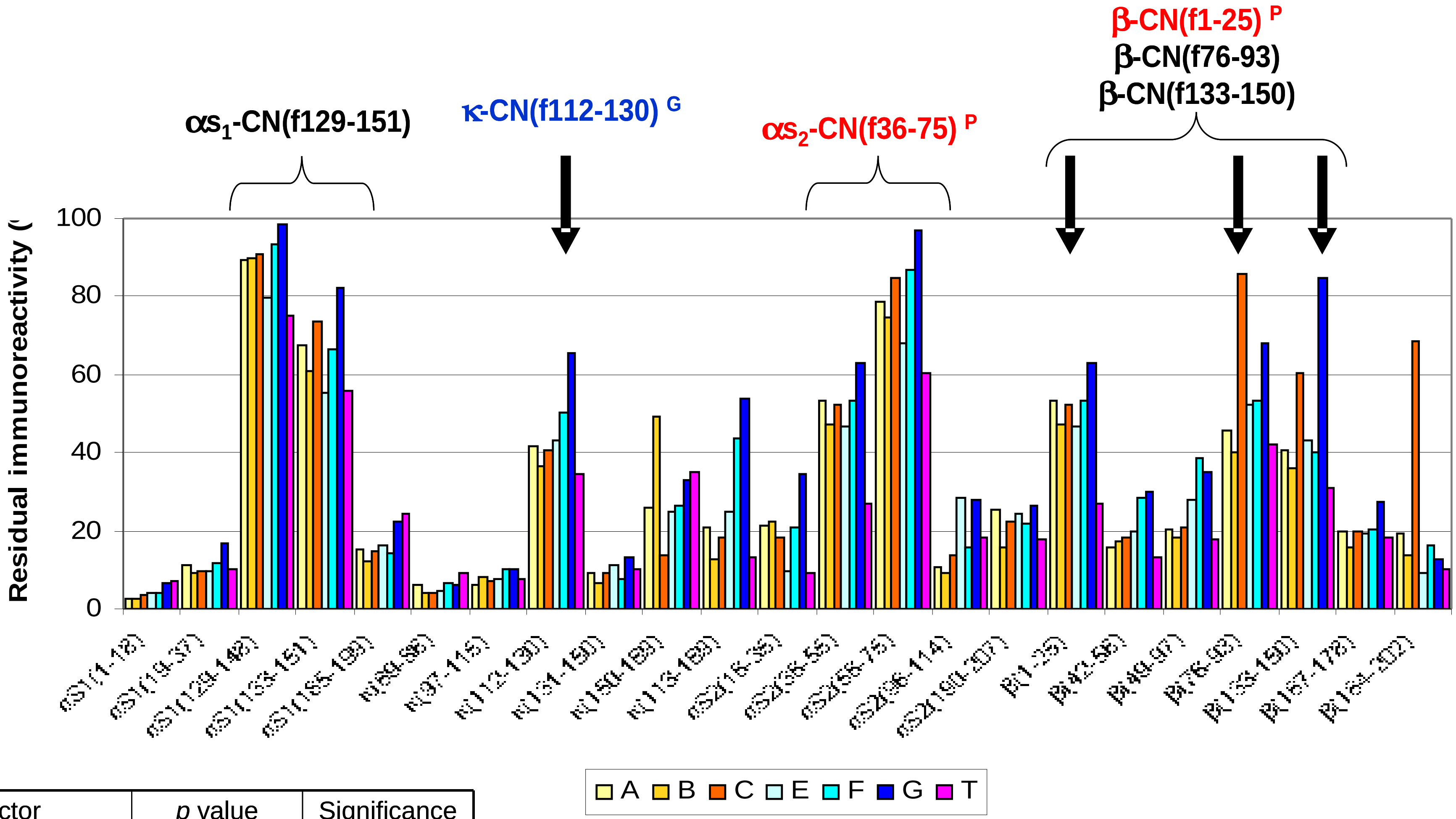
1728 Antigen-Antibody interactions simultaneously
2-3 µl of sample

Kinetics of β-casein digestion



□ Kinetics of □-casein digestion differ according to the area studied

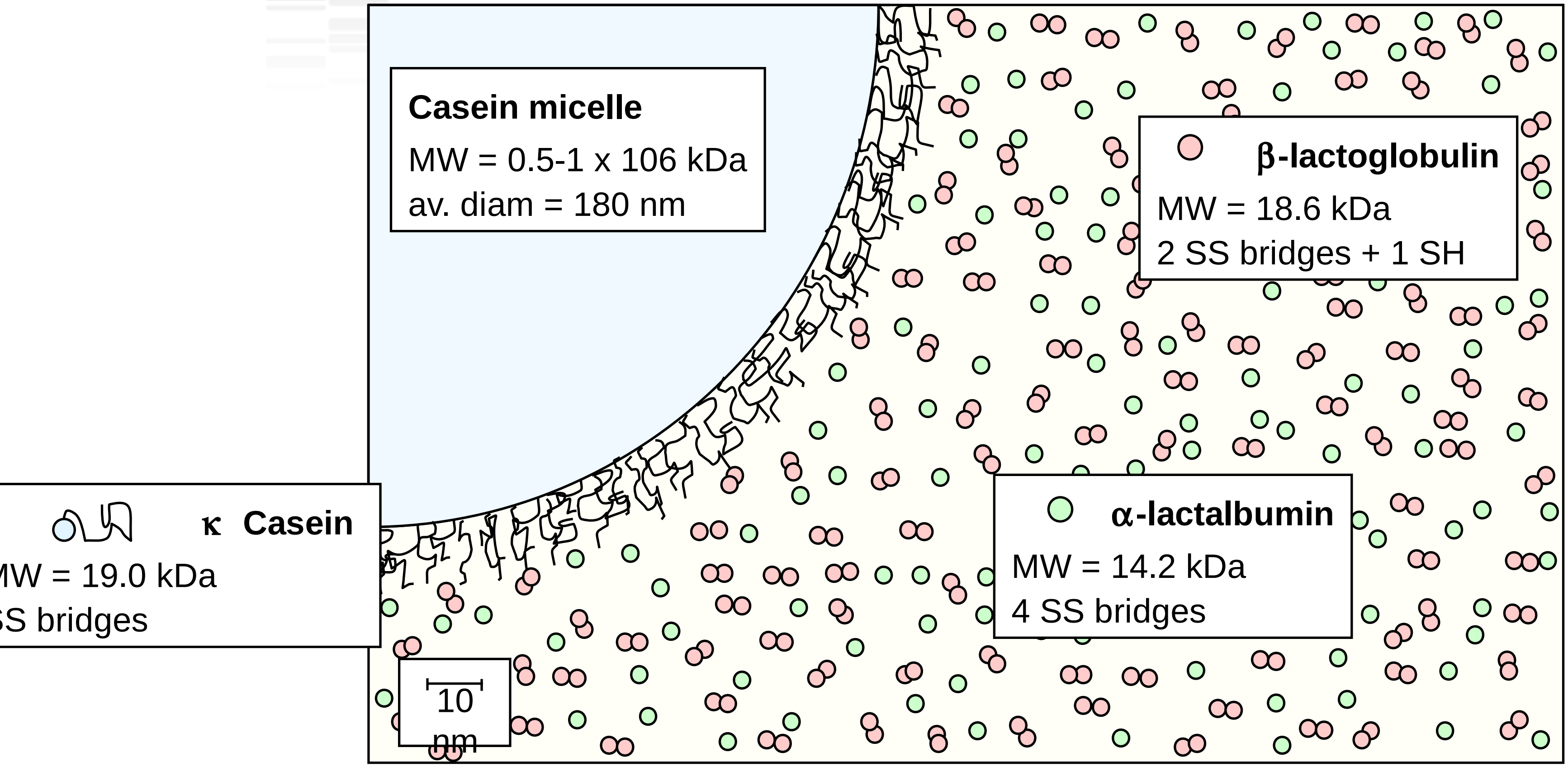
esidual immunoreactivity of casein fragments



Factor	*p* value	Significance
T	0.00001	***
% DM	0.00555	**
T:%DM	0.03262	*

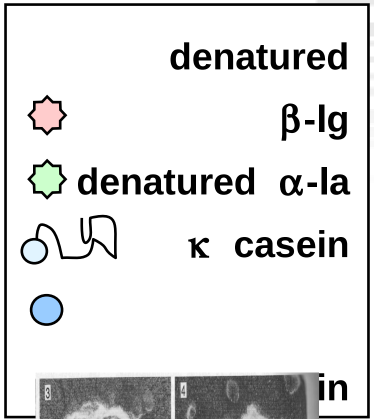
Increasing the heat-treatment makes casein more resistant to digestion

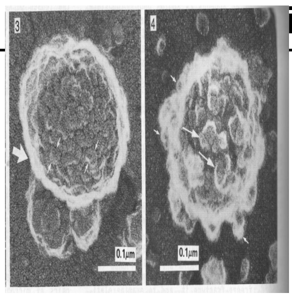
Thermal aggregation of whey proteins on the casein micelle



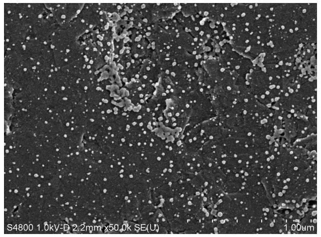
To scale schematic representation of the major whey proteins and of the casein micelle in unheated milk

Thermal aggregation of whey proteins on the casein micelle

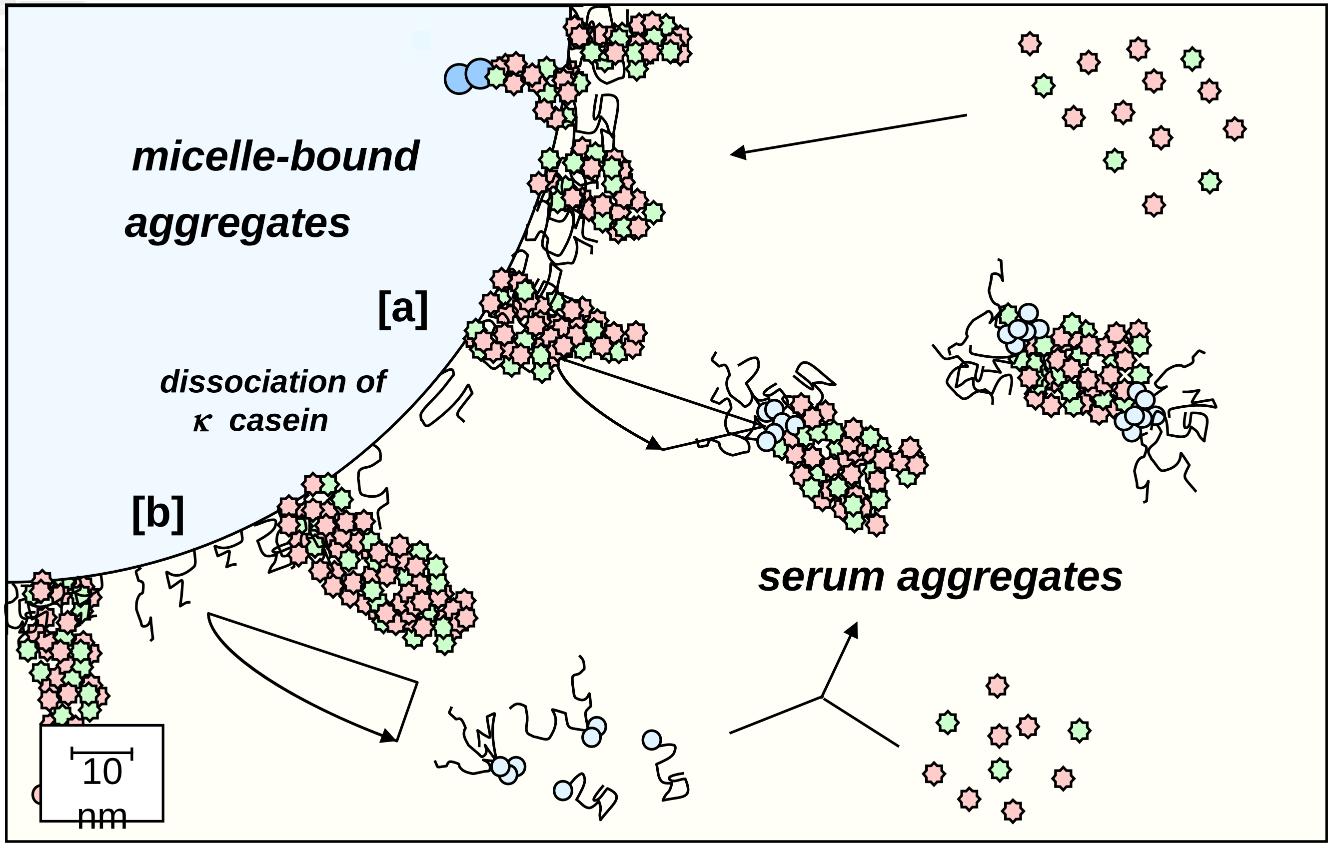




a (Harwalkar et al., 1989)

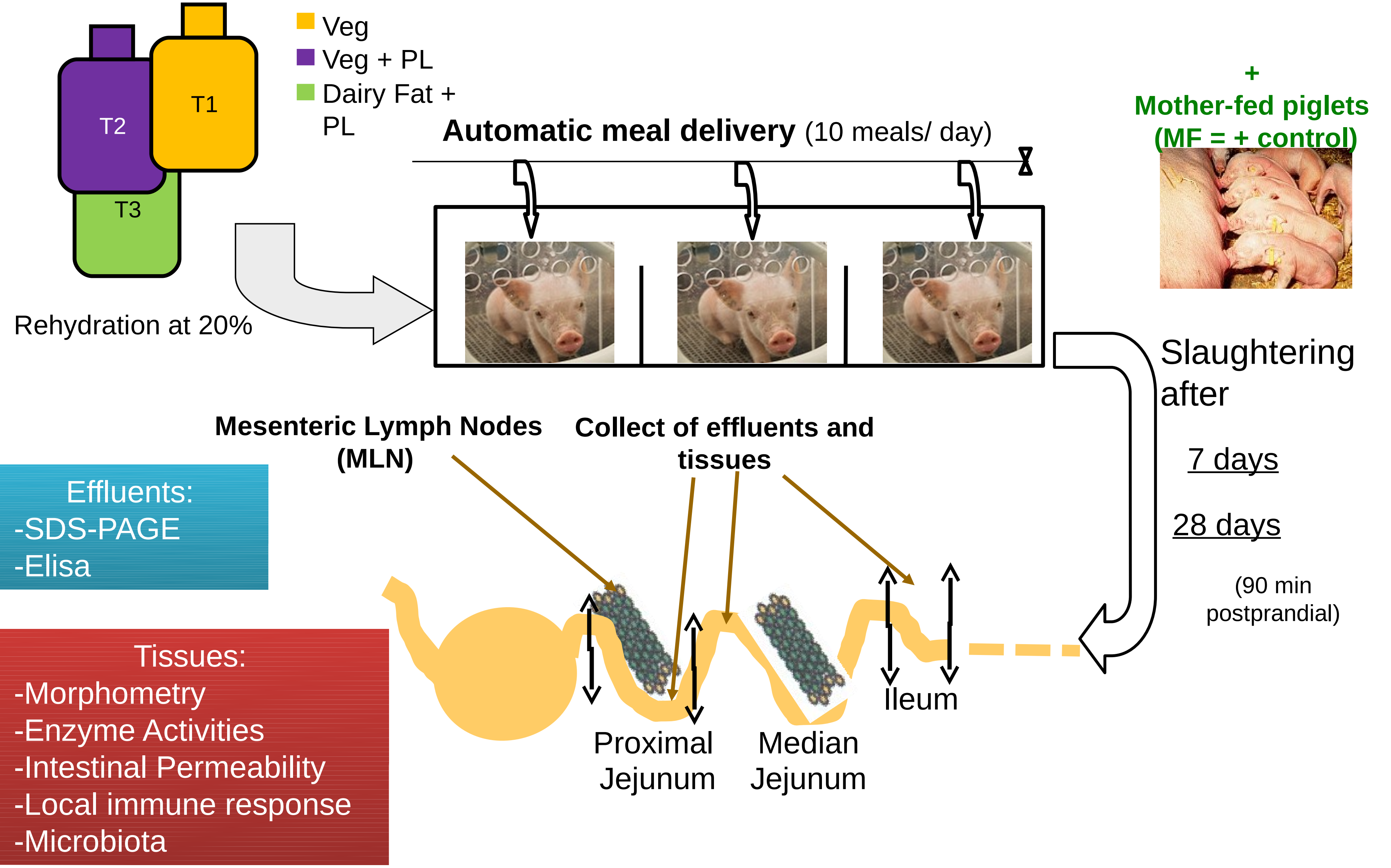


b (Rodriguez del Angel & Dalgleish, 2006)



Micelle-bound and serum aggregates are formed, containing denatured whey proteins, κ casein and possible traces of αs2 casein. [a] and [b] indicate the 2 possible ways for the formation of the serum aggregates.

Can IF of different composition modulate the physiological response of the host?

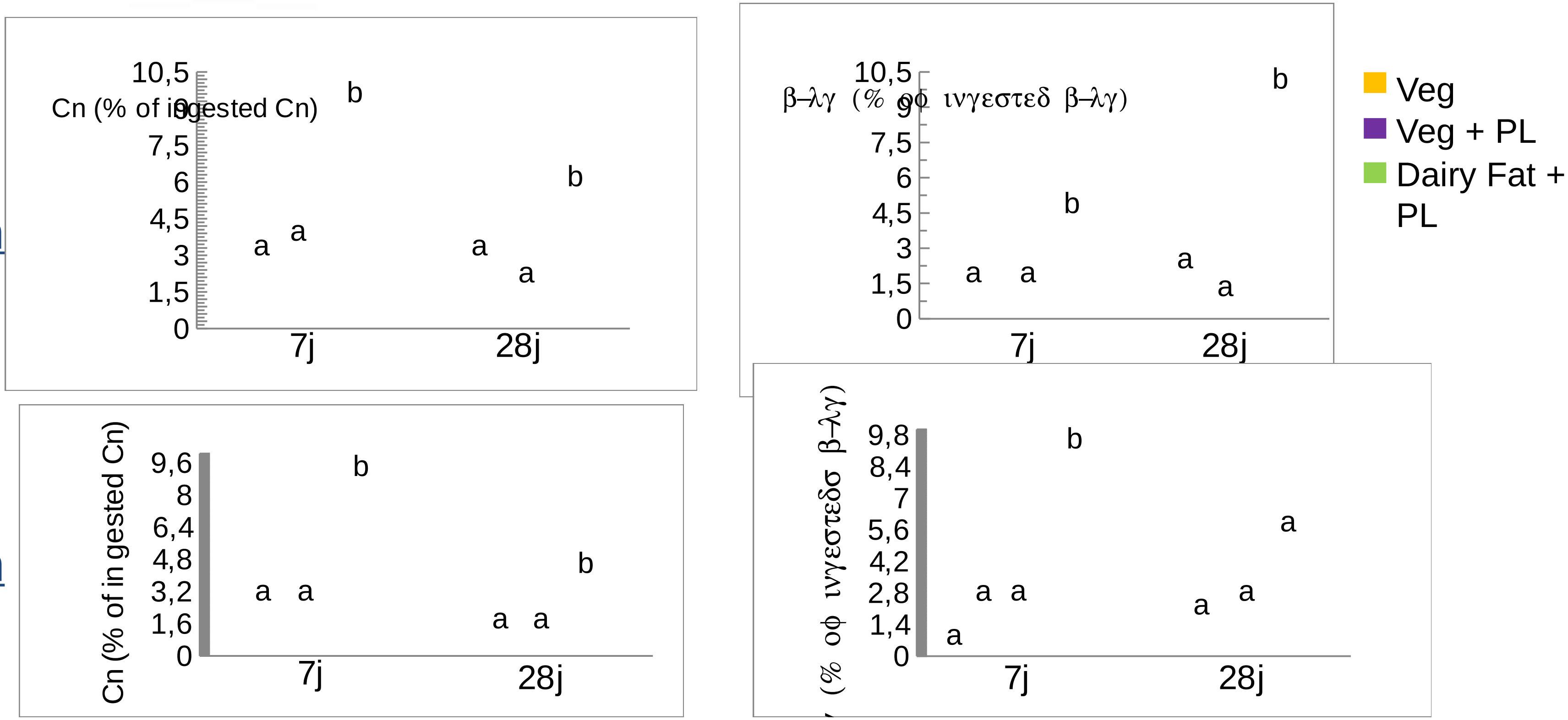


Protein Digestion

Casein | **β-lactoglobulin**

Jejunum

Ileum

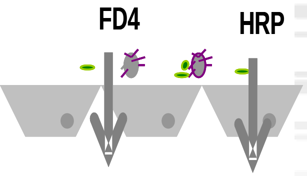


Milk Proteins better resist to intestinal digestion in the presence of dairy fat

 Modification of the interface

(Granger *et al* 2005; Davies *et al*, 2001)

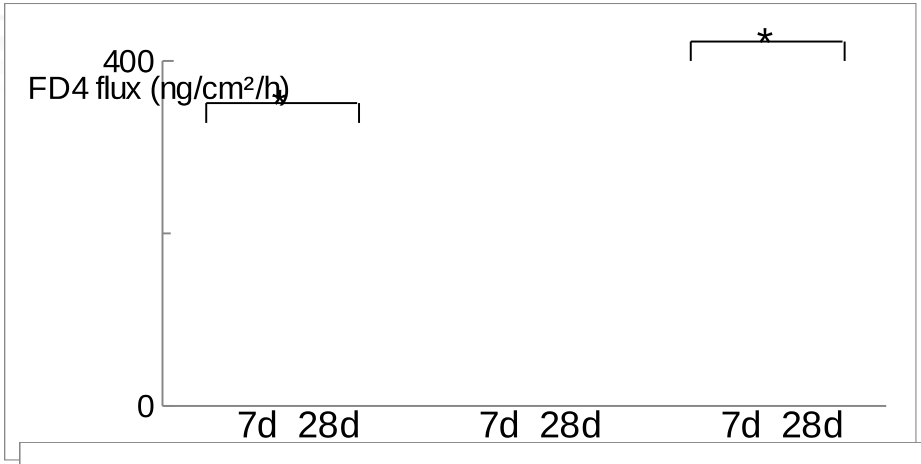
Paracellular Permeability



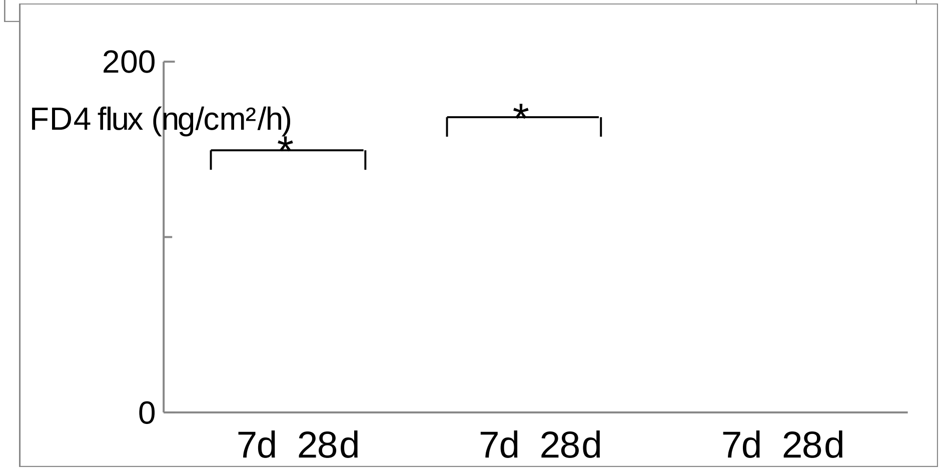
FD4 = FITC-Dextran (4kDa)

Veg
Veg + PL
Dairy Fat + PL

Jejunum



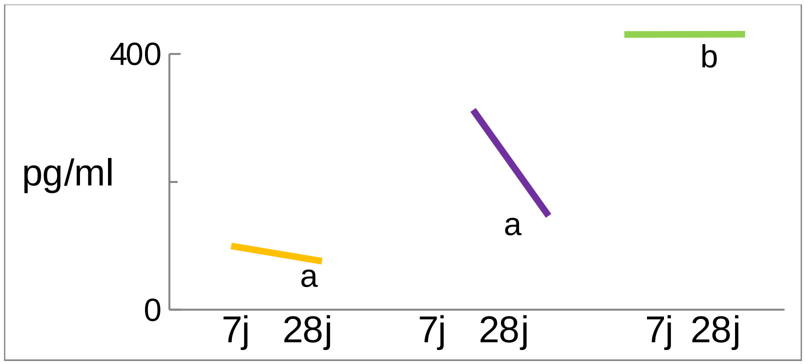
Ileum

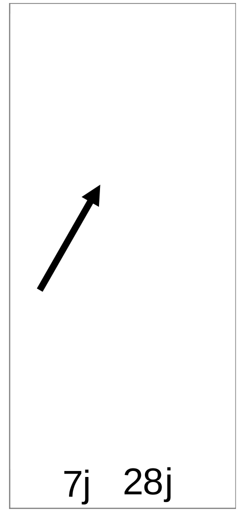


Limited effect of the infant formula structure/composition on paracellular permeability

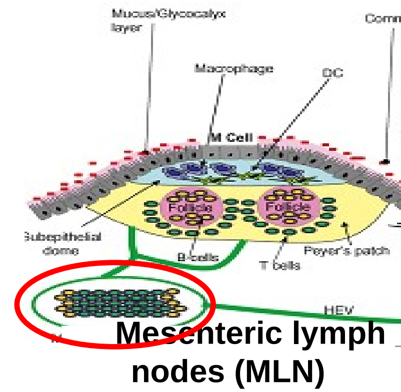
Secretory activity of MLN

Interferon-γ (Th1 pro-inflammatory)

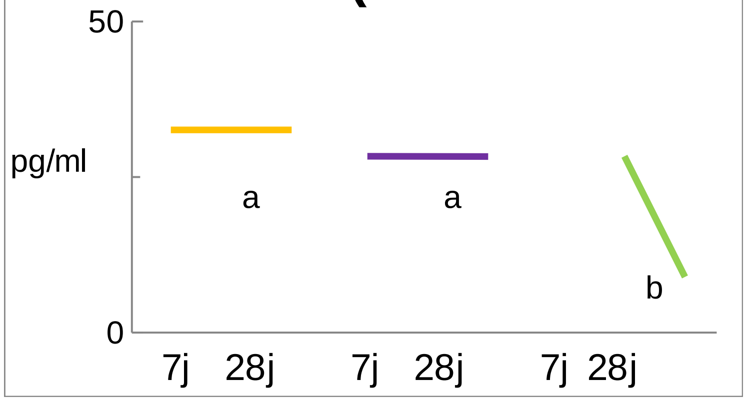


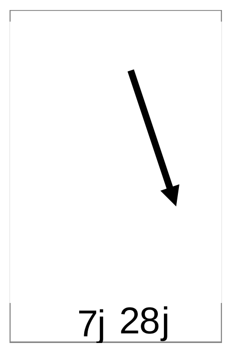


Veg
Veg + PL
Dairy Fat + PL
Porcelets SM

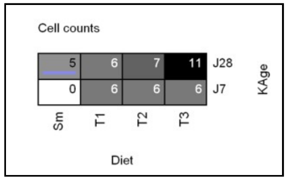


Interleukine-10 (Th2 anti-inflammatory)

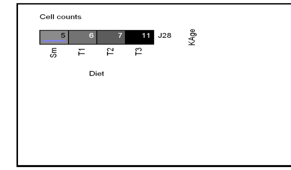




Milk lipids maturation of the piglet's immune system more similar than with sow's milk

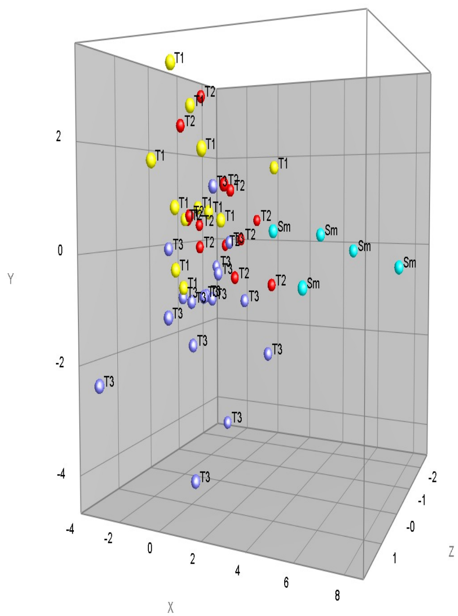


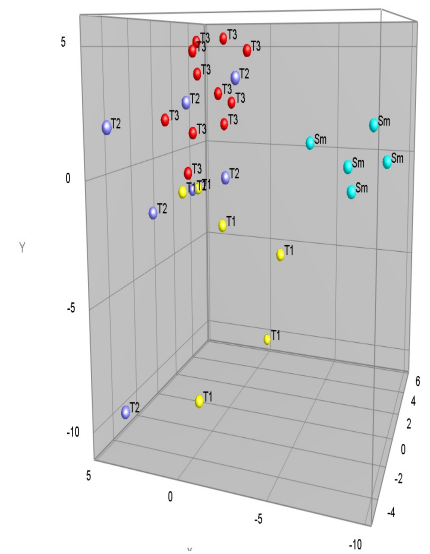
Microbiota by DHPLC

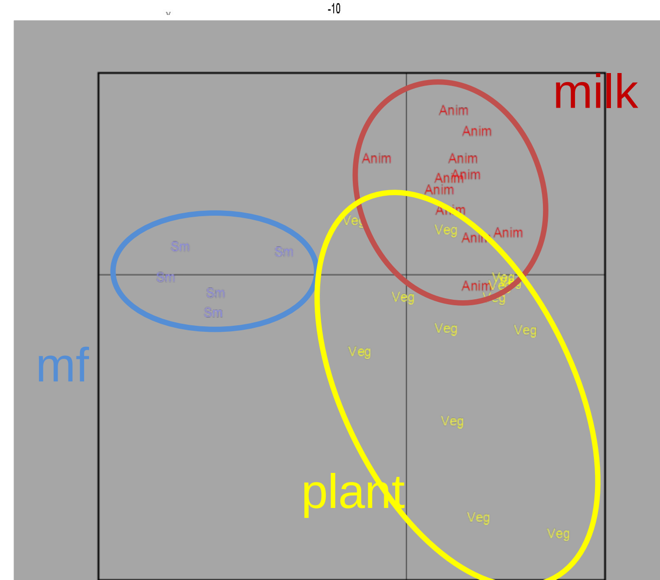


D7 & D28

D28







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

More Proteobacteria with milk fat / More Firmicutes with plant oil

BIOFORTIS
a Mérieux NutriSciences Company

Conclusion

The structure of dairy products, as modified by the processing conditions, regulates the kinetics of protein digestion and dietary amino acids bioavailability

For the neonate, substitution of vegetable oil by milk fat allows a better maturation of the immune system and a modification of the microbiota, but more work is needed to determine whether these modifications are transient or will remain with time

Understanding the disintegration of dairy products in the gastrointestinal tract is essential for designing new foods dedicated to specific sub-populations (elderly, athlete, infant, overweight people….)

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

COST Action FA1005

Dr. Didier DUPONT, Senior Scientist, INRA, France

INFOGEST

June 2011 – May 2015

320 scientists - 110 institutes – 34 countries

INFOGEST
International Conference
Naples, Italy
March 2015

We are pleased to announce the next

4th International Conference on Food Digestion

organized by the

COST Action FA1005 INFOGEST

in Naples, 17-19 March 2015