



# Combining selected immunomodulatory strains to develop an anti-inflammatory cheese

**Gwénaél JAN<sup>1,2</sup>**

<sup>1</sup>INRA, UMR 1253 Science et Technologie du Lait et de l'Œuf, Rennes

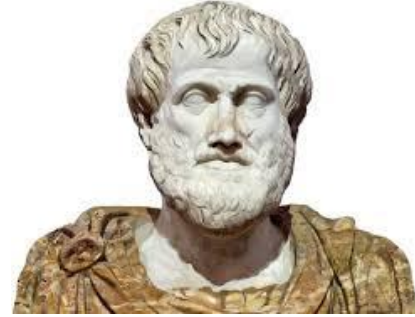
<sup>2</sup>Agrocampus Ouest, UMR 1253 Science et Technologie du Lait et de l'Œuf, Rennes





# Cheese, an old story ...

# Aristotle (384 BC –322 BC)



**Kykeon** (Gr. κυκεών, from κυκάω, "to stir, to mix"), an ancient greek made with **wine** and grated **cheese**.

A **magic** medicinal beverage



# Pliny the Elder (born Gaius Plinius Secundus, AD 23–79) « Natural History » «De diversitate caseorum»



Describes a ewe milk cheese from Babales (Lozère, France)



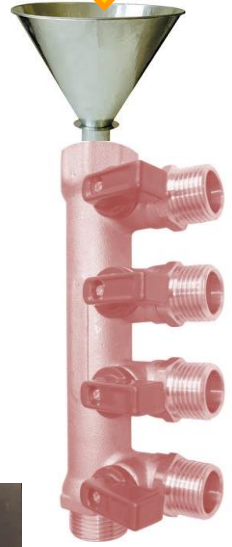
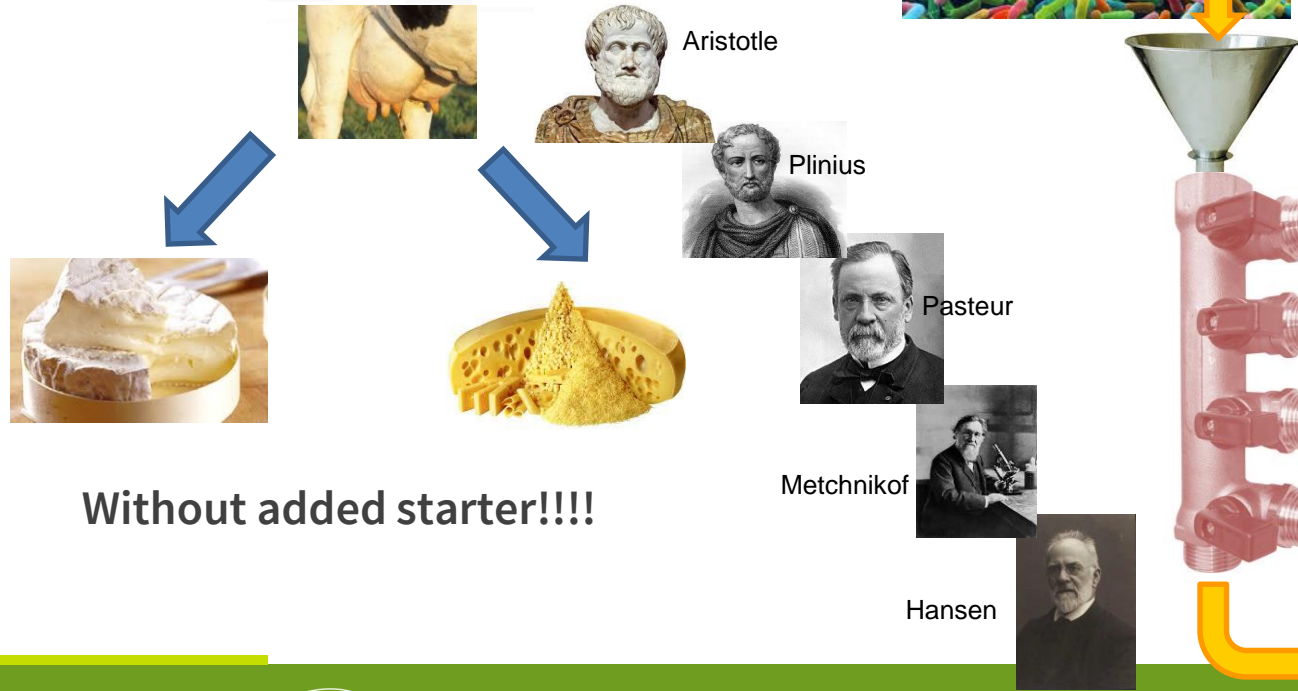
And a cow milk cheese from Arverni (Auvergnés, France)



All these cheeses without added starter !!!!

# The technological pathway use to select the bacteria

## And now we select the bacteria



- Texture
- Aroma
- Acidification

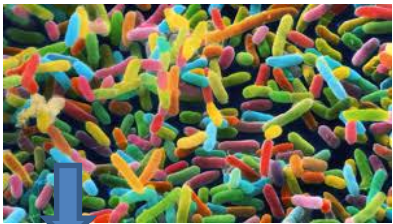
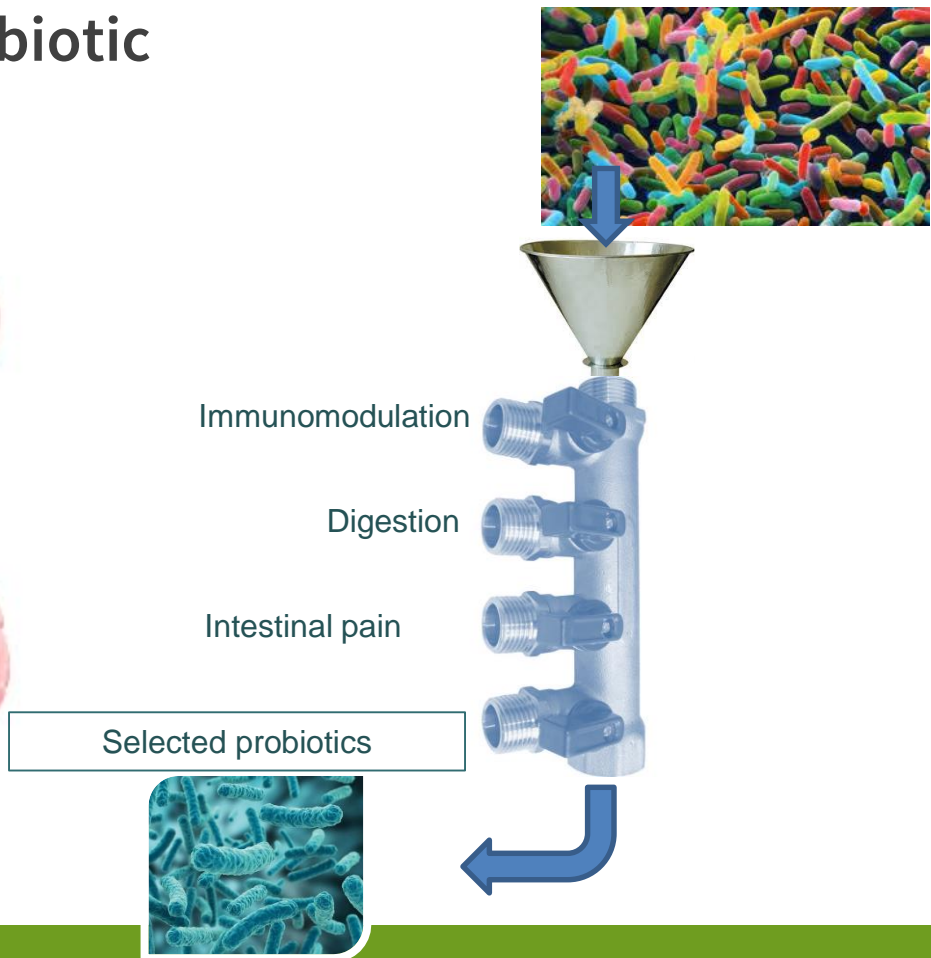
Selected starters



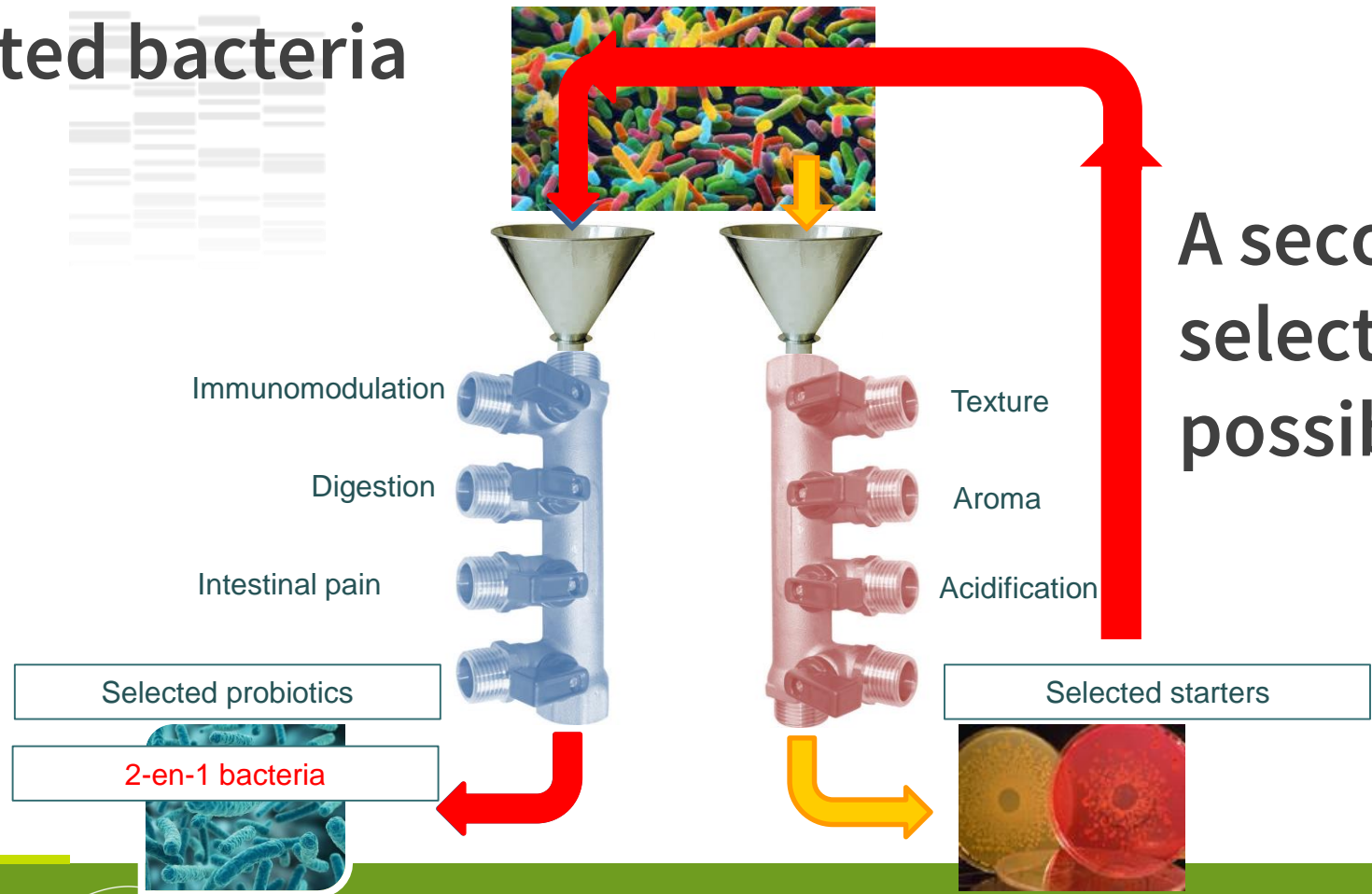
Without added starter!!!!

# Other bacteria are selected for probiotic properties

IBS, IBD, atopic, intolerance ...

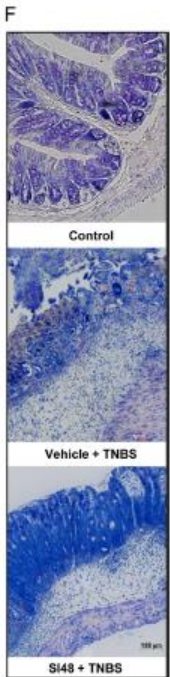


# Selected bacteria



A second selection is possible

# Examples of selected bacteria



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## Promising Immunomodulatory Effects of Selected Strains of Dairy Propionibacteria as Evidenced *In Vitro* and *In Vivo*<sup>†</sup>

Benoît Foligné,<sup>1,2,3,4</sup> Stéphanie-Marie Deutsch,<sup>5,6</sup> Jérôme Breton,<sup>1,2,3,4</sup> Fabien J. Cousin,<sup>5,6,7</sup>  
 Joëlle Dewulf,<sup>1,2,3,4</sup> Michel Samson,<sup>8</sup> Bruno Pot,<sup>1,2,3,4</sup> and Gwénaél Jan<sup>5,6\*</sup>

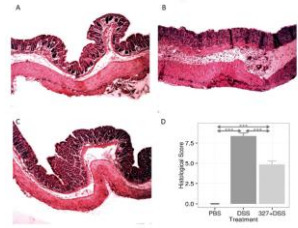


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## Local and Systemic Immune Mechanisms Underlying the Anti-Colitis Effects of the Dairy Bacterium *Lactobacillus delbrueckii*

Clarissa Santos Rocha<sup>1,3,4</sup>, Ana Cristina Gomes-Santos<sup>2</sup>, Thais Garcias Moreira<sup>2</sup>, Marcela de Azevedo<sup>1</sup>,  
 Tessalia Diniz Luerce<sup>1</sup>, Mahendra Mariadassou<sup>5</sup>, Ana Paula Longaray Delamare<sup>6</sup>, Philippe Langella<sup>3,4</sup>,  
 Emmanuelle Maguin<sup>3,4</sup>, Vasco Azevedo<sup>1</sup>, Ana Maria Caetano de Faria<sup>2</sup>, Anderson Miyoshi<sup>1,9</sup>,  
 Maarten van de Guchte<sup>3,4,9</sup>





# A reverse-engineered cheese



Microfiltr. Milk  
 ↓  
 Powder 100 g/L  
 ↓  
 Cream 150 g/L  
 ↓  
 Sterilisation  
 ↓  
 Culture *P. freudenreichii*  
 30°C, 72 h  
 ↓  
 Pre-cheese

UHT Milk  
 ↓  
 Culture *L. delbrueckii*  
 42°C, 4 h  
 ↓  
 Fermented Milk



Clotting, stirring, cooking,  
 moulding, pressing,  
 wrapping, ripening



Mol. Nutr. Food Res. 2016, 60, 935–948

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935

RESEARCH ARTICLE

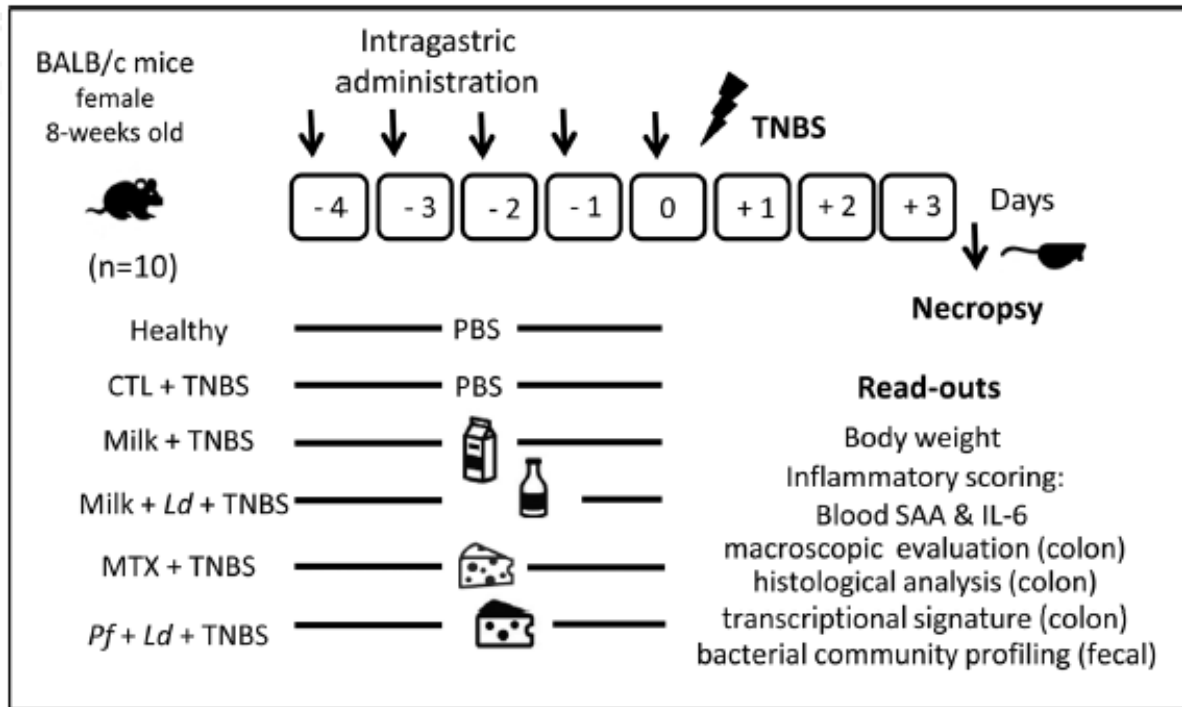


## Combining selected immunomodulatory *Propionibacterium freudenreichii* and *Lactobacillus delbrueckii* strains: Reverse engineering development of an anti-inflammatory cheese

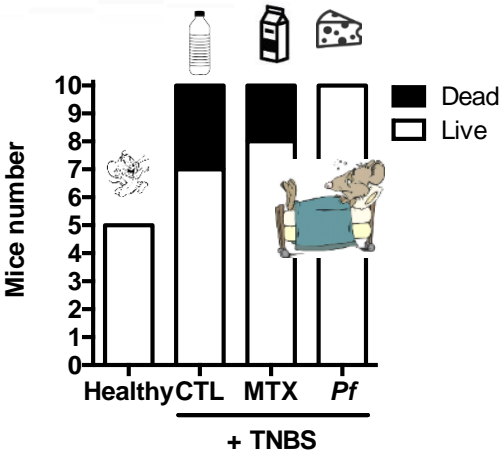
Coline Plé<sup>1</sup>, Jérôme Breton<sup>1</sup>, Romain Richoux<sup>2</sup>, Marine Nurdin<sup>2</sup>, Stéphanie-Marie Deutsch<sup>3,4</sup>,  
 Hélène Falentin<sup>3,4</sup>, Christophe Hervé<sup>5</sup>, Victoria Chuat<sup>3,4,6</sup>, Riwanon Lemée<sup>5</sup>,  
 Emmanuelle Maguin<sup>7,8</sup>, Gwénaél Jan<sup>3,4</sup>, Maarten Van de Guchte<sup>7,8</sup> and Benoit Foligné<sup>1</sup>



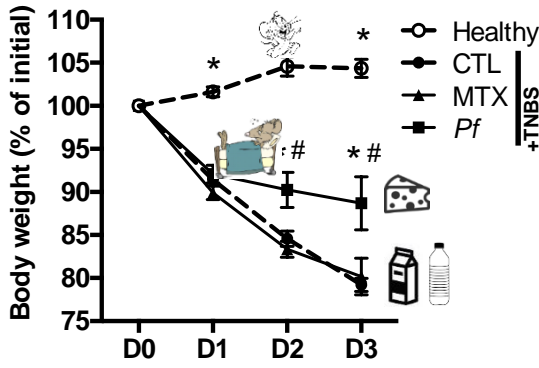
# Experimental design of the animal trial



# Cheese protects at the organism level



Survival

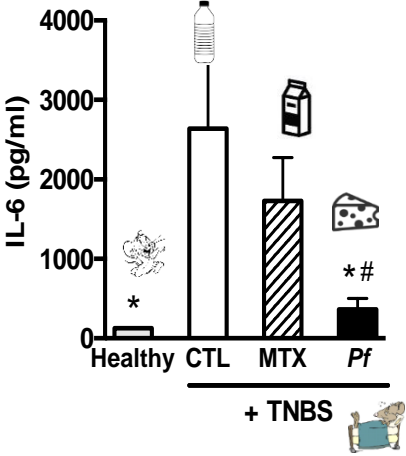


Body weight

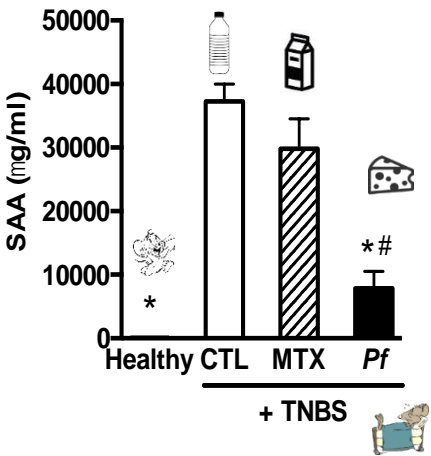
# Cheese protects at the systemic level



## Blood inflammation markers



Interleukin 6



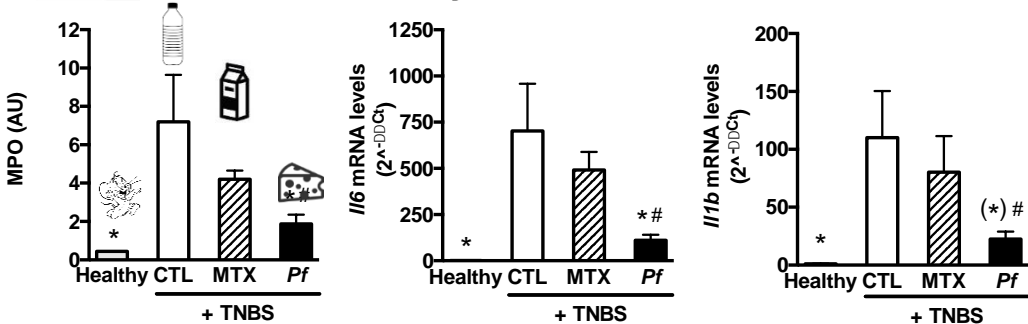
Serum Amyloid A



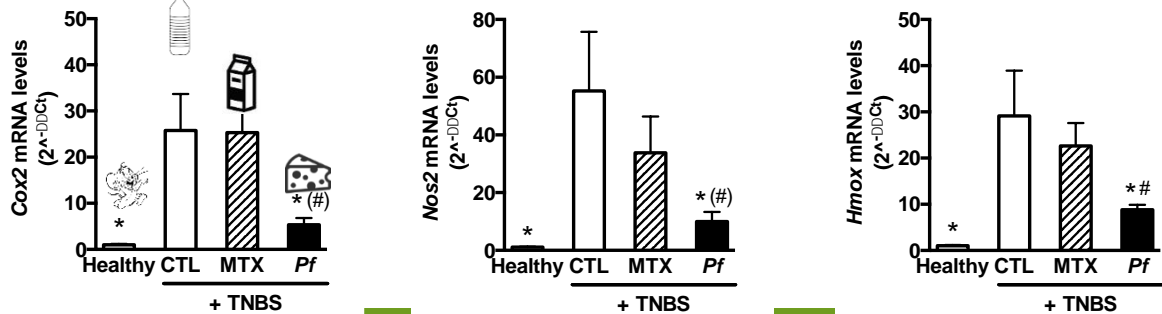


# Cheese protects at the tissue level

## Colonic inflammatory markers



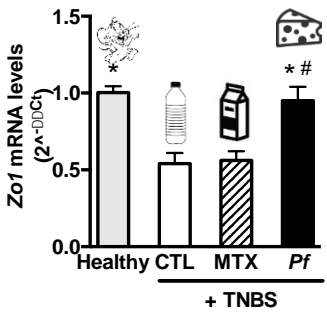
## Colonic oxidative stress markers



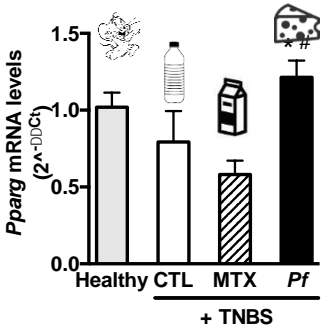
\* p<0.05: vs CTL  
# p<0.05: vs MTX

# Cheese protects at the cell level

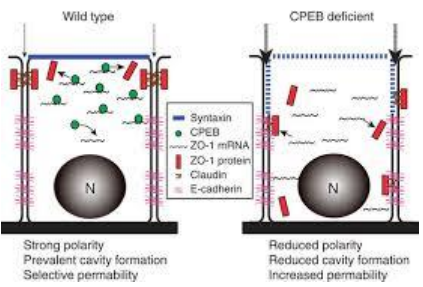
## Colonic epithelial cell markers



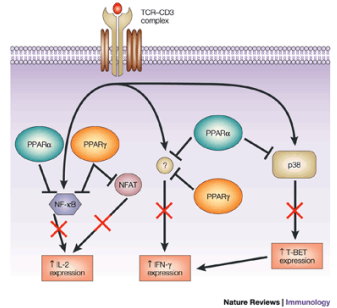
\* p<0.05: vs CTL  
# p<0.05: vs MTX



Nagaoka, Nature Communications, 2012



The zona occludens proteins (ZO-1, ZO-2 and ZO-3) : tight junction proteins that function as cross-linkers



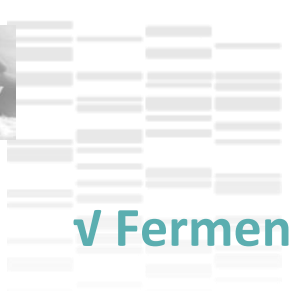
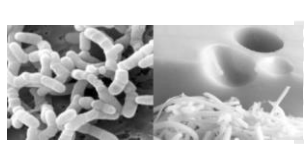
Peroxisome proliferator-activated receptors (PPARs) regulate T-cell cytokine production.



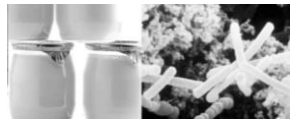
# More *in vivo* data



See Poster P90 by Houem Rabah !



## Conclusion:



✓ Fermented foods: a source of immunomodulatory bacteria

✓ Molecules and strains involved are being identified

## Perspectives :

✓ Preclinical and clinical studies with fermented products

✓ Fermented food for specific populations

AGRO  
CAMPUS  
OUEST



Fermented foods : 30% of our diet

A major source of bacteria :  $10^5$  to  $10^9$  per gram

A huge variety of bacteria



Thank  
you for  
your  
attention

Don't ask  
tough  
questions



Houem.Rabah@inra.fr

fillipelrc@gmail.com

SongHuang.suda@gmail.com



Agence Nationale de la Recherche  
ANR

Gwénaél JAN

<sup>1</sup>INRA, STLO, UMR 1253 Science et Technologie du Lait et de l'Œuf, Rennes

<sup>2</sup>Agrocampus Ouest, STLO, UMR 1253 Science et Technologie du Lait et de l'Œuf, Rennes

