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

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

**Gwénaél JAN<sup>1,2</sup>**

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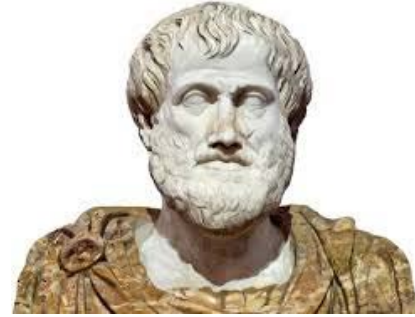
<sup>2</sup>Agrocampus Ouest, UMR 1253 Science et Technologie du Lait et de l'Œuf, Rennes





## 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)

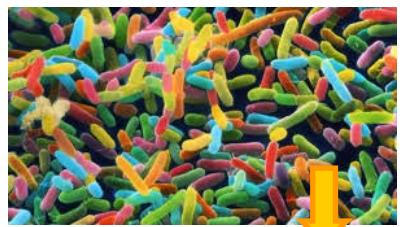
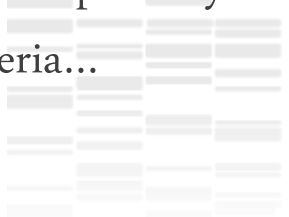


And a cow milk cheese from Arverni (Auvergnés, France)

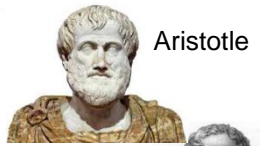
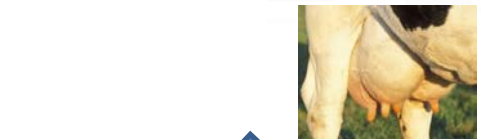


All these cheeses without added starter !!!!

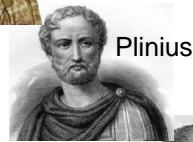
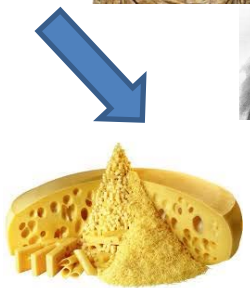
The technological pathway use to select the bacteria...



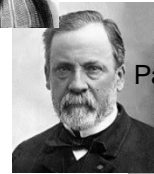
...but today, we select the bacteria



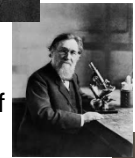
Aristotle



Plinius



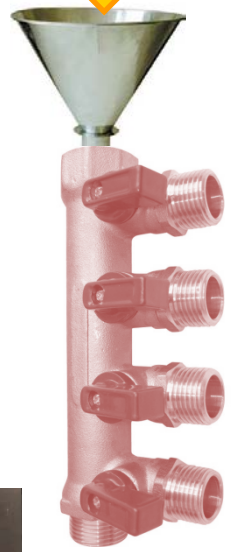
Pasteur



Metchnikof



Hansen



Texture

Aroma

Acidification

Selected starters

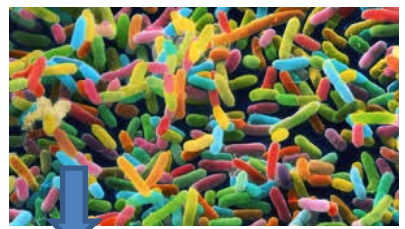


Without added starter!!!!

Other bacteria are selected for probiotic properties



IBS, IBD, atopie, intolérance ...



Immunomodulation

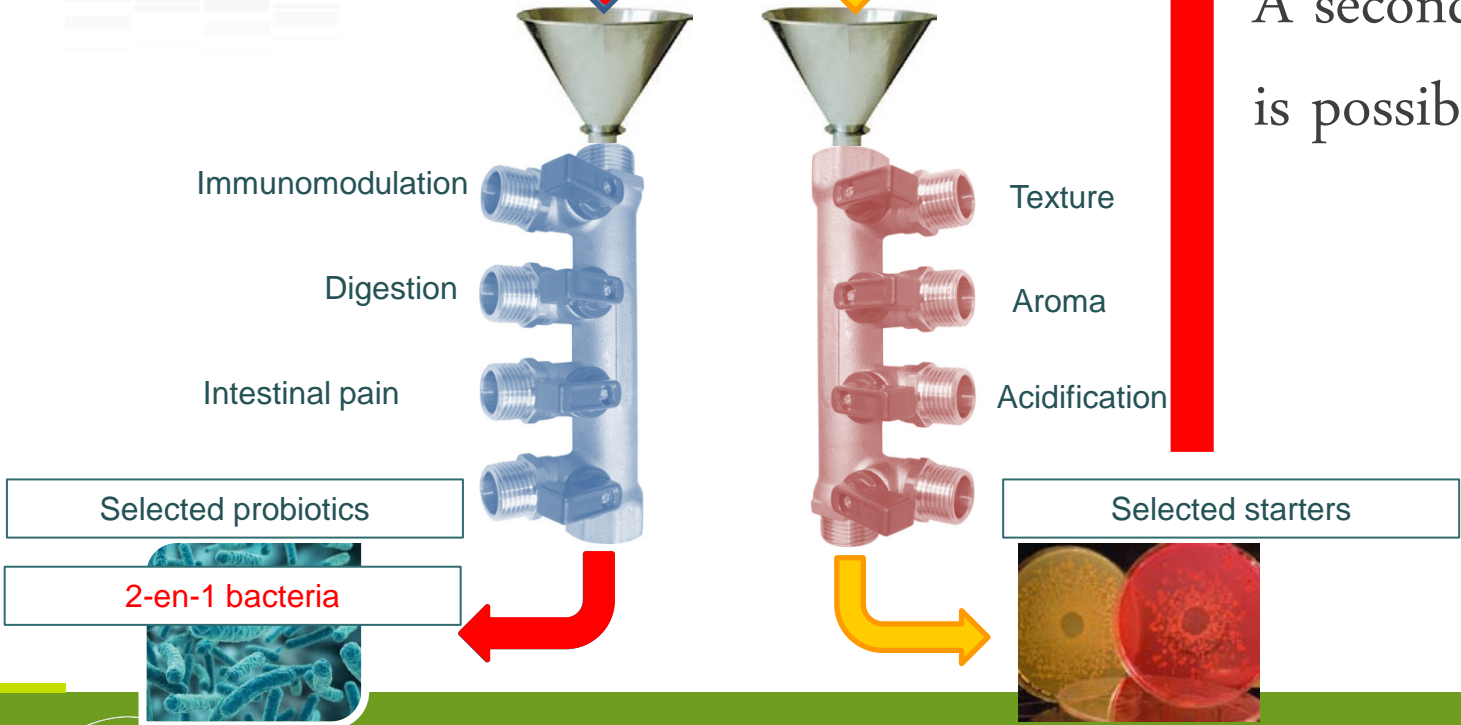
Digestion

Intestinal pain

Selected probiotics

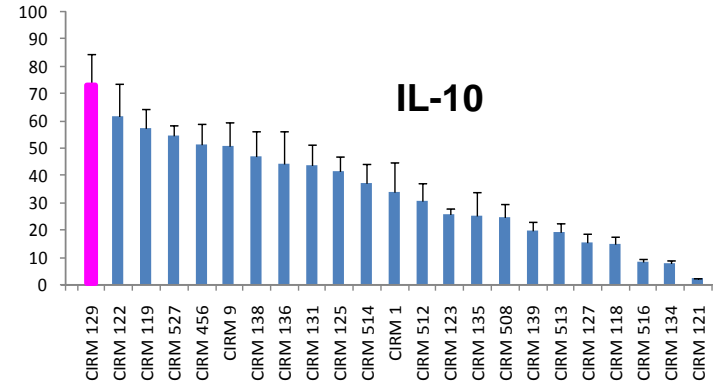
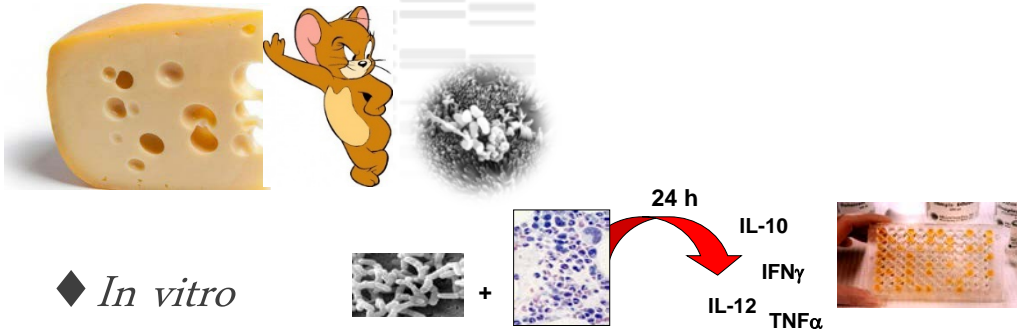


# Selected bacteria

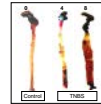
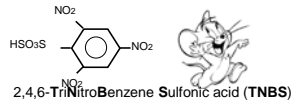




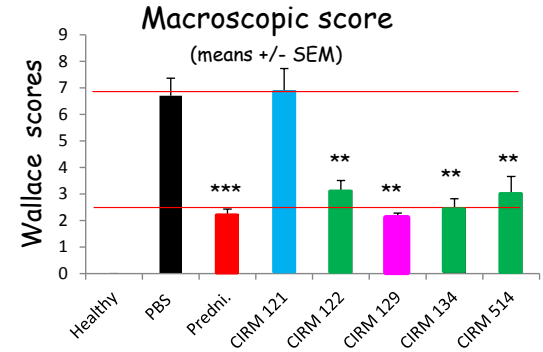
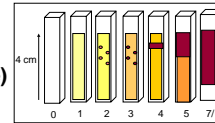
# Dairy propionibacteria : immunomodulatory?



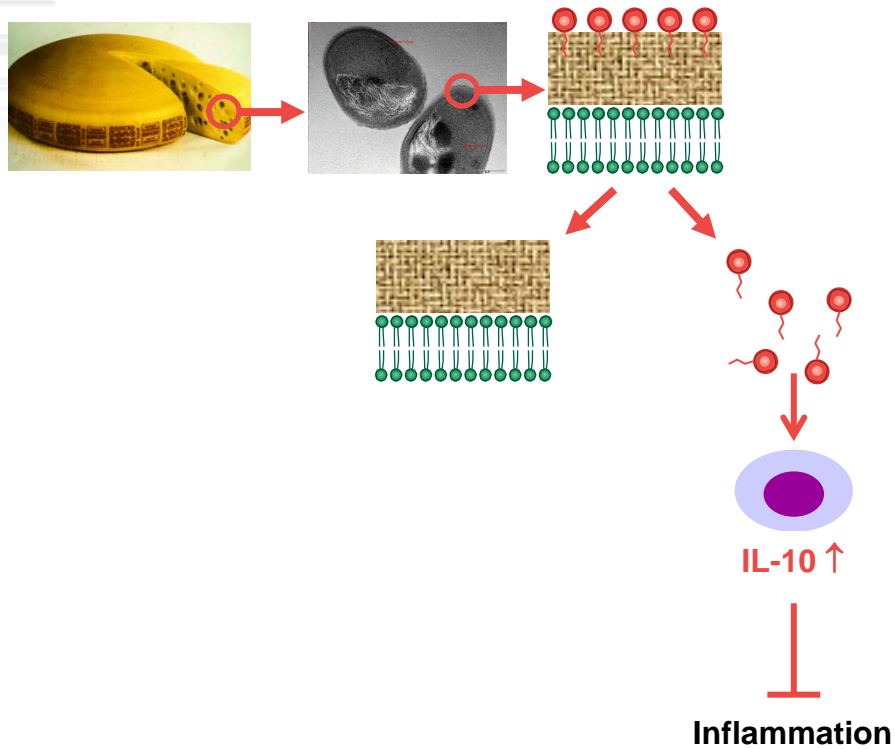
◆ *In vivo*



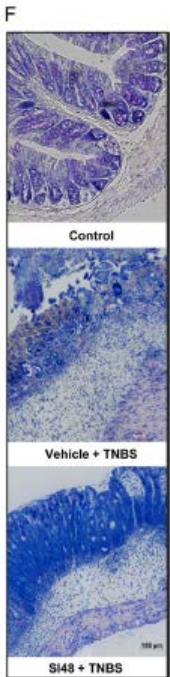
Macroscopic score (Wallace)



# Mechanisms investigated



# Examples of selected bacteria



APPLIED AND ENVIRONMENTAL MICROBIOLOGY, Dec. 2010, p. 8259–8264  
 0099-2240/10/\$12.00 doi:10.1128/AEM.01976-10  
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Vol. 76, No. 24

## 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>

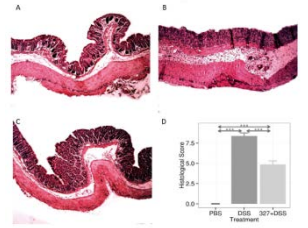


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## Local and Systemic Immune Mechanisms Underlying the Anti-Colitis Effects of the Dairy Bacterium *Lactobacillus delbrueckii*

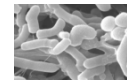
Clarissa Santos Rocha<sup>1,3,4</sup>, Ana Cristina Gomes-Santos<sup>2</sup>, Thais Garcia Moreira<sup>2</sup>, Marcela de Azevedo<sup>1</sup>,  
 Tessalia Diniz Luerce<sup>1</sup>, Mahendra Mariadassou<sup>5</sup>, Ana Paula Longaray Delamare<sup>6</sup>, Philippe Langella<sup>3,4</sup>,  
 Emmanuelle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

DOI 10.1002/mnfr.201500580

935

RESEARCH ARTICLE

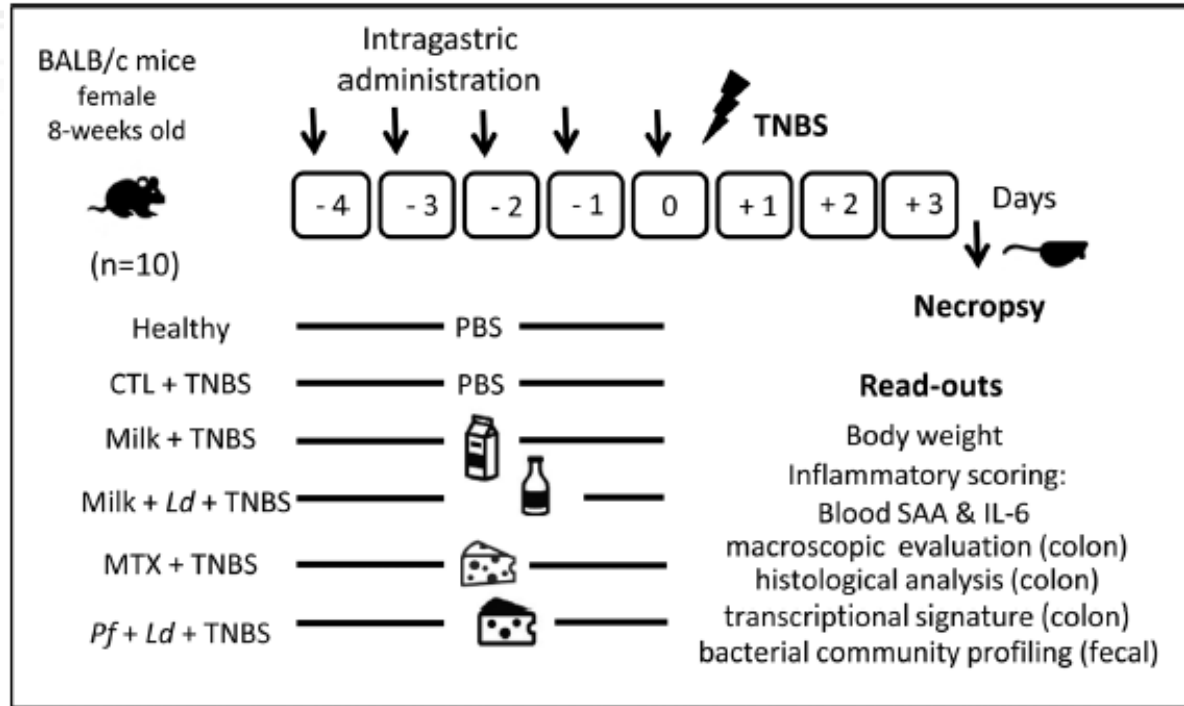


## Combining selected immunomodulatory *Propionibacterium freudenreichii* and *Lactobacillus delbrueckii* strains: Reverse engineering development of an anti-inflammatory cheese

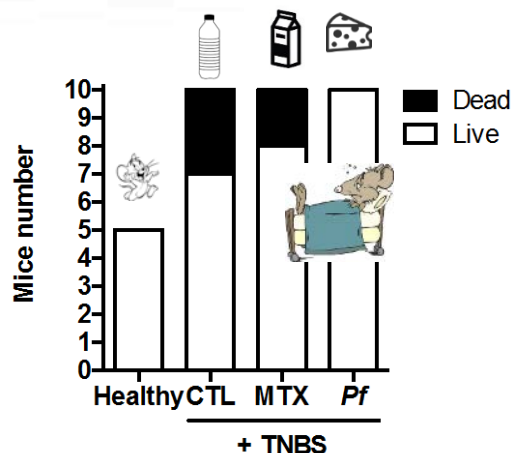
Coline Plé<sup>1</sup>, Jérôme Breton<sup>1</sup>, Romain Richoux<sup>2</sup>, Marine Nurdin<sup>2</sup>, Stéphanie-Marie Deutsch<sup>3,4</sup>,  
 Hélène Falentin<sup>3,4</sup>, Christophe Hervé<sup>5</sup>, Victoria Chuat<sup>3,4,6</sup>, Riwanon Lemée<sup>5</sup>,  
 Emmanuelle Maguin<sup>7,8</sup>,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



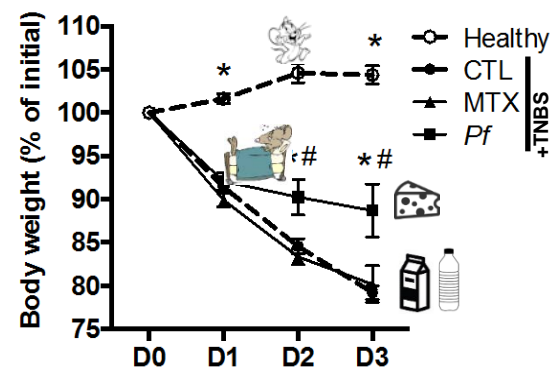
# Experimental design of the animal trial



# Cheese protects at the organism level



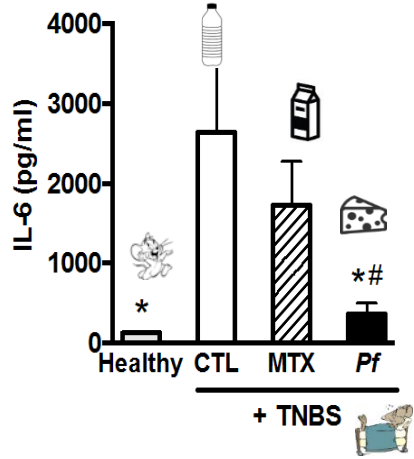
Survival



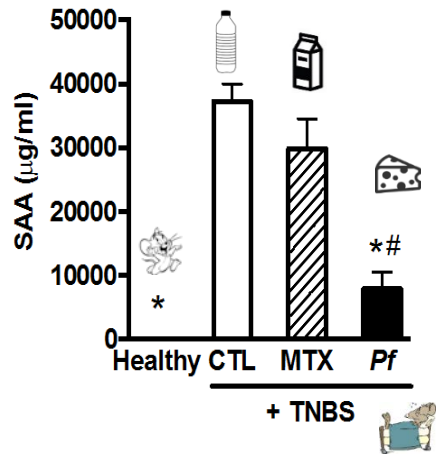
Body weight

# Cheese protects at the systemic level

## Blood inflammation markers

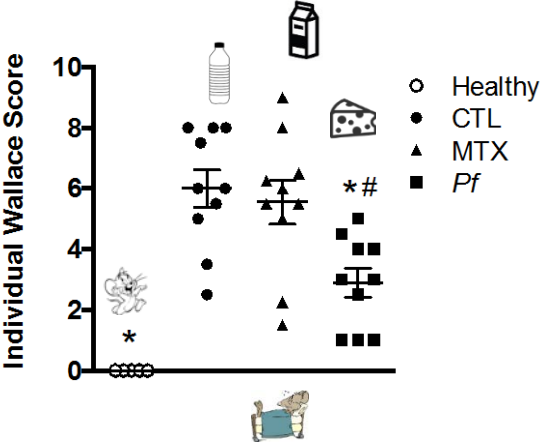
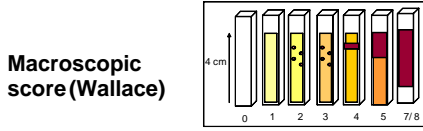
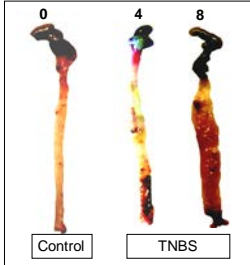
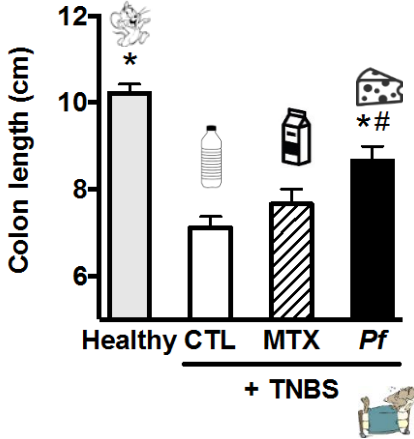


Interleukin 6



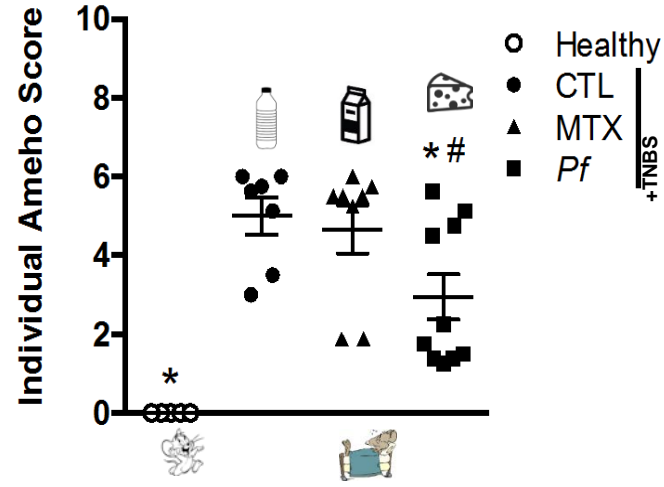
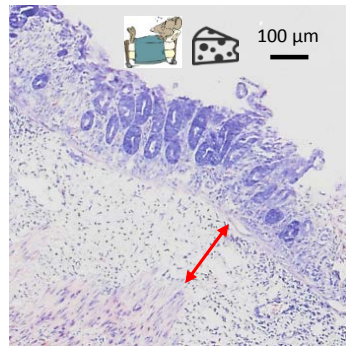
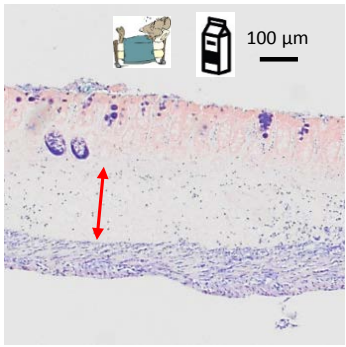
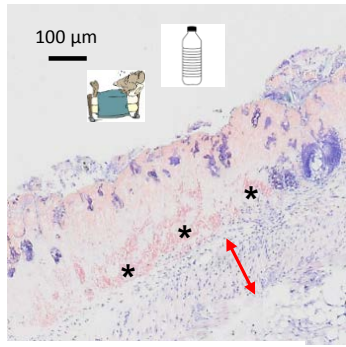
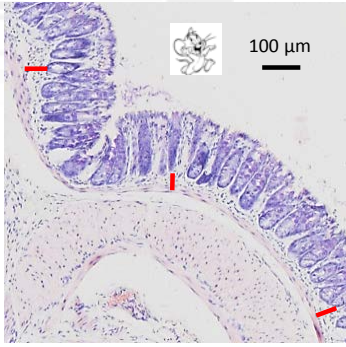
Serum Amyloid A

# Cheese protects at organ level



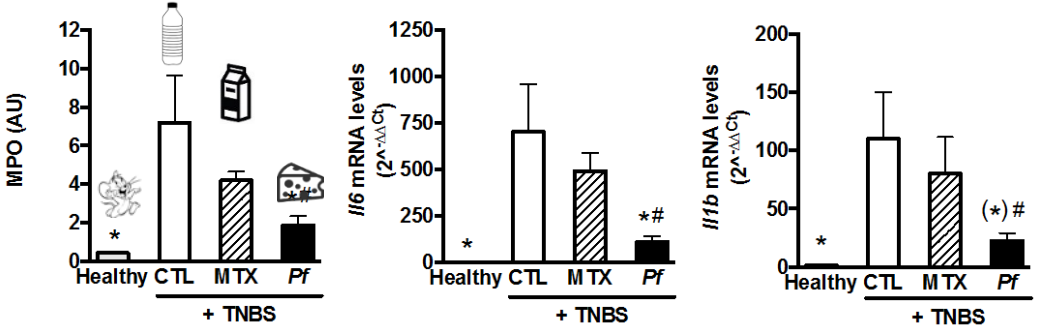


# Cheese protects at the tissue level

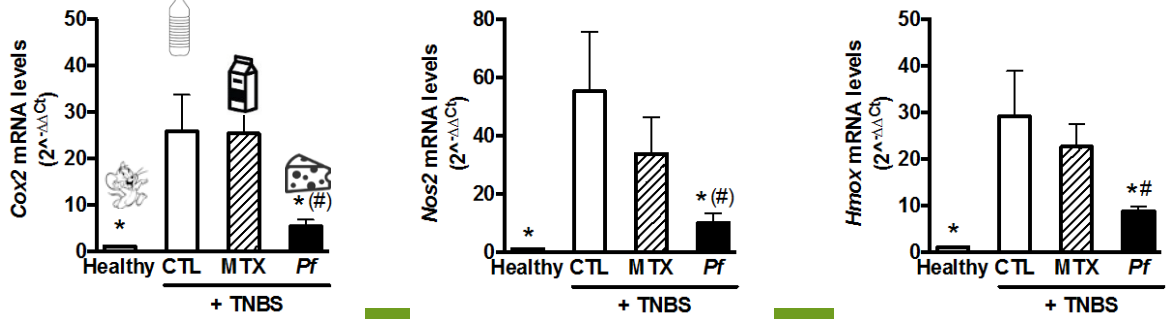


# Cheese protects at the tissue level

## Colonic inflammatory markers



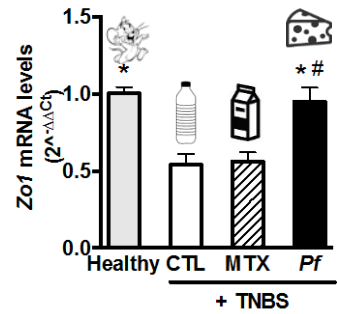
## Colonic oxidative stress markers



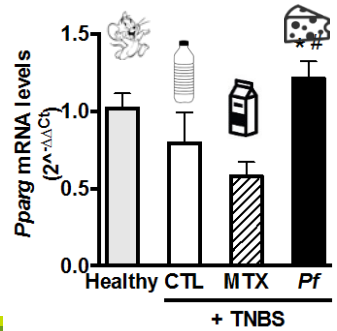
\* p<0.05: vs CTL  
# p<0.05: vs MTX

# Cheese protects at the cell level

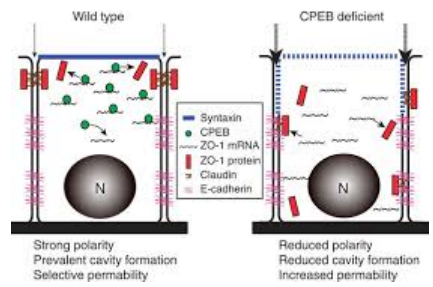
## Colonic epithelial cell markers



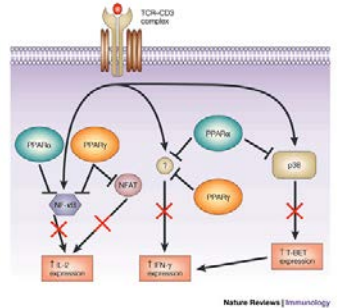
\* p<0.05: vs CTL  
# p<0.05: vs MTX



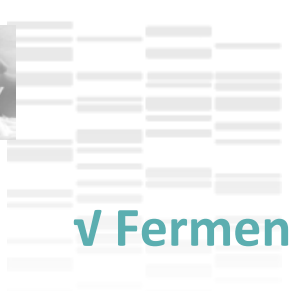
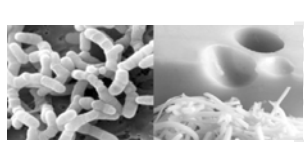
Nagaoka, Nature Communications, 2012



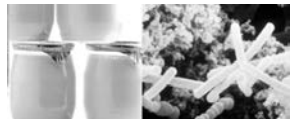
The zona occludens proteins (ZO-1, ZO-2 and ZO-3) : tight junction proteins that function as cross-linkers



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



## 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



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L'Europe s'engage  
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Agence Nationale de la Recherche  
ANR

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