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

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

Gwénaél JAN

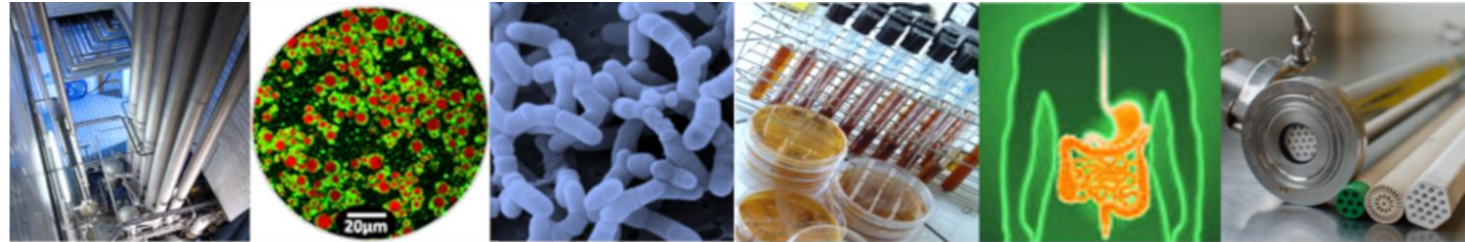
STLO, INRAE, Institut Agro, Science et Technologie du Lait et de l'Œuf, Rennes

gwenael.jan@inrae.fr

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



➤ Intestinal epithelial barrier: endangered...

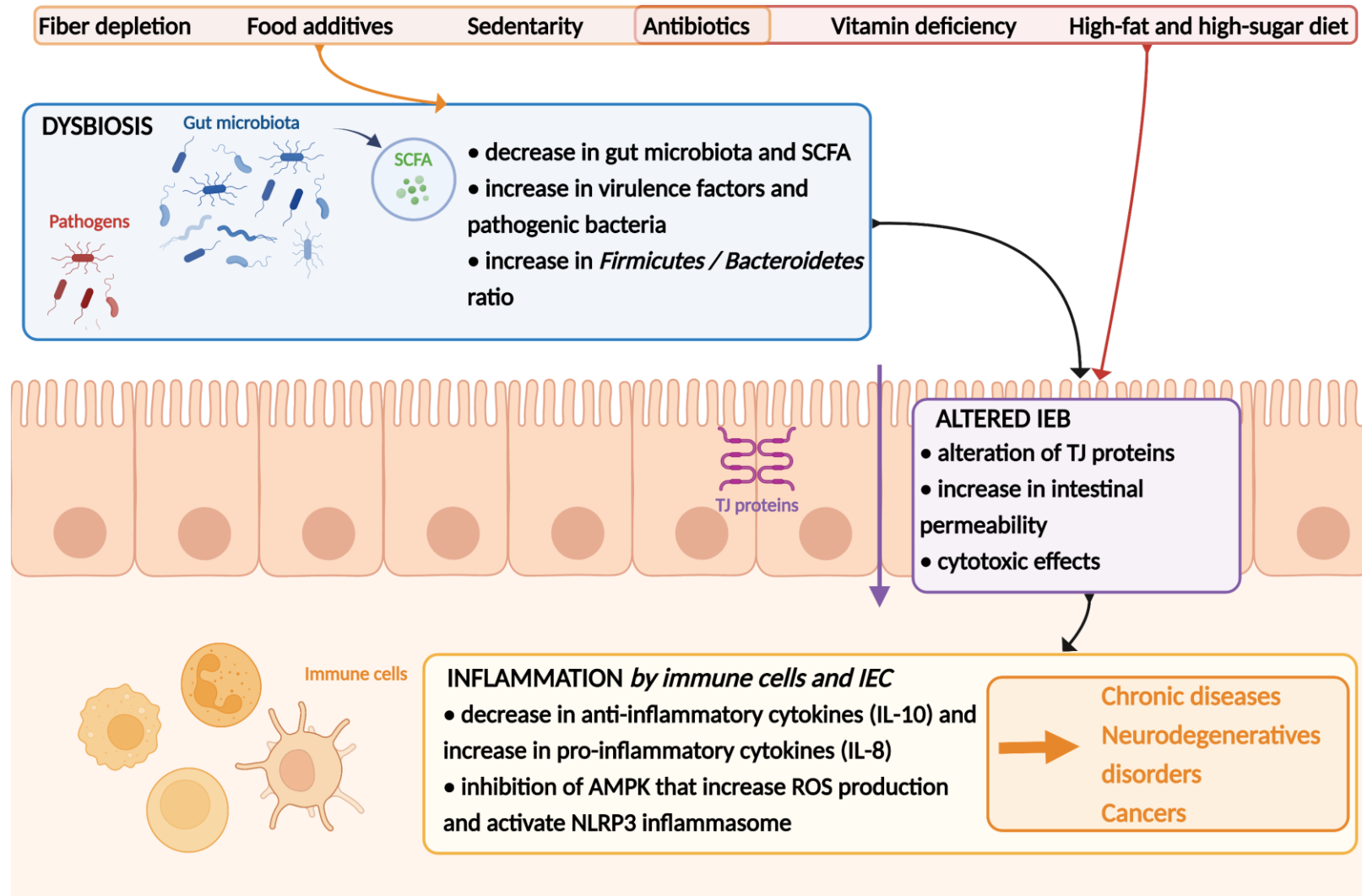


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Propionibacteria, Inflammation & SlpB

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> ... By modern lifestyle



➤ Examples of digestive inflammatory diseases

Colitis

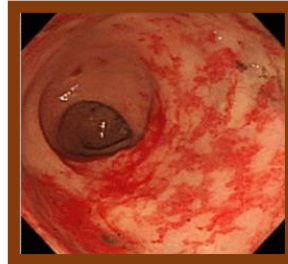
- GIT Chronic inflammation



Ulcerative Colitis



Mucositis



GI Mucositis



Oral mucositis

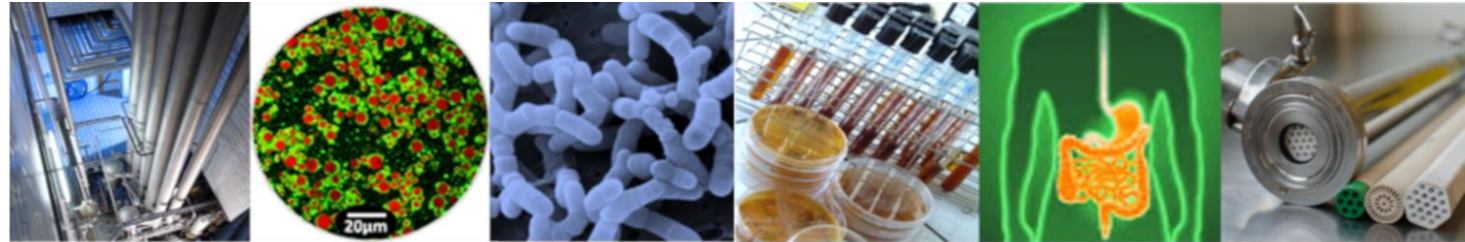
5-Fluoracil (5-FU)

- Head, neck and colon cancer.

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



➤ A key role of resident and ingested microorganisms...

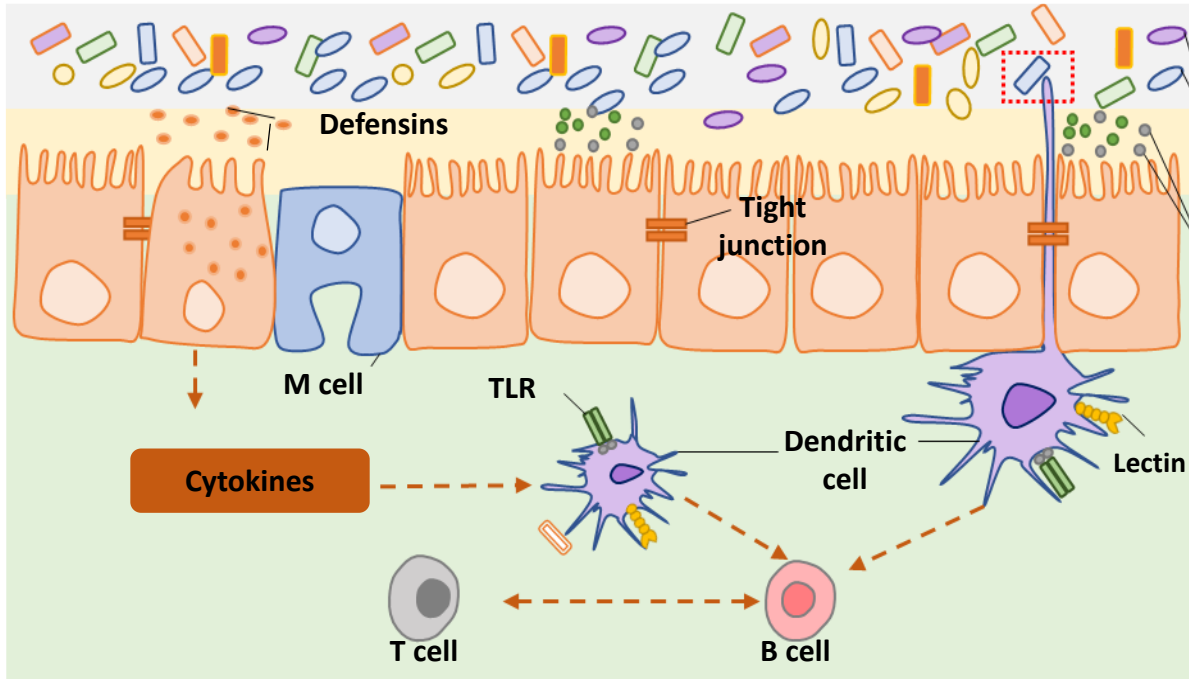


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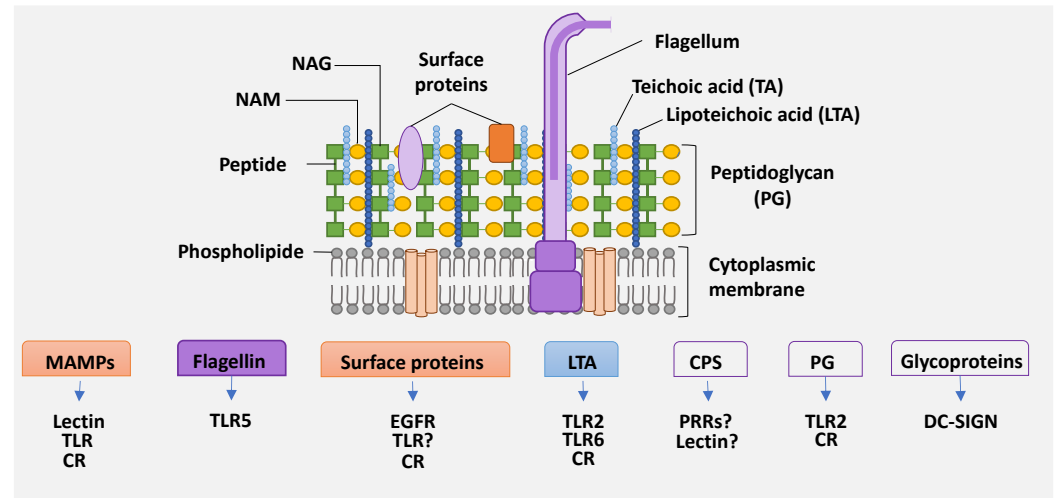
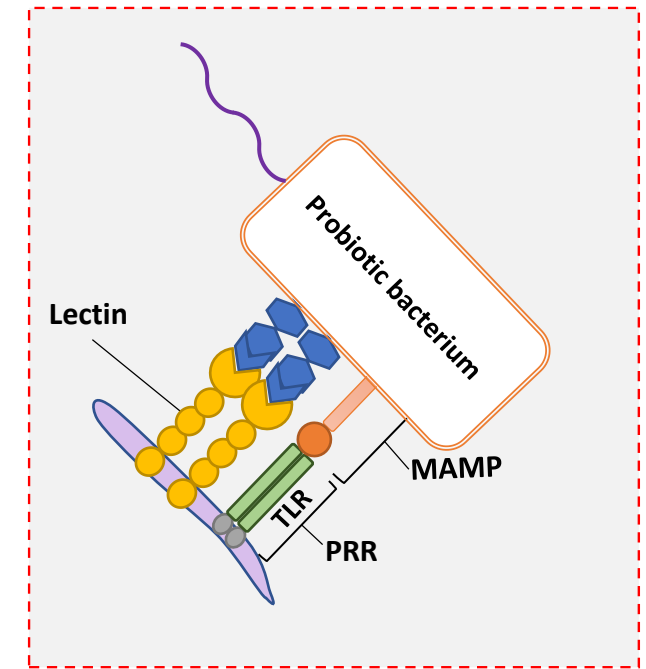
Propionibacteria, Inflammation & SlpB

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> ... Modulating the immune response



Intestinal microbiota
Antimicrobial peptides

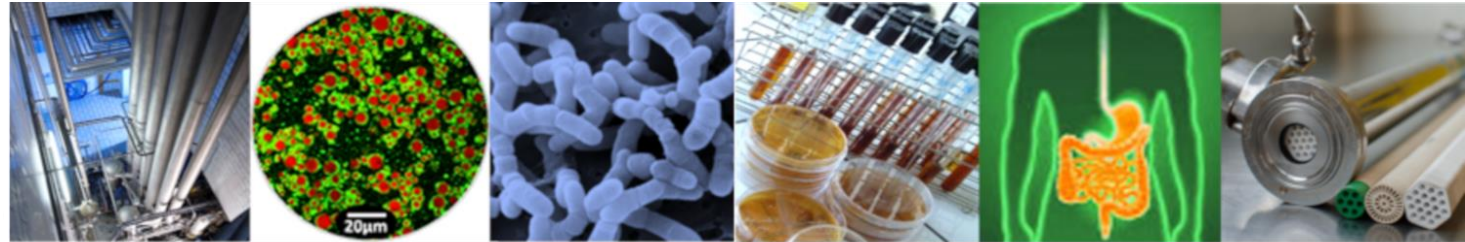


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➤ Introducing *Propionibacterium freudenreichii*...

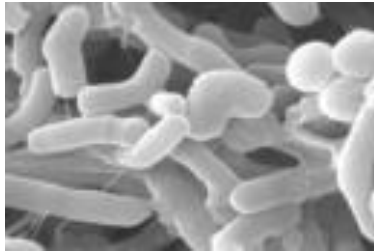


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Propionibacteria, Inflammation & SlpB

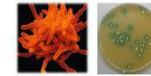
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> ... A sort of Swiss army knife



*Propionibacterium
freudenreichii*

→ Actinobacterium



→ Vitamin producer
B9, B12



→ Probiotic



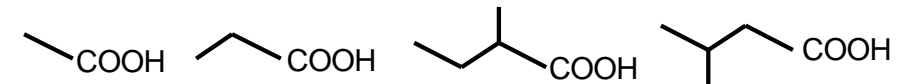
→ Food bio-preservative



→ Ripening starter



→ Short chain fatty acids



**Short Chain Fatty Acids
(SCFA)
Known effect on health**

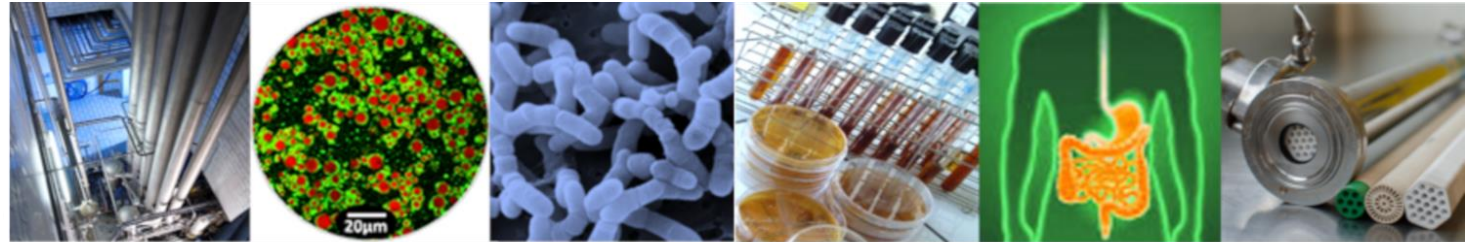


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➤ Immunomodulatory properties



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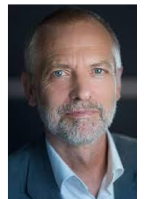
Propionibacteria, Inflammation & SlpB

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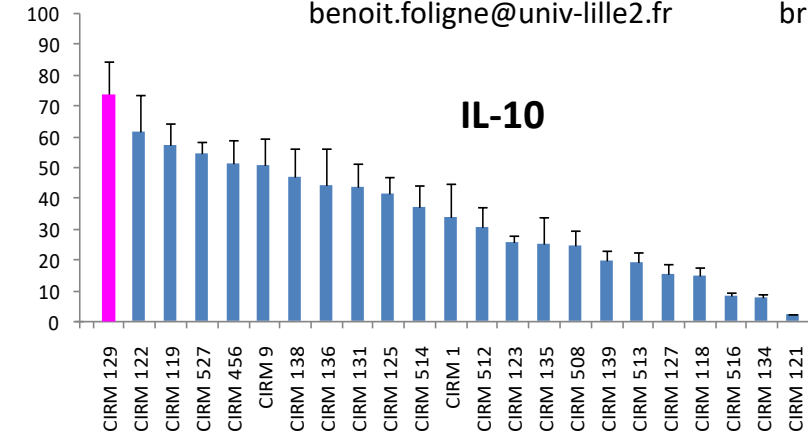
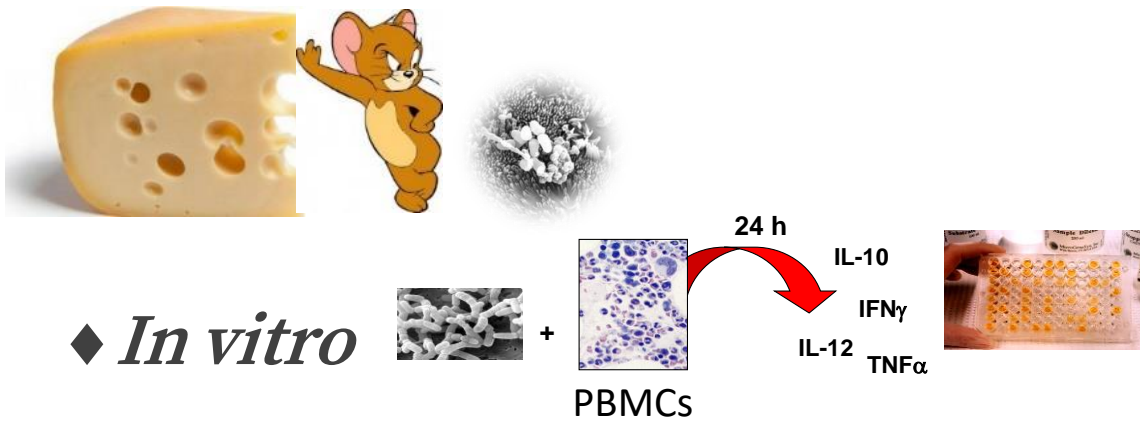
> ... *In vitro* and *in vivo*



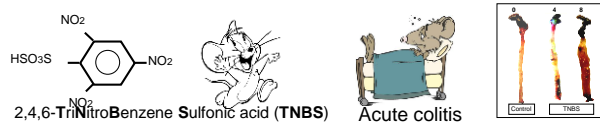
benoit.foligne@univ-lille2.fr



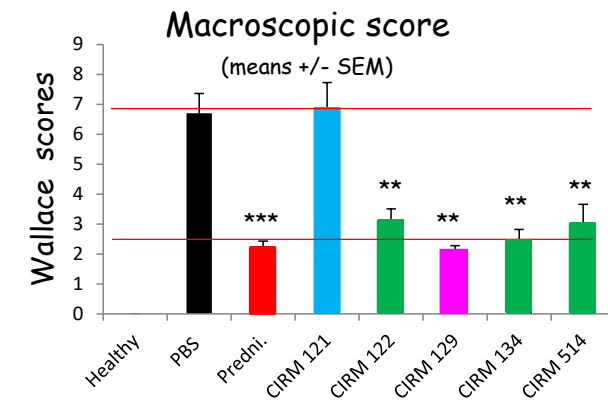
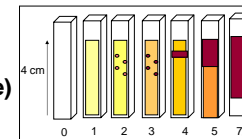
bruno.pot1@telenet.be



◆ *In vivo*



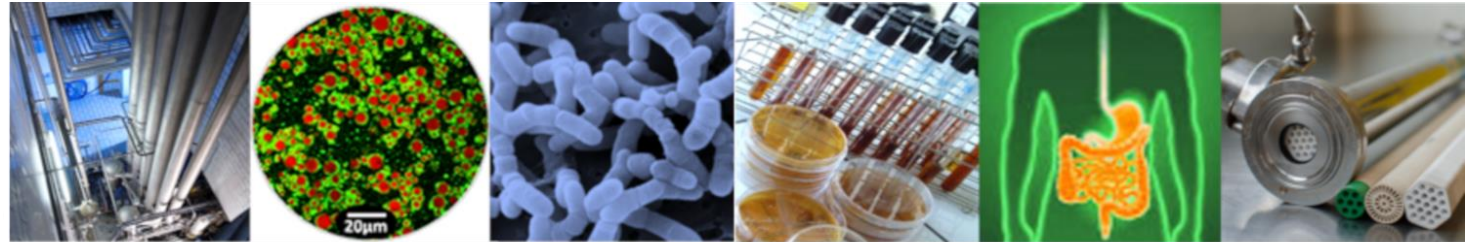
Macroscopic score (Wallace)



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➤ The healing effect of *Propionibacterium freudenreichii*

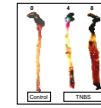
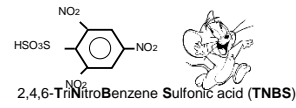


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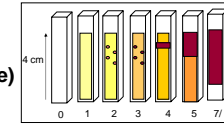
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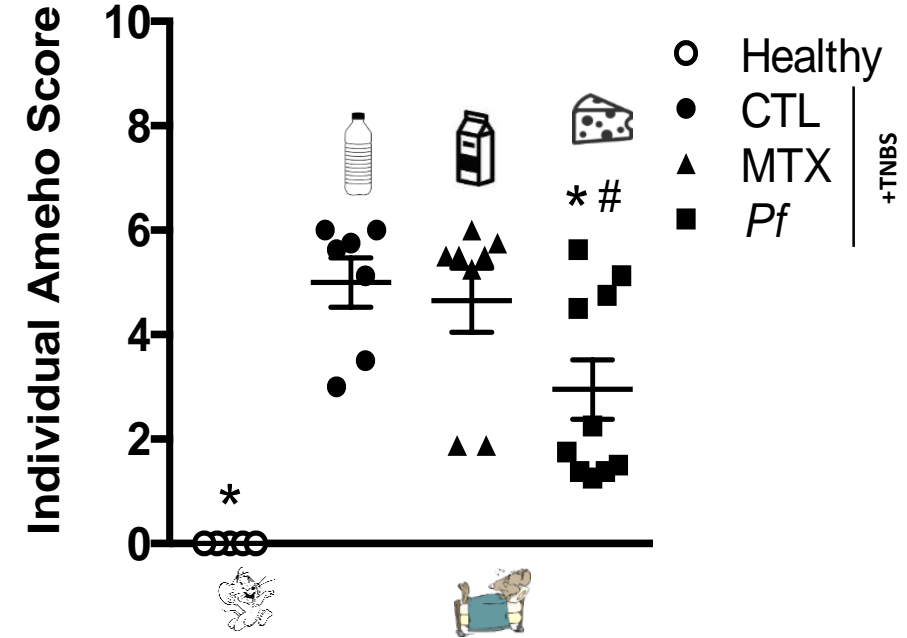
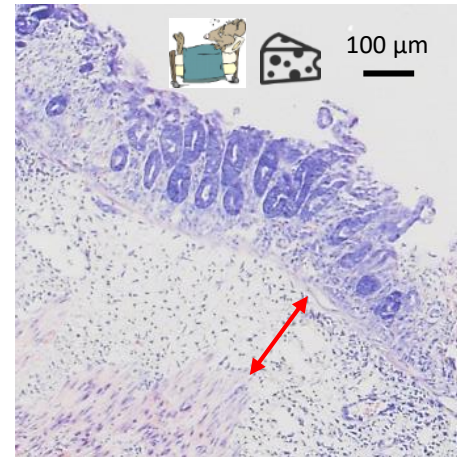
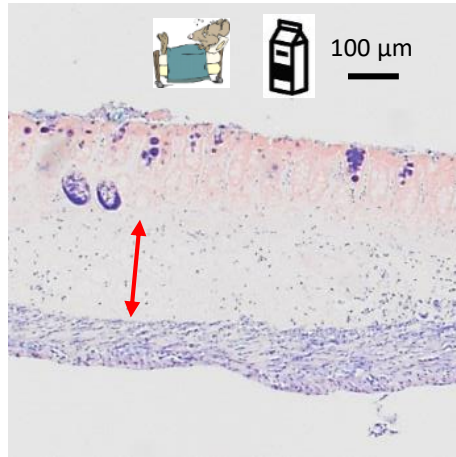
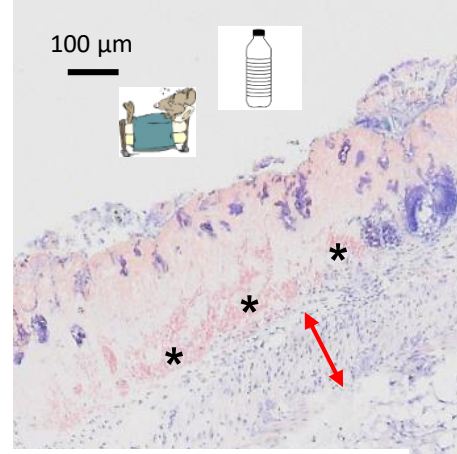
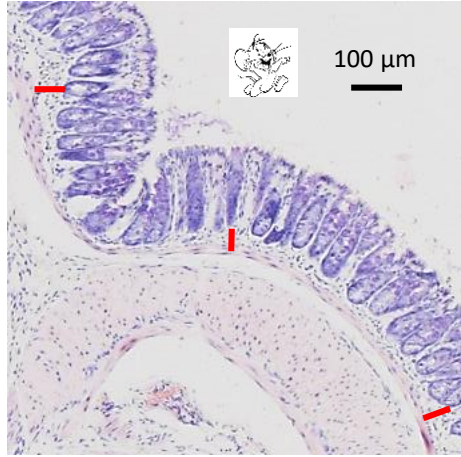
➤ In TNBS-induced colitis



Macroscopic score (Wallace)



A model cheese



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ID2Santé



➤ In DSS-induced colitis

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

C57BL6
8th week age



1st Day

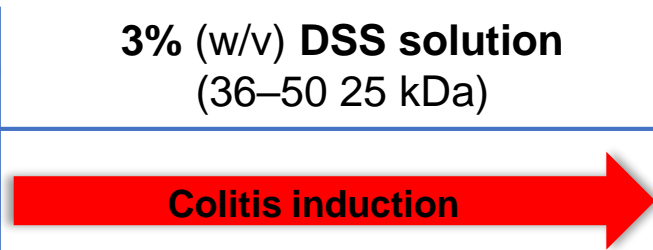


5th Day

12th Day



Gavage 500 μ L
(400 mg cheese in
500 μ L PBS pH 7.4)

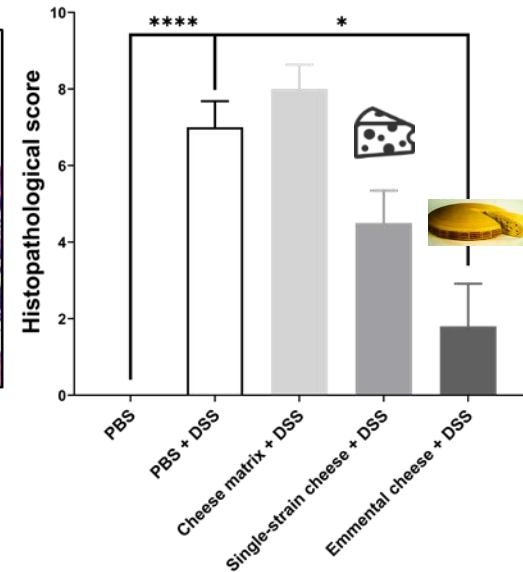
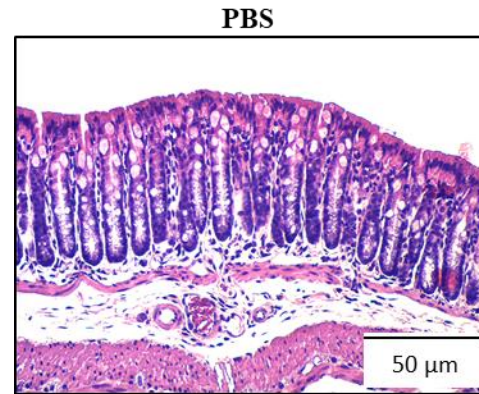
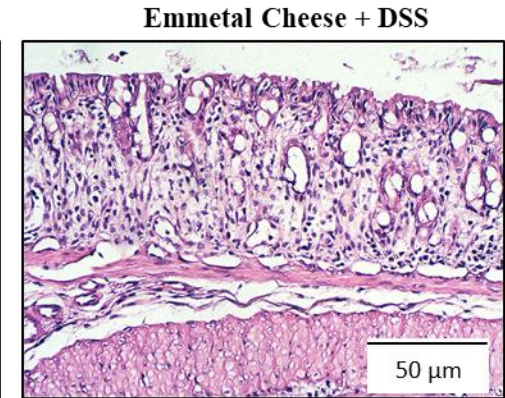
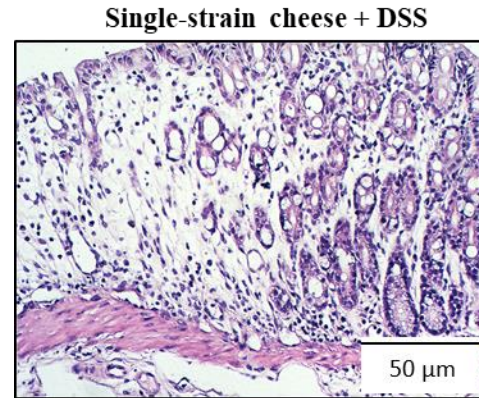
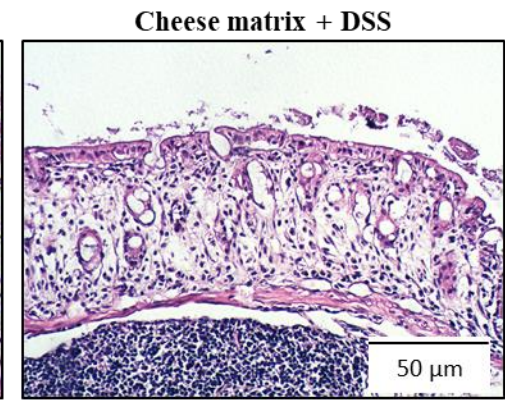
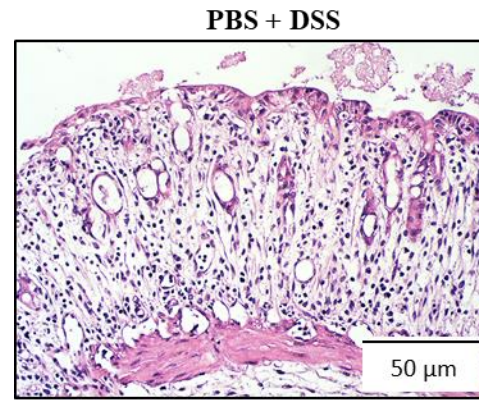


Beginning

Euthanasia



Vasco Azevedo



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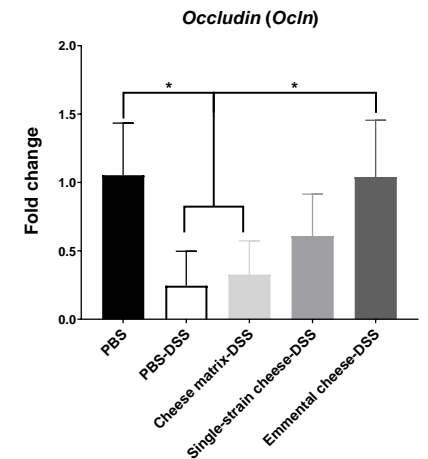
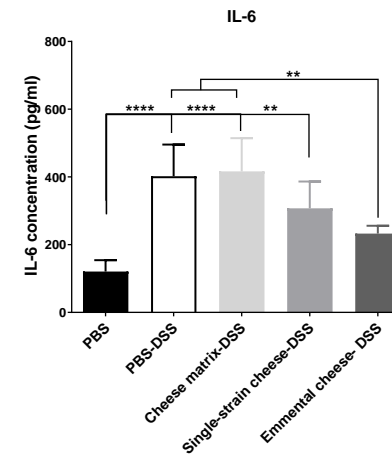
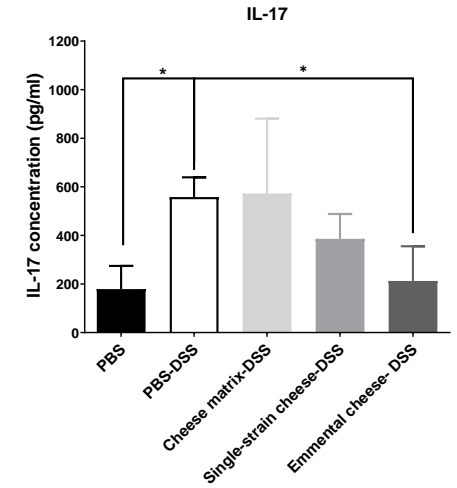
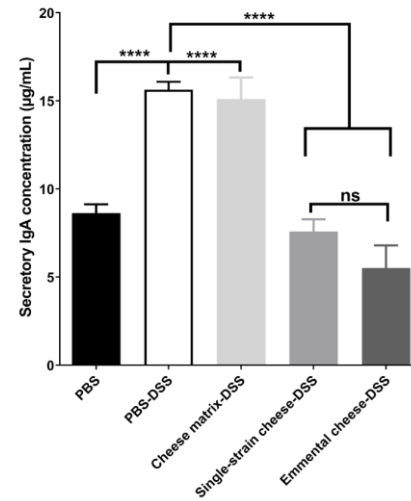
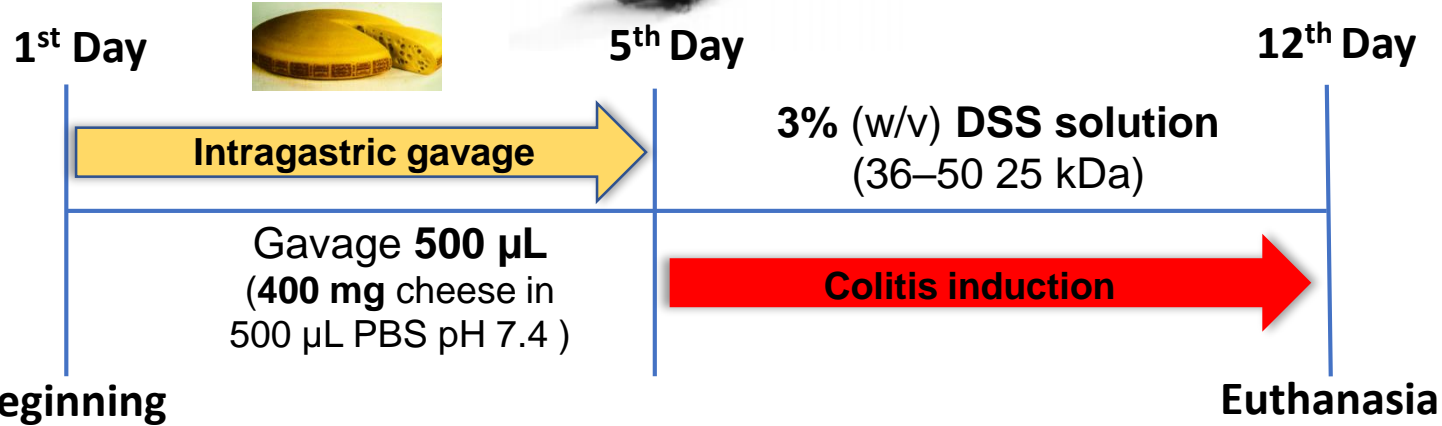
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➤ In DSS-induced colitis

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

C57BL6
8th week age



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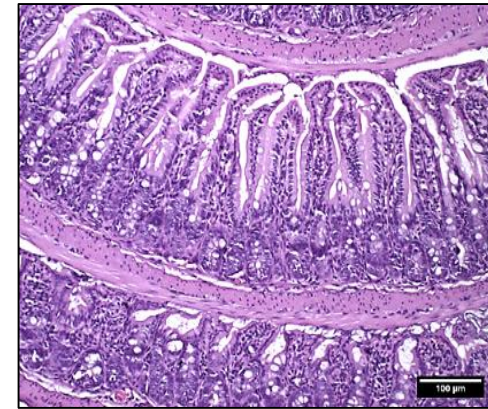


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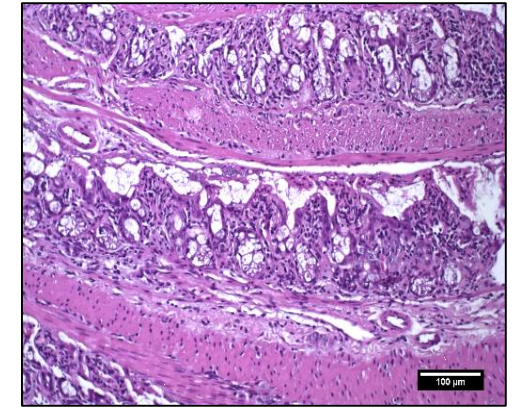


➤ In 5FU-induced mucositis

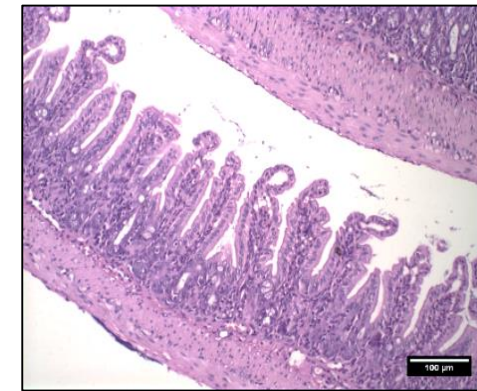
Representative images from mucosal histopathology (H&E)



Healthy Ileum

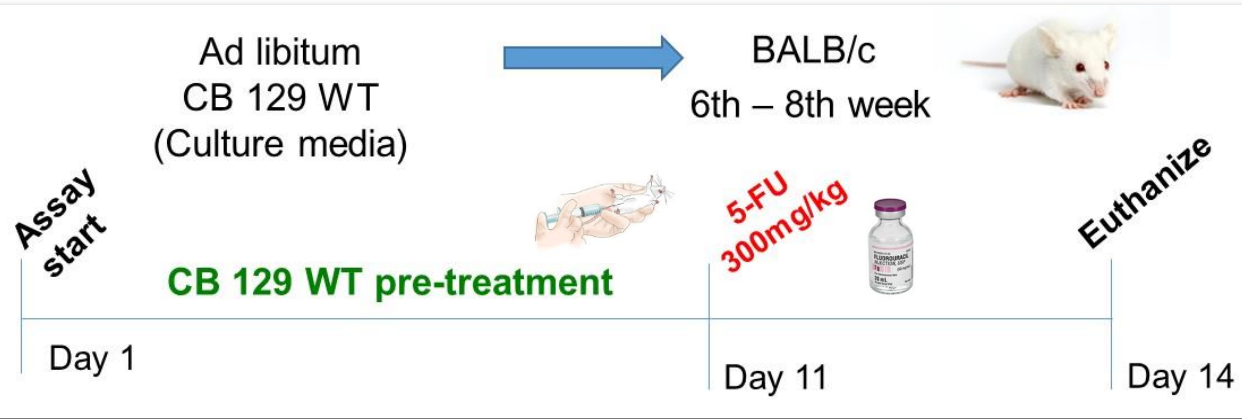
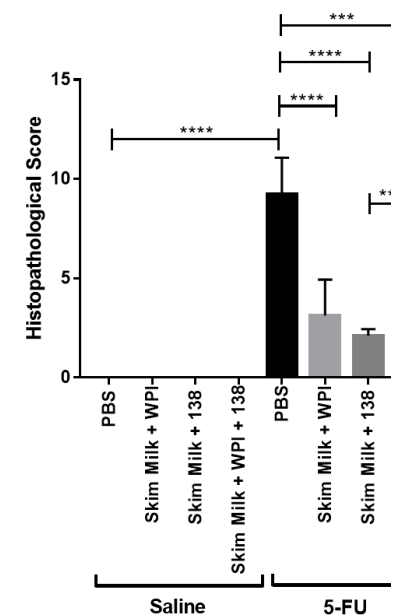


PBS + 5-FU



Skim milk + propio

Histopathological scores



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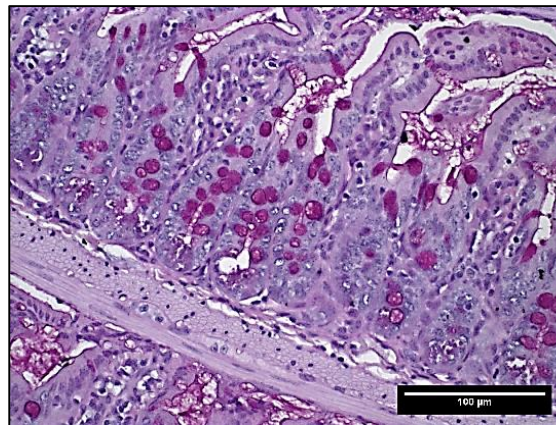
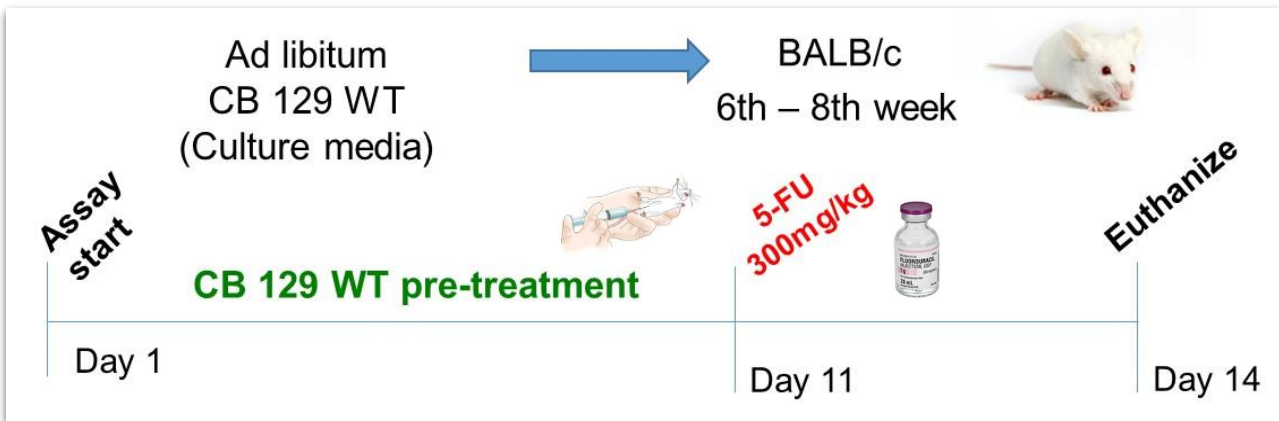


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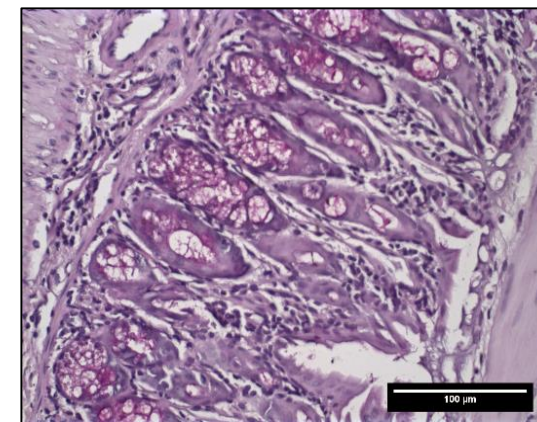


➤ In 5FU-induced mucositis

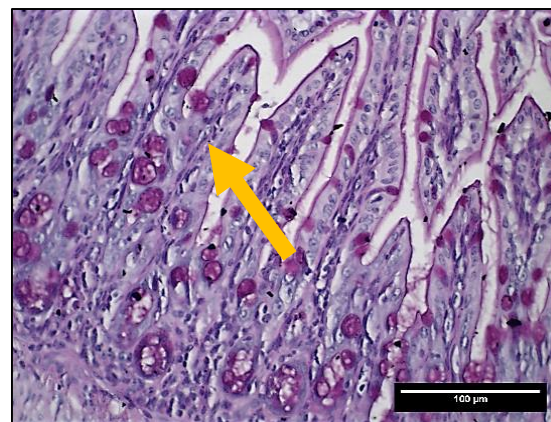
Representative images of stained goblet cells (PAS)



Healthy ileum

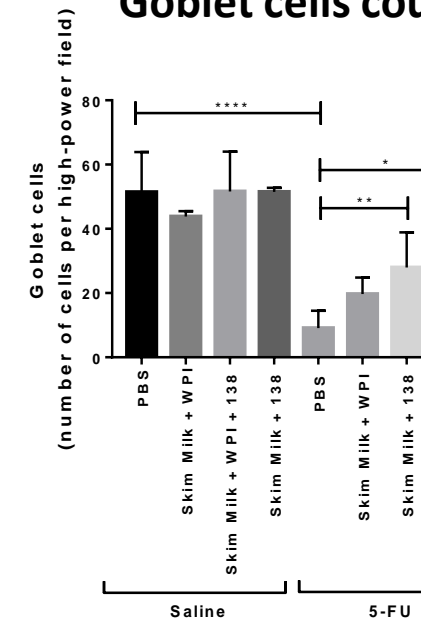


PBS + 5FU



LDF + 138 + 5FU

Goblet cells counts



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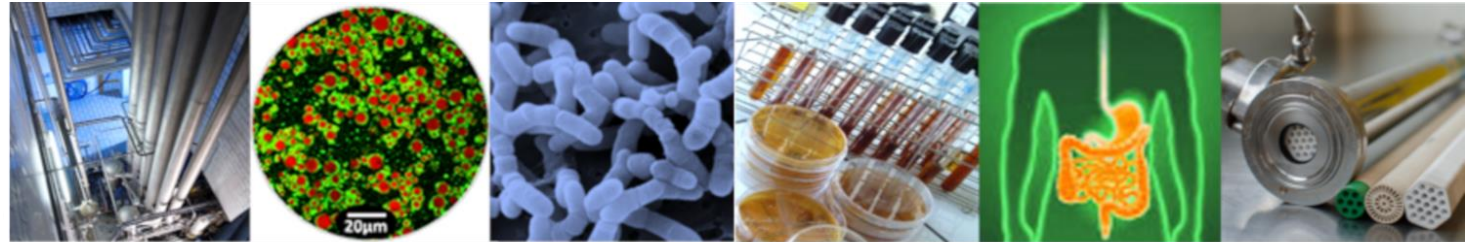


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> How does it work?



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➤ If we remove surface proteins: PBMC assay

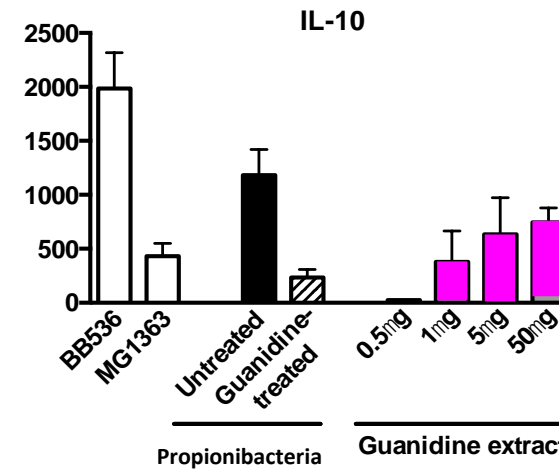
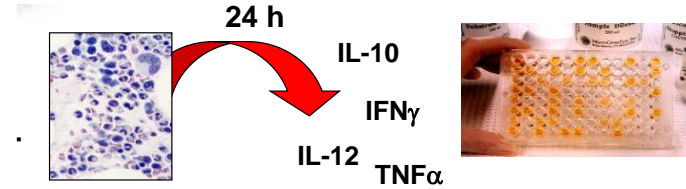
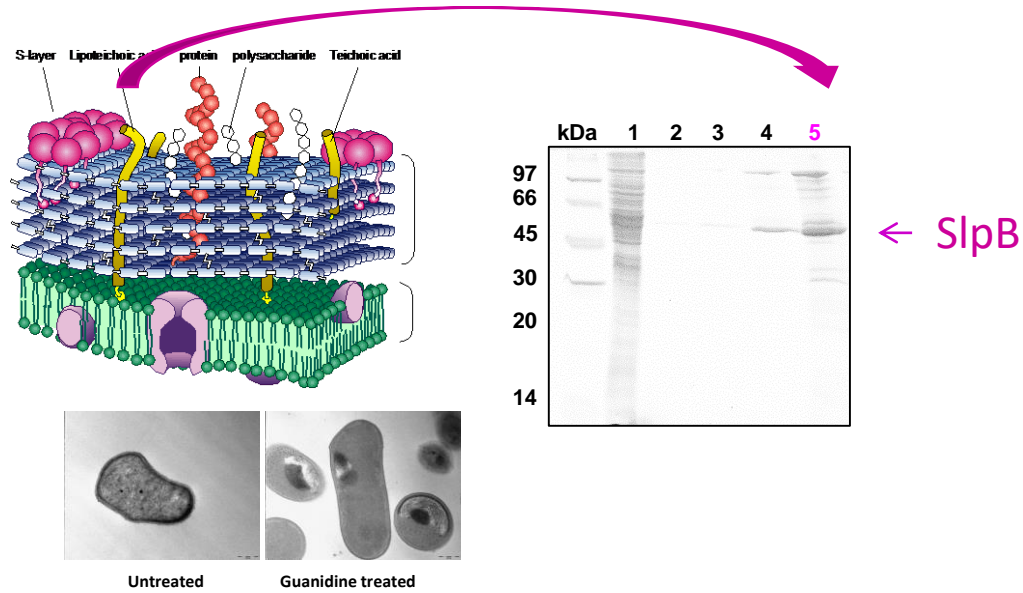


Table 1 – *Propionibacterium freudenreichii* proteins identified by nano-LC-MS/MS after guanidine hydrochloride (shaving column) or in-situ fluorescence labeling (CyDye column).

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 lose immunomodulatory properties

But extracted proteins induce IL-10

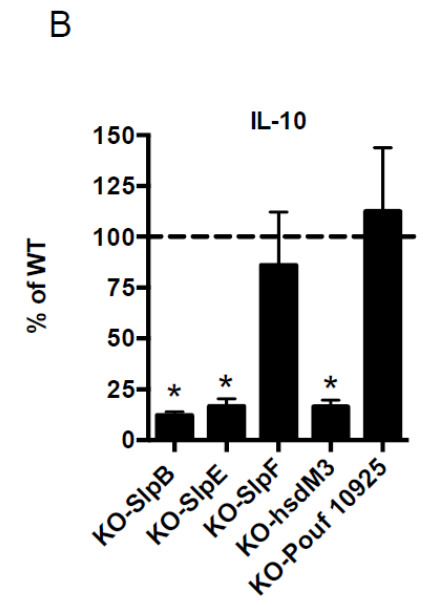
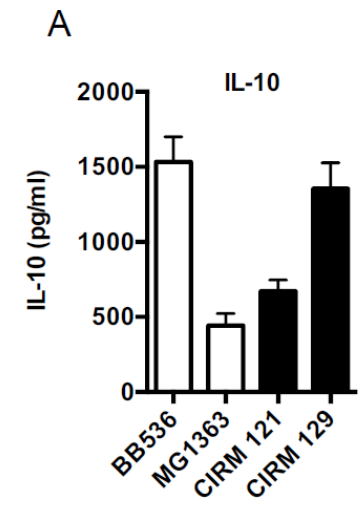
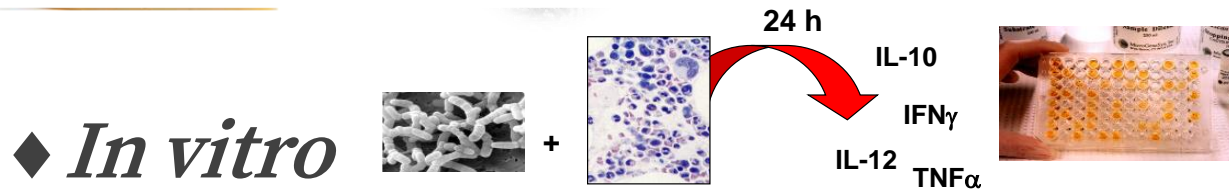
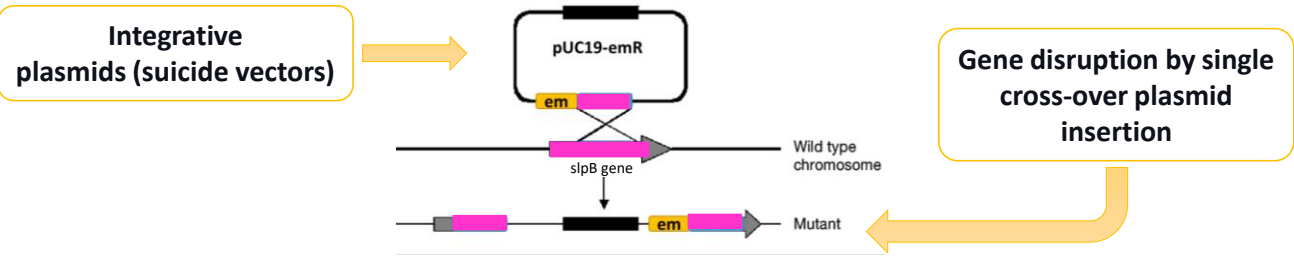


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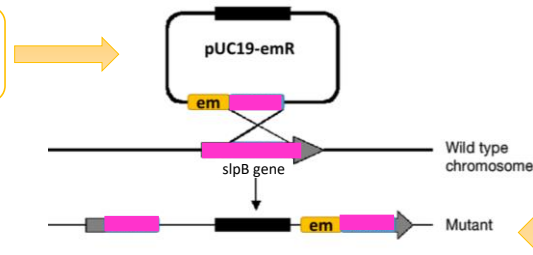
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➤ If we mutate Surface Layer Protein genes: PBMC assay

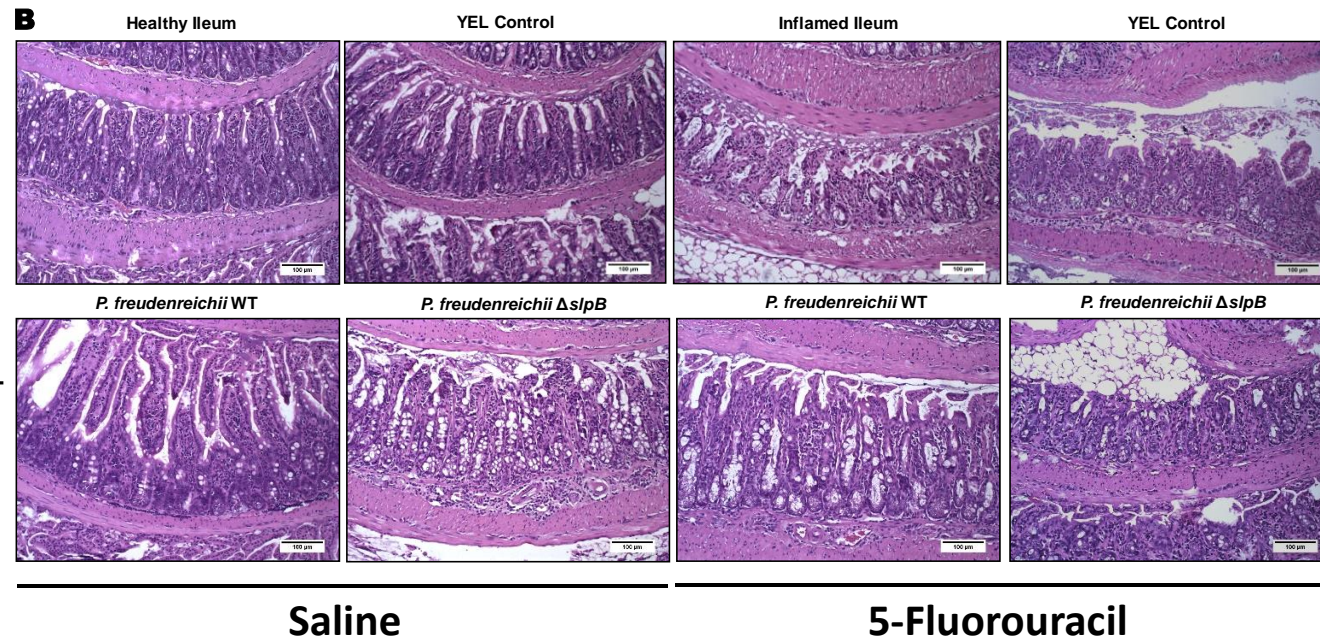
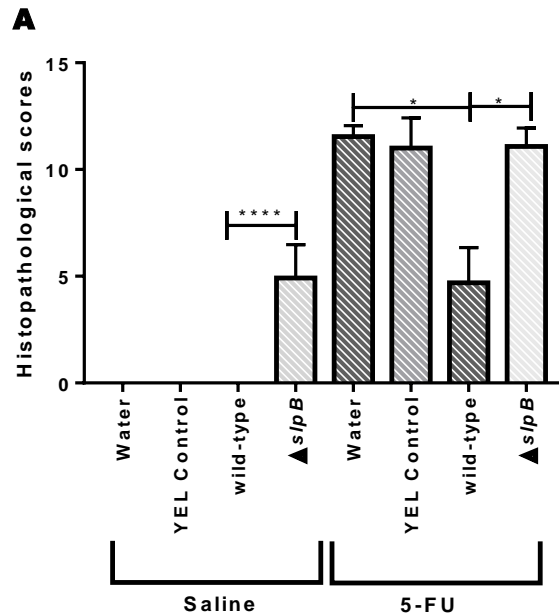
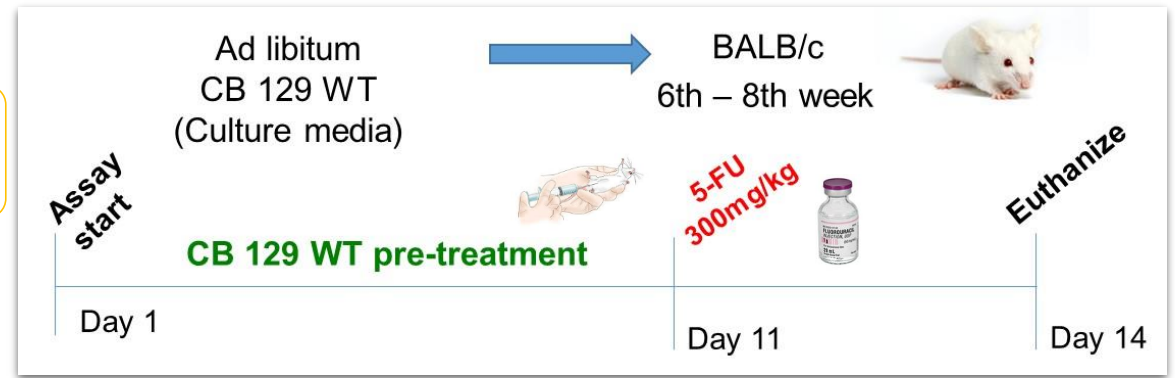


➤ If we mutate Surface Layer Protein SlpB gene: mucositis challenge

Integrative plasmids (suicide vectors)



Gene disruption by single cross-over plasmid insertion



Fillipe Luiz Carmo
fillipelrc@gmail.com



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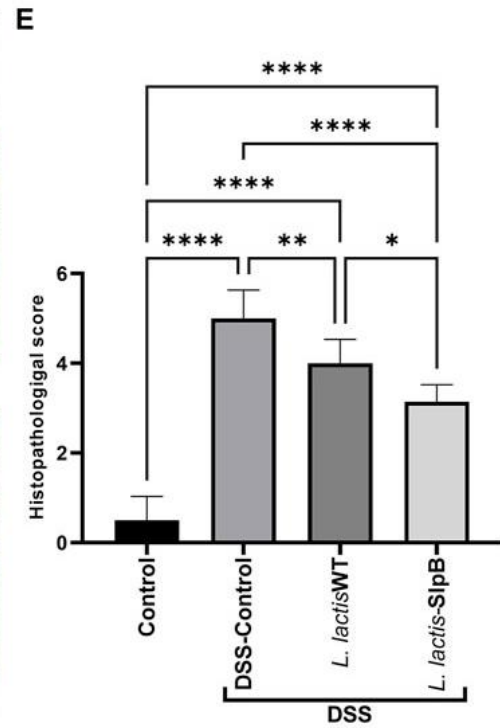
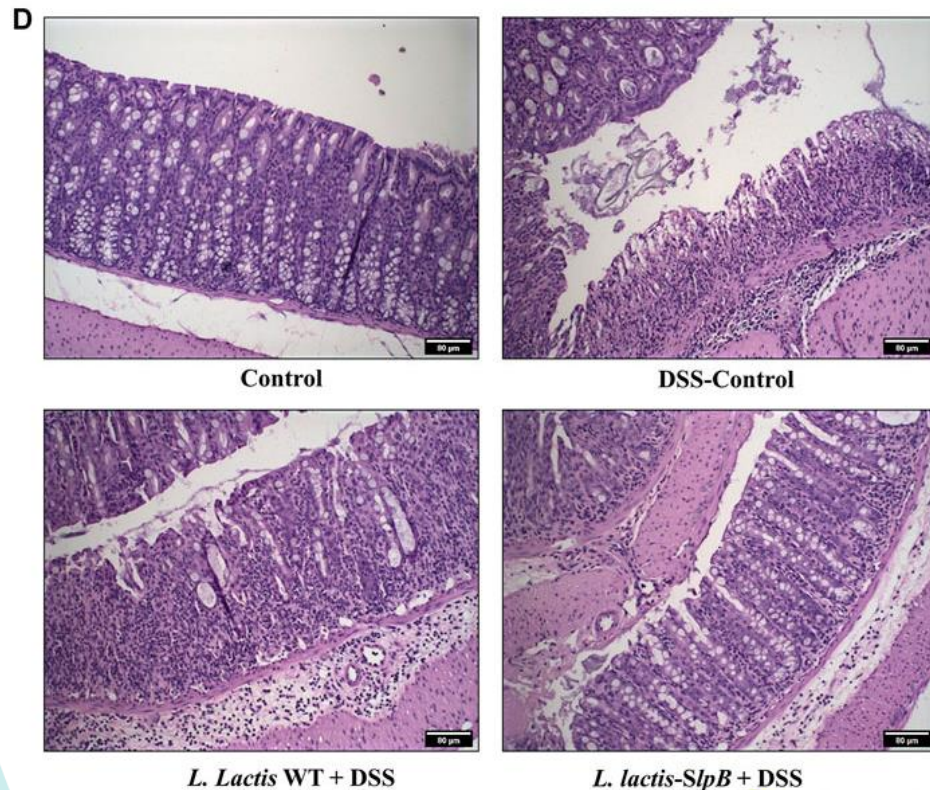
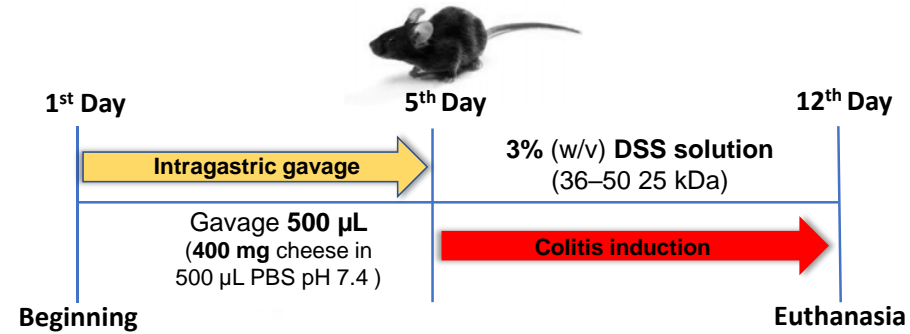
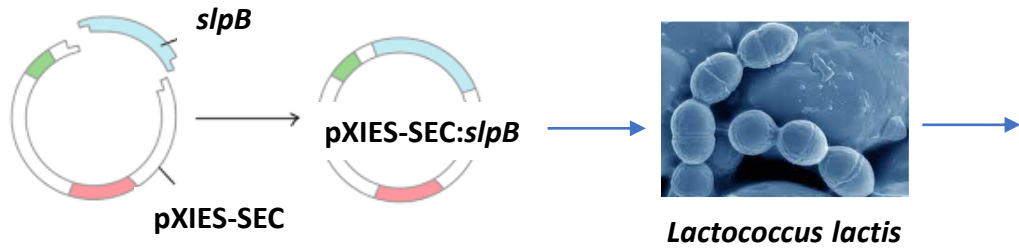


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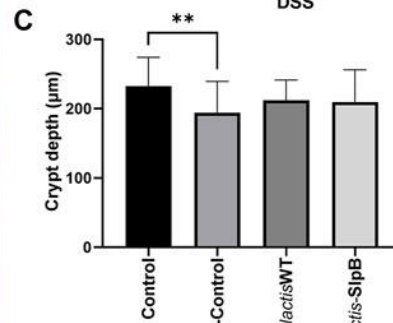
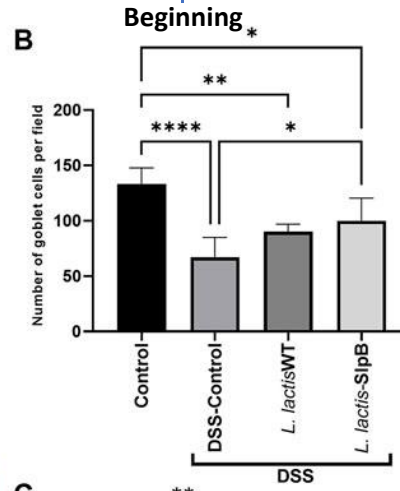
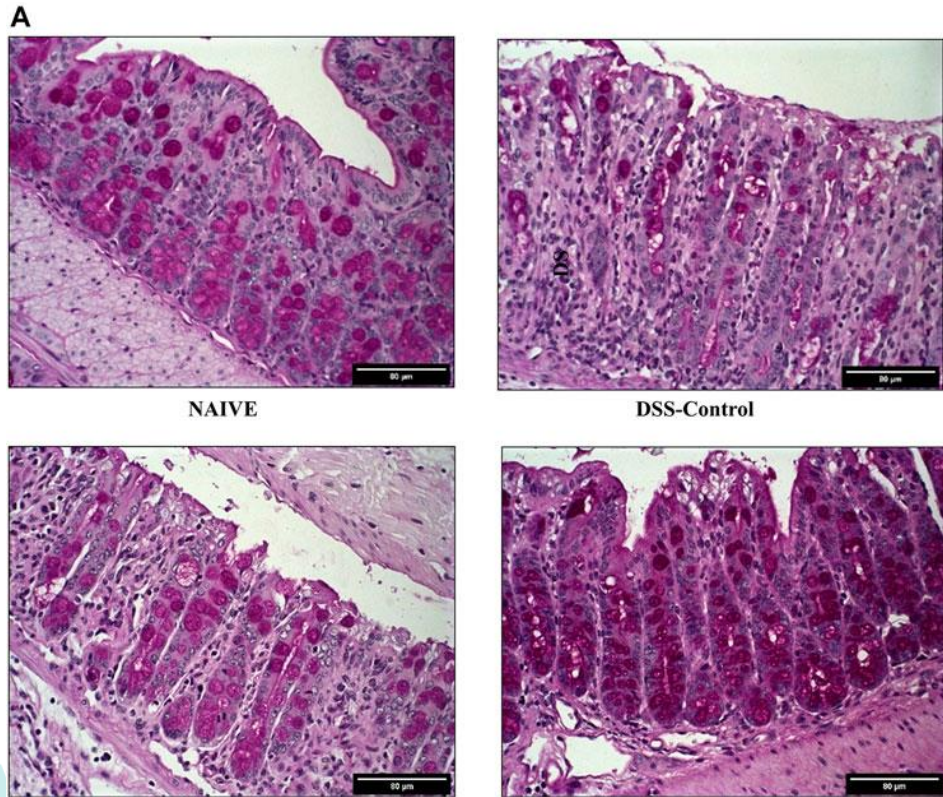
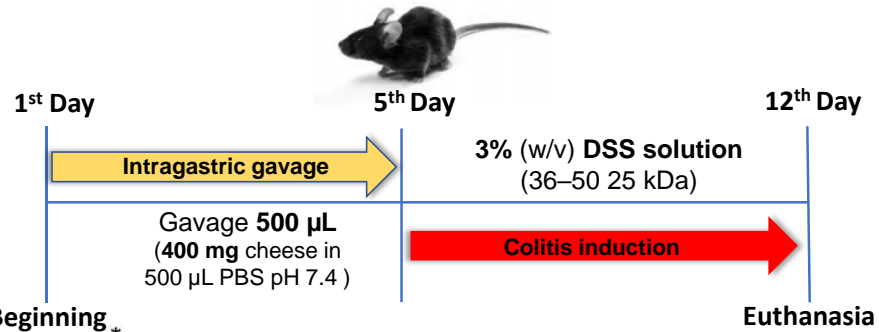
➤ If we express SlpB in *Lactococcus lactis*: colitis challenge



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



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



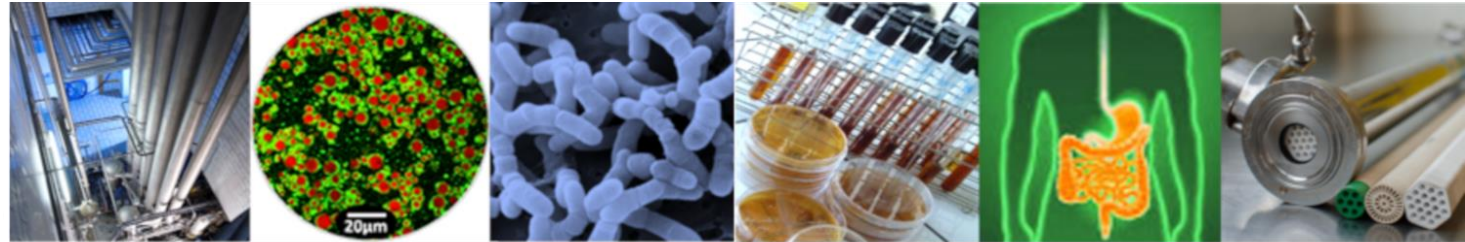
➤ **SlpB expression protects from mucus and goblet cells depletion**

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



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➤ Take-home messages



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Propionibacteria, Inflammation & SlpB

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- **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

