



# Fermented milks, using *Lactobacillus casei* or *Propionibacterium freudenreichii*, prevent mucositis, a side effect of chemotherapy, in mice



**Gwénaél JAN**

UMR 1253 STLO

INRA Agrocampus Ouest, Rennes, France





Société Française  
de Microbiologie

**MICROBES**  
15<sup>e</sup> congrès national  
de la SFMM ●●●●●

Du  
30 septembre  
au 2 octobre  
**2019**

Cité des sciences et de l'industrie, Paris 19<sup>ème</sup> ●●●

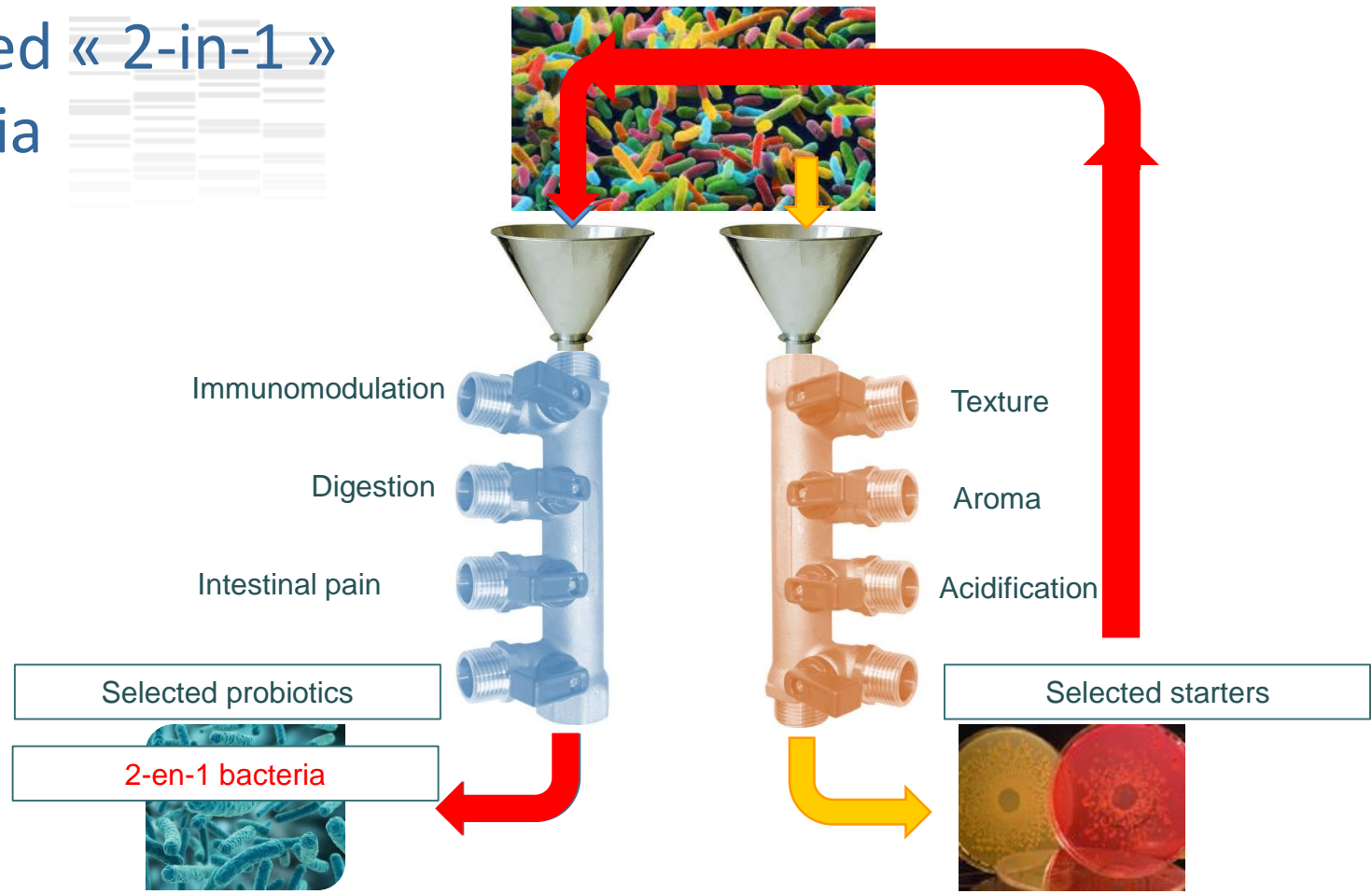
## Déclaration de conflit d'intérêt

Pour cette présentation, je déclare n'avoir aucun conflit d'intérêt.

LIA, Laboratoire International  
Associé, BactInflam

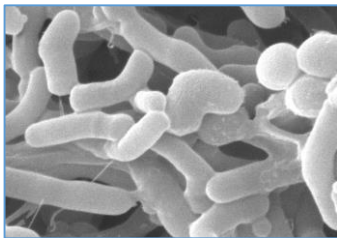


# Selected « 2-in-1 » bacteria



# Example of selected bacteria: propionibacteria

Gram +  
pleiomorphic  
anaerobic to microaérophilic  
non motiles et non sporulated  
actinobacterium



GC Rich : 67%

« Dairy » :  
***P. freudenreichii***  
*P. jensenii* - *P. thoenii* -

→ Vitamin producer  
B9, B12



→ Probiotics



→ Food bio-preservative



→ Ripening starter



→ Commensal/probiotic





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 journal homepage: [www.elsevier.com/locate/jff](http://www.elsevier.com/locate/jff)



## Single-strain starter experimental cheese reveals anti-inflammatory effect of *Propionibacterium freudenreichii* CIRM BIA 129 in TNBS-colitis model

Coline Plé<sup>a</sup>, Romain Richoux<sup>b</sup>, Julien Jardin<sup>c,d</sup>, Marine Nurdin<sup>b</sup>, Valérie Briard-Bion<sup>c,d</sup>, Sandrine Parayre<sup>c,d</sup>, Stéphanie Ferreira<sup>e</sup>, Bruno Pot<sup>a</sup>, Guillaume Bouguen<sup>f,g</sup>, Stéphanie-Marie Deutsch<sup>c,d</sup>, Hélène Falentin<sup>c,d</sup>, Benoit Foligné<sup>a,1</sup>, Gwénaél Jan<sup>c,d,\*1</sup>



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# SCIENTIFIC REPORTS

Vol. 76, No. 24

Dairy

5,6,7

Calmette,  
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## OPEN Identification of proteins involved in the anti-inflammatory properties of *Propionibacterium freudenreichii* by means of a multi-strain study

Received: 29 September 2016  
 Accepted: 09 March 2017  
 Published: 13 April 2017

Stéphanie-Marie Deutsch<sup>1</sup>, Mahendra Mariadassou<sup>1</sup>, Pierre Nicolas<sup>2</sup>, Sandrine Parayre<sup>1</sup>, Rozenn Le Guellec<sup>1</sup>, Victoria Chuat<sup>1</sup>, Vincent Peton<sup>1</sup>, Caroline Le Maréchal<sup>1</sup>, Julien Burati<sup>1</sup>, Valentin Loux<sup>2</sup>, Valérie Briard-Bion<sup>1</sup>, Julien Jardin<sup>1</sup>, Coline Plé<sup>1</sup>, Benoit Foligné<sup>1</sup>, Gwénaél Jan<sup>1,2</sup> & Hélène Falentin<sup>1,2</sup>



## Surface proteins of *Propionibacterium freudenreichii* are involved in its anti-inflammatory properties

Caroline Le Maréchal<sup>a,b</sup>, Vincent Peton<sup>a,b</sup>, Coline Plé<sup>c</sup>, Christophe Vroland<sup>a,b</sup>, Julien Jardin<sup>a,b</sup>, Valérie Briard-Bion<sup>a,b</sup>, Gaël Durant<sup>a,b</sup>, Victoria Chuat<sup>a,b,d</sup>, Valentin Loux<sup>e</sup>, Benoit Foligné<sup>c</sup>, Stéphanie-Marie Deutsch<sup>a,b</sup>, Hélène Falentin<sup>a,b,1</sup>, Gwénaél Jan<sup>a,b,\*1</sup>



## Microbiome functionality: *Propionibacterium freudenreichii* species

Denis Mater, et al.

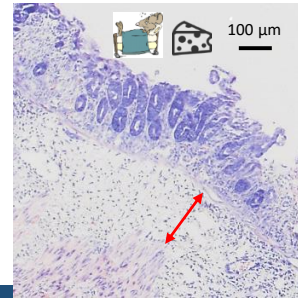
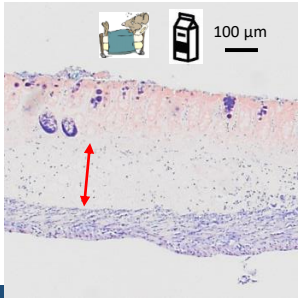
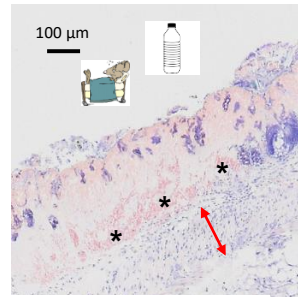
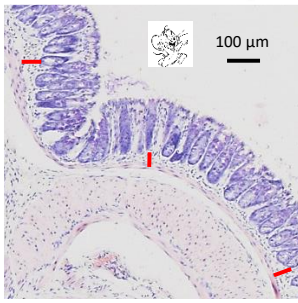
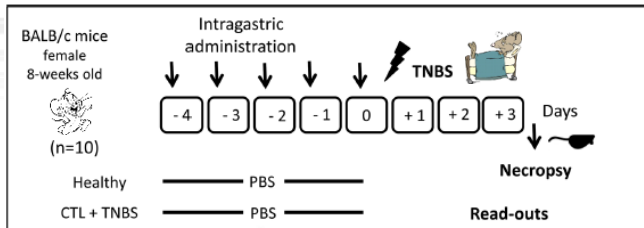
First published online February 6, 2013  
 04393



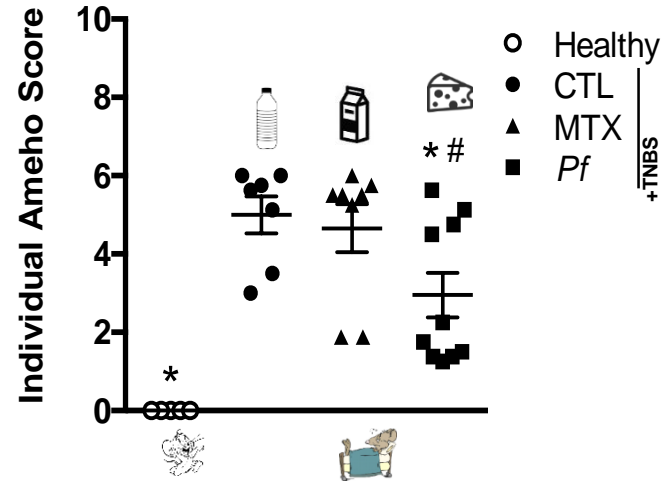
benoit.foligne@univ-lille.fr

<sup>a</sup>INRA, UMR1253 STLO, Science et Technologie du Lait et de l'Œuf, F-35042 Rennes, France  
<sup>b</sup>AGROCAMPUS OUEST, UMR1253 STLO, F-35042 Rennes, France  
<sup>c</sup>Lactic Acid Bacteria & Mucosal Immunity, Center for Infection and Immunity of Lille, Institut Pasteur de Lille, U 1019, UMR8204 Université Lille Nord de France, 1 rue du Pr Calmette, BP 245, F-59019 Lille, France  
<sup>d</sup>INRA, UMR1253 STLO, CIRM-BIA, F-35042 Rennes, France  
<sup>e</sup>INRA, UR MIG, F-78352 Jouy-en-Josas, France

# Focus on *Propionibacterium freudenreichii* ITG P20 alias CIRM-BIA 129



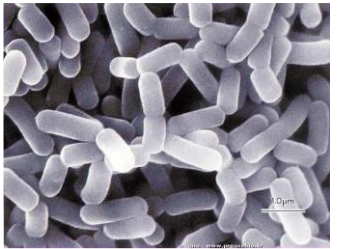
...in TNBS-induced acute colitis



benoit.foligne@univ-lille.fr

# Example of selected bacteria: *Lactobacillus casei*

Gram +  
rods bacilli



Facultative anaerobic  
non motiles et non sporulated  
Firmicute, lactobacillales

GC low : 48%

→ Olive fermentation



→ Ripening starter



→ Commensal/probiotic



# Focus on *Lactobacillus casei* BL23



## Attenuation of Colitis by *Lactobacillus casei* BL23 Is Dependent on Dairy Delivery Matrix

Bokyung Lee,<sup>a</sup> Xiaochen Yin,<sup>a</sup> Stephen M. Griffey,<sup>b</sup> Maria L. Marco<sup>a</sup>

Department of Food Science and Technology, University of California, Davis,<sup>a</sup> and Comparative Pathology Laboratory, University of California, Davis, School of Veterinary Medicine,<sup>b</sup> Davis, California, USA

*Beneficial Microbes*, 2017, 8(3): 433-438



## Intragastric administration of *Lactobacillus casei* BL23 induces regulatory FoxP3+RORγt+ T cells subset in mice

N.G. Cortes-Perez<sup>a</sup>, D. Lozano-Ojalvo, M.A. Maiga, S. Hazebrouck and K. Adel-Patient

UMR Service de Pharmacologie et d'Immuno-Analyse, CEA, INRA, Université Paris-Saclay, 91191 Gif-sur-Yvette, France; [naima.cortes-perez@cea.fr](mailto:naima.cortes-perez@cea.fr)

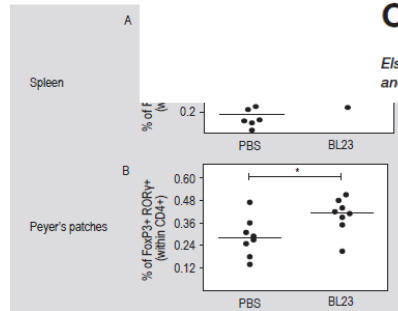


ORIGINAL RESEARCH  
published: 17 November 2017  
doi: 10.3389/fimmu.2017.01563



## Probiotic Strain *Lactobacillus casei* BL23 Prevents Colitis-Associated Colorectal Cancer

Elsa Jacouton<sup>1</sup>, Florian Chain<sup>1</sup>, Harry Sokol<sup>1,2</sup>, Philippe Langella<sup>1</sup> and Luis G. Bermúdez-Humarán<sup>1\*</sup>





## GI inflammatory diseases

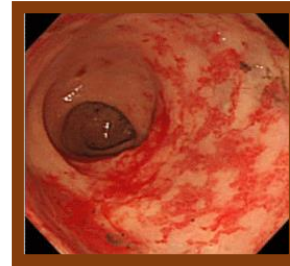
IBD

- GIT Chronic inflammation

Ulcerative  
Colitis



Mucositis



Oral mucositis

GI Mucositis

5-Fluoracil (5-FU)

- Head, neck and colon cancer.

(Chang *et al.*, 2012; Falvey *et al.*, 2015)



# Probiotics in inflammatory intestinal conditions

→ NO CURE AVAILABLE

IBD available treatment

Mucositis available treatment

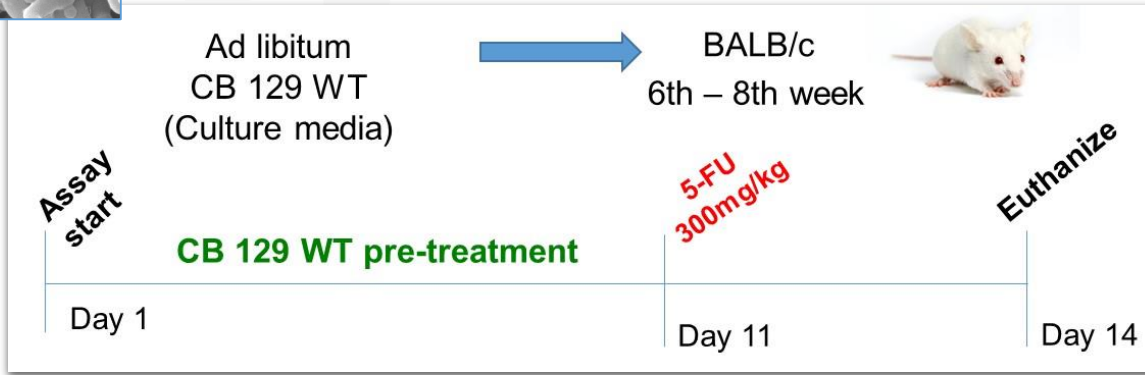
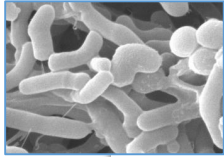
- Treatment for **mucositis** and **IBD** are limited;
- Development of **new therapies** is **necessary**.

Strong side effects!!!

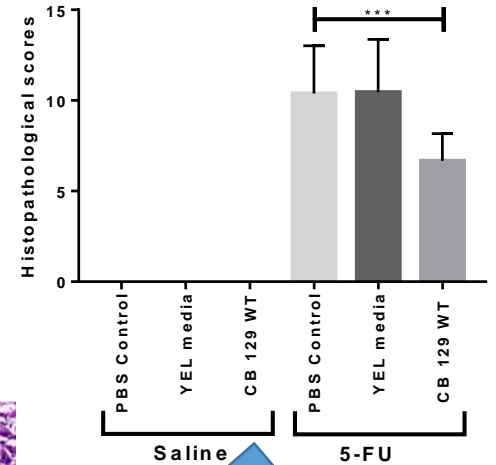
Temporary benefit!!!



# *P. freudenreichii* ameliorates mucositis in mouse model (5-FU)



*P. freudenreichii* CB 129 x Mucositis



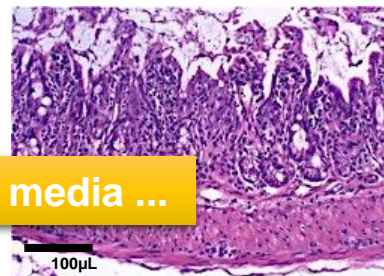
Healthy Ileum



Inflamed Ileum- 5-FU



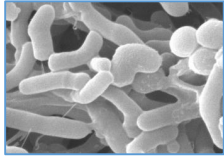
*P. f* CB129 5-FU



However, nobody drinks culture media ...

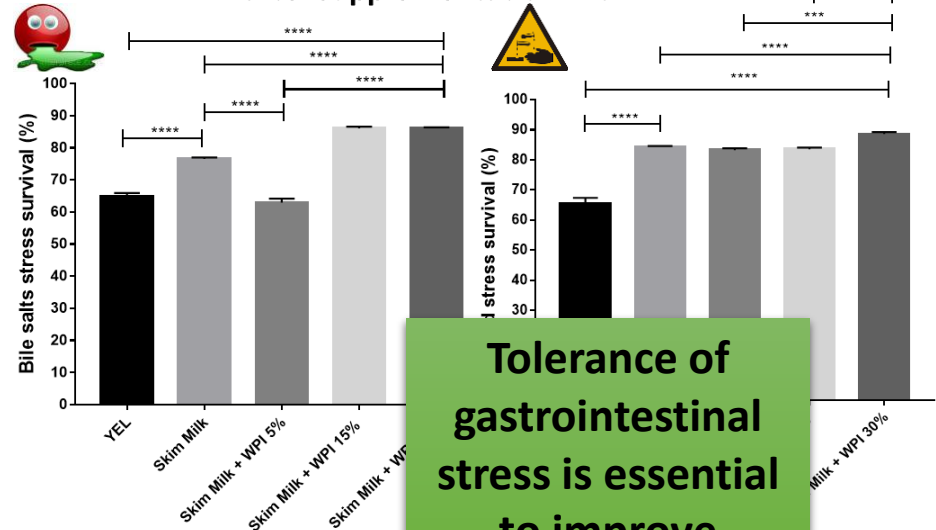
**MAKE A PROBIOTIC BEVERAGE!!!**

# Why Protein Isolate enhances *P. freudenreichii* stress tolerance



Strain	Genotype	Stress Tolerance
1	WT	Low
2	WT + WPI	High
3	WT + WPI	High
4	WT + WPI	High
5	WT + WPI	High
6	WT + WPI	High
7	WT + WPI	High
8	WT + WPI	High
9	WT + WPI	High
10	WT + WPI	High

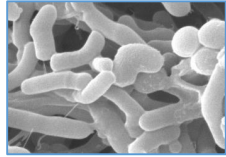
Stress tolerance of *P. freudenreichii* 138 is improved after supplementation with WPI



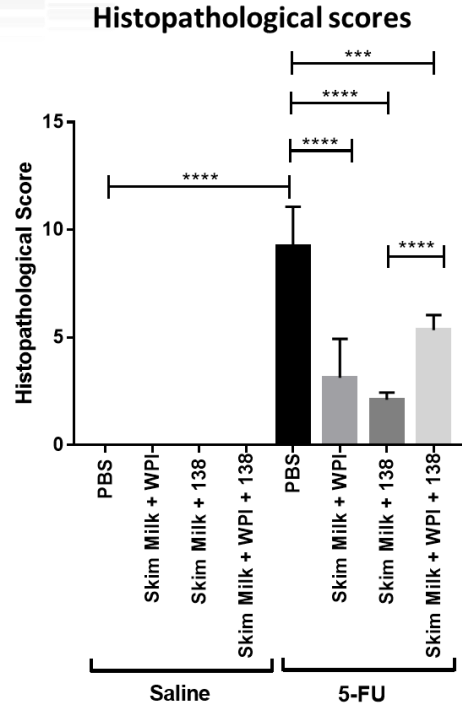
*P. freudenreichii* Fermented Milk supplemented with Whey Protein Isolate (WPI).

Tolerance of gastrointestinal stress is essential to improve probiotic survival and therapeutics effects.

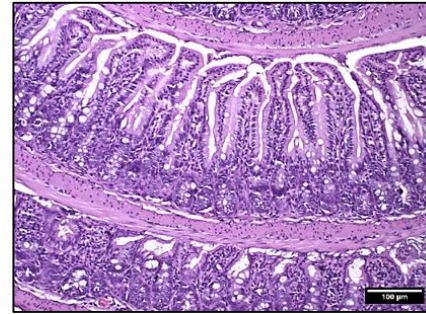
# *P. freudenreichii*-fermented milk ameliorates mucositis in mouse model (5-FU)



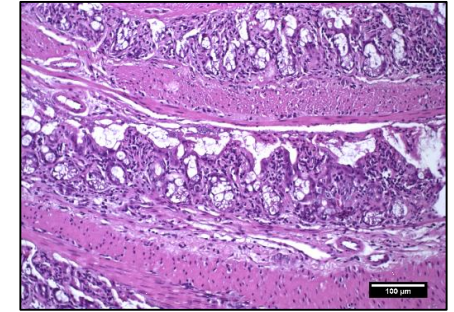
Fermented Milk by *P. freudenreichii* 138 supplemented with Whey Protein Isolate (WPI).



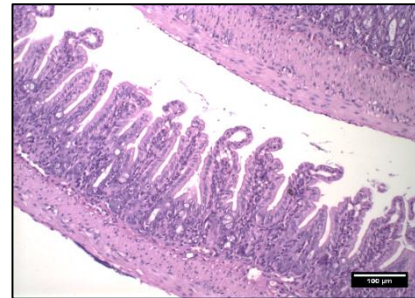
## Representative images from mucosal histopathology (H&E)



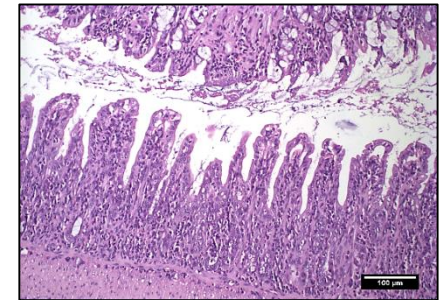
Healthy Ileum



PBS + 5-FU

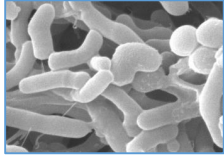


PF-fermented milk + 5-FU

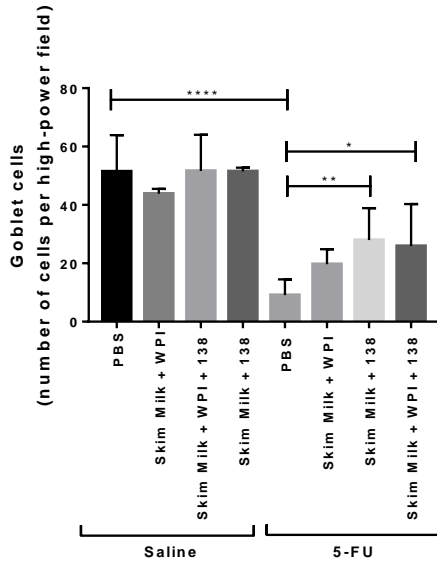


PF-fermented milk + WPI + 5-FU

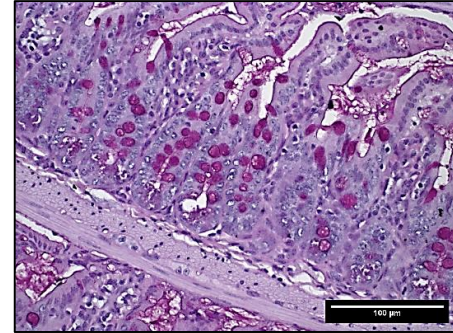
# *P. freudenreichii*-fermented milk ameliorates mucositis in mouse model (5-FU)



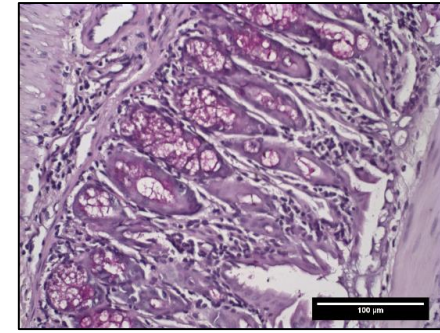
## Goblet cells counts



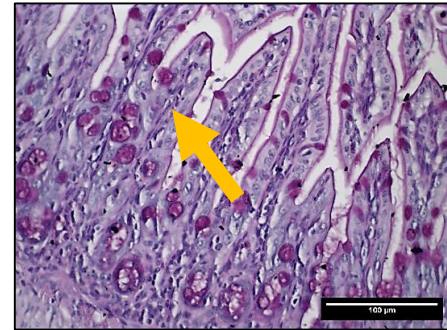
## Representative images of stained goblet cells (PAS)



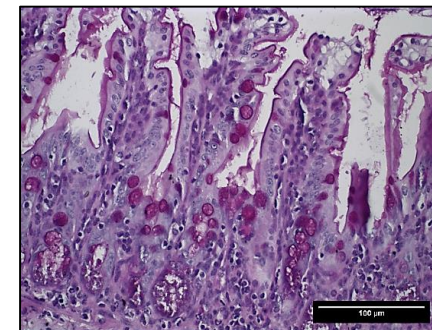
Healthy Ileum



PBS + 5FU



LDF + PF + 5FU



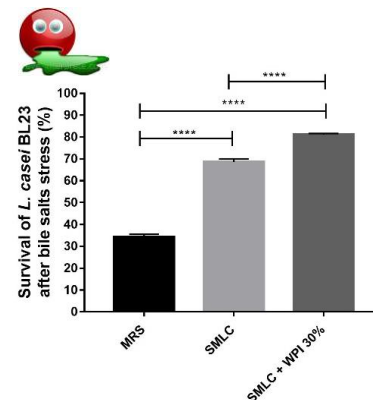
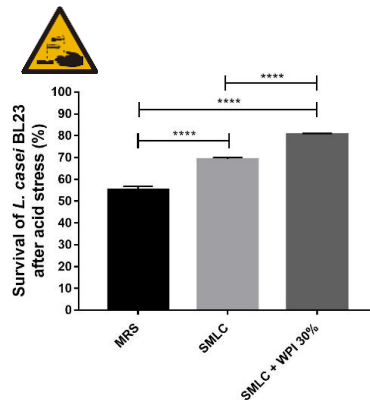
LDFWPI + PF + 5FU

What about *Lactobacillus casei* BL23?

# Why Protein Isolate enhances *L. casei* stress tolerance



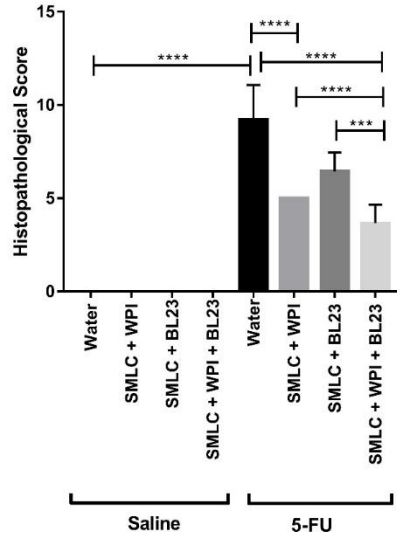
*L. casei*-fermented Milk supplemented with Whey Protein Isolate (WPI).



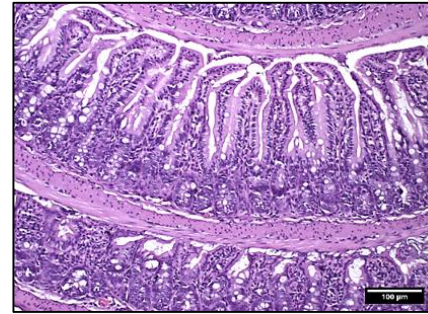
# L. casei-fermented milk ameliorates mucositis in mouse model (5-FU)



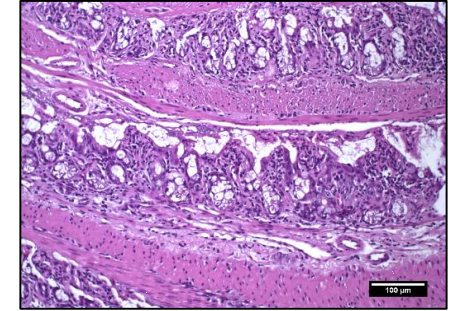
L. casei-fermented Milk supplemented with Whey Protein Isolate (WPI).



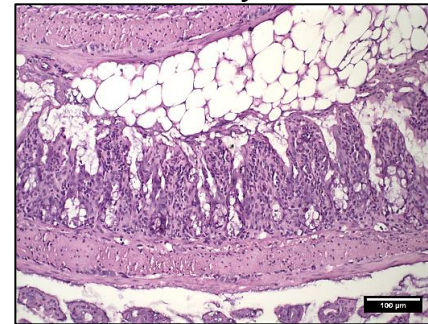
## Representative images from mucosal histopathology (H&E)



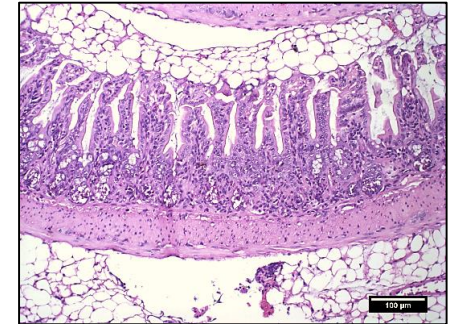
Healthy Ileum



PBS + 5-FU

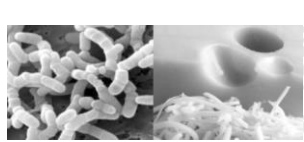


LC-fermented milk + 5-FU

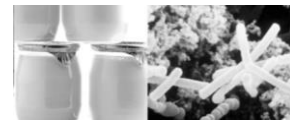


LC-fermented milk + WPI + 5-FU





## Conclusion:



✓ Fermented foods: a source of immunomodulatory bacteria

✓ Fermented foods may protect from colitis and mucositis

## 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 :  $10^{10}$  per day!

A huge variety of bacteria

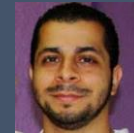


A  
PACT



Thank  
you for  
your  
attention

Don't ask  
tough  
questions



Fillipe Luiz Rosa do Carmo  
fillipeirc@gmail.com



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