HAL open science

The dairy bacterium Propionibacterium freudenreichii against colitis and mucositis: a key role of the surface layer protein SlpB

Gwénaël Jan, Benoît Foligné, Fillipe Luiz Rosa Do Carmo, Houem Rabah, Floriane Gaucher, Vasco Azevedo, Eric Guédon

To cite this version:

Gwénaël Jan, Benoît Foligné, Fillipe Luiz Rosa Do Carmo, Houem Rabah, Floriane Gaucher, et al.. The dairy bacterium Propionibacterium freudenreichii against colitis and mucositis: a key role of the surface layer protein SlpB. FoodMicro 2022, Aug 2022, Athènes, Greece. hal-03781529

HAL Id: hal-03781529

https://hal.inrae.fr/hal-03781529

Submitted on 20 Sep 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Distributed under a Creative Commons Attribution - NonCommercial - NoDerivatives 4.0 International License

The dairy probiotic bacterium *Propionibacterium freudenreichii* against colitis and mucositis: a key role of the surface layer protein SlpB

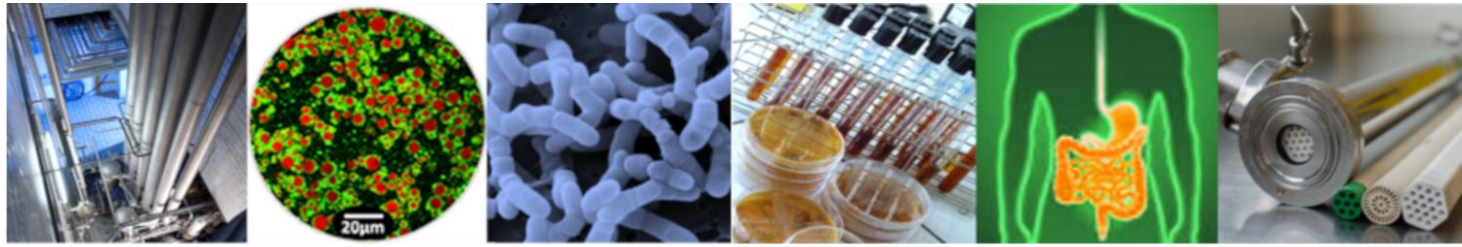
Gwénaël JAN

STLO, INRAE, Institut Agro, Science et Technologie du Lait et de l'Œuf, Rennes

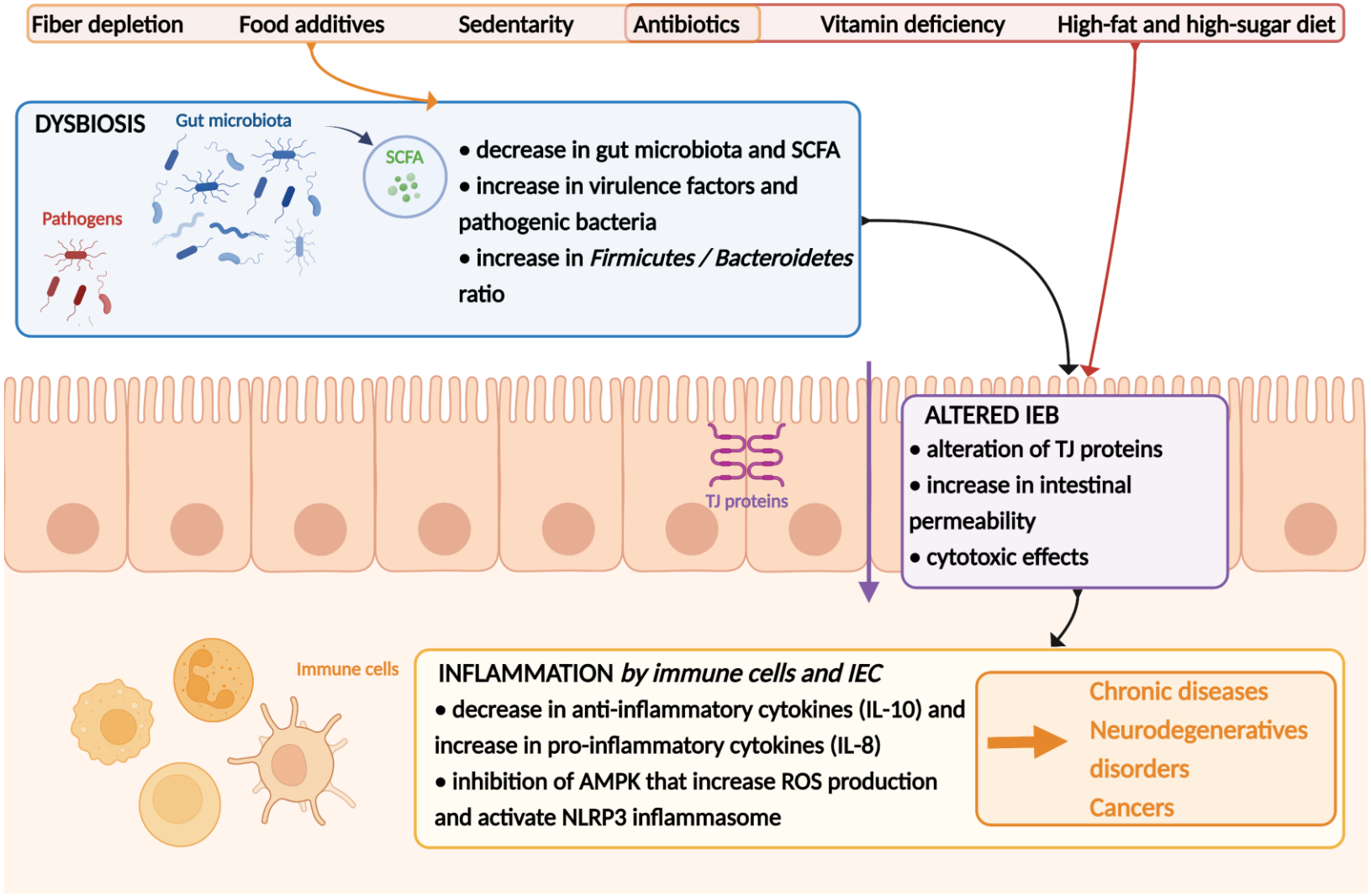
gwenael.jan@inrae.fr@inrae.fr

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

Intestinal epithelial barrier: endangered…



… By modern lifestyle



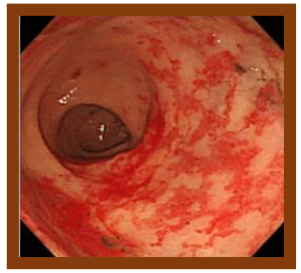
Examples of digestive inflammatory diseases

Colitis

- GIT Chronic inflammation

Ulcerative Colitis

Mucositis



GI Mucositis

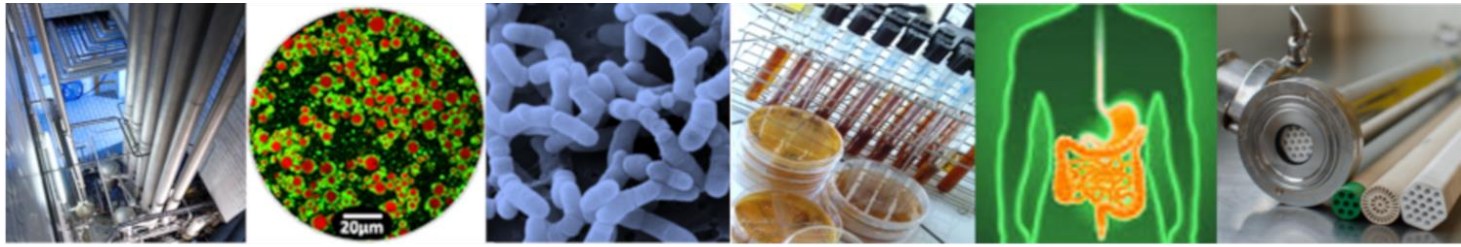
Oral mucositis

5-Fluoracil (5-FU)

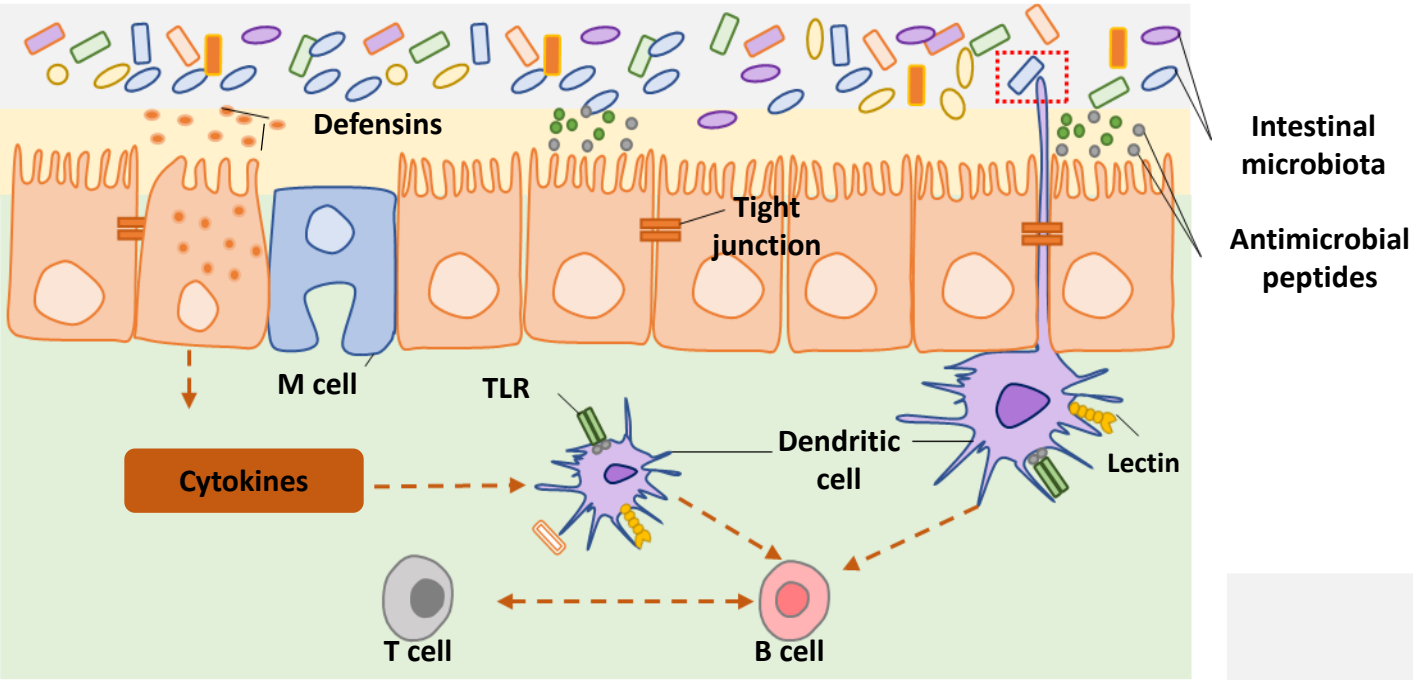
- Head, neck and colon cancer.

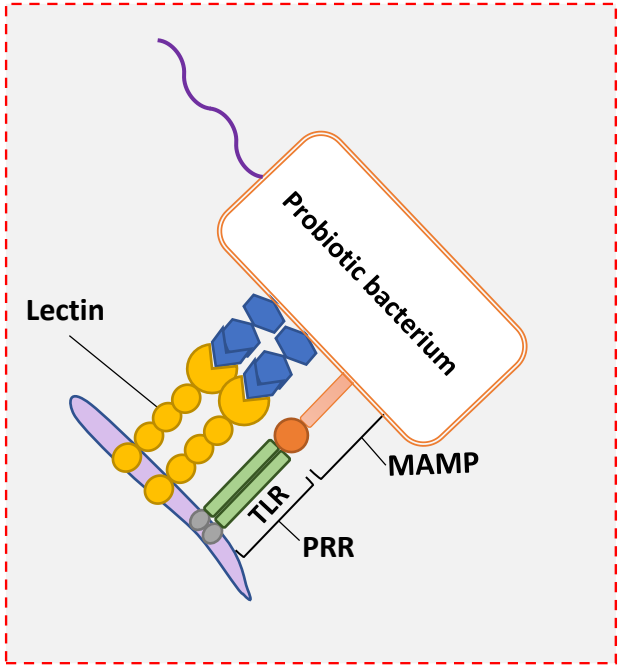
(Chang *et al*., 2012; Falvey *et al*., 2015)

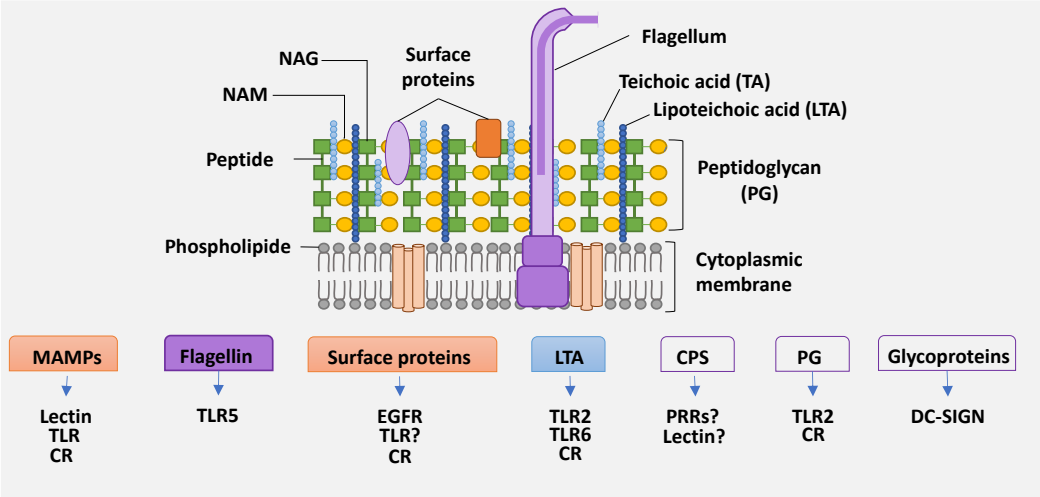
A key role of resident and ingested microorganisms…



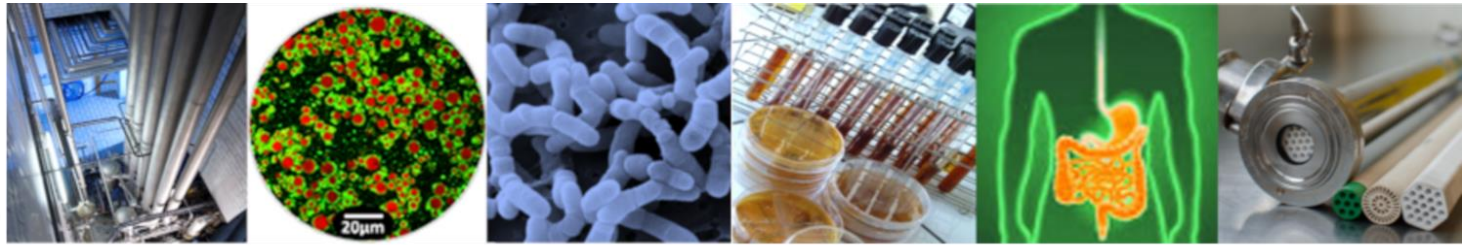
… Modulating the immune response



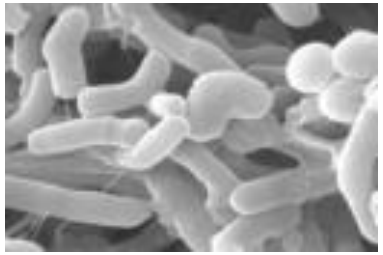




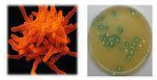
Introducing *Propionibacterium freudenreichii*…

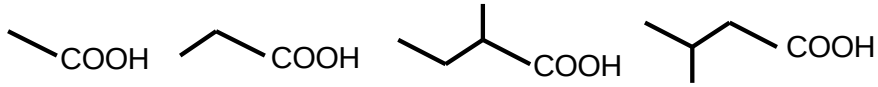


… A sort of Swiss army knife



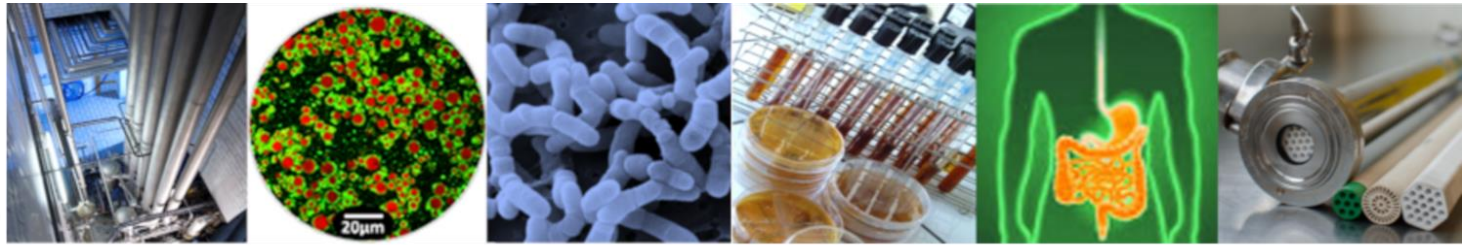
Propionibacterium freudenreichii

- ➔ Actinobacterium 
- ➔ Vitamin producer B9, B12
- ➔ Probiotic
- ➔ Food bio-preservative
- ➔ Ripening starter
- ➔ Short chain fatty acids



Short Chain Fatty Acids (SCFA)
Known effect on health

Immunomodulatory properties

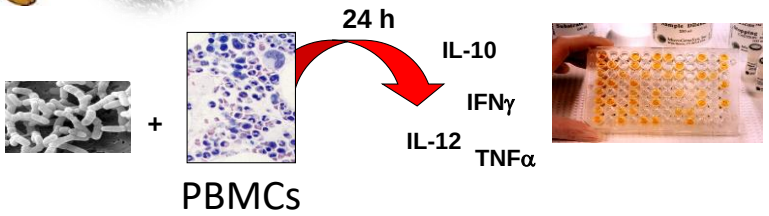


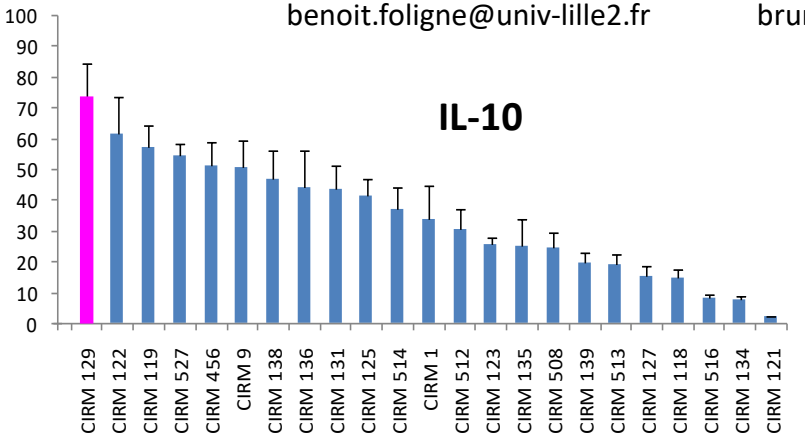
… *In vitro* and *in vivo*

benoit.foligne@univ-lille2.fr

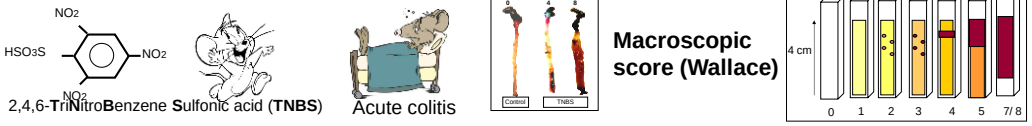
bruno.pot1@telenet.be

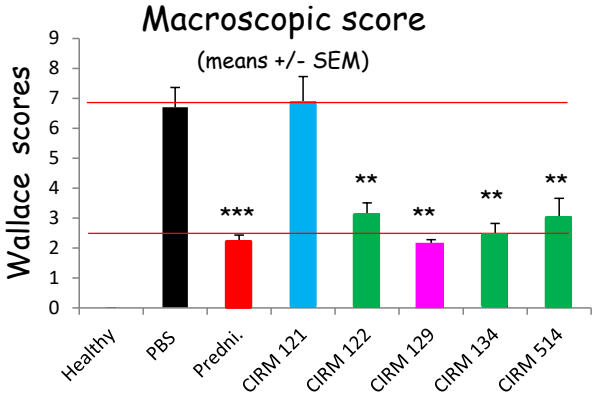
♦ *In vitro*





♦ *In vivo*





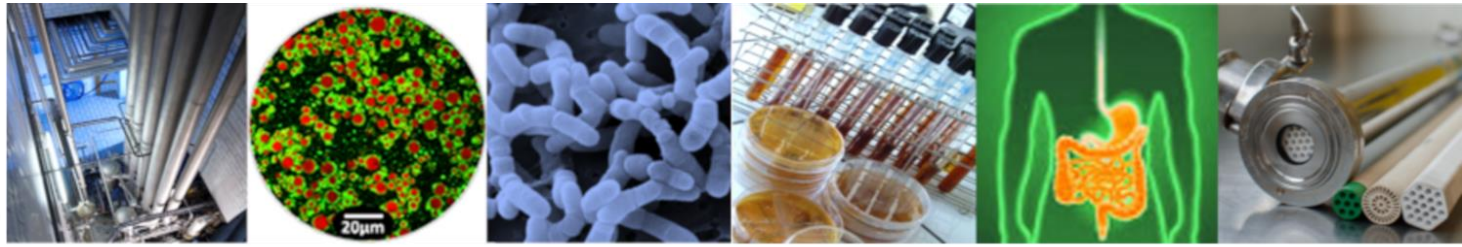
SURFING
Starter Surface against Inflammation of the Gut

CIIL
CENTER FOR INFECTION & IMMUNITY OF LILLE

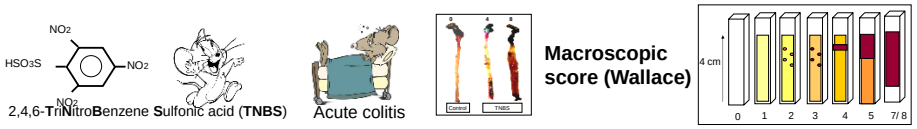
INRAE

Cniel · iD2Santé · STLO · Nutrition Santé Longévité · Région Bretagne · ACTALIA · Valorial · ANR · Institut Pasteur de Lille

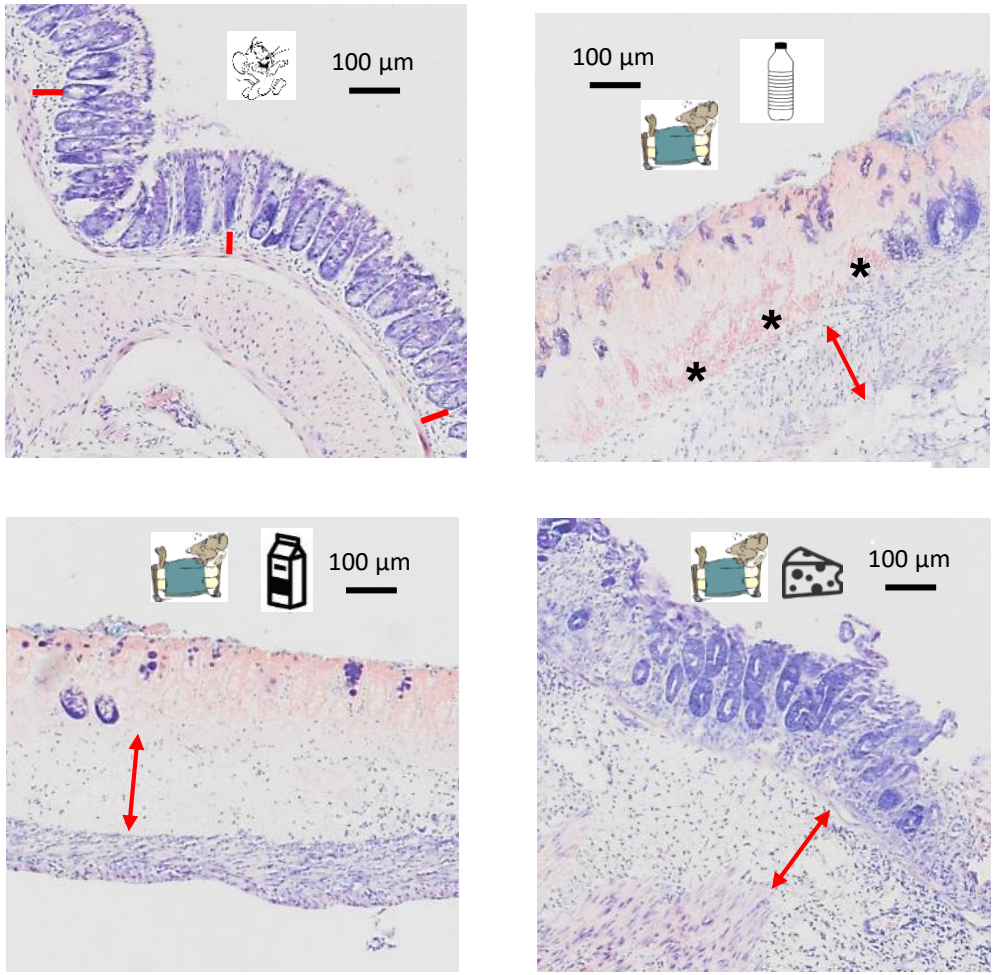
The healing effect of *Propionibacterium freudenreichii*

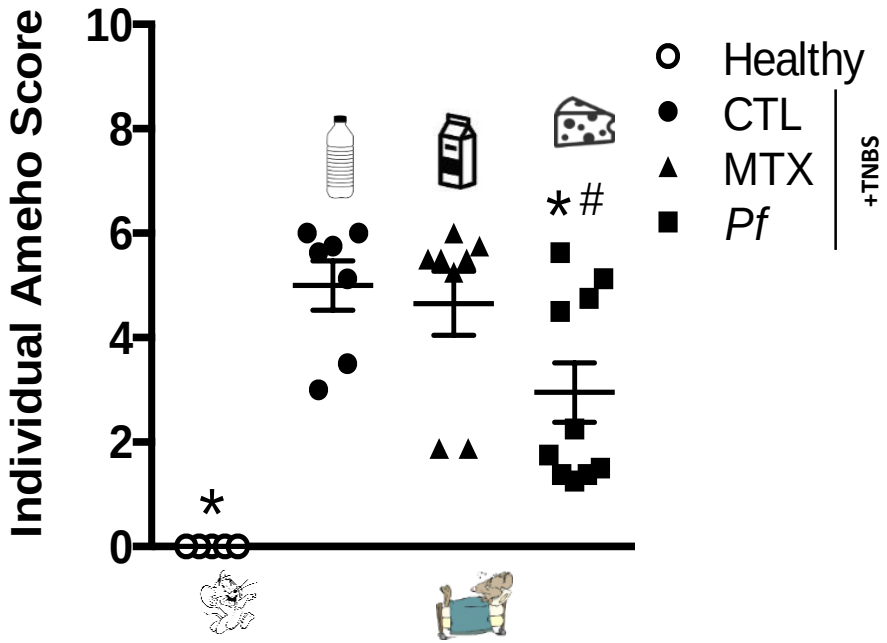


In TNBS-induced colitis



A model cheese





In DSS-induced colitis

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

C57BL6
8th week age

1st Day

5th Day

12th Day

Intragastric gavage

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

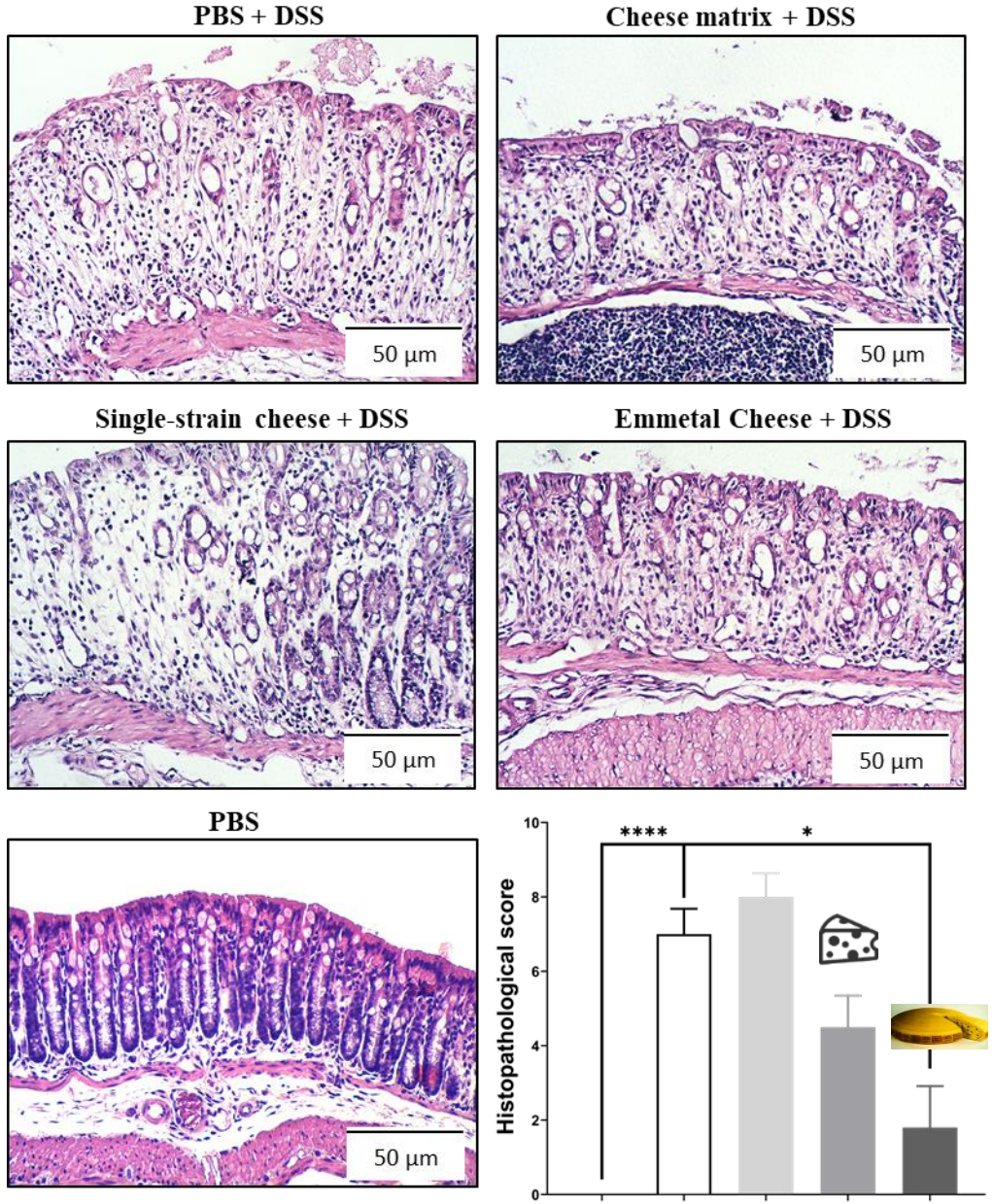
Gavage **500 µL**
(**400 mg** cheese in
500 µL PBS pH 7.4)

Colitis induction

Beginning

Euthanasia

Vasco Azevedo



In DSS-induced colitis

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

C57BL6
8th week age

1st Day — **5th Day** — **12th Day**

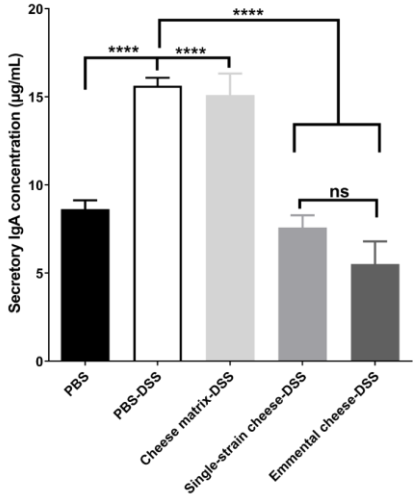
Intragastric gavage

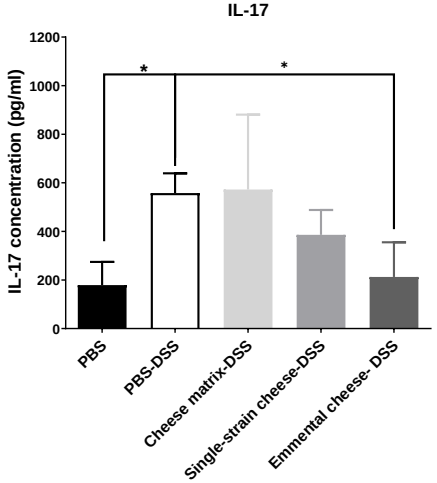
Gavage **500 µL**
(**400 mg** cheese in
500 µL PBS pH 7.4)

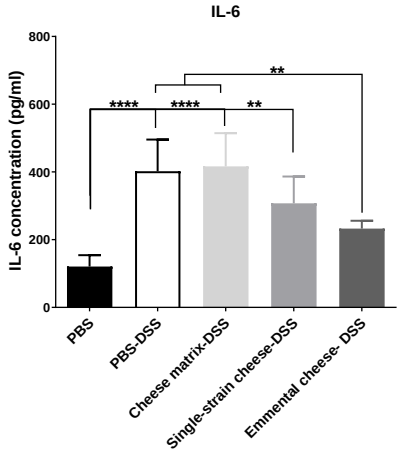
3% (w/v) **DSS solution**
(36–50 25 kDa)

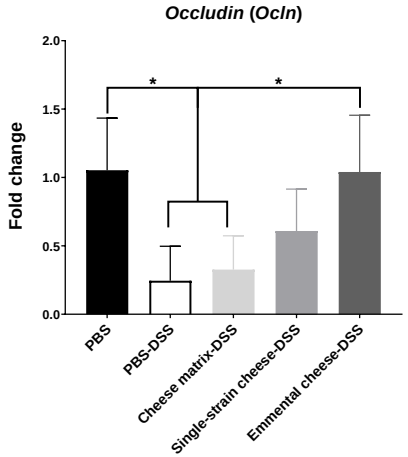
Colitis induction

Beginning — **Euthanasia**

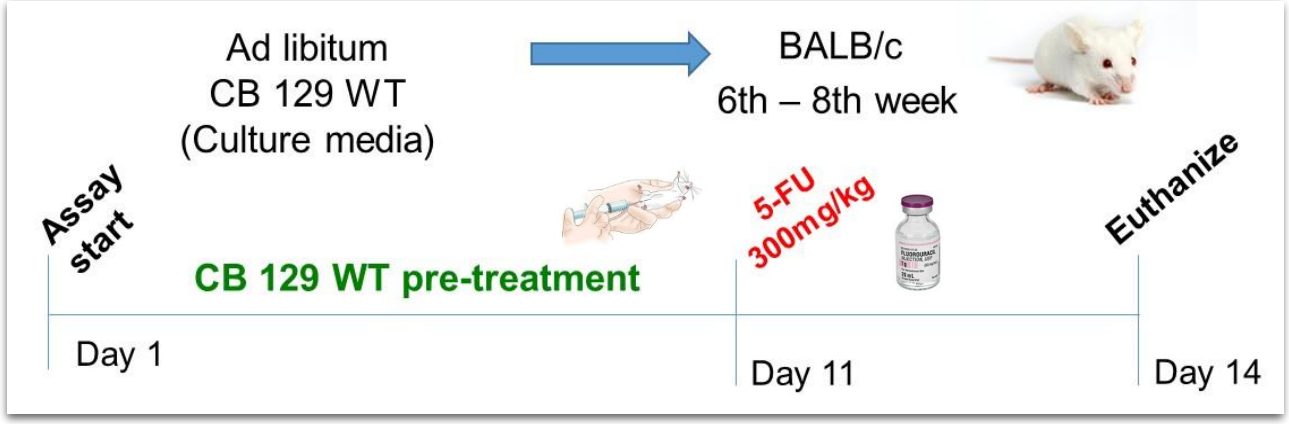




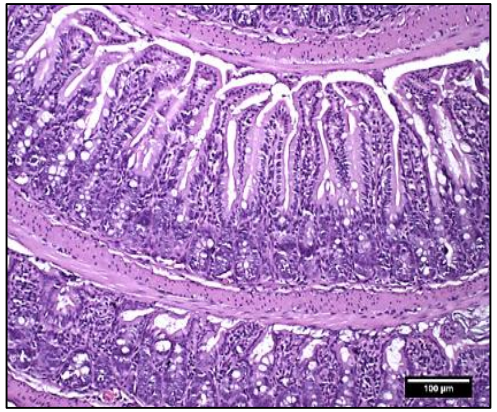




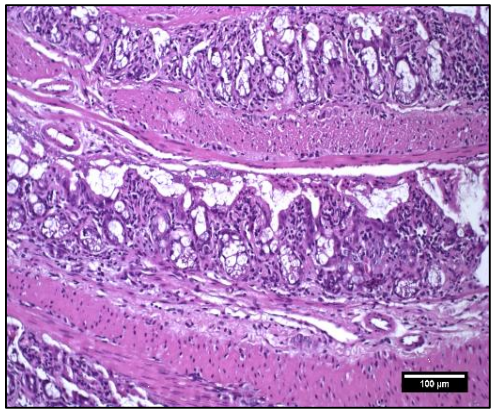
In 5FU-induced mucositis



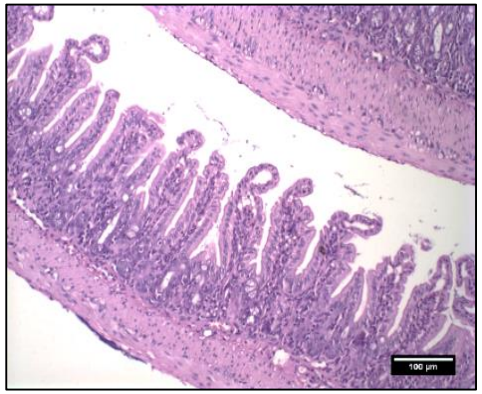
Representative images from mucosal histopathology (H&E)



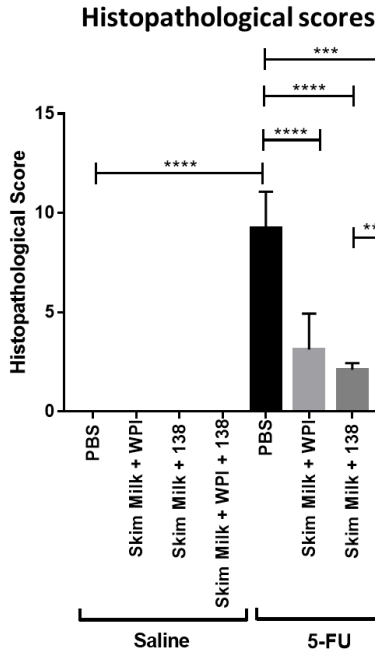
Healthy Ileum



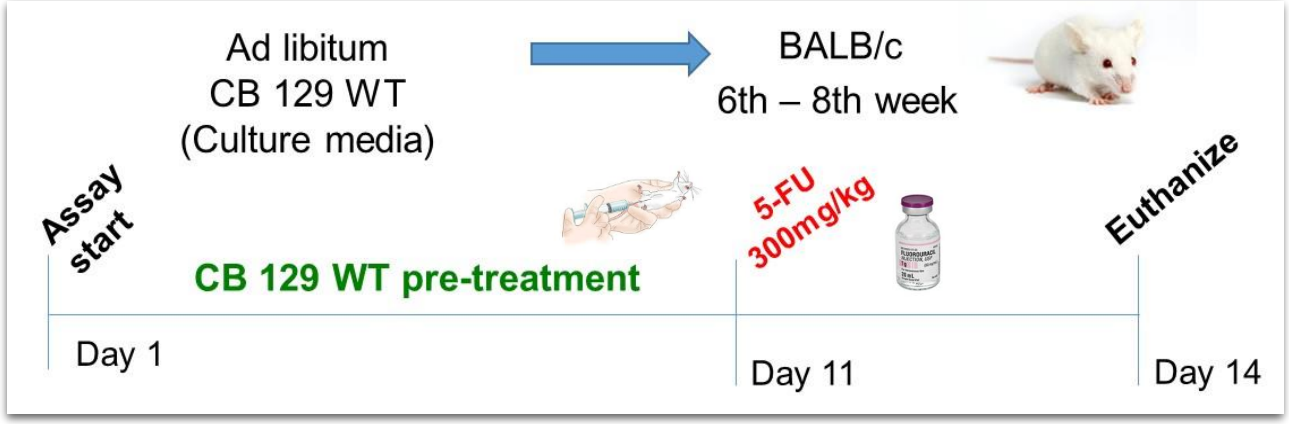
PBS + 5-FU



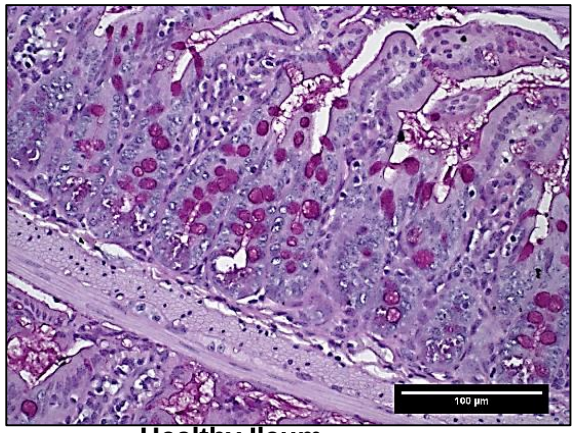
Skim milk + propio



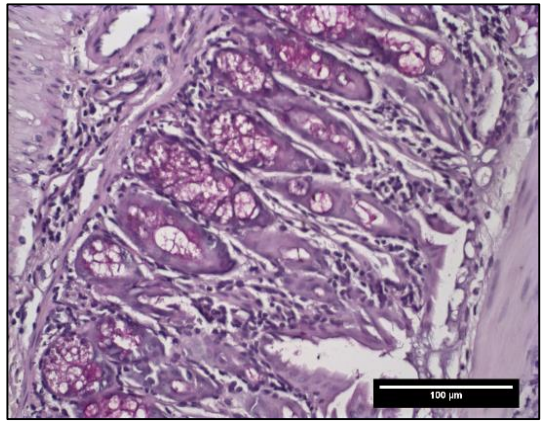
In 5FU-induced mucositis



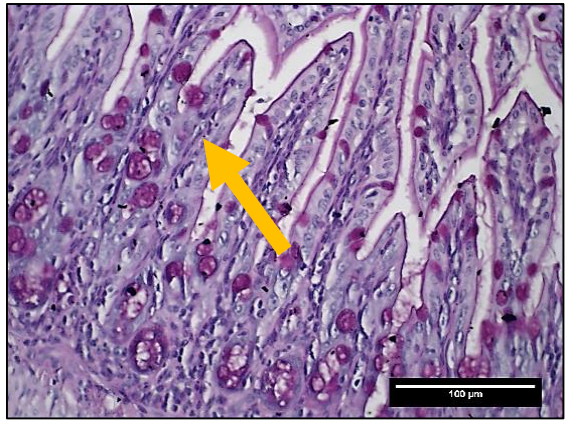
Representative images of stained goblet cells (PAS)



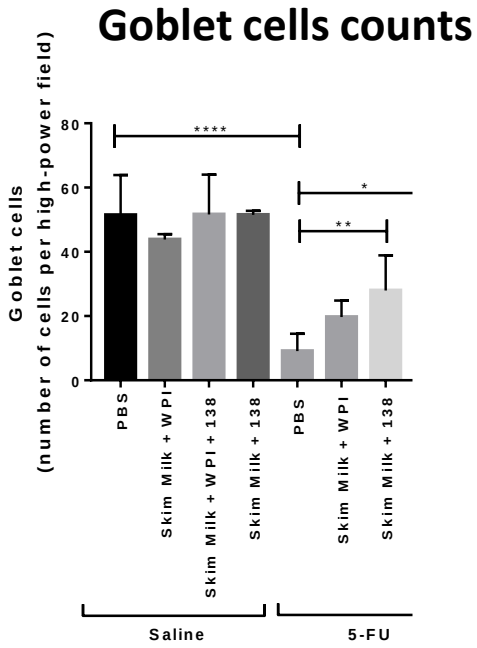
Healthy Ileum



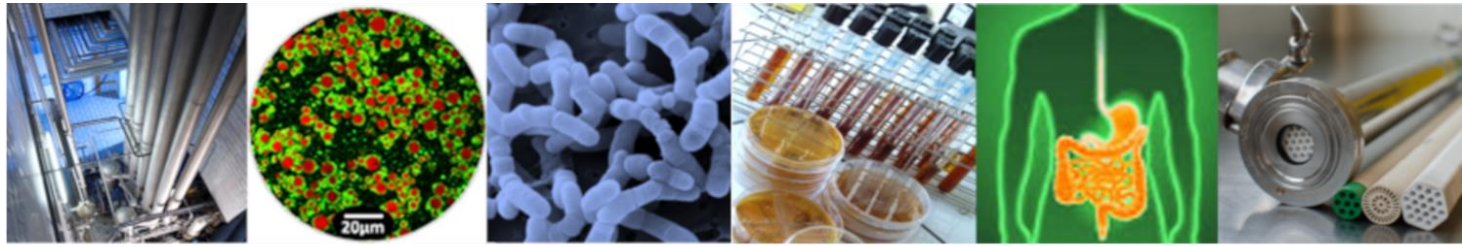
PBS + 5FU



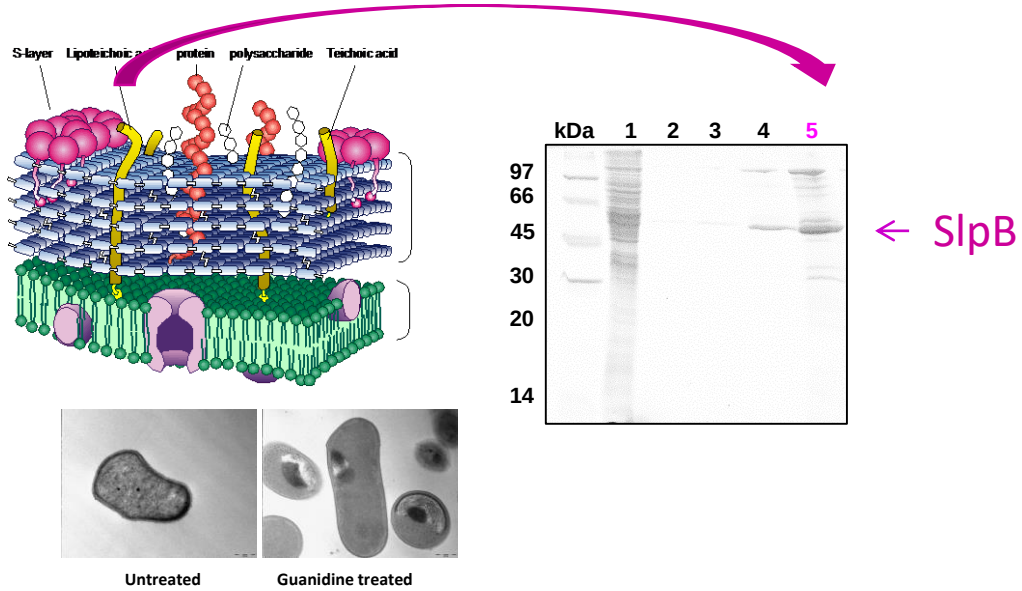
LDF + 138 + 5FU

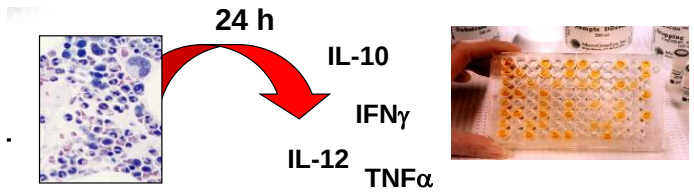


How does it work?



If we remove surface proteins: PBMC assay





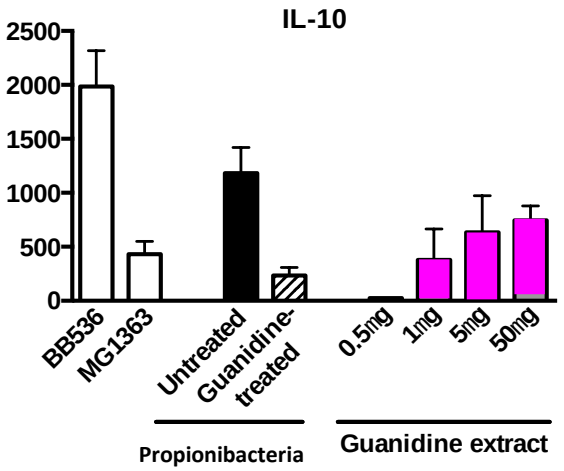


Table 1 – *Propionibacterium freudenreichii* proteins identified by nano-LC-MS/MS after guanidine hydrochl (shaving column) or in-situ fluorescence labeling* (CyDye column).

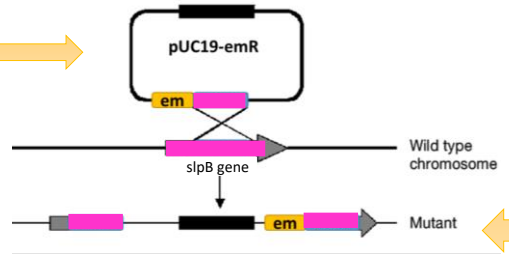
Locus Tag	Description	Gene	Function
PFCIRM129_12235	Internalin A	inlA	Miscellaneous
PFCIRM129_05460	Surface protein with SLH domain	slpE	Cell wall
FCIRM129_09350	Surface layer protein A	slpA	Cell wall
PFCIRM129_00700	Surface layer protein B	slpB	Cell wall
PFCIRM129_11445	Large surface protein A	lspA	Cell wall

Stripped propionibacteria loose immunomodulatory properties

But extracted proteins induce IL-10

If we mutate Surface Layer Protein genes: PBMC assay

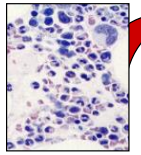
Integrative plasmids (suicide vectors)



Gene disruption by single cross-over plasmid insertion

♦ *In vitro*

+



24 h

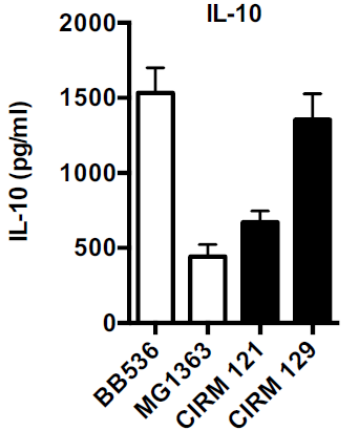
IL-10

IFNγ

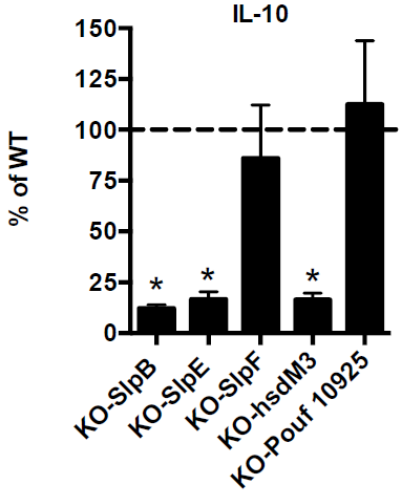
IL-12

TNFα

A

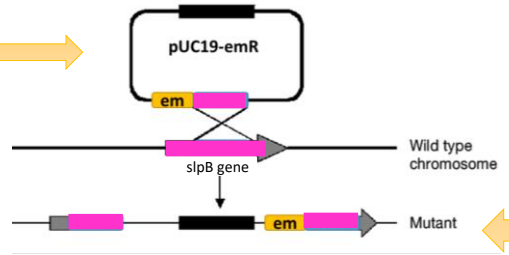


B

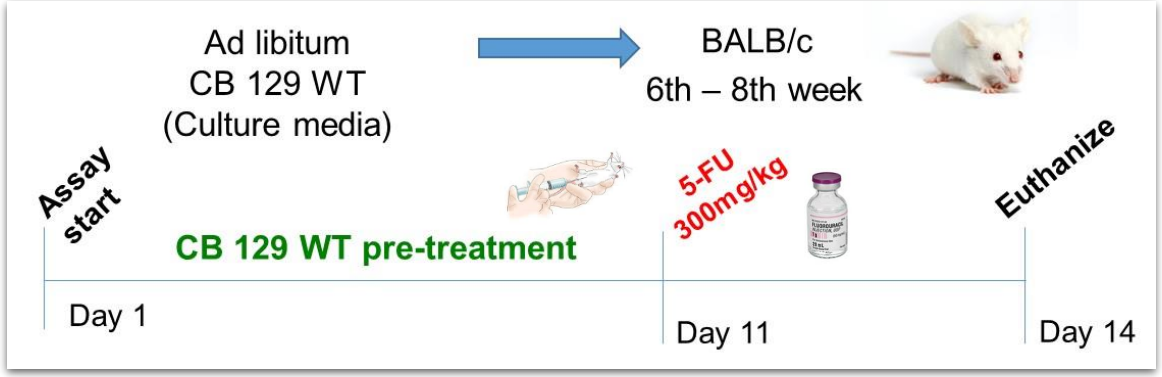


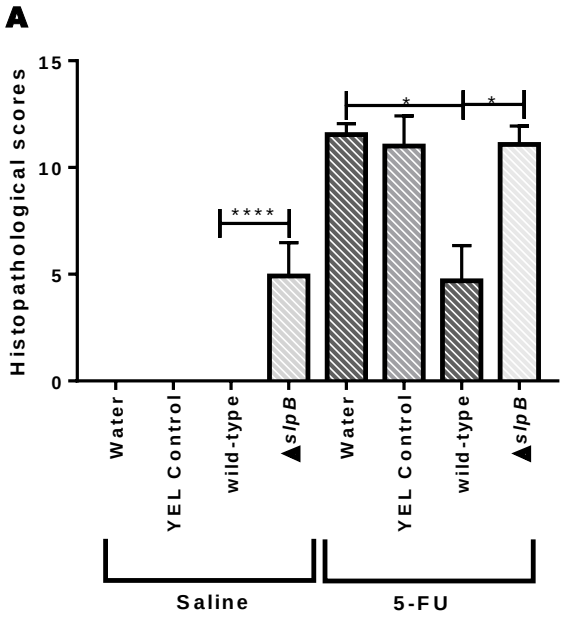
If we mutate Surface Layer Protein SlpB gene: mucositis challenge

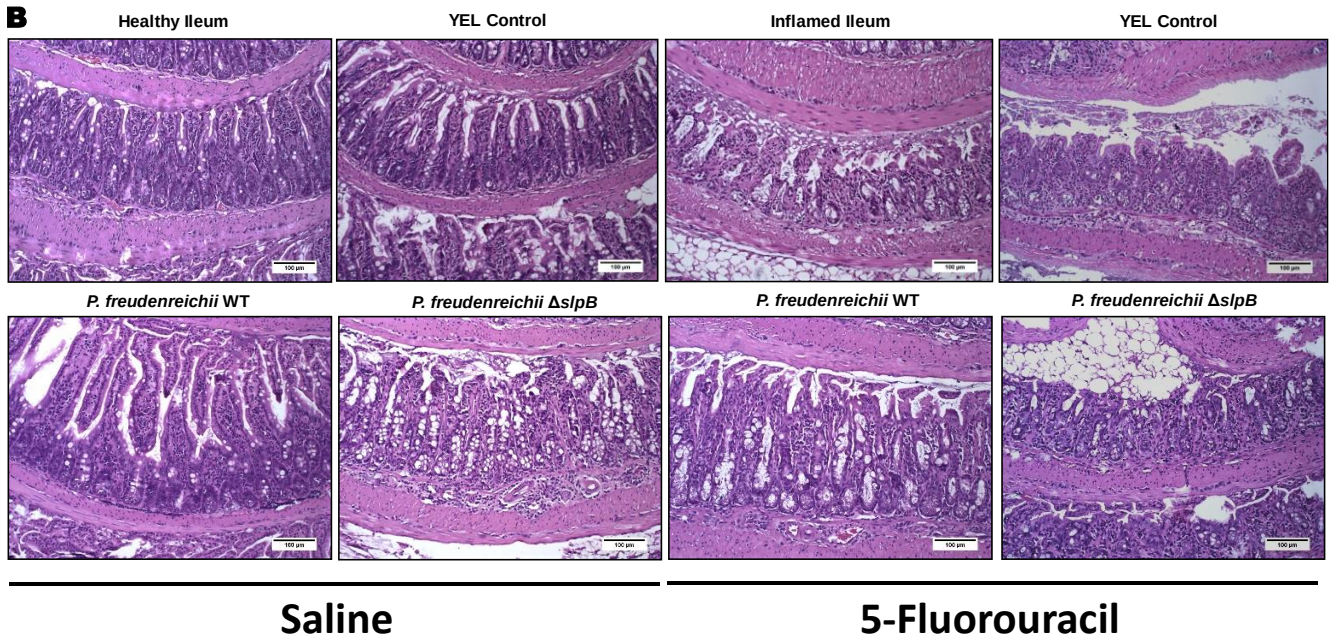
Integrative plasmids (suicide vectors)



Gene disruption by single cross-over plasmid insertion







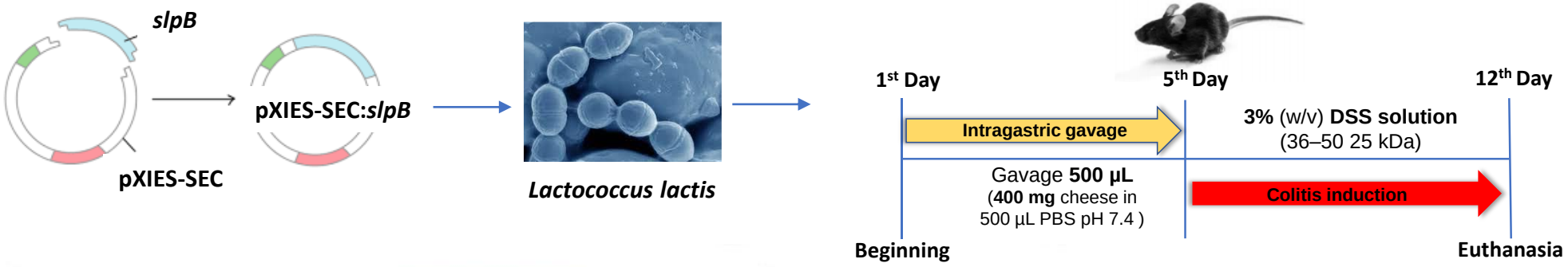
Fillipe Luiz Carmo
fillipelrc@gmail.com

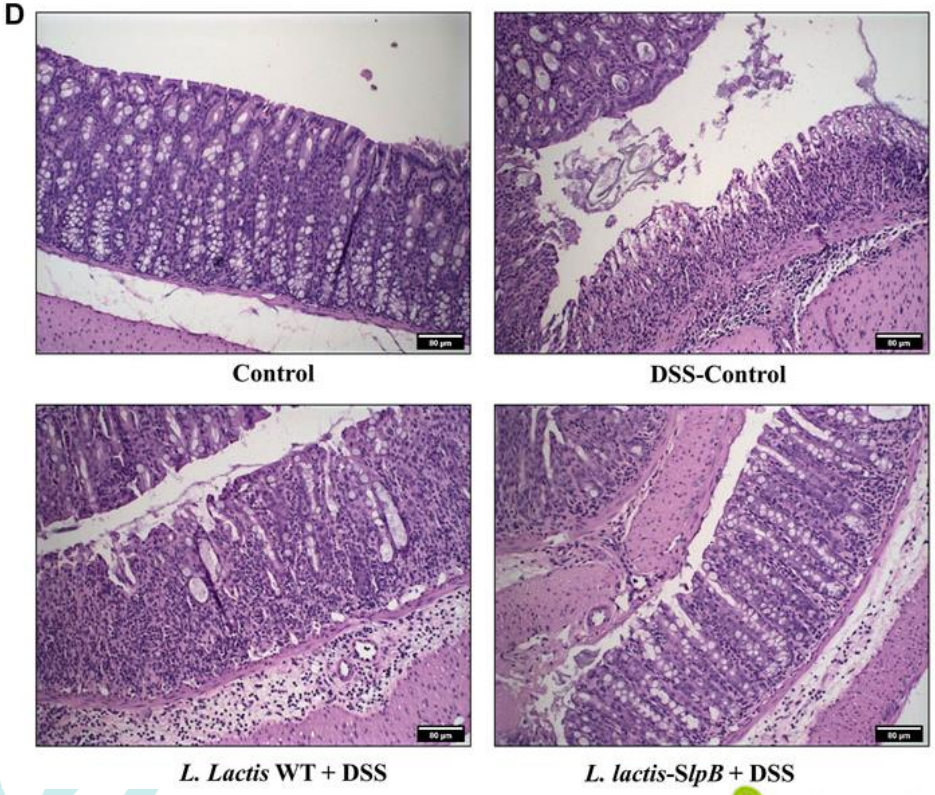
STLO

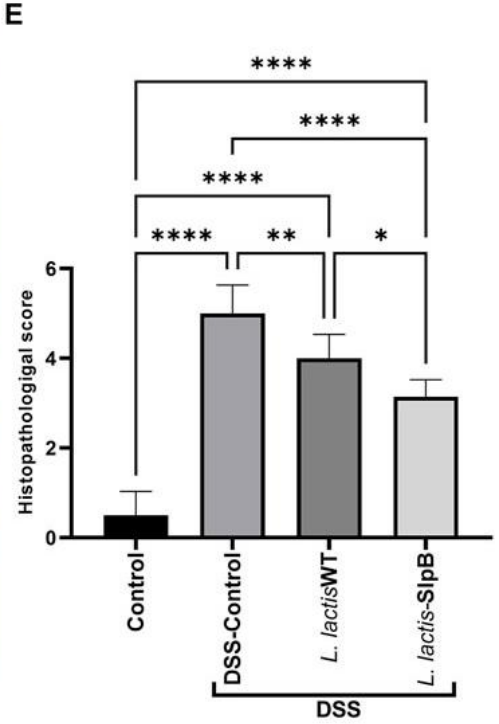
UFMG UNIVERSIDADE FEDERAL DE MINAS GERAIS

LGCM Laboratório de Genética Celular e Molecular

If we express SlpB in *Lactococcus lactis*: colitis challenge



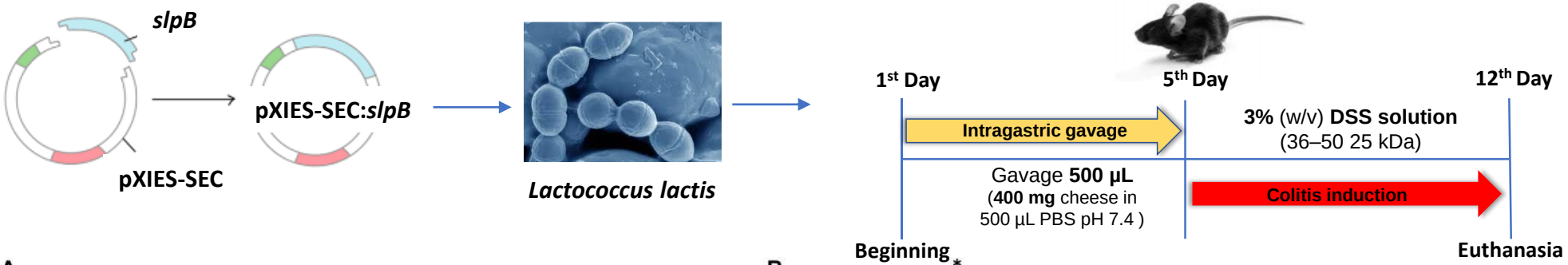


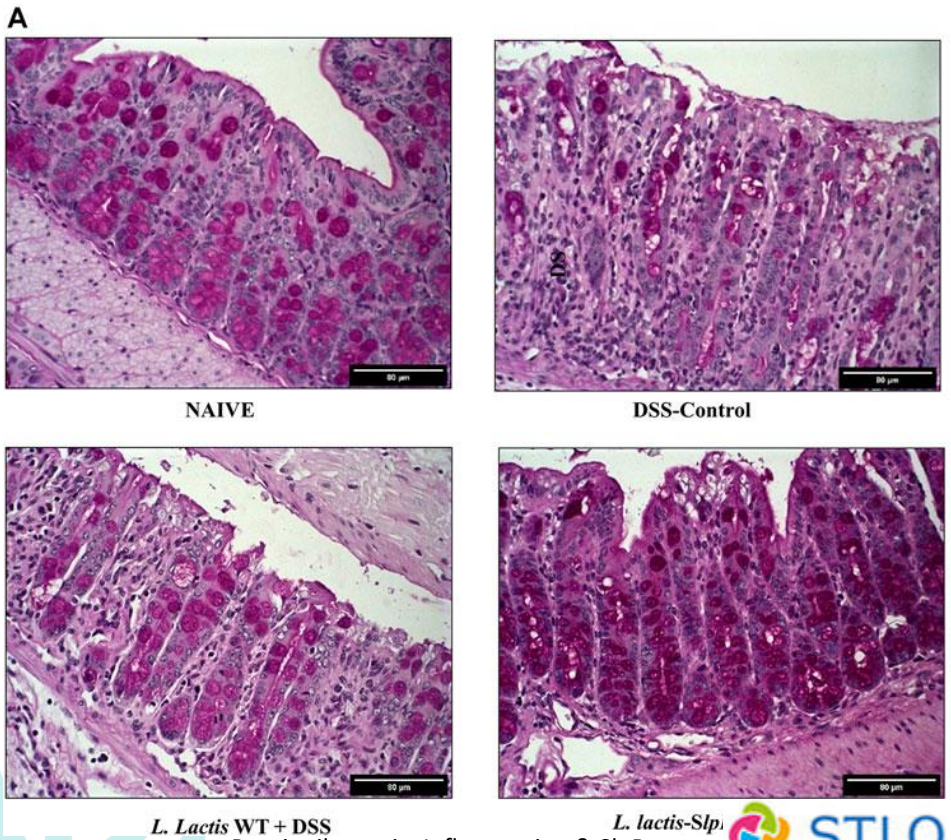


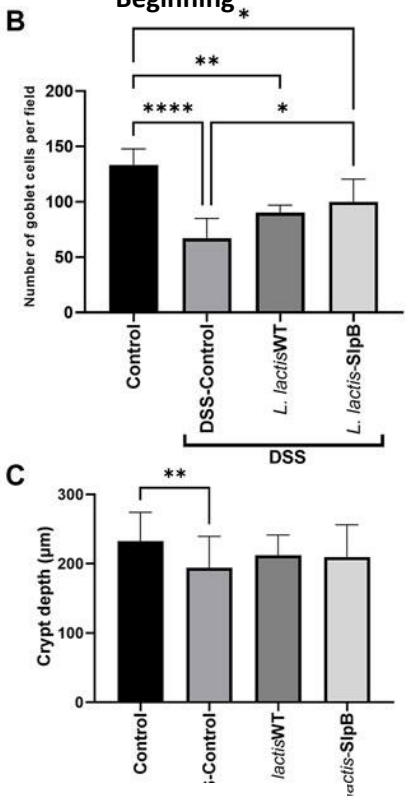
SlpB expression provides *L. lactis* with enhanced anti-inflammatory properties

Fillipe Luiz Carmo
fillipelrc@gmail.com

If we express SlpB in *Lactococcus lactis*: colitis





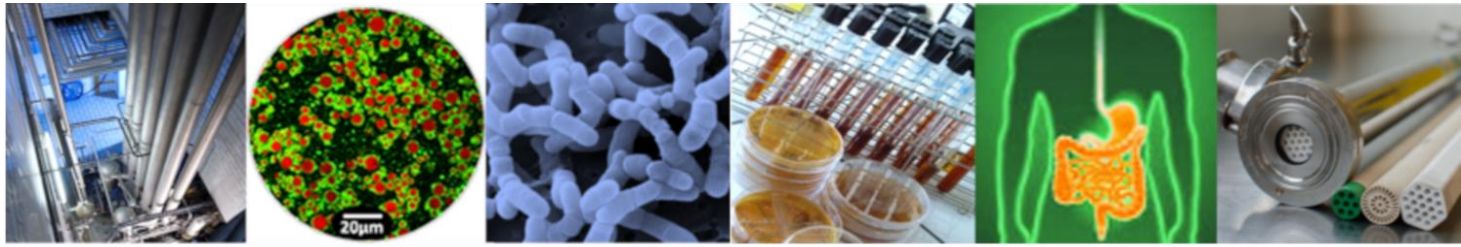


SlpB expression protects from mucus and goblet cells depletion

Do Carmo et.al., 2021, **Front. Pharmacol.** SlpB Protein Enhances the Probiotic Potential of L. lactis NCDO 2118 in Colitis Mice Model

Fillipe Luiz Carmo
fillipelrc@gmail.com

Take-home messages

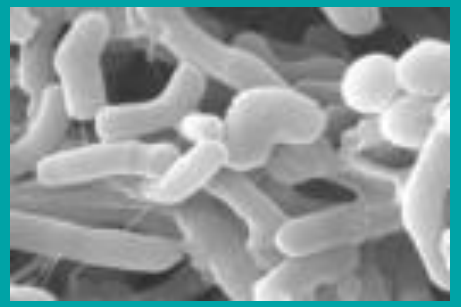


- Propionibacteria: strain-dependent immunomodulatory properties
- Anti-inflammatory effect of propionibacteria-containing cheese in different models of inflammatory diseases
- Surface layer protein SlpB plays a key role in this interaction
- This can be transferred to another bacterium via heterologous expression

I ♥ Γραβιέρα Κρήτης

INRAE

Thank you for your attention



I ♥ Emmental

L'INSTITUT agro Rennes Angers

RÉPUBLIQUE FRANÇAISE Liberté Égalité Fraternité INRAE

UFMG UNIVERSIDADE FEDERAL DE MINAS GERAIS

AGROCAMPUS OUEST

CIIL CENTER FOR INFECTION & IMMUNITY OF LILLE