Effects of Lactobacillales Supplementation in a Rat Model of Short Bowel Syndrome (SBS)

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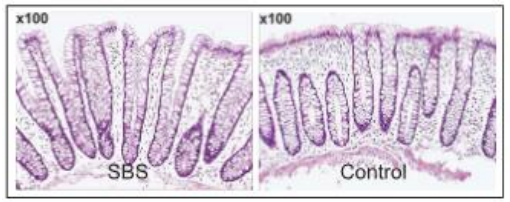
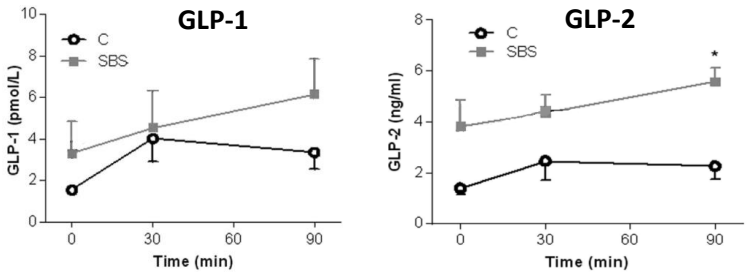
Short Bowel Syndrome (SBS)

Spontaneous adaptations

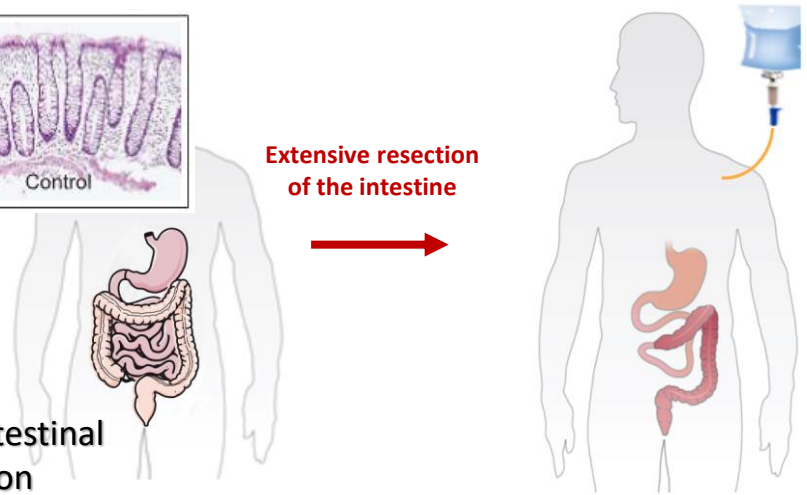
Morphological intestinal adaptation



Functional intestinal adaptation



Extensive resection of the intestine



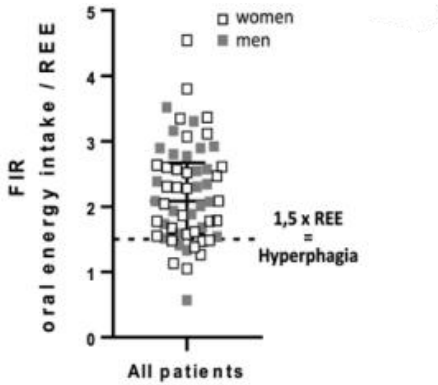
Nutritional support through parenteral nutrition

Post-duodenal length
< 1,5 - 2m

Severe MALABSORPTION

First cause of chronic intestinal failure

Modification of eating behavior



Microbiota modification

Control **SBS**

90% *Lactobacillus*

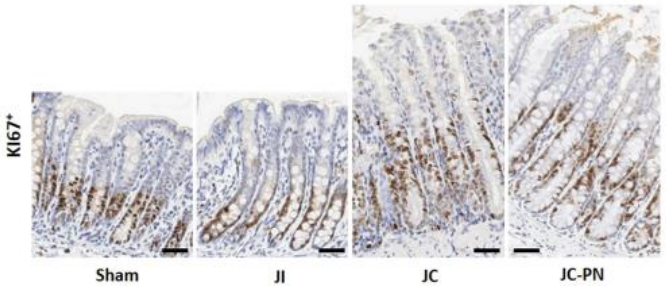
Lactobiota

Fourati et al., 2023
Joly et al., 2009
Gillard et al., 2016

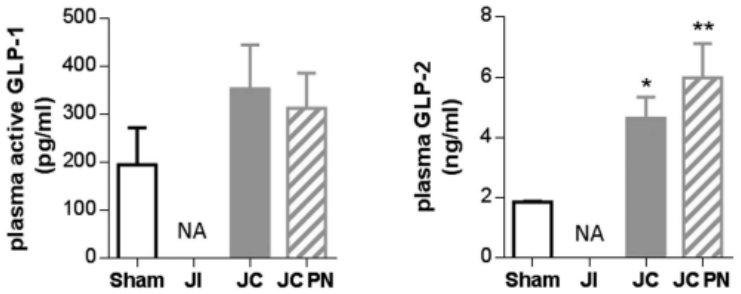
Adaptations in a pre-clinical model of SBS

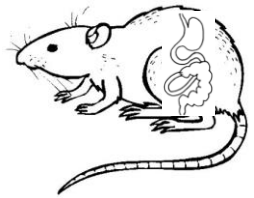
Spontaneous adaptations

Morphological intestinal adaptation

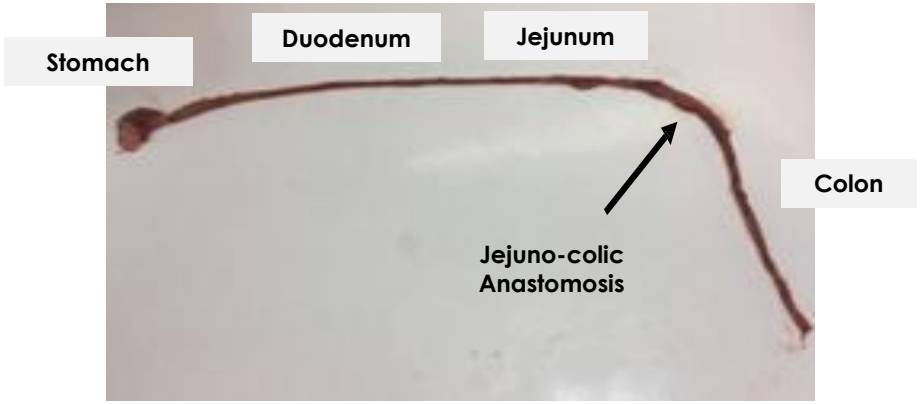


Functional intestinal adaptation

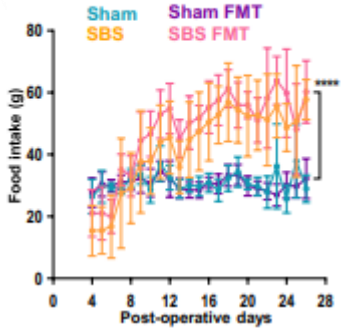




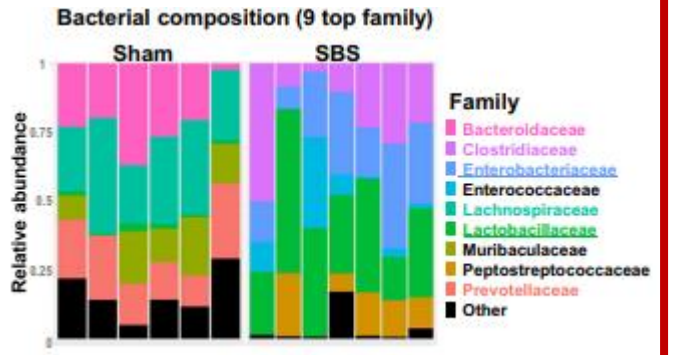
SBS rats



Modification of eating behavior



Microbiota modification



Key factor?

Fourati et al., 2023

Gillard et al., 2016

SBS Microbiota : Role in the adaptations setting

Previous studies in our team:

- Transfer of SBS microbiota to axenic rats

→ Setting of adaptations observed in SBS patients : SBS-like Microbiota + High concentrations of GLP-1 and ghrelin

Gillard et al, 2017

- Level of food intake in SBS rats positively correlated with Lactobacillaceae abundance

Fourati et al, 2023

- Muriel Thomas' team (INRAE, Micalis) → Isolation of probiotic *Lactobacillus* strains from the SBS microbiota

Giron et al, 2021

AIM :

→ Study the effect of supplementation with 2 strains on the setting of spontaneous adaptations in a rat model of short bowel syndrome.

Gillard et al, 2017
Fourati et al, 2023

Design of the experiment

♂ Wistar Rats
7 weeks

J0
Surgery

SHAM

SBS

SBS + A

SBS + B

4 weeks
treatment

Strain A ou Strain B

D7 *D14* *D21* *D28*

Daily: Phenotype monitoring

- Weight/Food Intake
- Feces score

Weekly :
- Blood and feces collection

Sacrifices

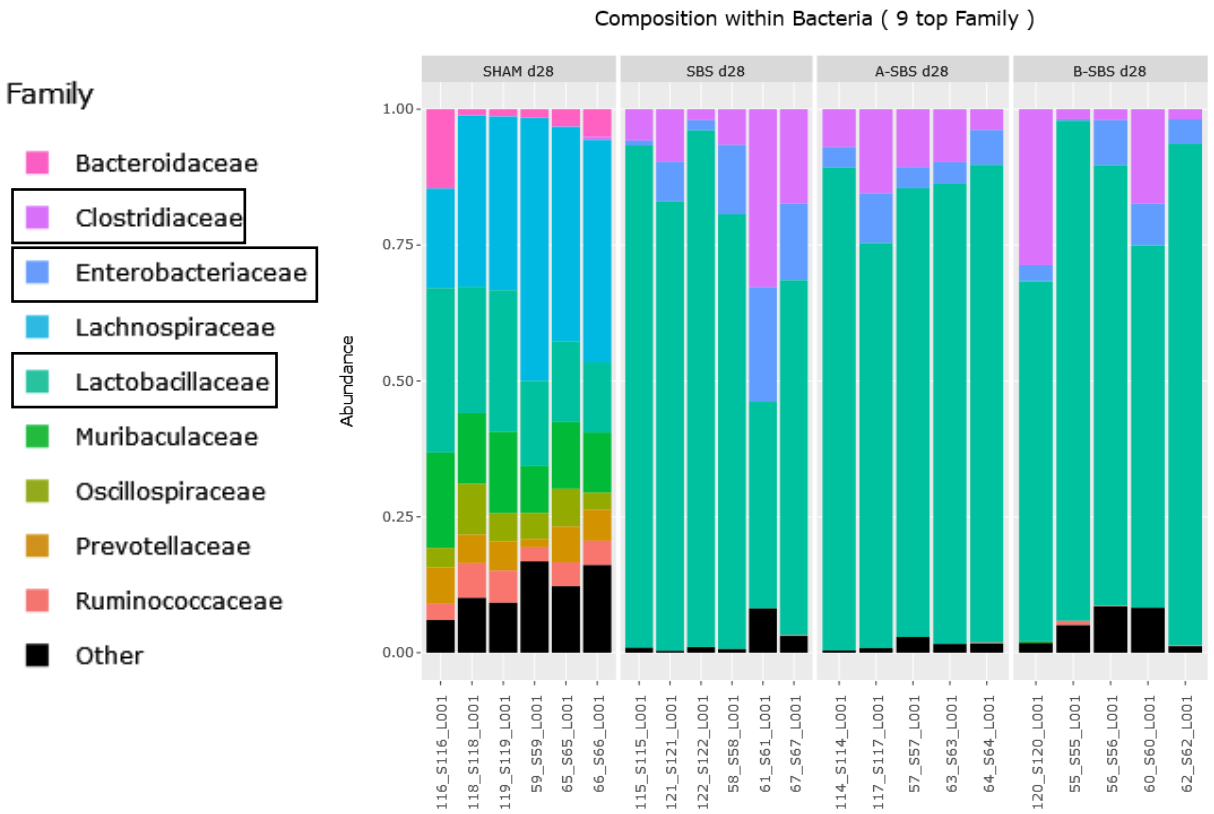
Transit study
(carmine red)

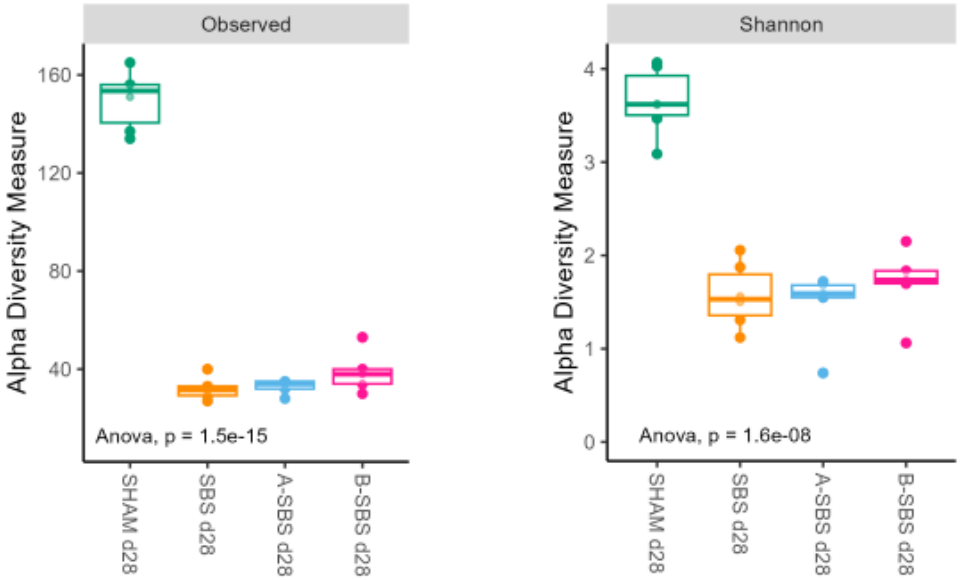
Samples :
- Hypothalamus
- Jejunum
- Colon
- Blood
- Feces

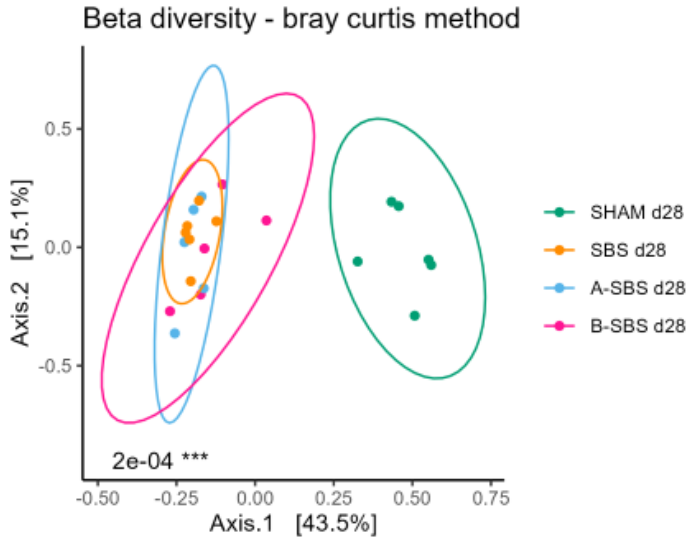
Analyses:
- Microbiota study
- Morphometric measurements
- RT qPCR

Microbiota composition and alpha/beta diversity after 1 month of supplementation

D28





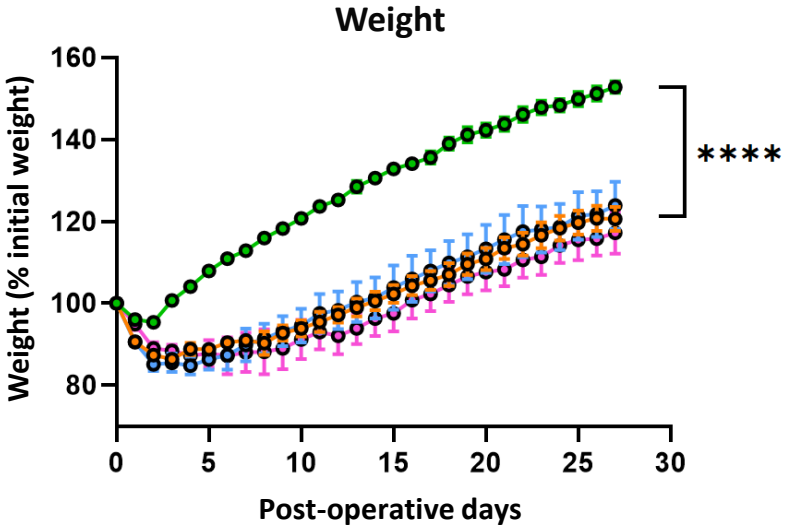


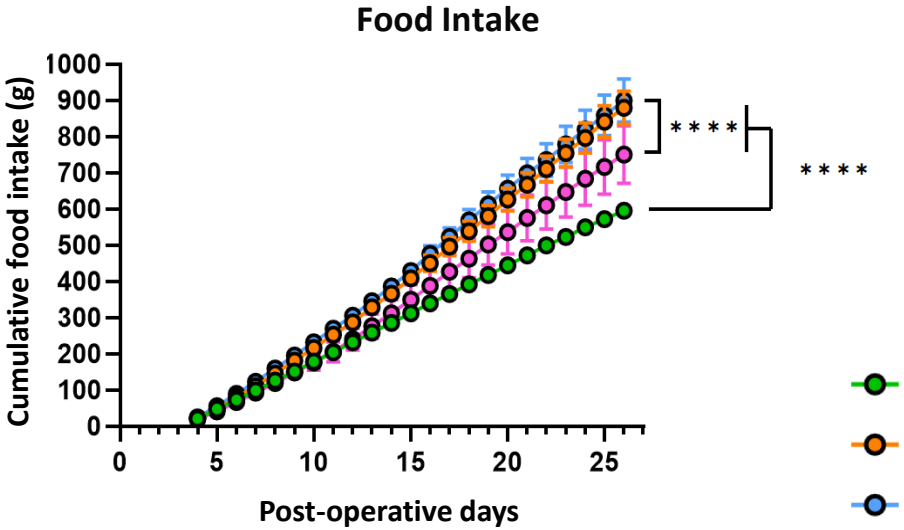
- Large majority of Lactobacillaceae in the SBS microbiota
- Reduced alpha and beta diversities in SBS rats

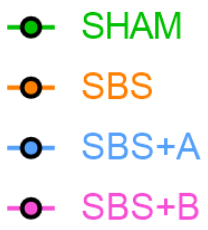
→ No major changes in the microbiota composition with the supplementation

In collaboration with
Anne DUMAY and Maryline ROY

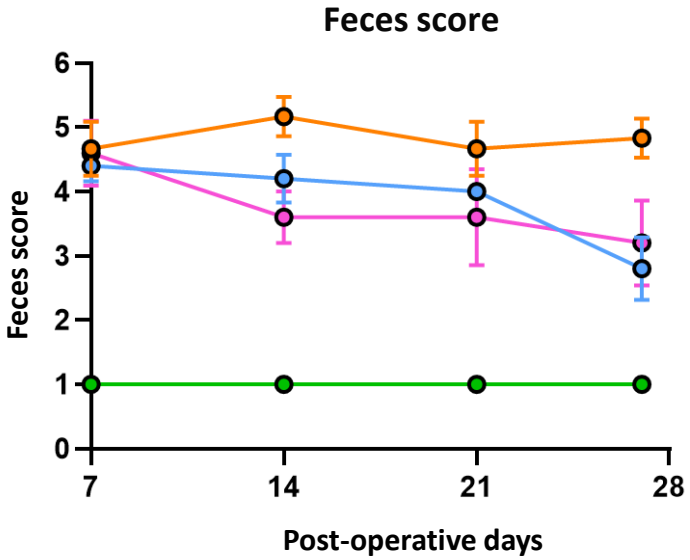
Impact of strains A or B supplementation on SBS phenotype





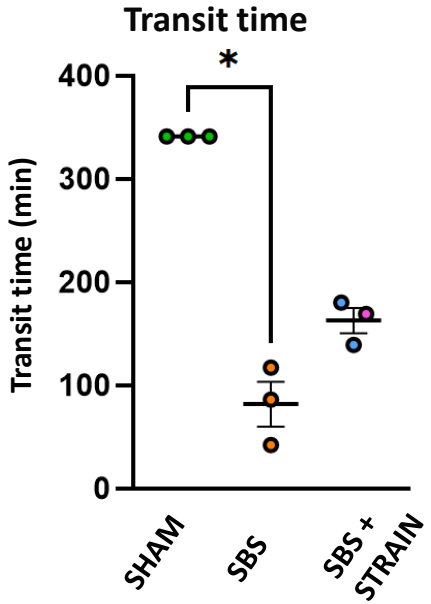


- Increased food intake in SBS rats
- SBS+B rats eat less than the others SBS groups



Feces score:

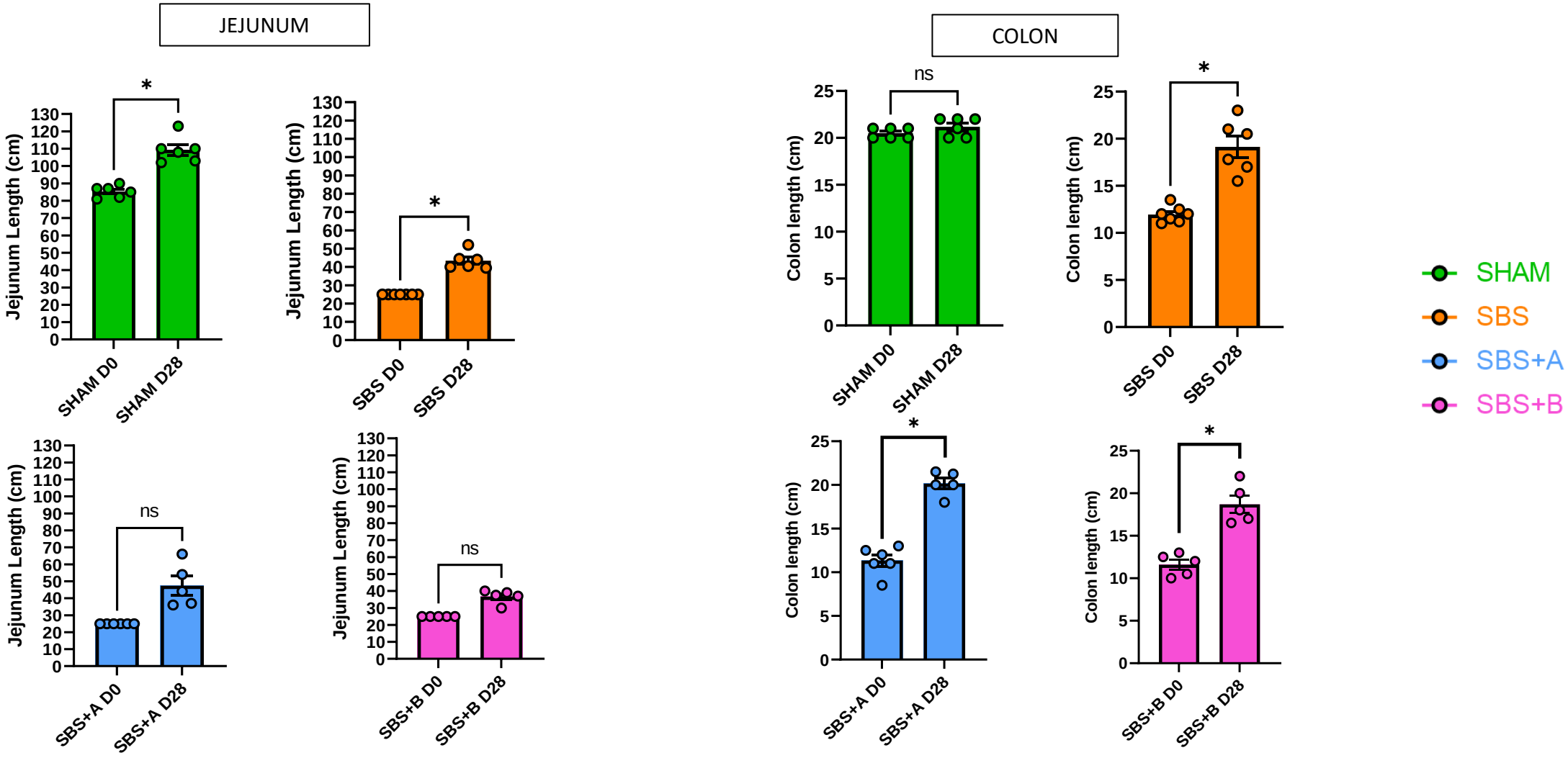
6 = severe diarrhea
5 = diarrhea
4 = soft feces + diarrhea
3 = soft feces
2 = moulded feces + soft feces
1 = moulded feces



Less diarrhea with slowed transit time in SBS supplemented groups

Kruskal-Wallis test
2 way ANOVA

Measurements of jejunum and colon lengths in SBS rats



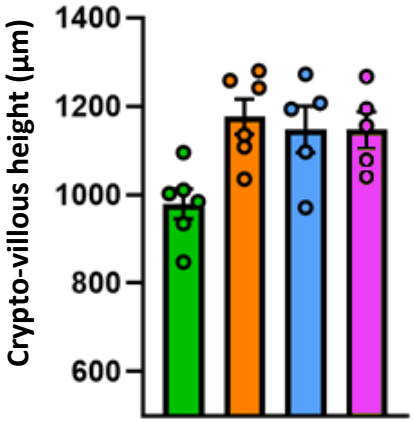
- Increased jejunum and colon lengths in SBS rats at D28
- No effect of the supplementation with the two strains on these parameters

T-test

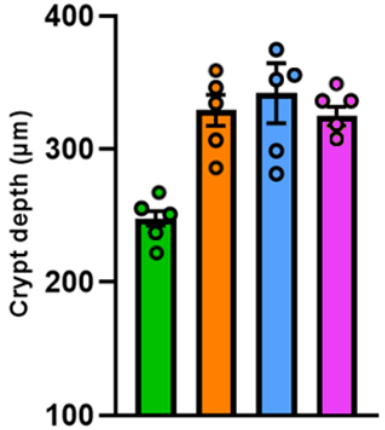
Jejunal and colonic hyperplasia analysis

D28

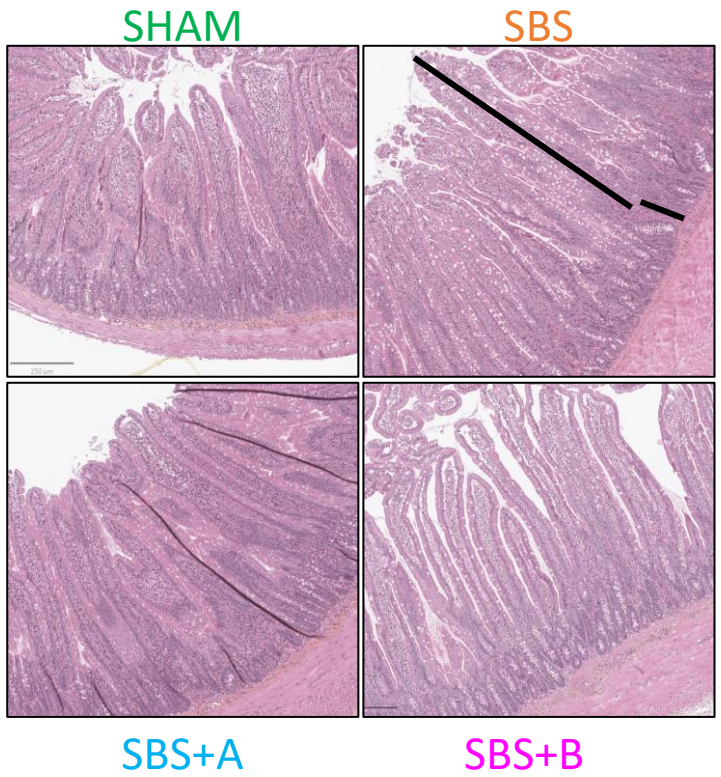
JEJUNUM

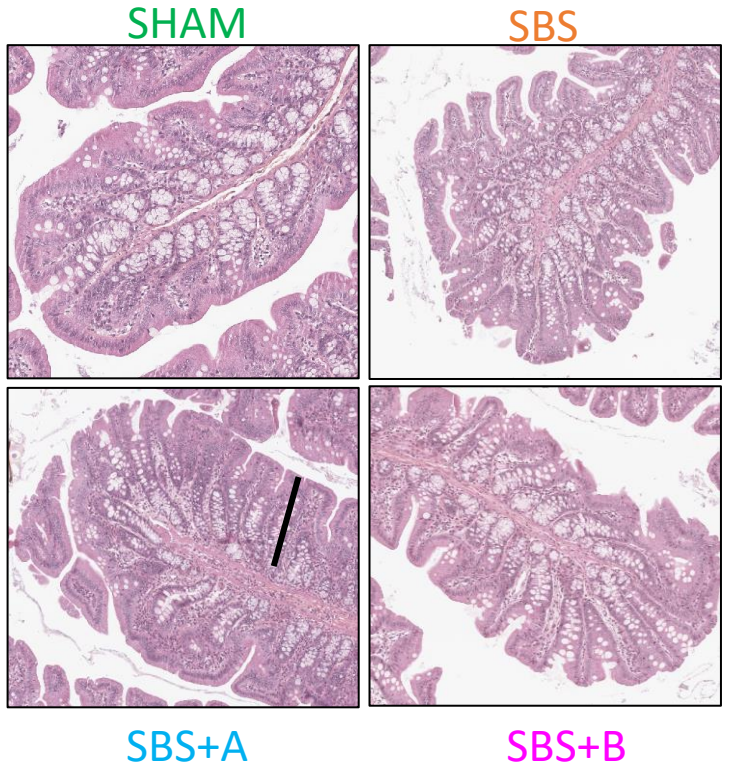


COLON



SHAM
SBS
SBS+A
SBS+B



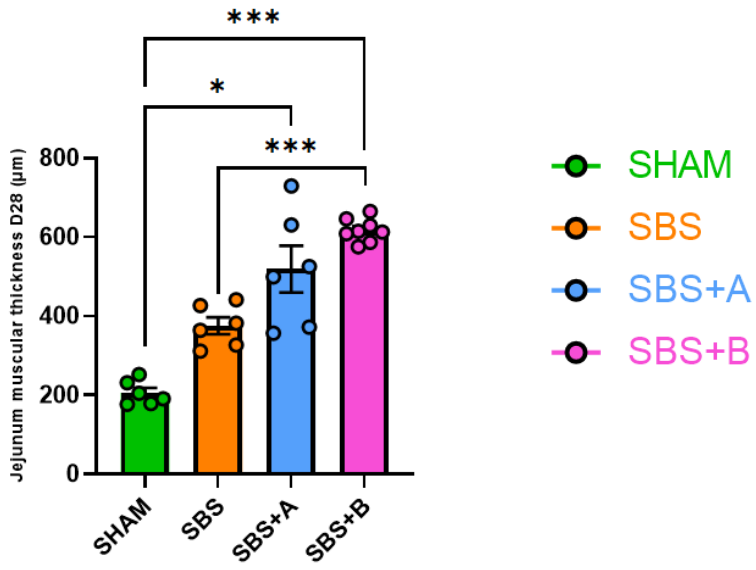


- Increased depth of the jejunal and colic crypts in all SGC rats
- No major effects of the supplementation on these parameters

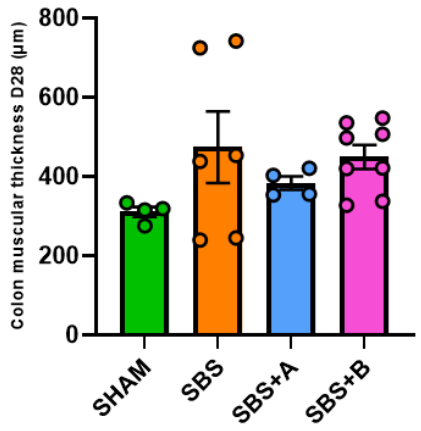
Kruskal-Wallis test

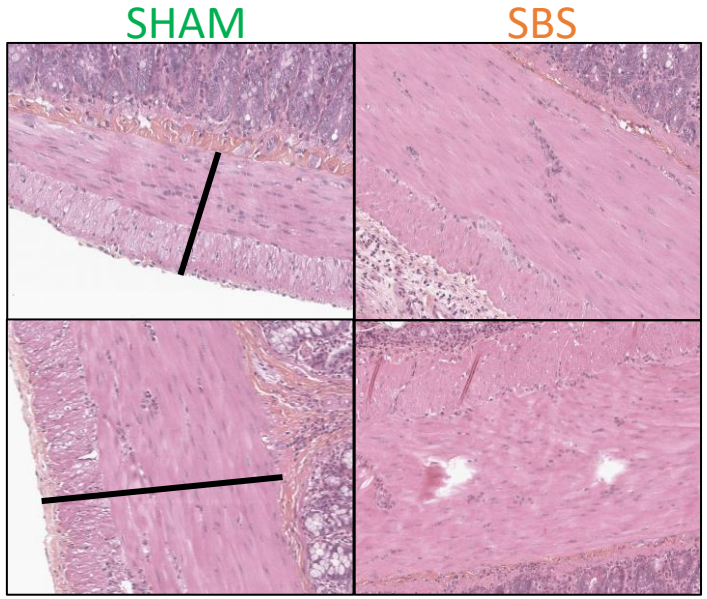
Measurement of the Thickness of the Jejunal Muscularis in SBS Rats

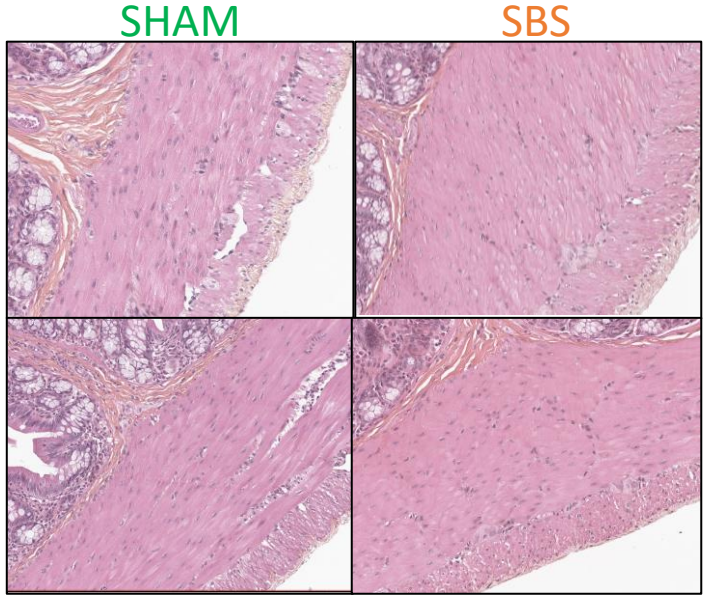
JEJUNUM



COLON







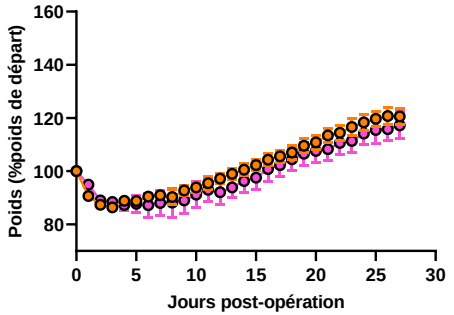
- Significant increase in jejunal muscularis thickness in treated SBS rats, particularly in SBS+B rats.

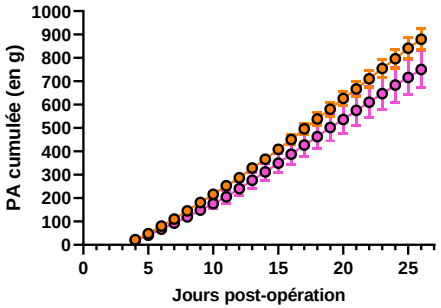
Kruskal-Wallis test

Conclusion

Impact of *Lactobacillales* Supplementation

- ↘ of food intake in **SGC+B :** gain as many weight as the other groups
  → **positive effect of the strain B on weight gain?**
- Improvement in faeces : less diarrhea
  → **better water absorption?**
- Improved transit time : more time for nutrient absorption
  → **positive effect on absorption?**
- ↗ in the thickness of the jejunal muscularis
  → **positive effect on absorption?**





Strains A and B appear to have had a positive effect on different parameters

→ Could they be an effective therapy?

→ Efficacy compared to existing therapies?

Acknowledgements to all AdMIR project partners

U1149, PIMS team :

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