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## Food or probiotic for IBD? Both!

Gwénaél Jan

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# INRAE

## ➤ Food or probiotics for IBD? Why choose? Both!

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<https://www6.rennes.inrae.fr/stlo>



# ➤ Milk & Egg Science and Technology



Departments: MICA, CEPIA, P3AN  
Carnot Institute « Qualiment » (since 2016)

140 people

80 tenure staff (34 researchers and professors;  
42 technicians and engineers)

~25 Docs and Post-Docs / year

~15 Students (Master)

16 members of R&D dept (private sector)



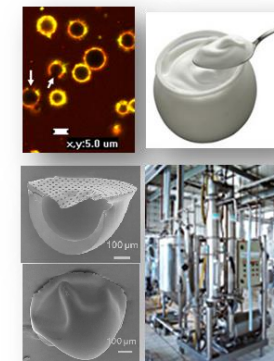
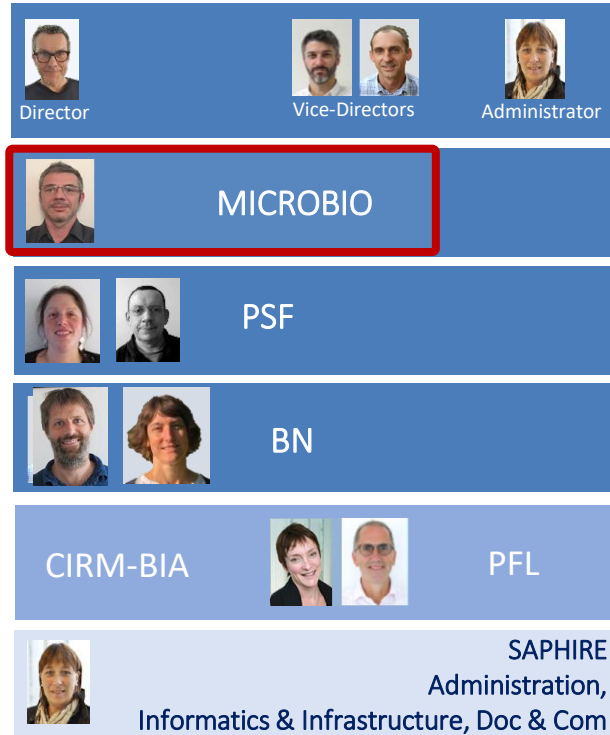
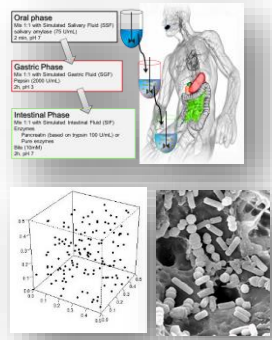
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IBD - Next

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# ➤ Organization





# MICROBIO

### Food quality & safety



Develop safe, healthy, sustainable and hedonic fermented foods

### Food spoilage



Reduce health risks and food losses and waste

Characterize interactions between bacteria/environment

### Animal health

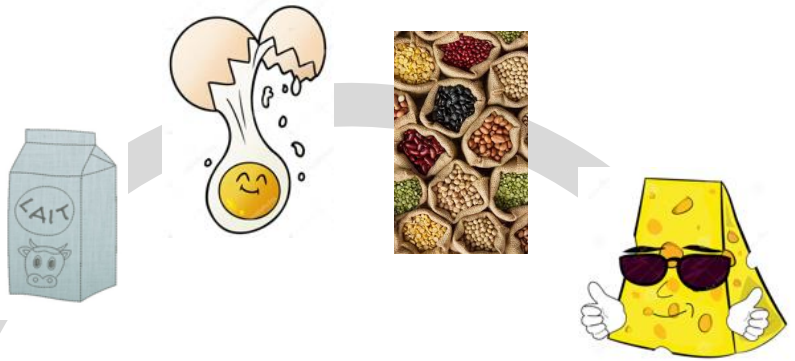


Offer alternatives to antibiotic treatments (probiotics)

### Health & wellbeing



Develop functional food against modern lifestyle diseases or promoting health in infants



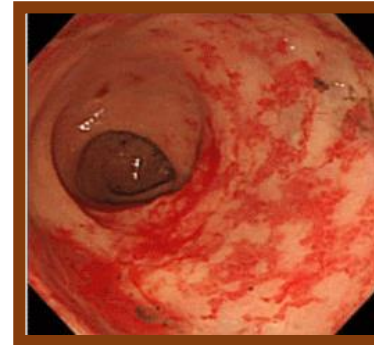
## > A growing incidence of inflammatory ailments

### IBD

- GIT Chronic inflammation



### Mucositis



GI Mucositis



Oral mucositis

5-Fluoracil (5-FU)

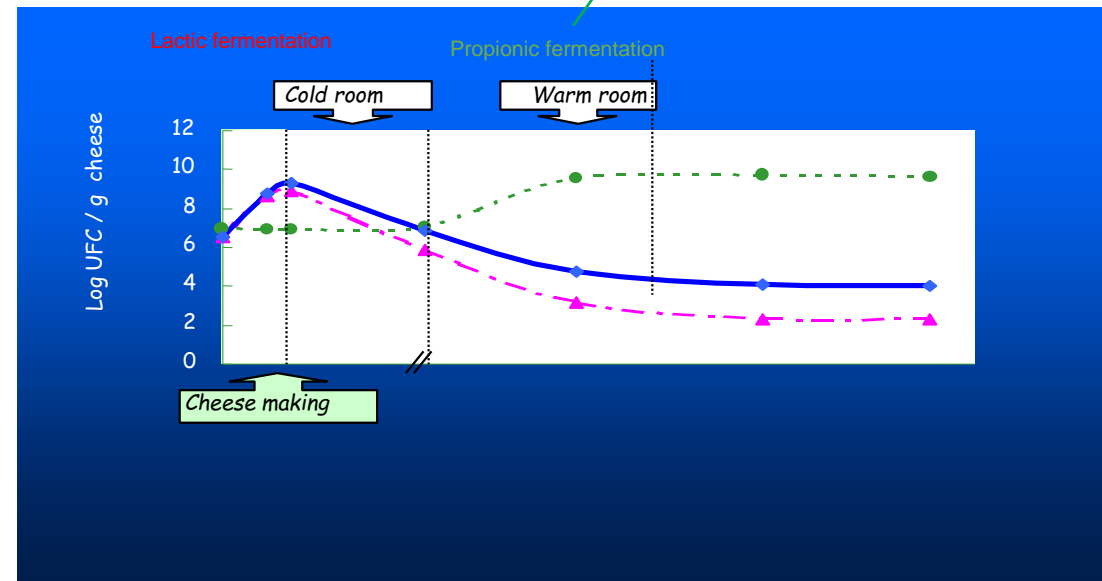
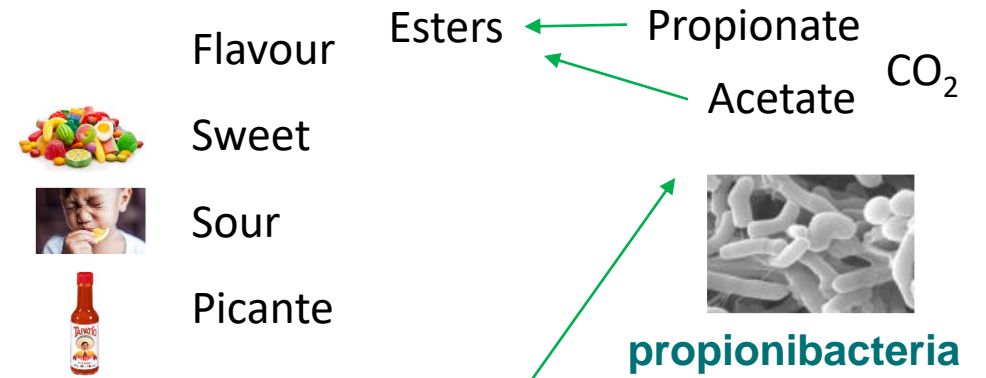
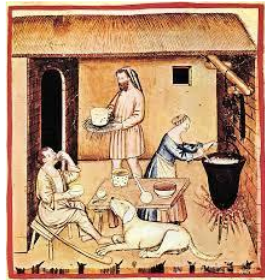
- Head, neck and colon cancer.

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



## > A seek for immunomodulatory biotherapies

# ➤ Seeking in a cheese with a long history: Emmental



## ➤ Propionibacteria, the main microbes in Emmental



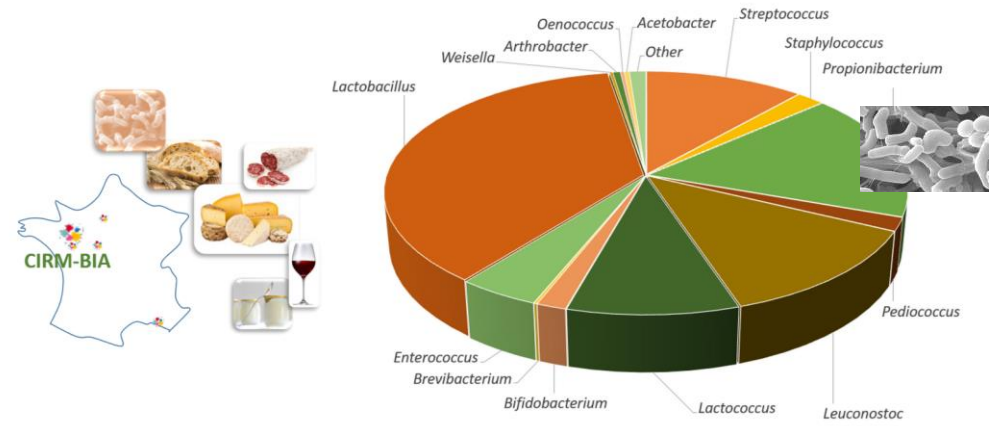
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# ➤ Many propionibacteria strains were collected



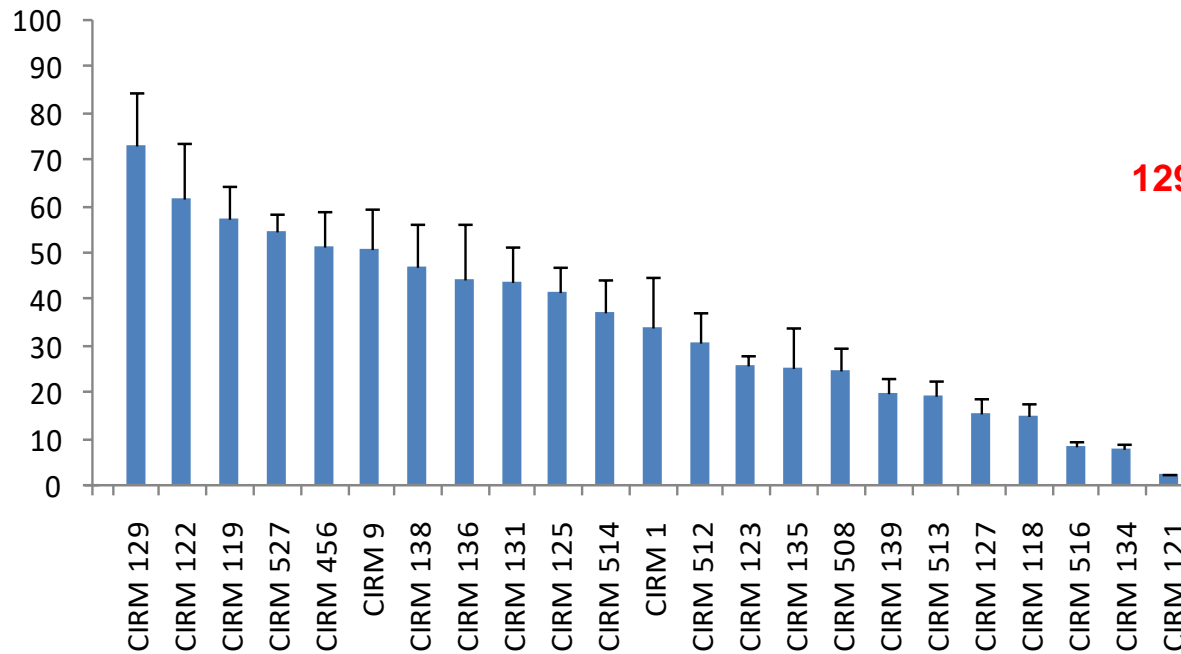
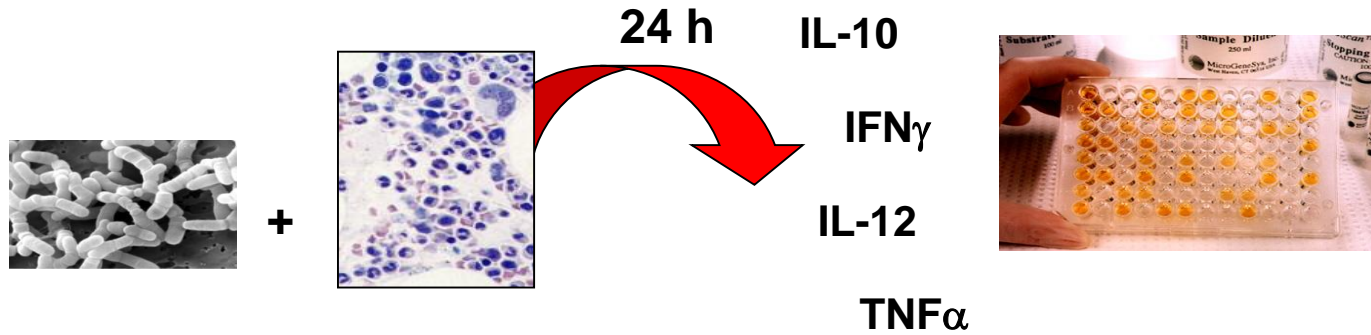
The CIRM-BIA Biological Resource Centre



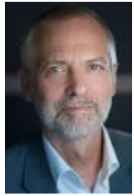
# ➤ Ready to be screened



# ➤ Screening on human immune cells: PBMCs



**129, The best anti-inflammatory strain**



Bruno Pot



Benoit Foligné



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## ➤ Test in colitis conditions

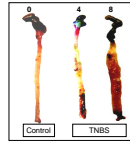
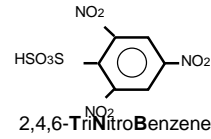
IBD

- GIT Chronic inflammation

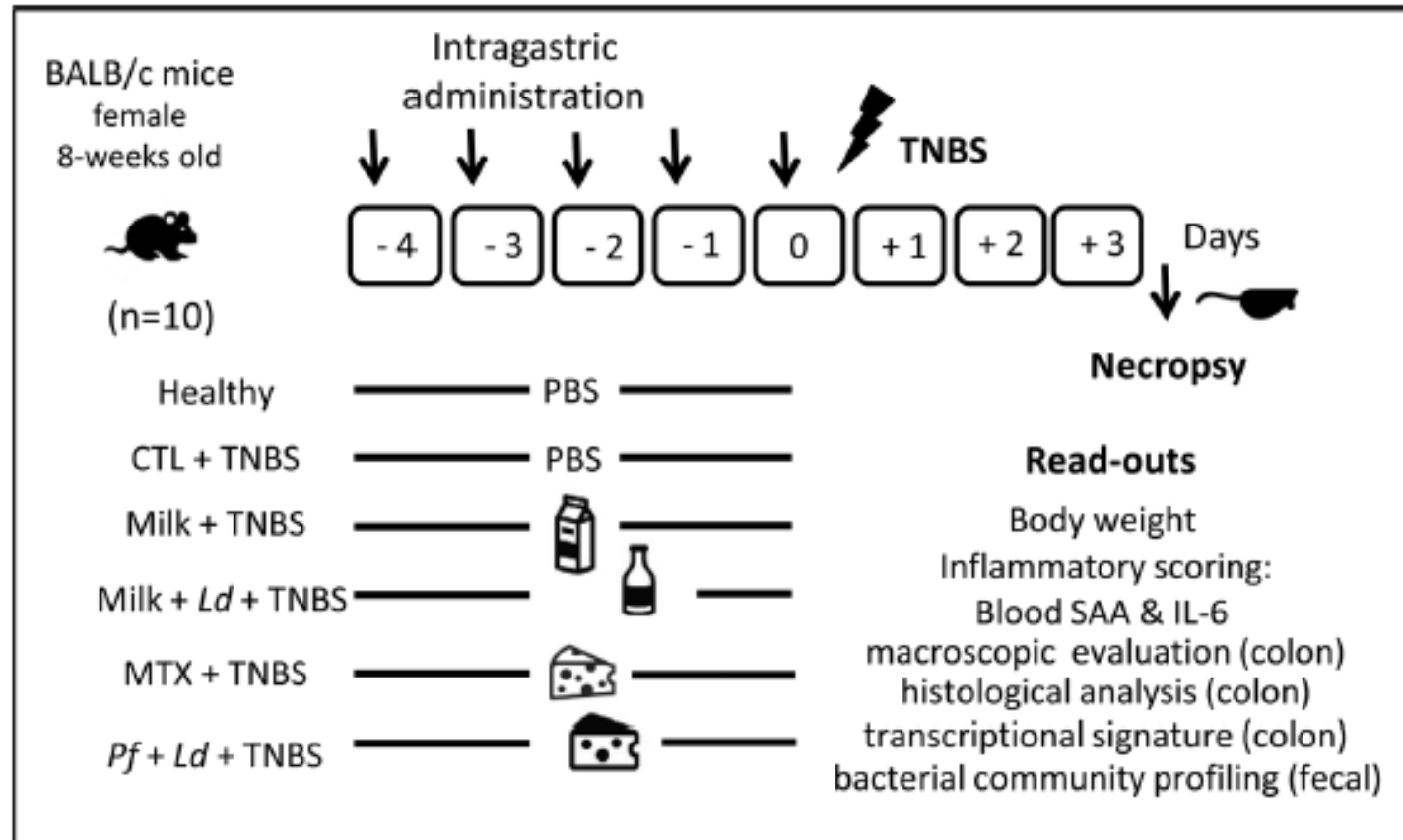
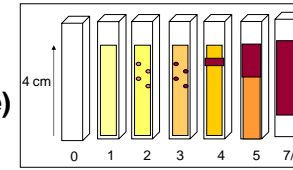
Ulcerative  
Colitis



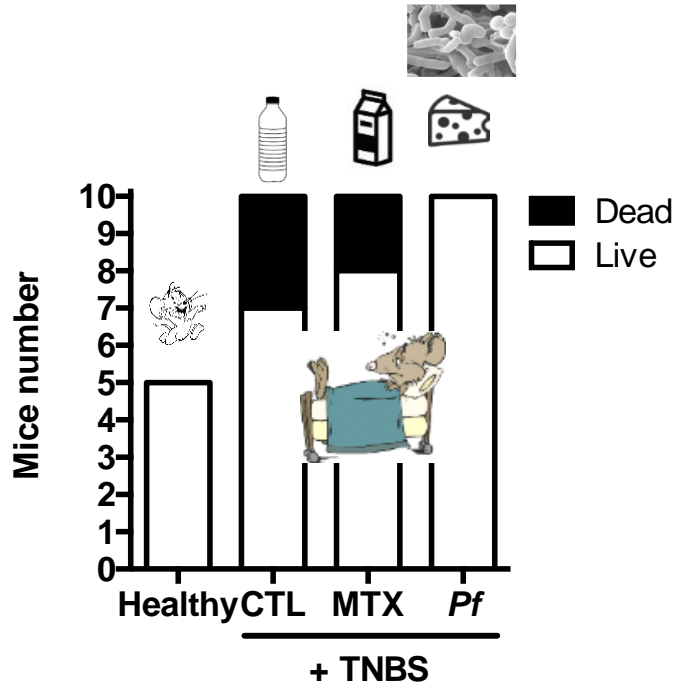
# ➤ In an acute colitis mice model induced by TNBS



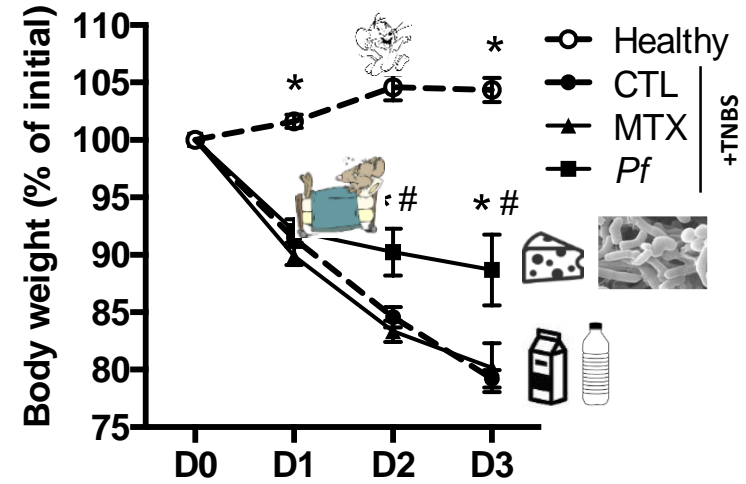
Macroscopic score (Wallace)



# ➤ *P. freudenreichii* mitigates TNBS-induced colitis in mice



Survival

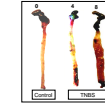
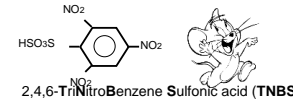
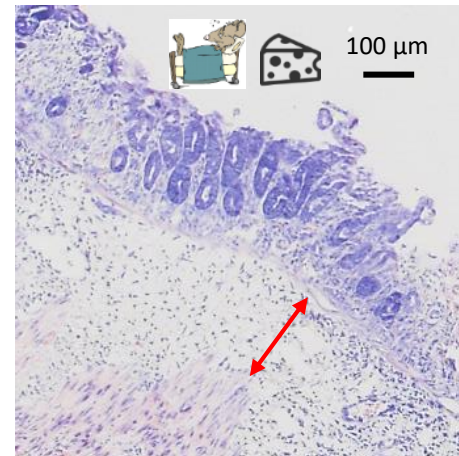
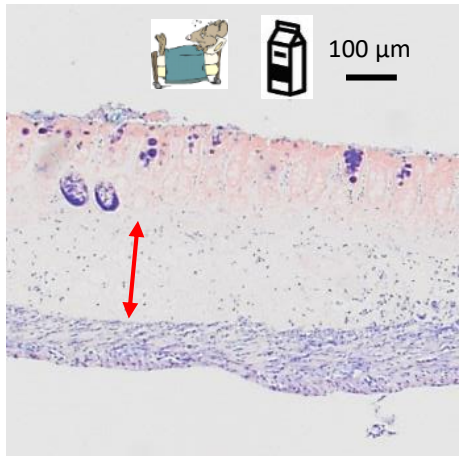
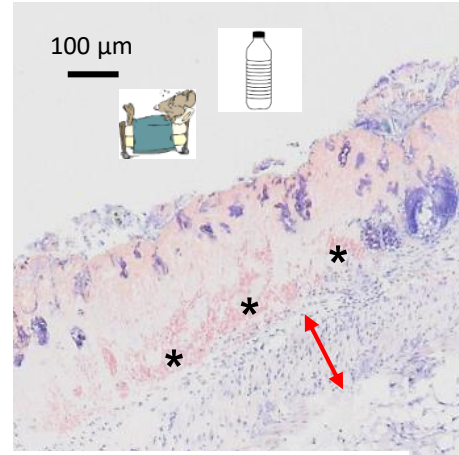
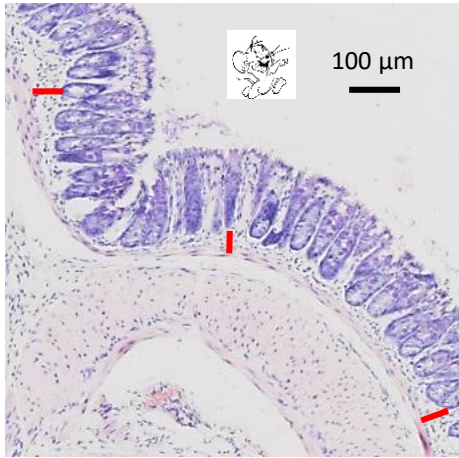


Body weight

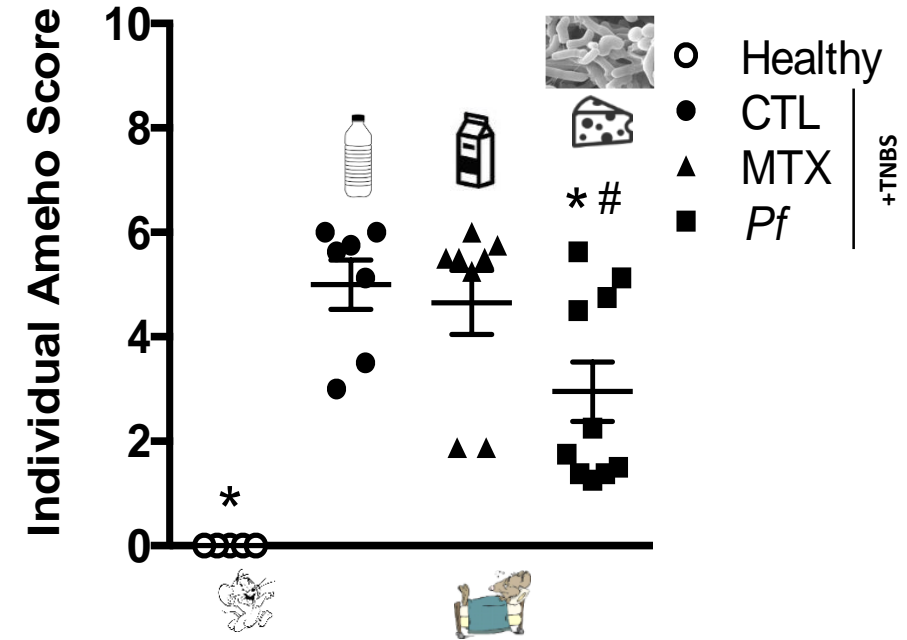
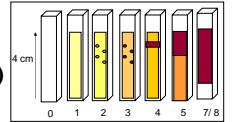




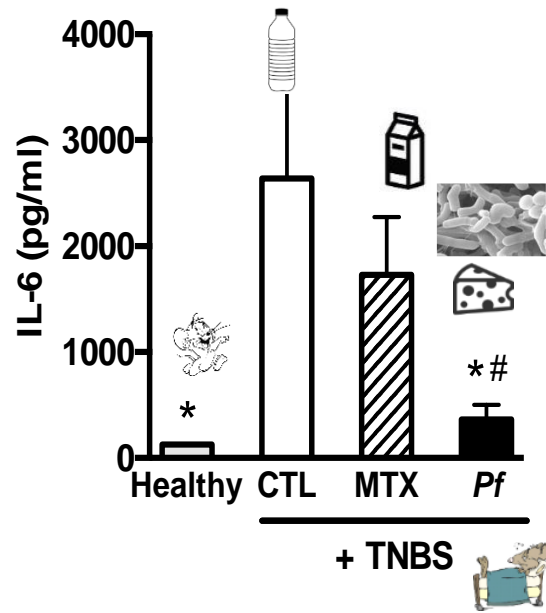
# ➤ *P. freudenreichii* mitigates TNBS-induced colitis in mice



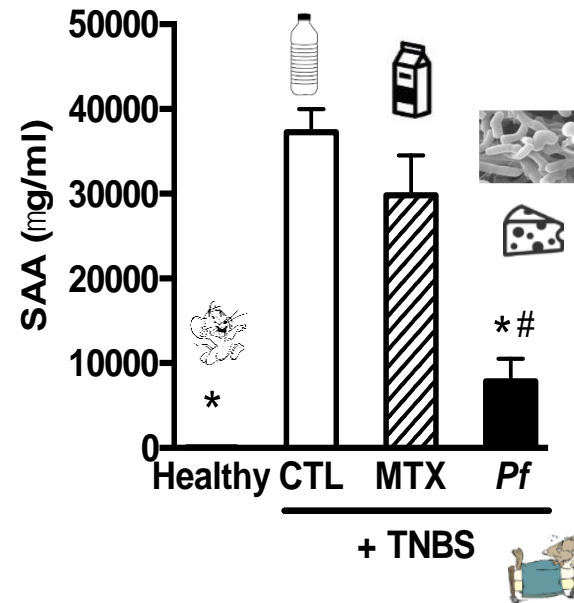
Macroscopic score (Wallace)



# ➤ *P. freudenreichii* mitigates blood inflammation markers



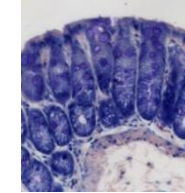
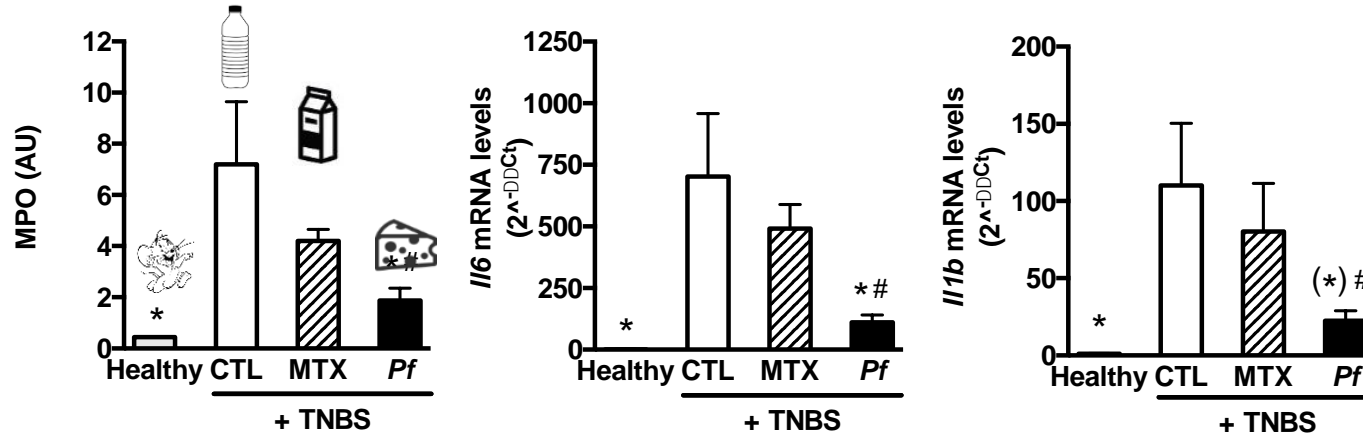
Interleukin 6



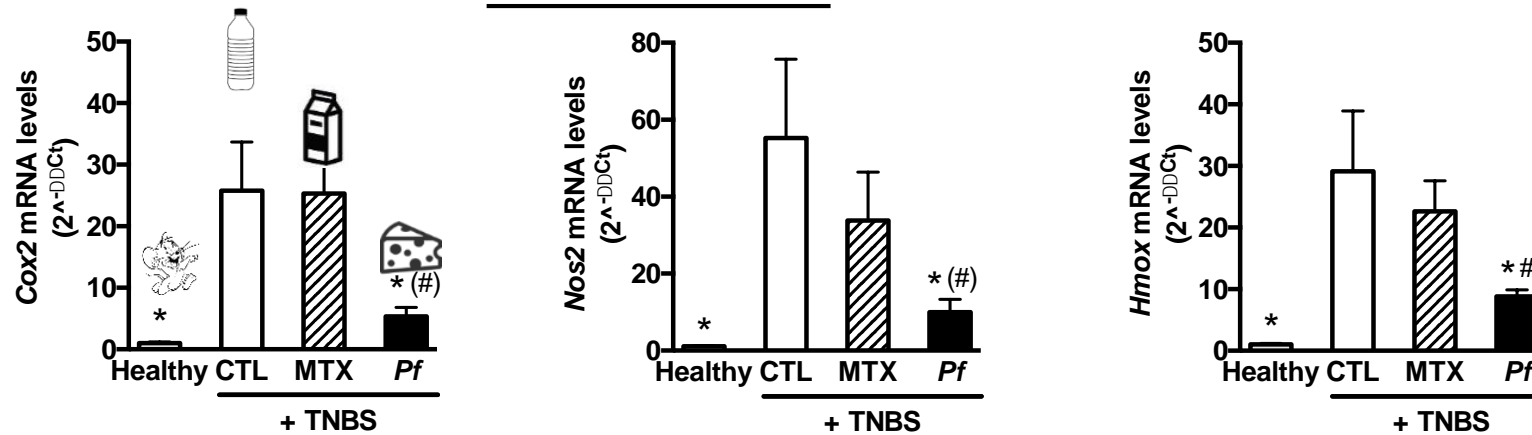
Serum Amyloid A

# ➤ *P. freudenreichii* mitigates colon inflammation markers

## Colonic inflammatory markers



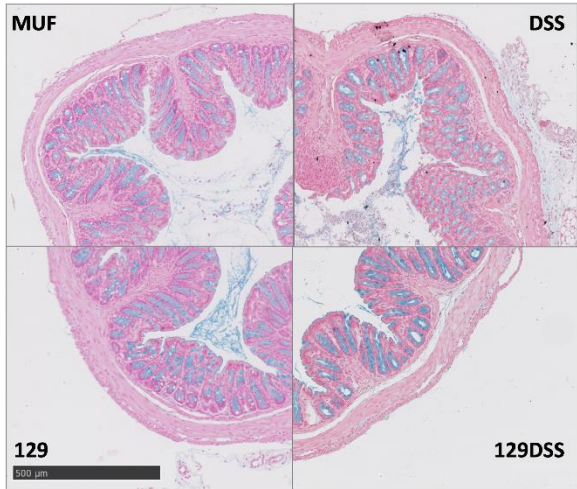
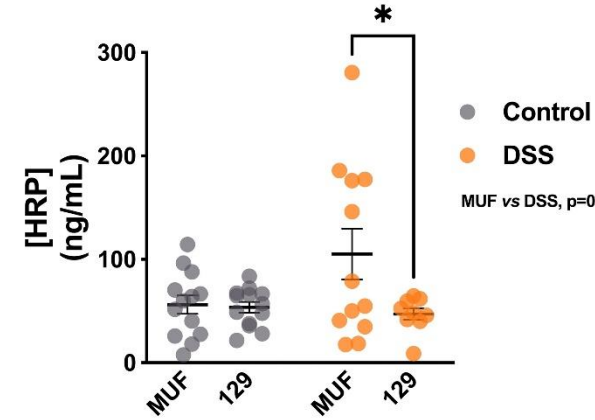
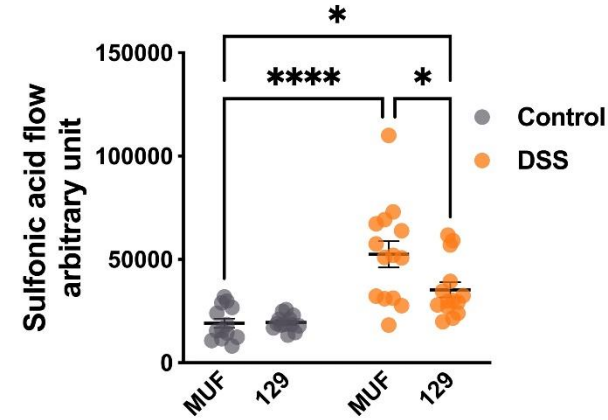
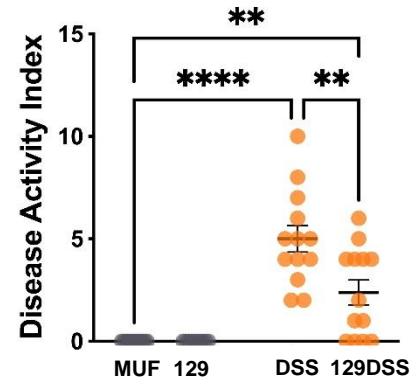
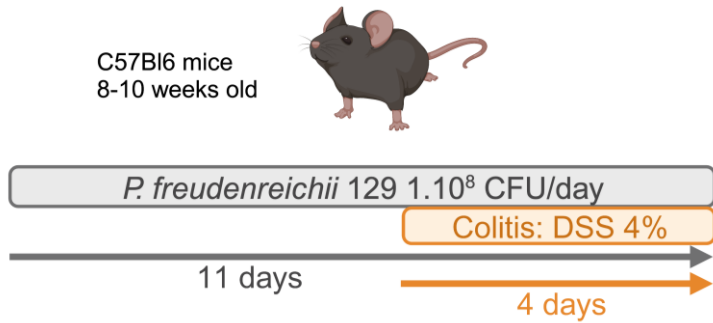
## Colonic oxidative stress markers



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



# ➤ *P. freudenreichii* protects gut architecture and integrity *in vivo*

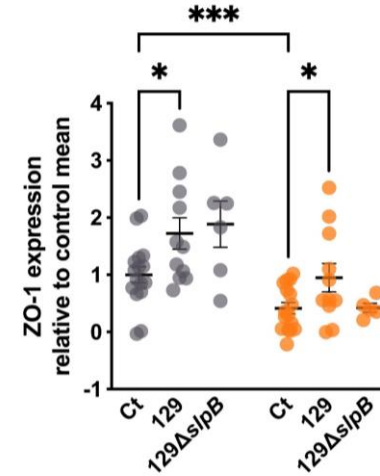
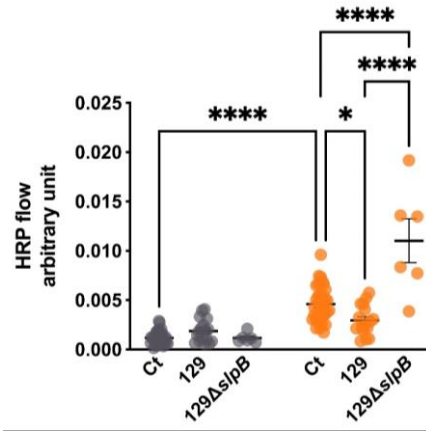
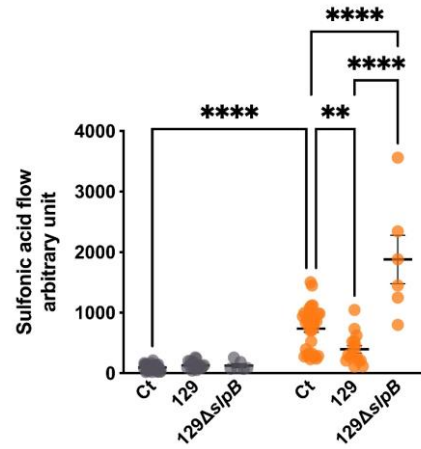
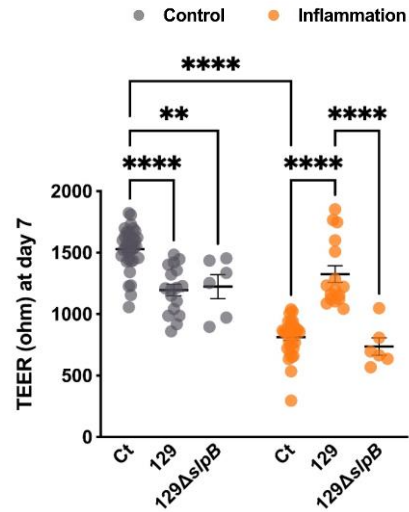
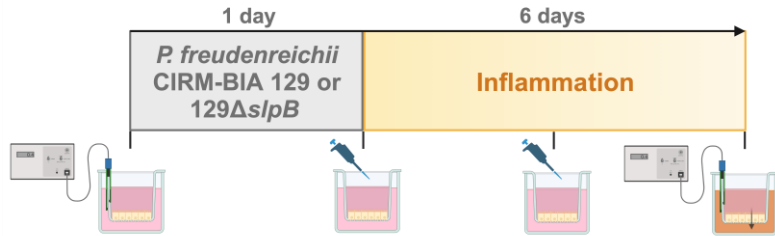


Malvyné Rolli-Derkinderen

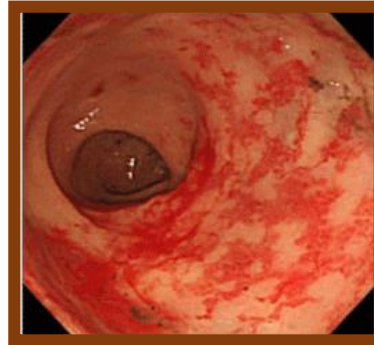


Marine Mantel

# ➤ *P. freudenreichii* protects intestinal epithelial barrier *in vitro*



# Mucositis



**GI Mucositis**



**Oral mucositis**

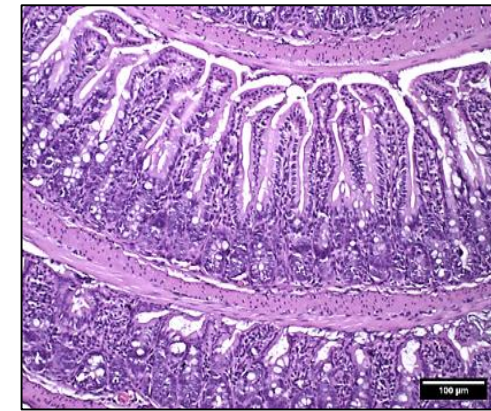
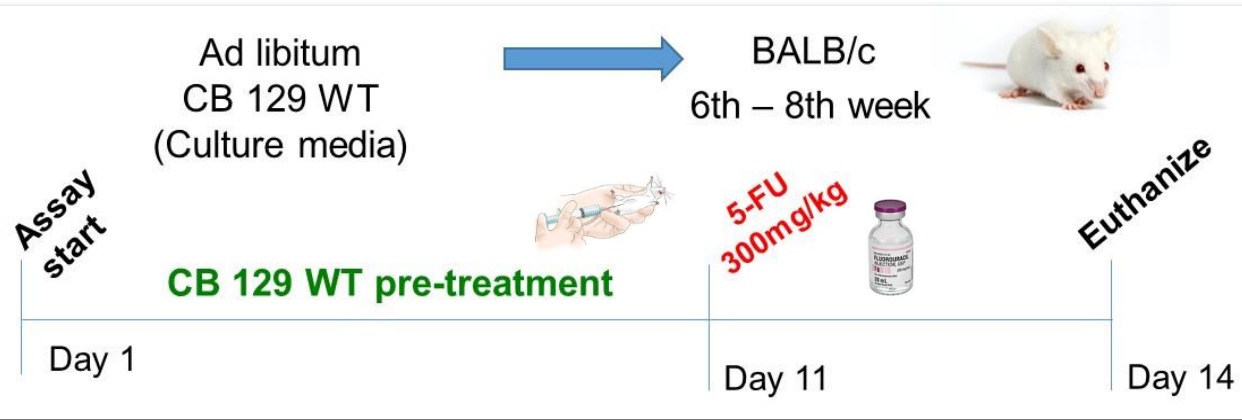
## 5-Fluoracil (5-FU)

- Head, neck and colon cancer.

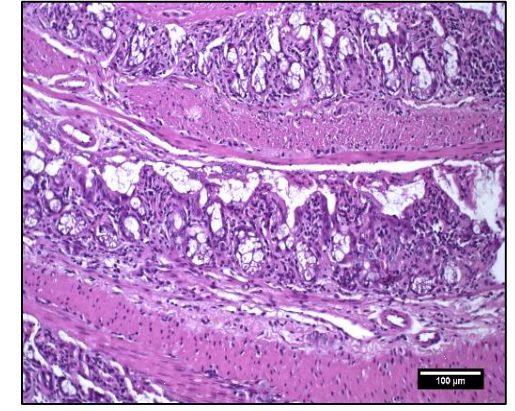
(Chang *et al.*, 2012; Falvey *et al.*, 2015)



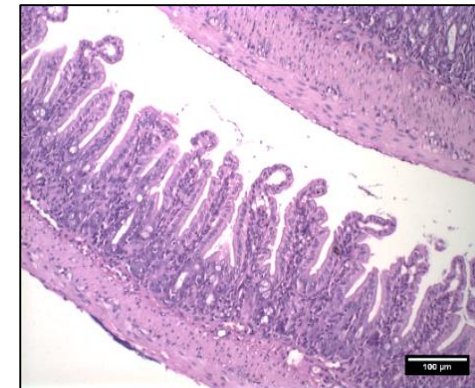
# ➤ Propionibacteria mitigate cancer chemotherapy-induced mucositis in mice



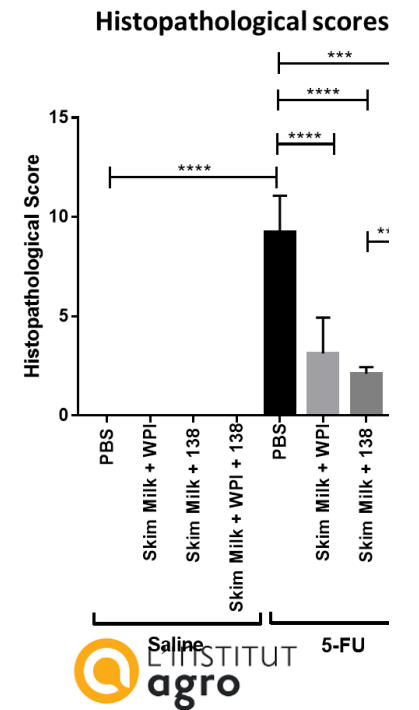
Healthy Ileum



PBS + 5-FU



Skim milk + propio



Vasco Azevedo

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UFMG

UNIVERSIDADE FEDERAL  
DE MINAS GERAIS

LGCM  
Laboratório de Genética  
Celular e Biotecnologia



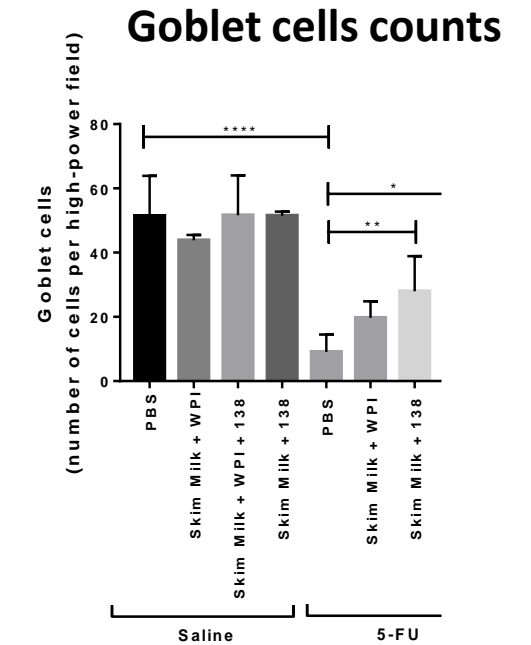
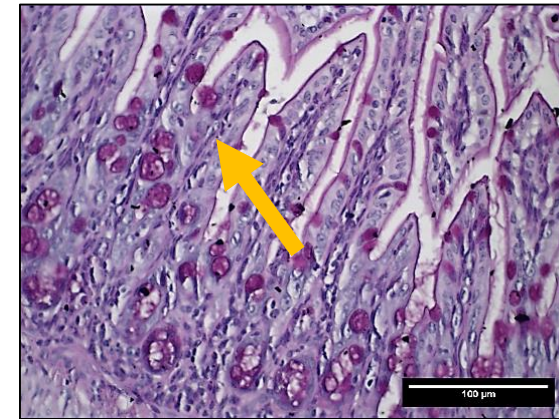
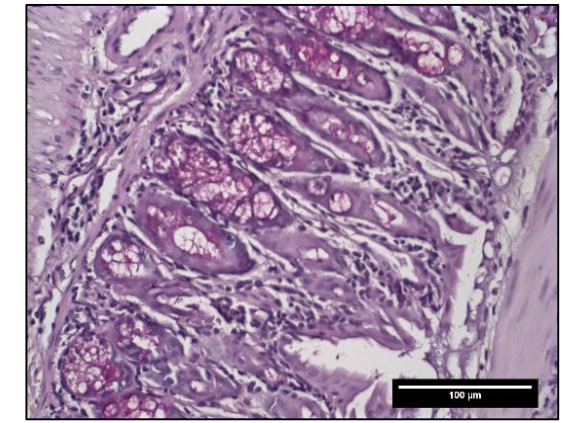
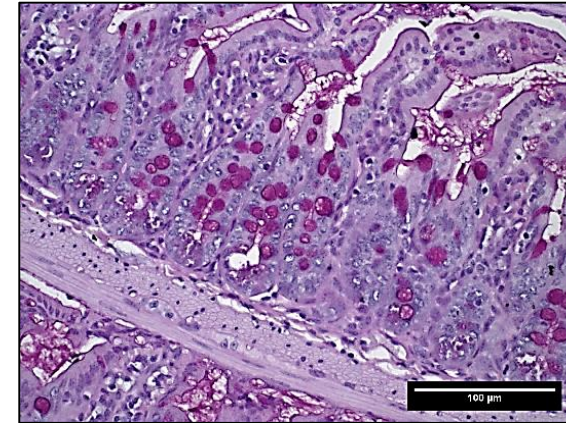
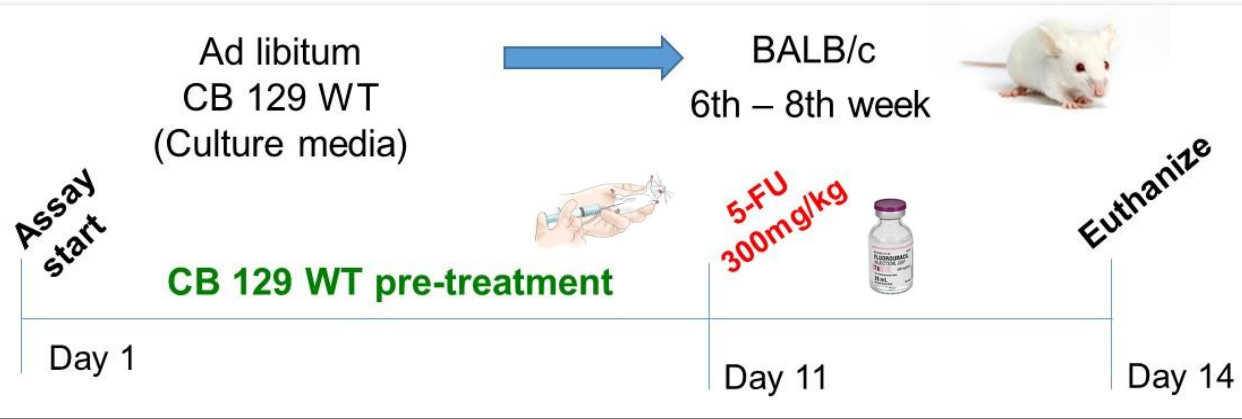
STLO

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agro



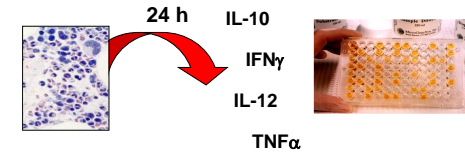
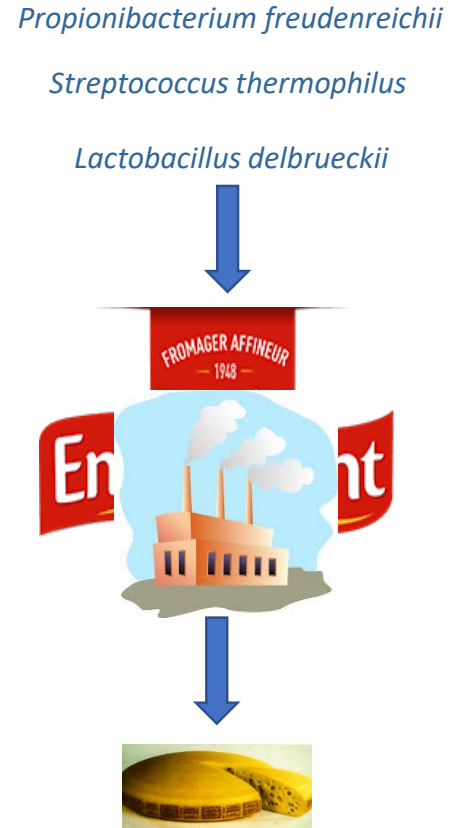
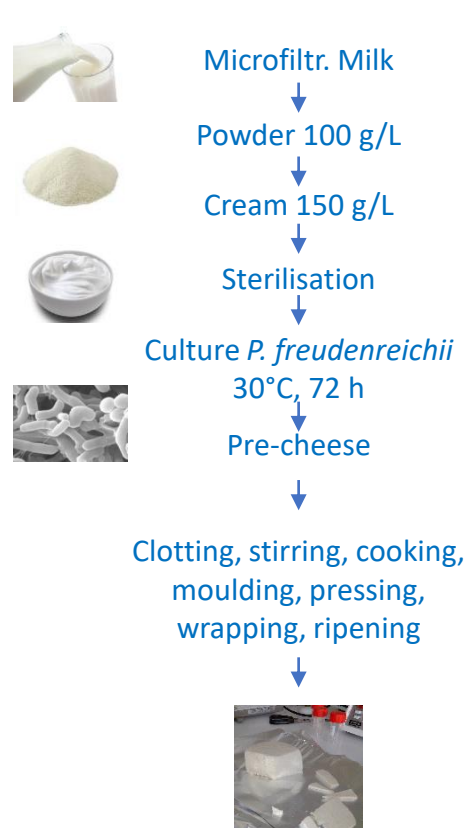
# ➤ Propionibacteria mitigate cancer chemotherapy-induced mucositis in mice



➤ OK, but this is pure culture of *P. freudenreichii*.....

➤ What about cheese?

# ➤ Model cheese or industrial cheese?



➤ Both!



# ➤ Propionibacteria: prevention of DSS-in

Emmental cheese with  
*P. freudenreichii*  
*S. thermophilus*  
*L. delbrueckii*

C57BL6  
8<sup>th</sup> week age



1<sup>st</sup> Day



5<sup>th</sup> Day

12<sup>th</sup> Day

Intragastric gavage

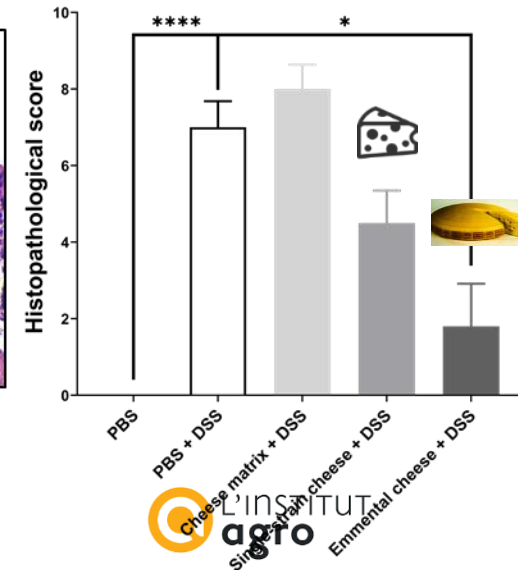
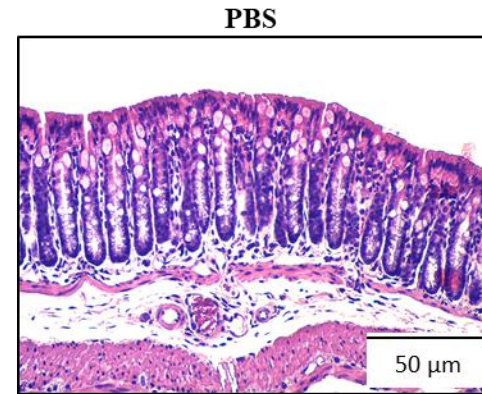
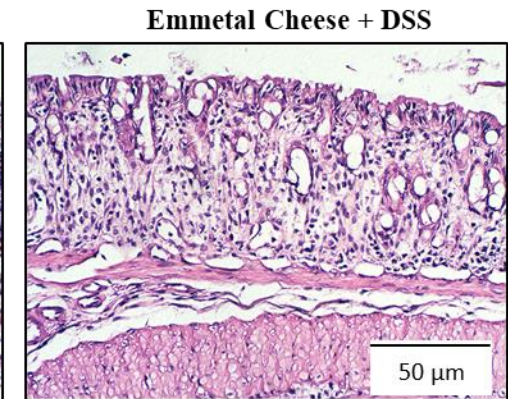
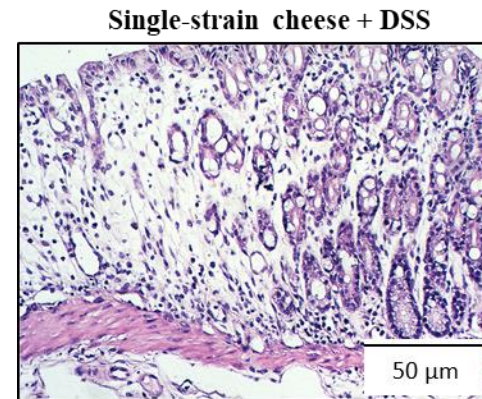
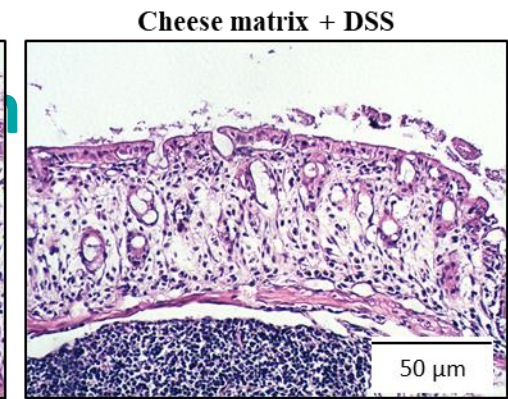
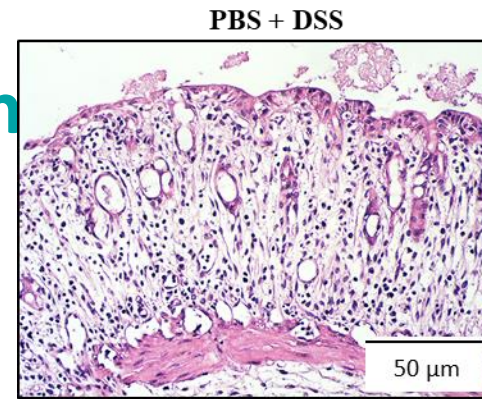
Gavage 500  $\mu$ L  
(400 mg cheese in  
500  $\mu$ L PBS pH 7.4)

3% (w/v) DSS solution  
(36–50 25 kDa)

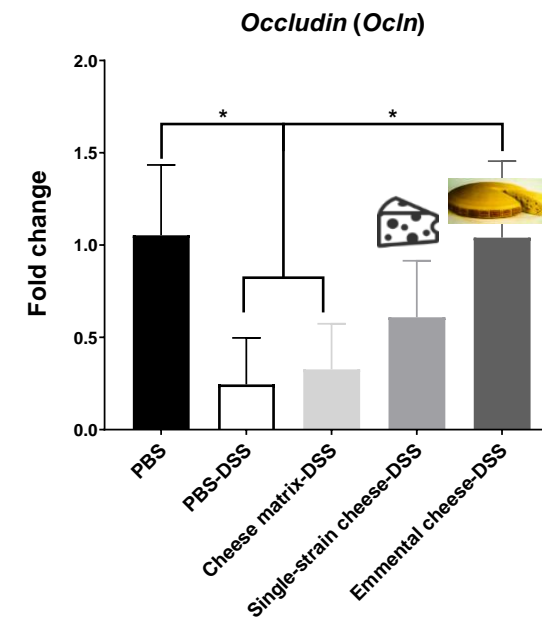
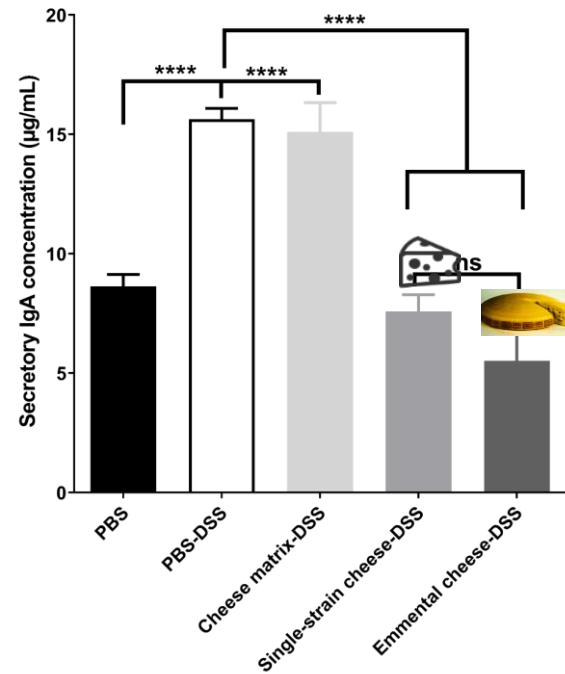
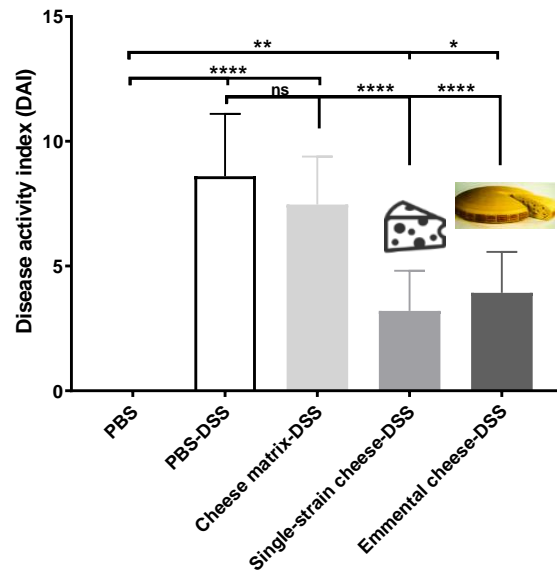
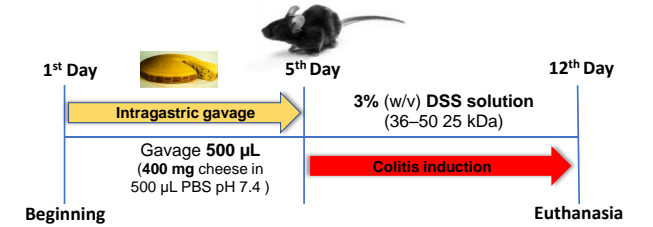
Colitis induction

Beginning

Euthanasia



# ➤ Propionibacteria: prevention of DSS-induced colitis in mice



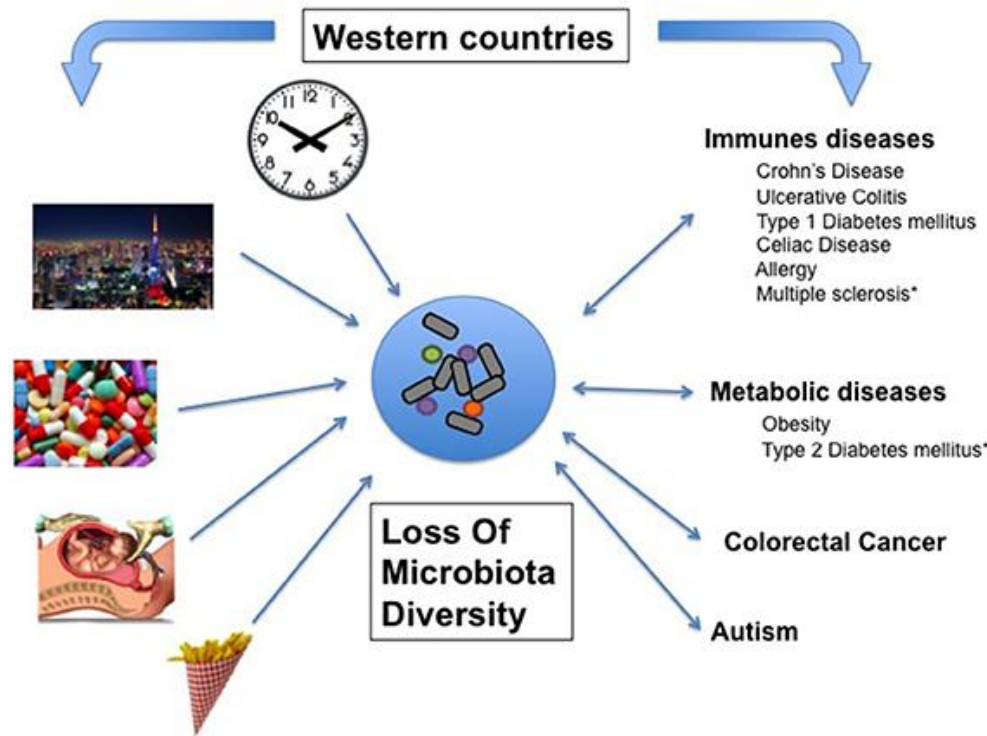




- **Propionibacteria: strain-dependent immunomodulatory properties**
- **Mitigate the pro-inflammatory response**
- **Protect IEB integrity**
- **Propionibacteria and Emmental cheese, a perspective to help IBD treatment ?**



# ➤ Loss of gut microbial diversity



Mosca et al. Front. Microbiol. (2016)

Disease	LOMD	References	Increased prevalence in western countries	References
<b>IMMUNE DISEASES</b>				
Crohn's Disease	+	Manichanh et al., 2006; Dey et al., 2013; Sha et al., 2013; Matsuoka and Kanai, 2015	+	Lehtinen et al., 2011
Ulcerative Colitis	+	Michail et al., 2012; Sha et al., 2013	+	Lehtinen et al., 2011
Type 1 diabetes mellitus	+	Giongo et al., 2010; De Goffau et al., 2013; Kostic et al., 2015	+	Harjutsalo et al., 2008; Andersson et al., 2014
Multiple Sclerosis	ND	Bhargava and Mowry, 2014	+	Mayr et al., 2003
Celiac Disease	+	Schippa et al., 2010	+	Lohi et al., 2007
Allergy	+	Wang et al., 2008; Ismail et al., 2012; Abrahamsson et al., 2014	+	Latvala et al., 2005; Eder et al., 2006
<b>METABOLIC DISEASES</b>				
Obesity	+	Turnbaugh et al., 2009	+	WHO   Obesity and overweight
Type 2 diabetes mellitus	-		+	WHO   Diabetes
<b>CANCER</b>				
Colorectal cancer	+	Ahn et al., 2013	+	European Cancer Observatory <a href="http://eco.iarc.fr/">http://eco.iarc.fr/</a>
<b>OTHERS</b>				
Irritable Bowel Syndrome	+	Carroll et al., 2012; Durbán et al., 2012	-	Lovell and Ford, 2012
Recurrent <i>Clostridium difficile</i> Infection	+	Chang et al., 2008	ND	
Autism	+	Kang et al., 2013	+	Atladdottir et al., 2015
Necrotising Enterocolitis	+	Stewart et al., 2013	ND	
Graft Versus Host Disease	+	Jenq et al., 2012	ND	

WHO | Diabetes WHO. Available at: <http://www.who.int/mediacentre/factsheets/fs312/en/> [Accessed September 29, 2015].

WHO | Obesity and overweight WHO. Available at: <http://www.who.int/mediacentre/factsheets/fs311/en/> [Accessed September 29, 2015].  
ND, No Data.

## ➤ Any link with a loss of microbial diversity in our food?



# INRAE

➤ Thank you for your attention!  
Any kind question?



Bruno Pot



Benoit Foligné



Malvyne Rolli-Derkinderen



Marine Mantel



Vasco Azevedo, UFMG, Brazil

