IAFP'S EUROPEAN SYMPOSIUM ON FOOD SAFETY
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Do polysorbate 80 and sodium nitrite affect differently the gut microbiota of healthy individuals and IBD patients ?

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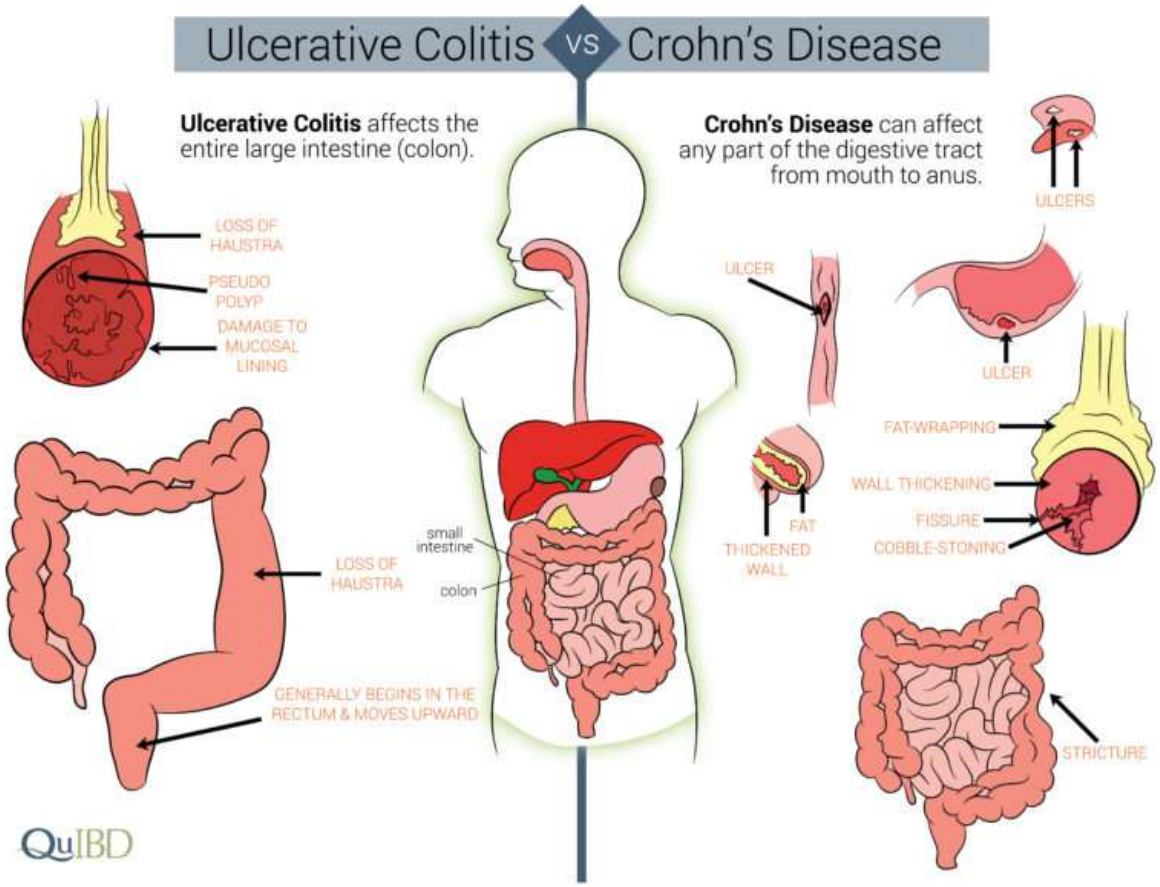
Inflammatory Bowel Diseases – IBD

Food additives ↔ IBD



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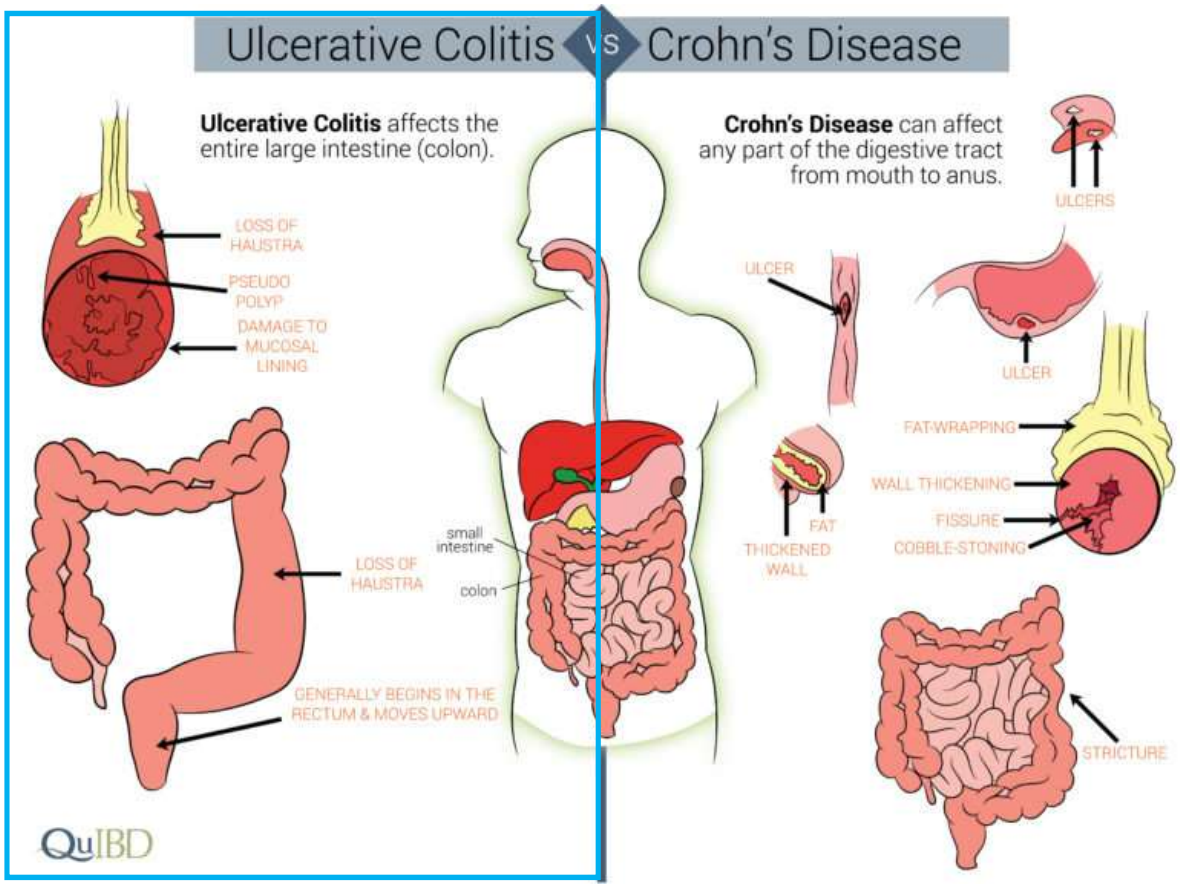

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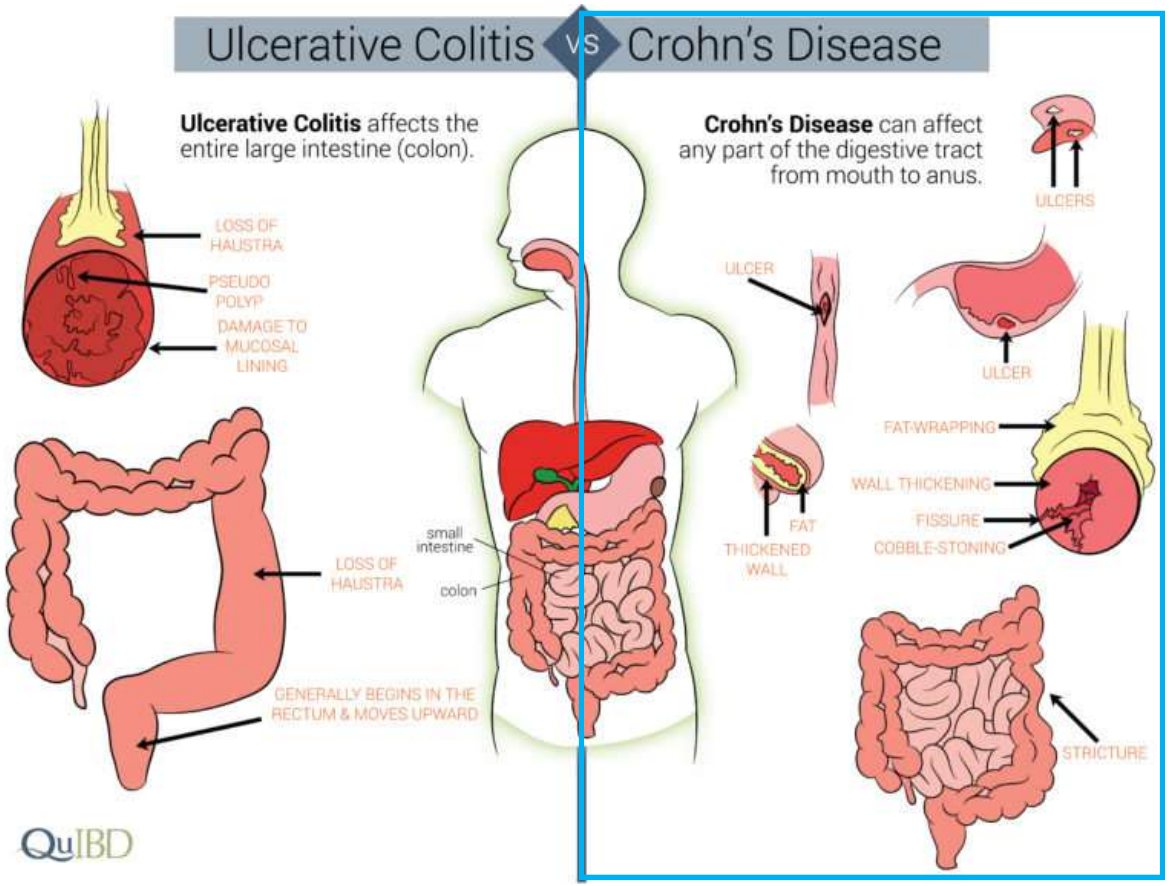

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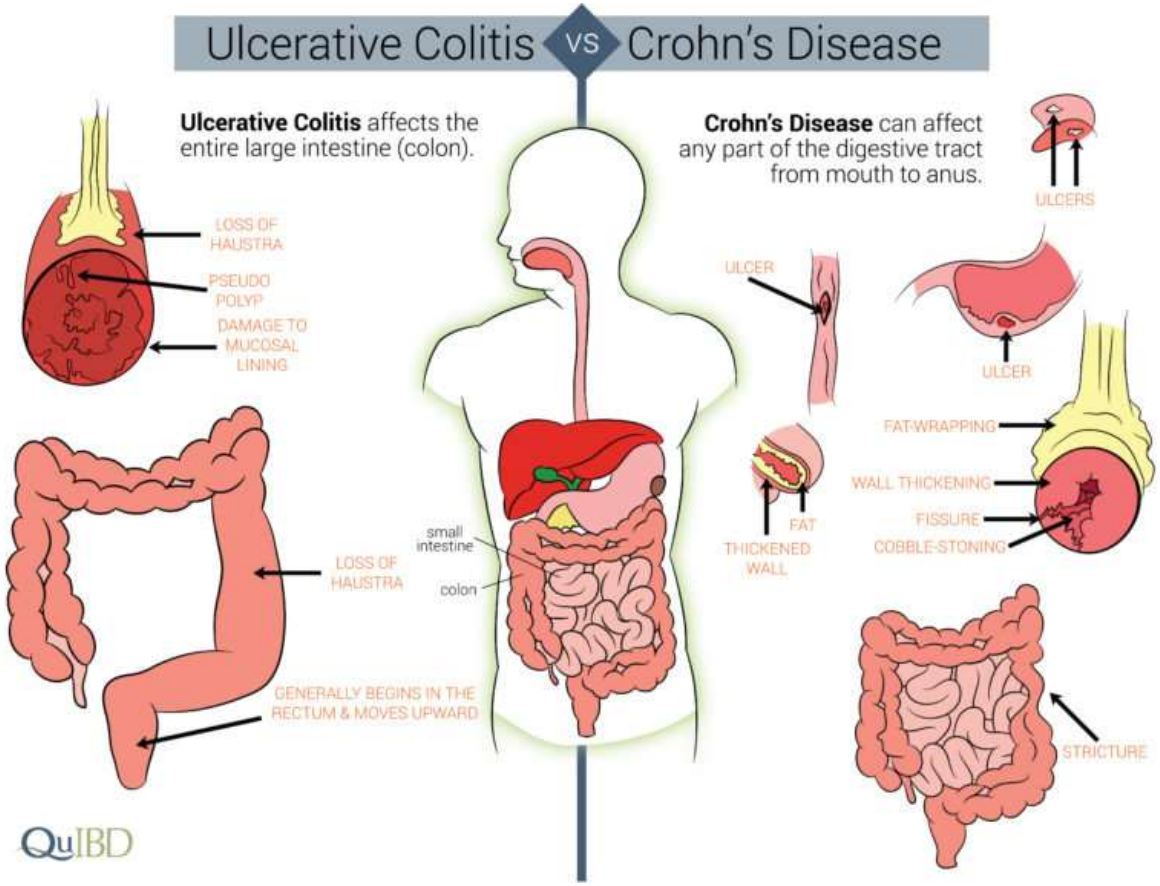

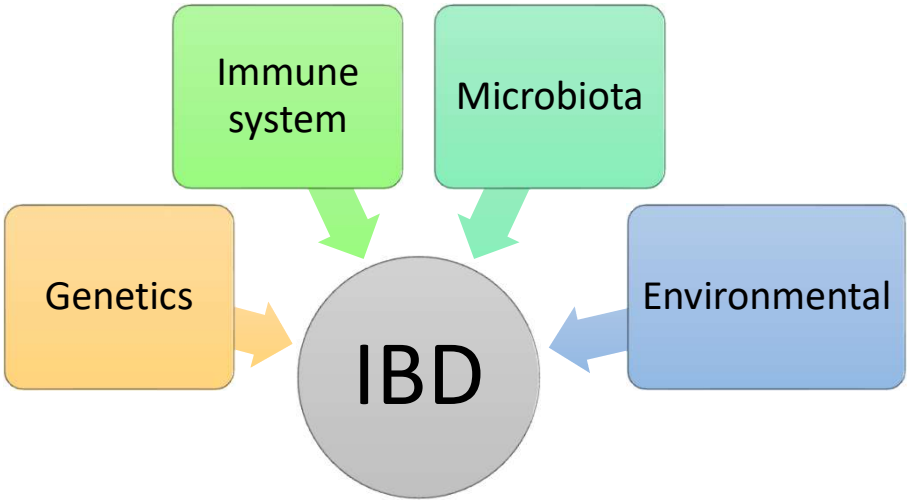

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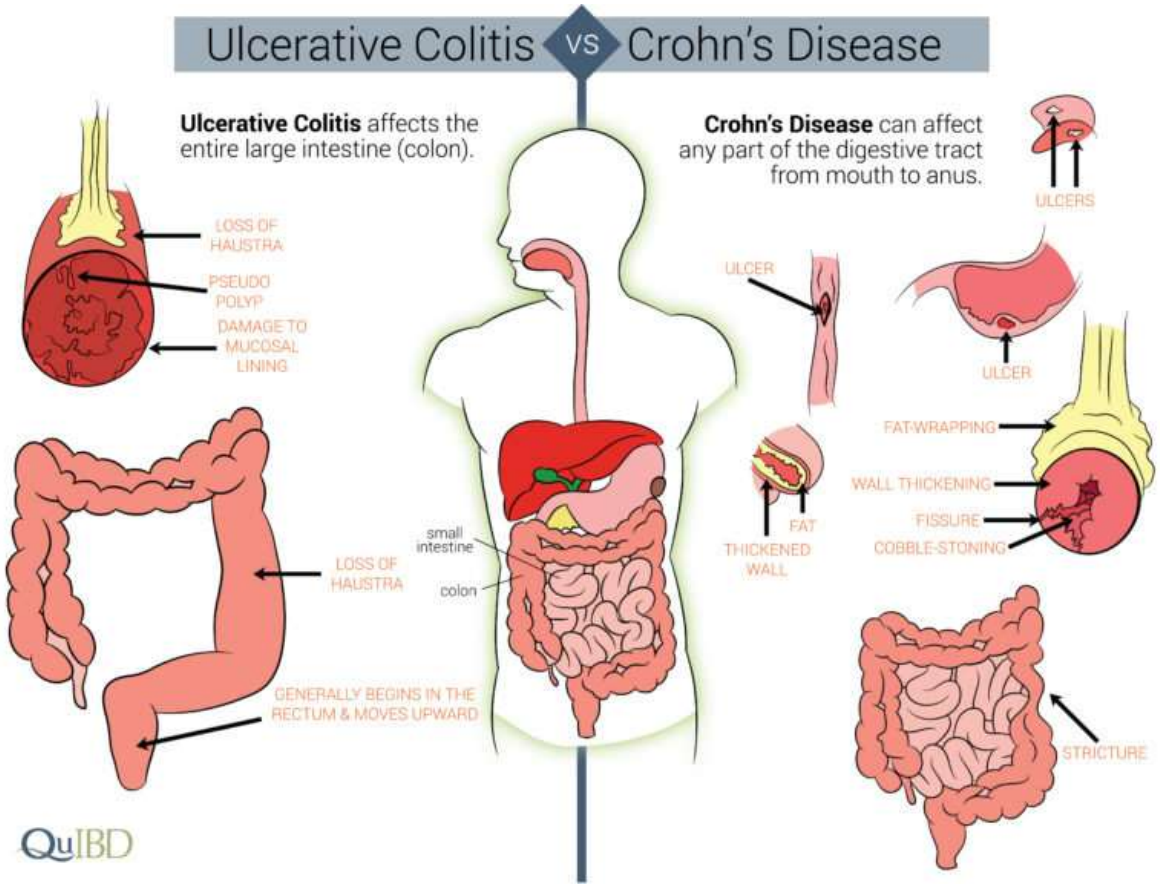
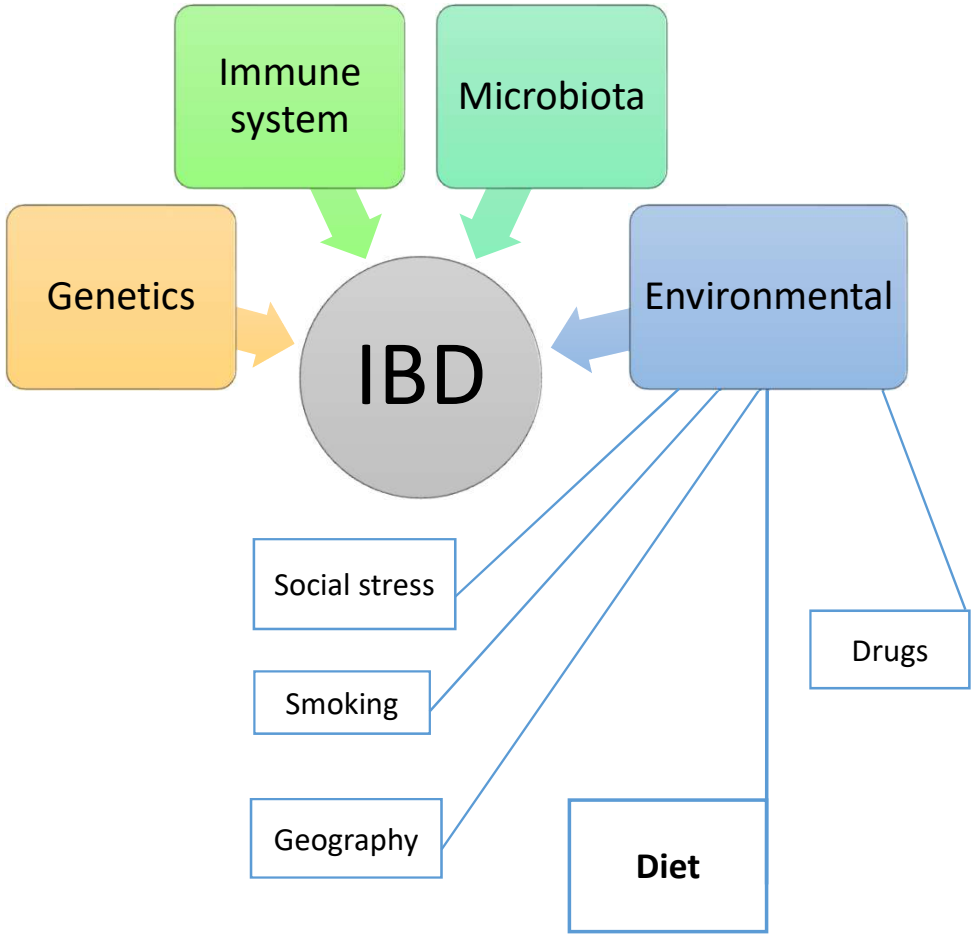
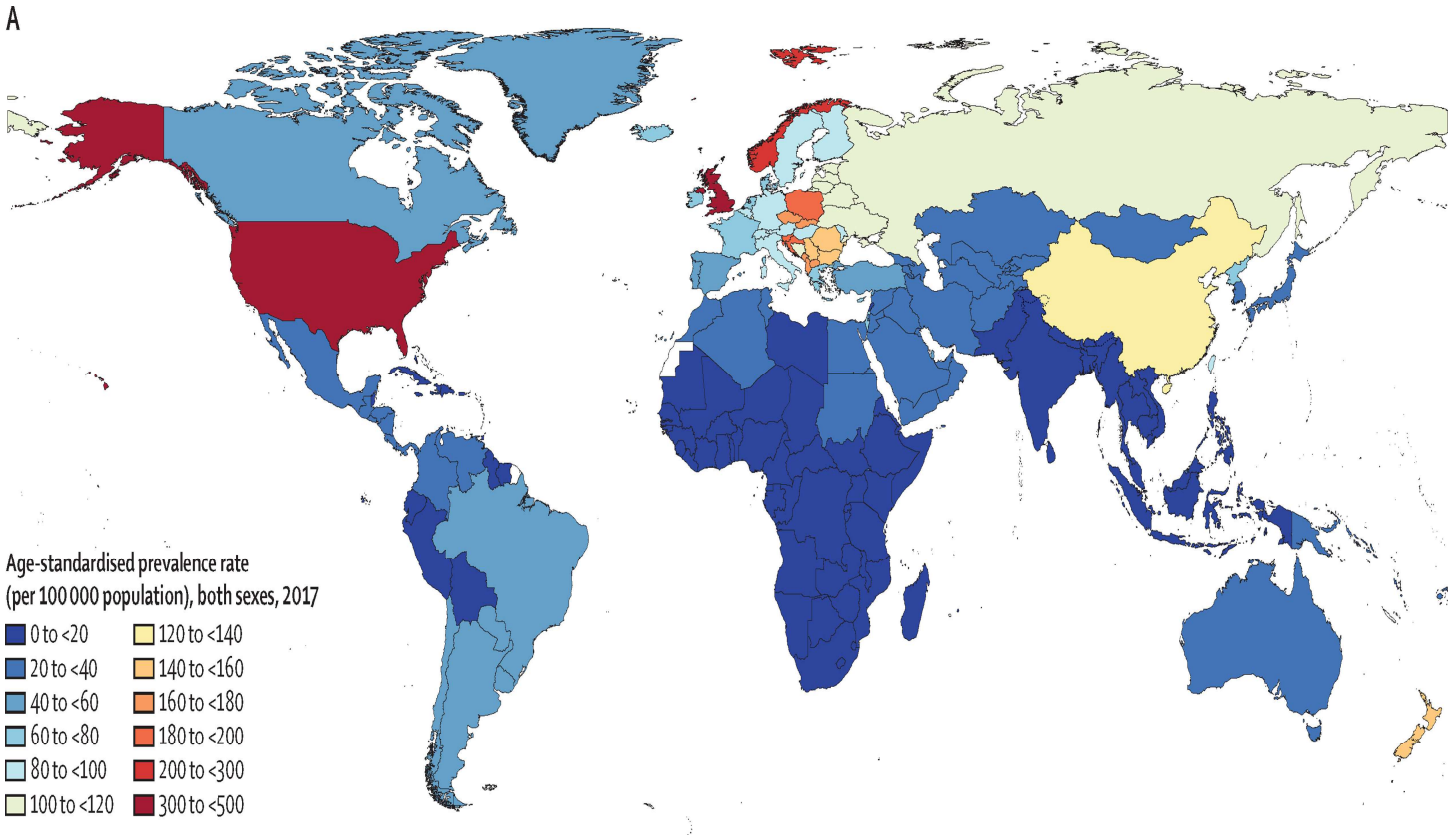




IBD prevalence



~ 0,2% European population suffer from IBD (Zhao *et al., 2021)*

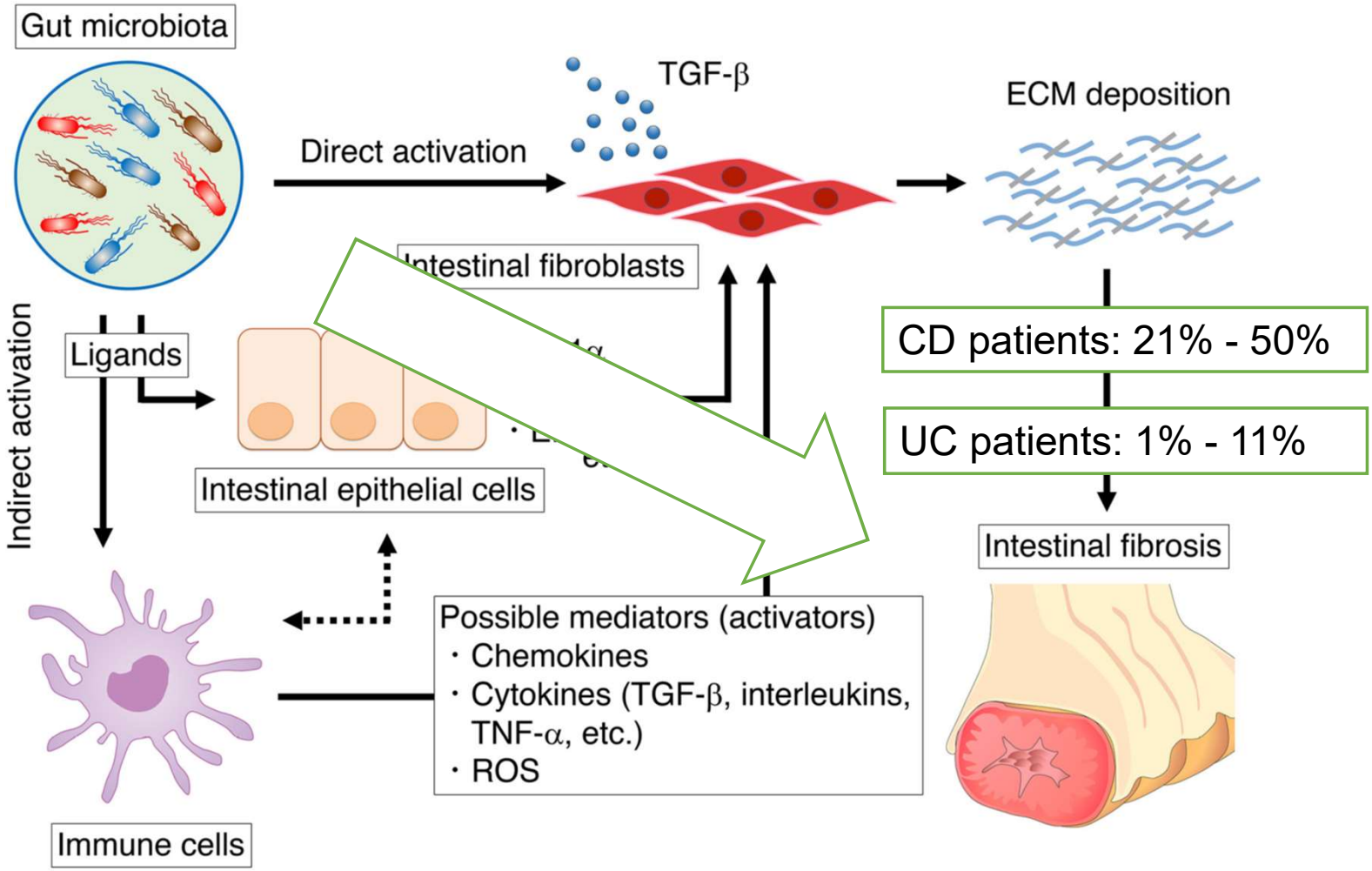
Western diets

e.g., Fast-food diet

Red and processed meat, high-energy dense foods, refined carbohydrates, added sugar

The Lancet Gastroenterology & Hepatology 2020 517-30 DOI: (10.1016/S2468-1253(19)30333-4)

Intestinal fibrosis



Watanabe D, Kamada N. Front Med 2022;9:1–14.

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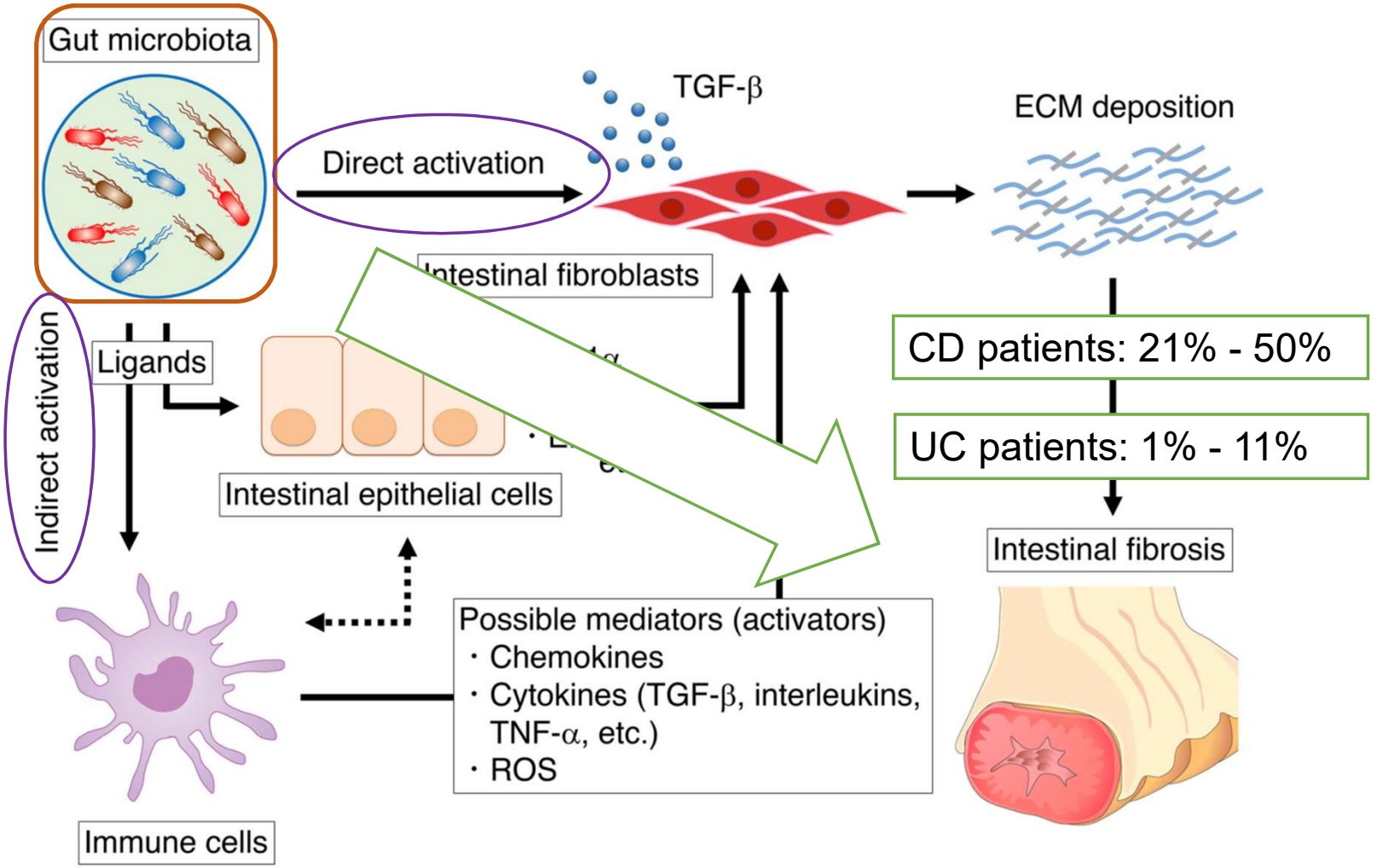

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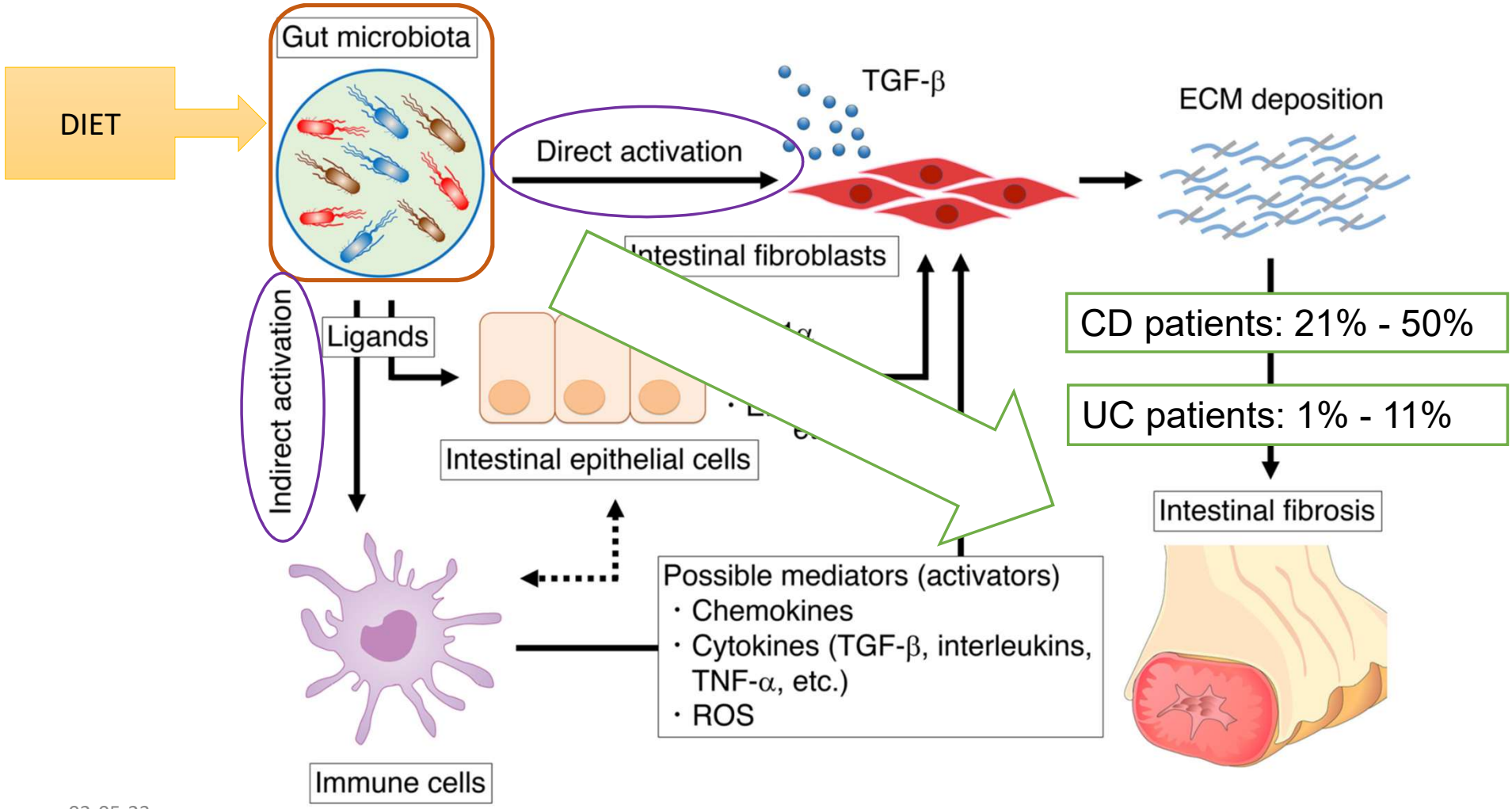

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Diet (food additives) & IBD

Emulsifiers

- ↑ *Escherichia/ Shigella*
- ↓ *Faecalibacterium*
- **↓ Bacterial diversity**
- ↓ SCFAs
- **↑ Intestinal inflammation**

Colorants

- ↑ Firmicutes
- **↓ Bacterial diversity**
- **↑ Intestinal inflammation**

Preservatives

- ↑ *Proteobacteria*
- ↓ *Clostridiales*
- **↓ Bacterial diversity**
- **↑ Intestinal inflammation**

Sweeteners

- ↑ *Escherichia/ Shigella*
- ↑ Proteobacteria
- ↓ *Clostridium cluster XIVa*
- **↓ Bacterial diversity**
- **↑ Pro-inflammatory cytokines**

Raoul *et al.,Microorganisms* ***2022****, 10, 167*

Goals

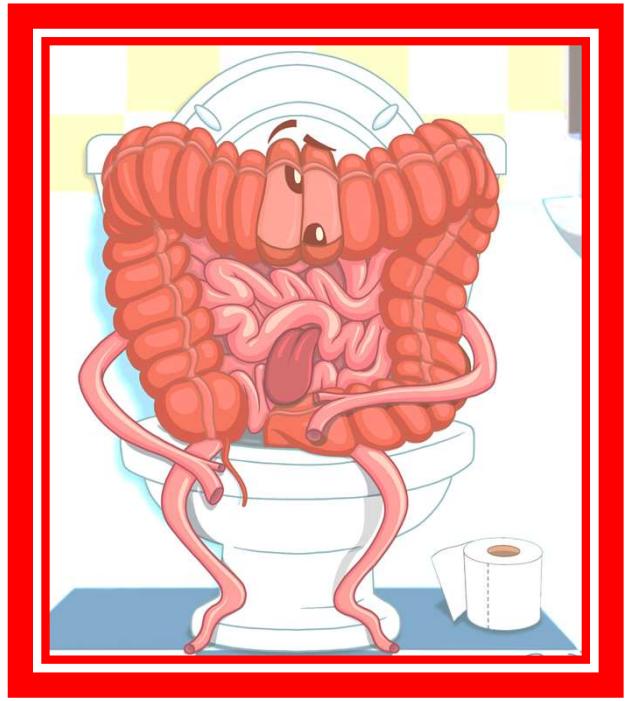
- ✓ Short – term *in vitro* fermentations
- ✓ Gut microbiota of healthy individuals and IBD patients
- ✓ Evaluate the impact of several compounds
- ✓ Measure microbial metabolites
- ✓ Changes in bacterial populations

Methodology – Donors

- 3 groups

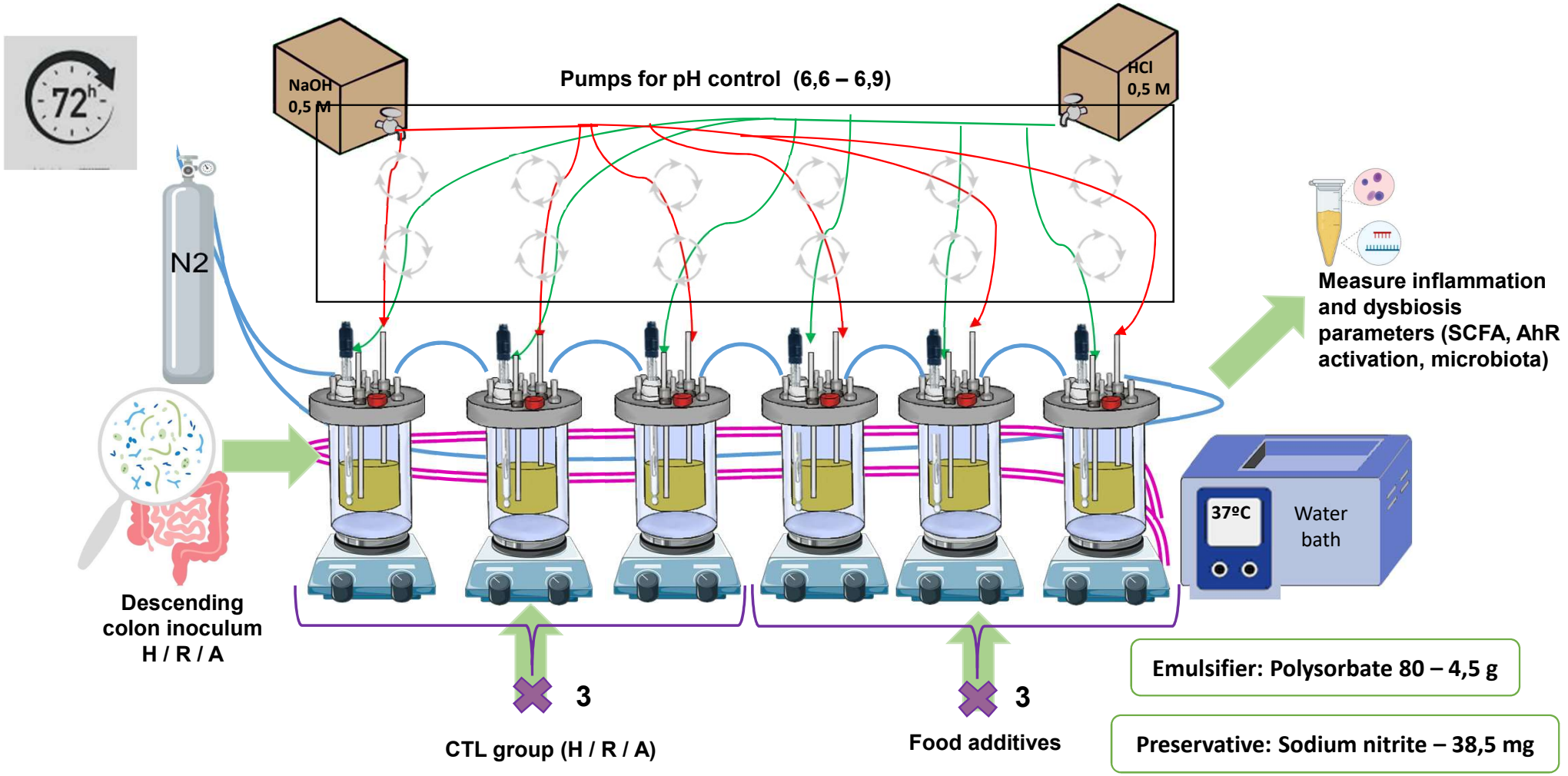
Healthy (n = 5)

Remission of IBD (n = 5)



Active IBD (n = 5)

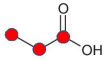
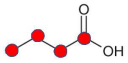
Methodology: Short – term *in vitro* fermentations



Methodology – Short chain fatty acid (SCFA) production

SCFA → ↓IBD

Gas chromatography + mass spectrometry (SPME)

 Acetate (C2)	Anti – inflammatory effects Promote T cells differentiation Reduction of epithelial permeability
 Propionate (C3)	Antimicrobial effect (C3, C4) ↓ Cancer cells proliferation (C3, C4)
 Butyrate (C4)	Increase mucin production (C4) Energy source for colonocytes (C4)
BCFA [iso – butyric (iC4); iso – valeric (iC5)]	Markers for colonic protein fermentation High ammonia and biogenic amines production

Methodology – Microbial population changes

SCFA	Bacterial populations
Acetate	Bacteroidetes, ***Akkermansia muciniphila***, *Bifidobacterium* spp., ***Bacteroides* spp.**, ***Prevotella* spp.**, ***Ruminococcus* spp**., *Clostridium* spp., Streptococcus spp.
Propionate	Bacteroidetes, ***Akkermansia muciniphila***, *Bacteroides* spp., ***Veillonella* spp.**, *Dialister* spp., *Salmonella* spp., *Megasphaera elsdenii*, *Coprococcus catus, Ruminococcus obeum, Phascolarctobacterium succinatutens*
Butyrate	Firmicutes, ***Faecalibacterium prausnitzii***, ***Roseburia* spp.**, ***Coprococcus*** *(eutactus, comes, catus), Anaerostipes* spp., *Eubacterium rectale, Eubacterium hallii,* ***Oscillospira* spp.**, *C. leptum*
BCFA	*Bacteroides* spp., *Clostridium* spp.

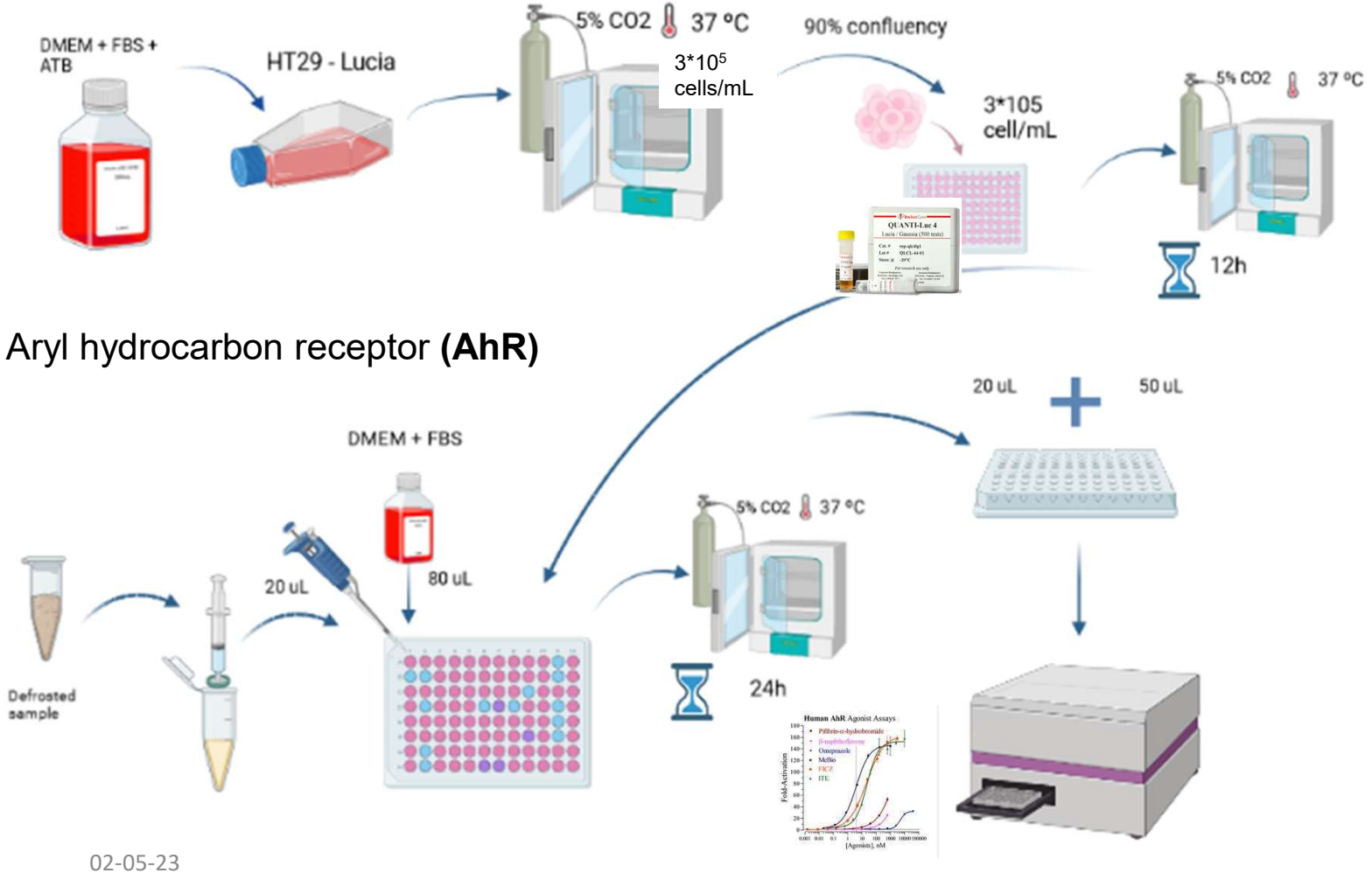
qPCR analysis

↓ IBD

↑ IBD

Fibrosis

Methodology – Microbial derived AhR agonist



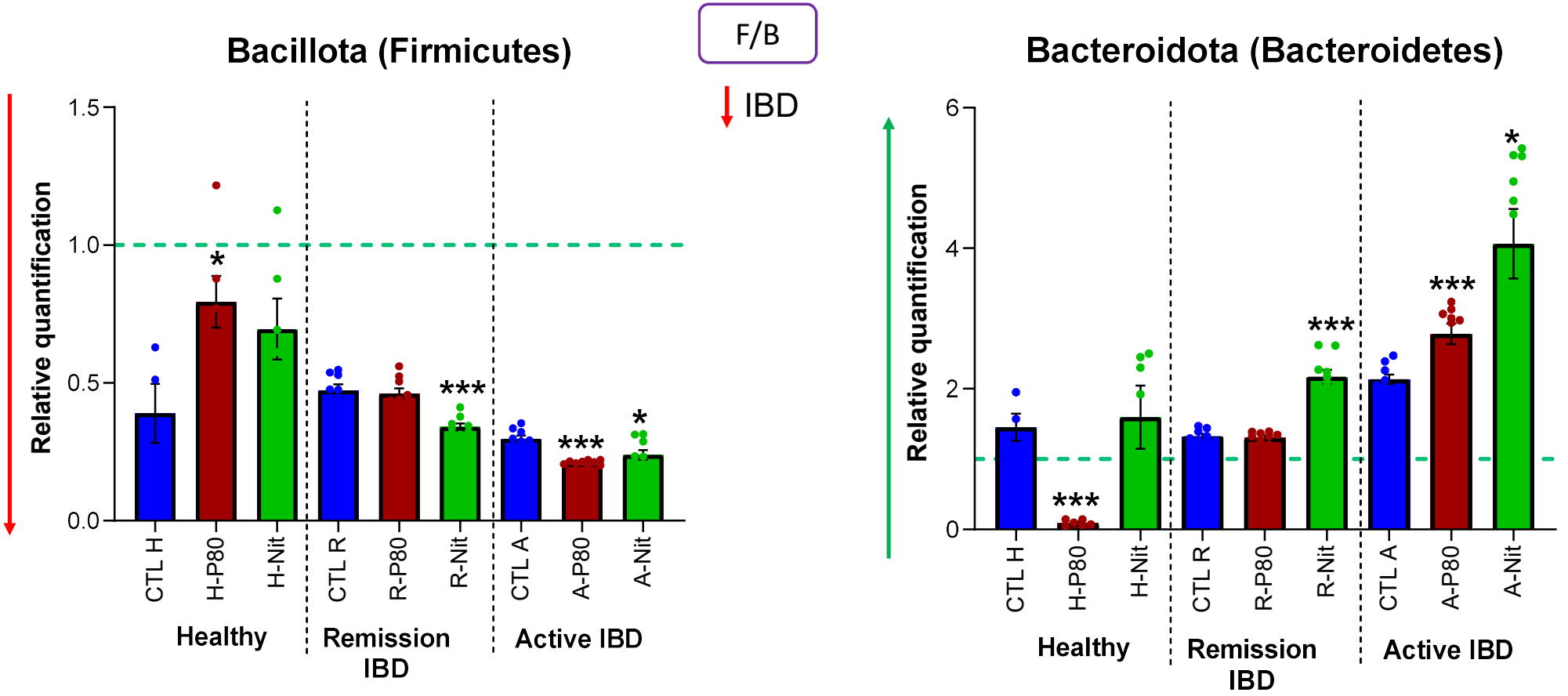
Aryl hydrocarbon receptor **(AhR)**

↑ **AhR activation**

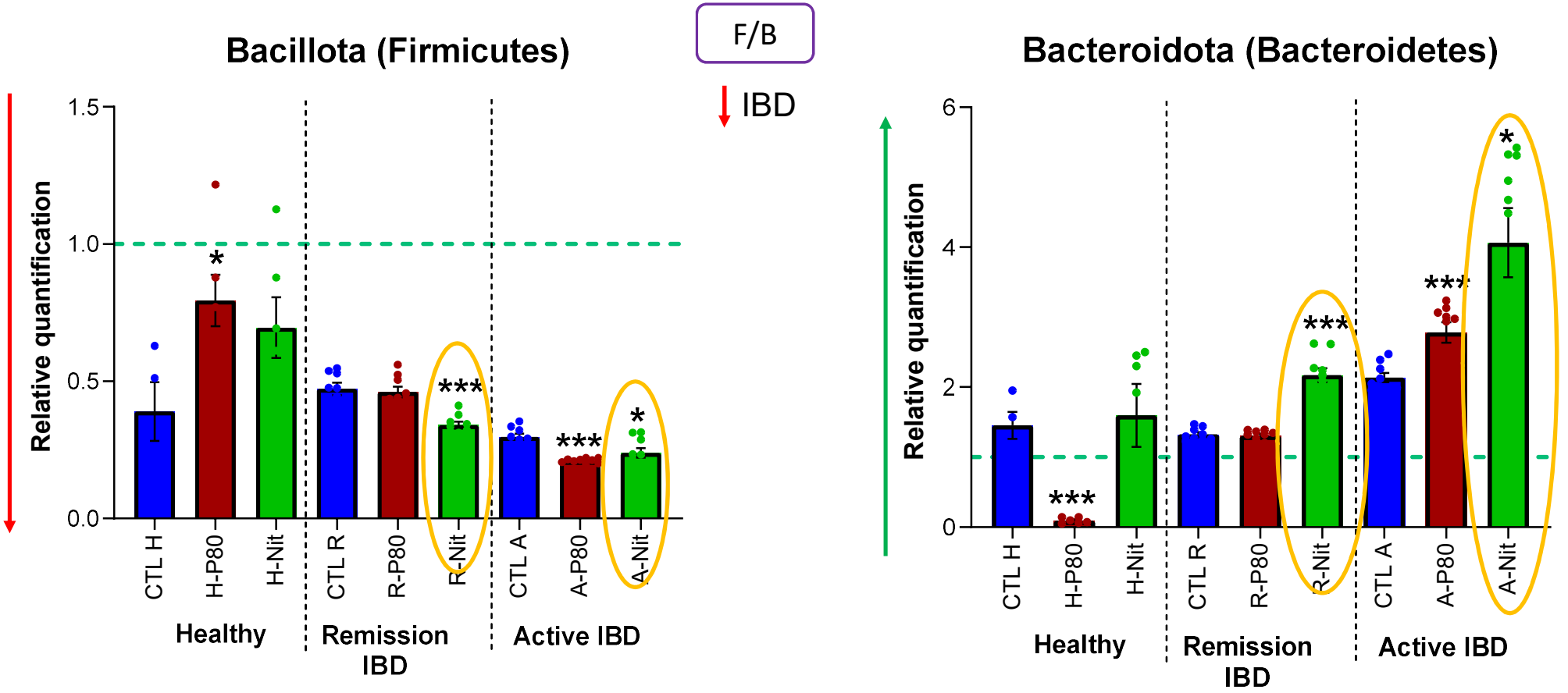
↓ Pro – inflammatory cytokines
Collagen synthesis

↑ Anti – inflammatory cytokines
Mucus production

Results – Phylum analysis

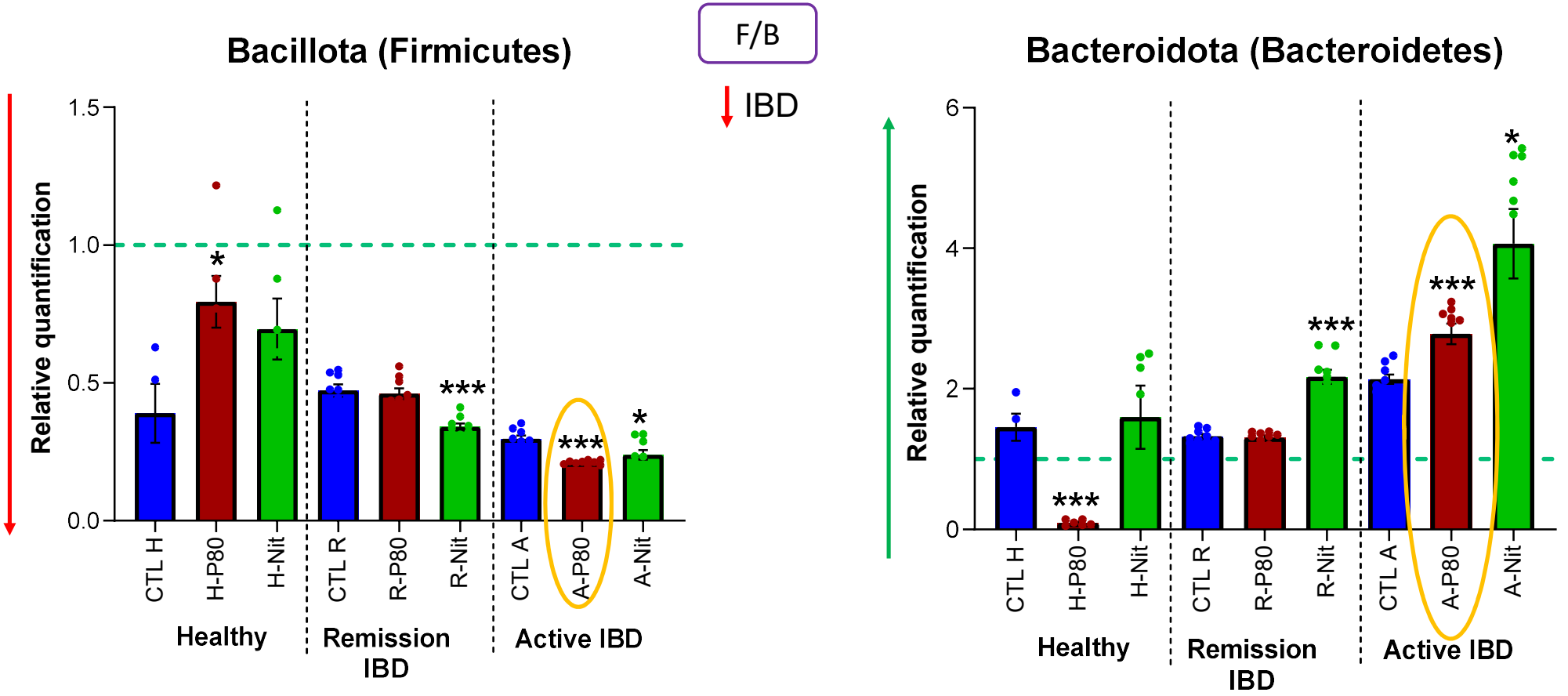


Results – Phylum analysis



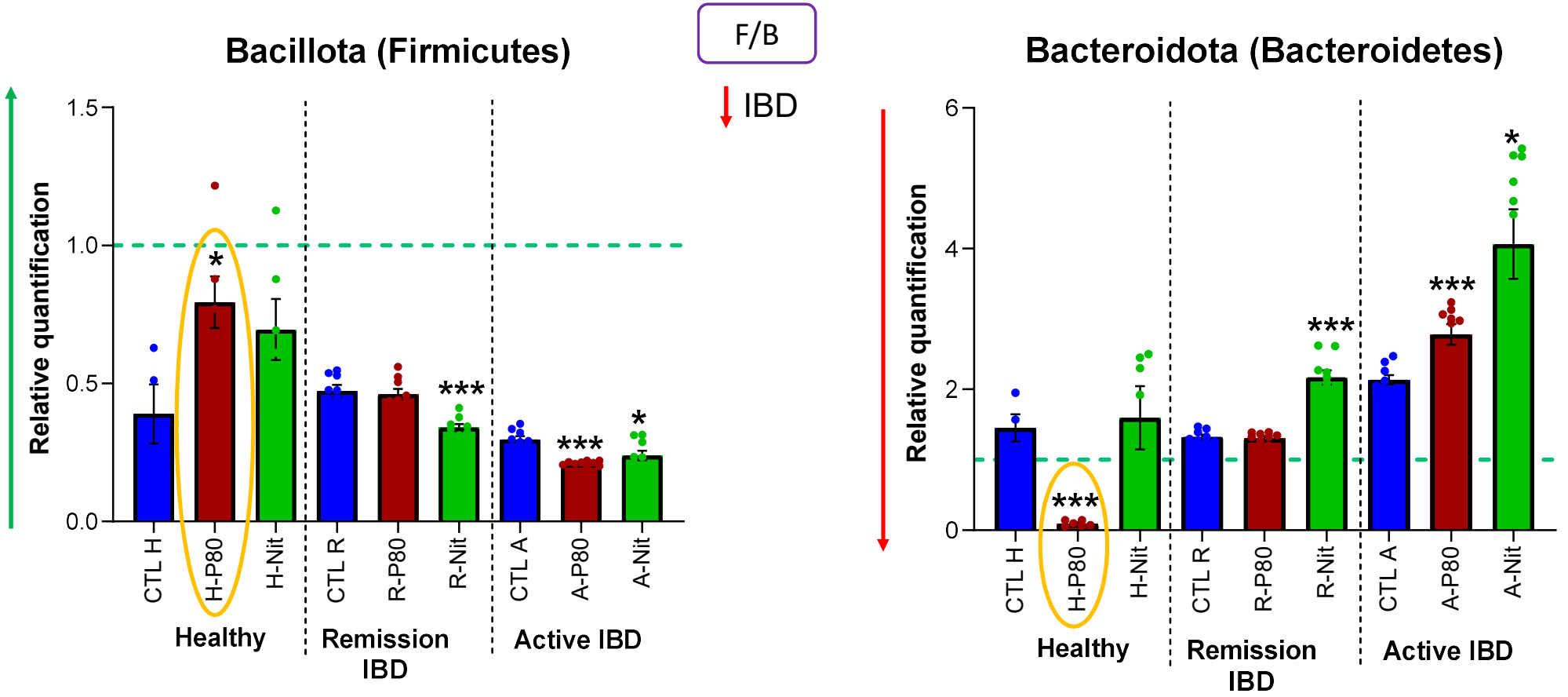
Sodium nitrite: ↓ F/B in R and A

Results – Phylum analysis



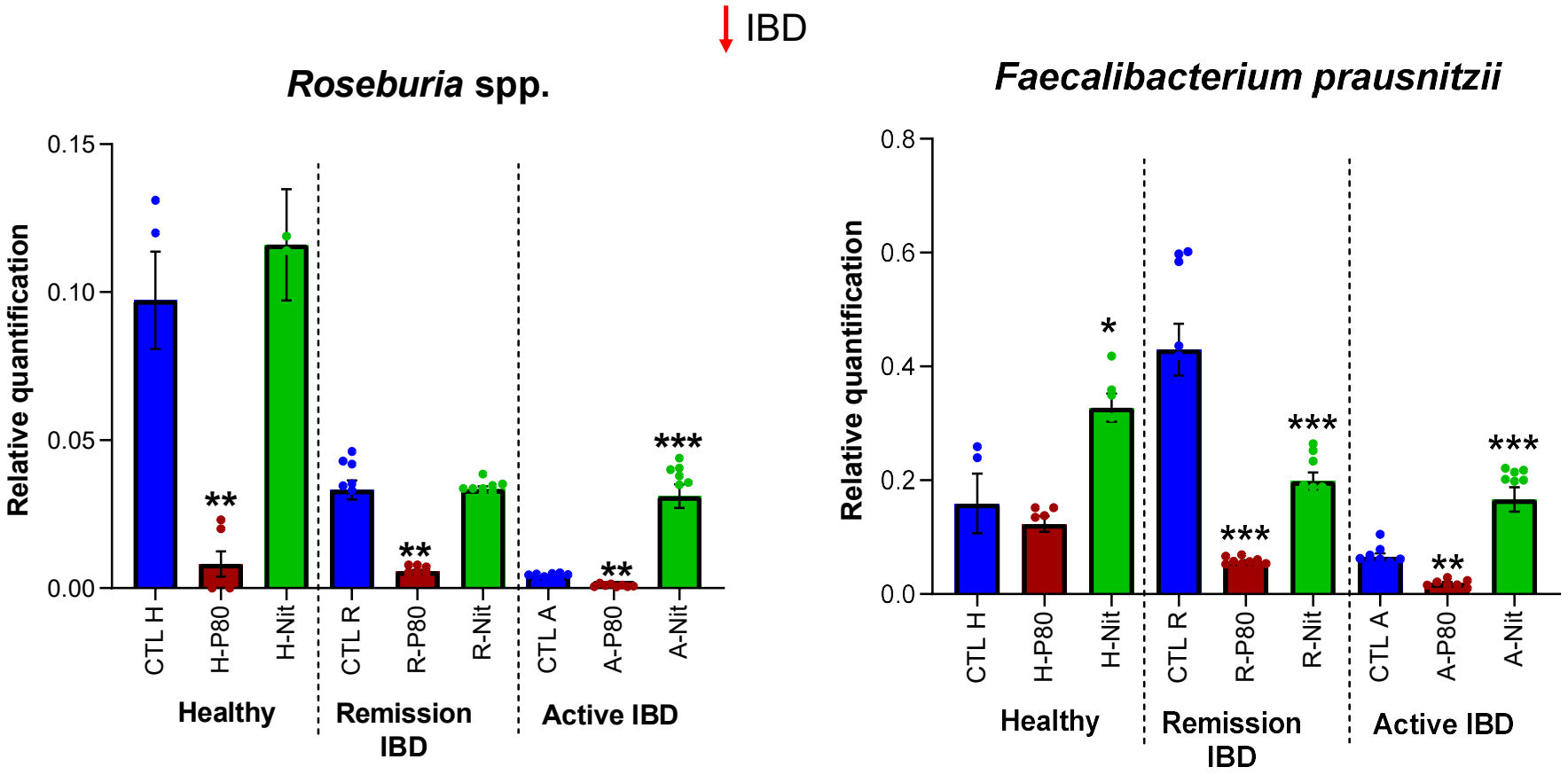
Polysorbate 80: ↓ F/B in A

Results – Phylum analysis



Polysorbate 80: ↑ F/B in H

Results – Butyrate producers



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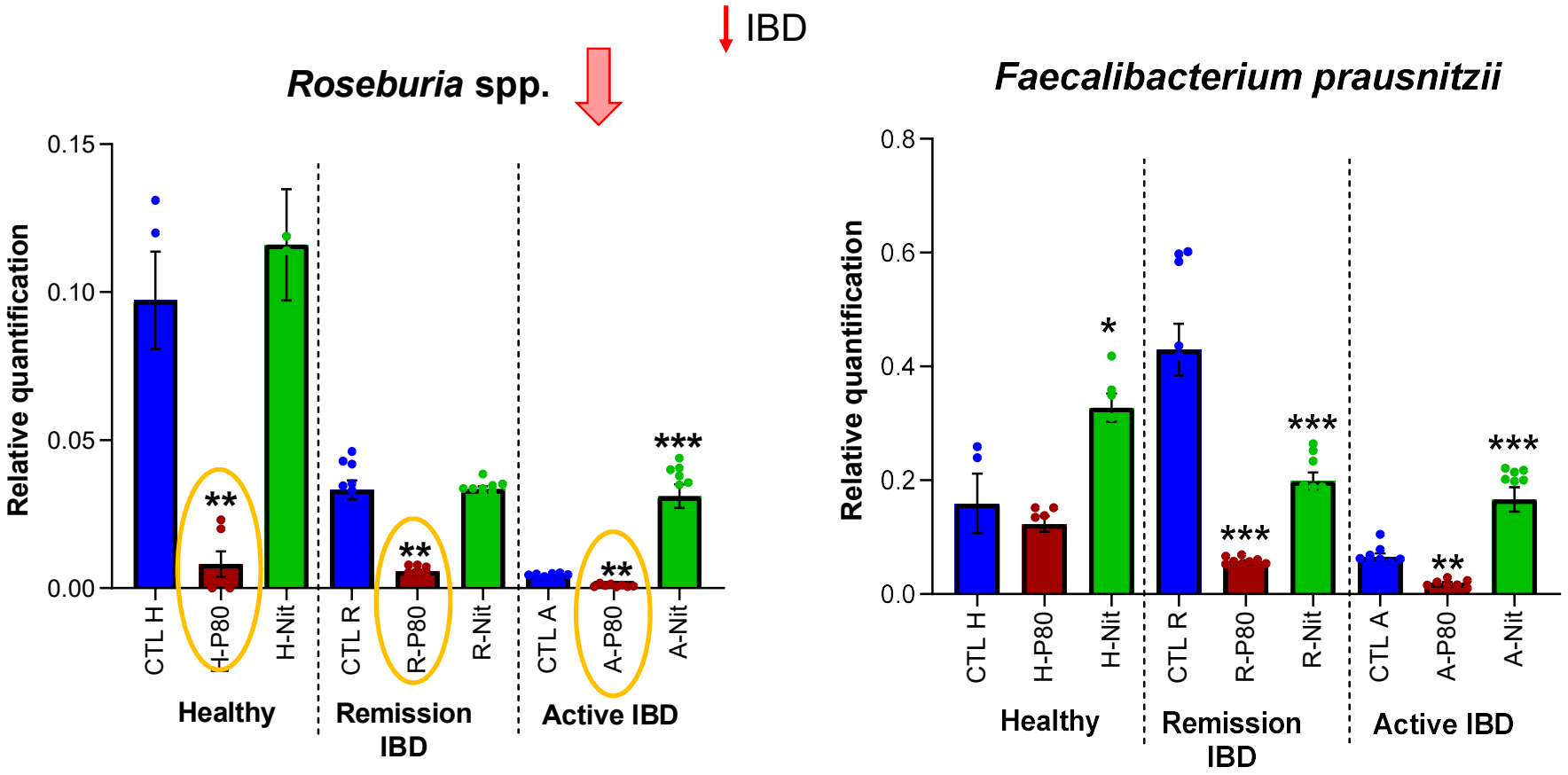
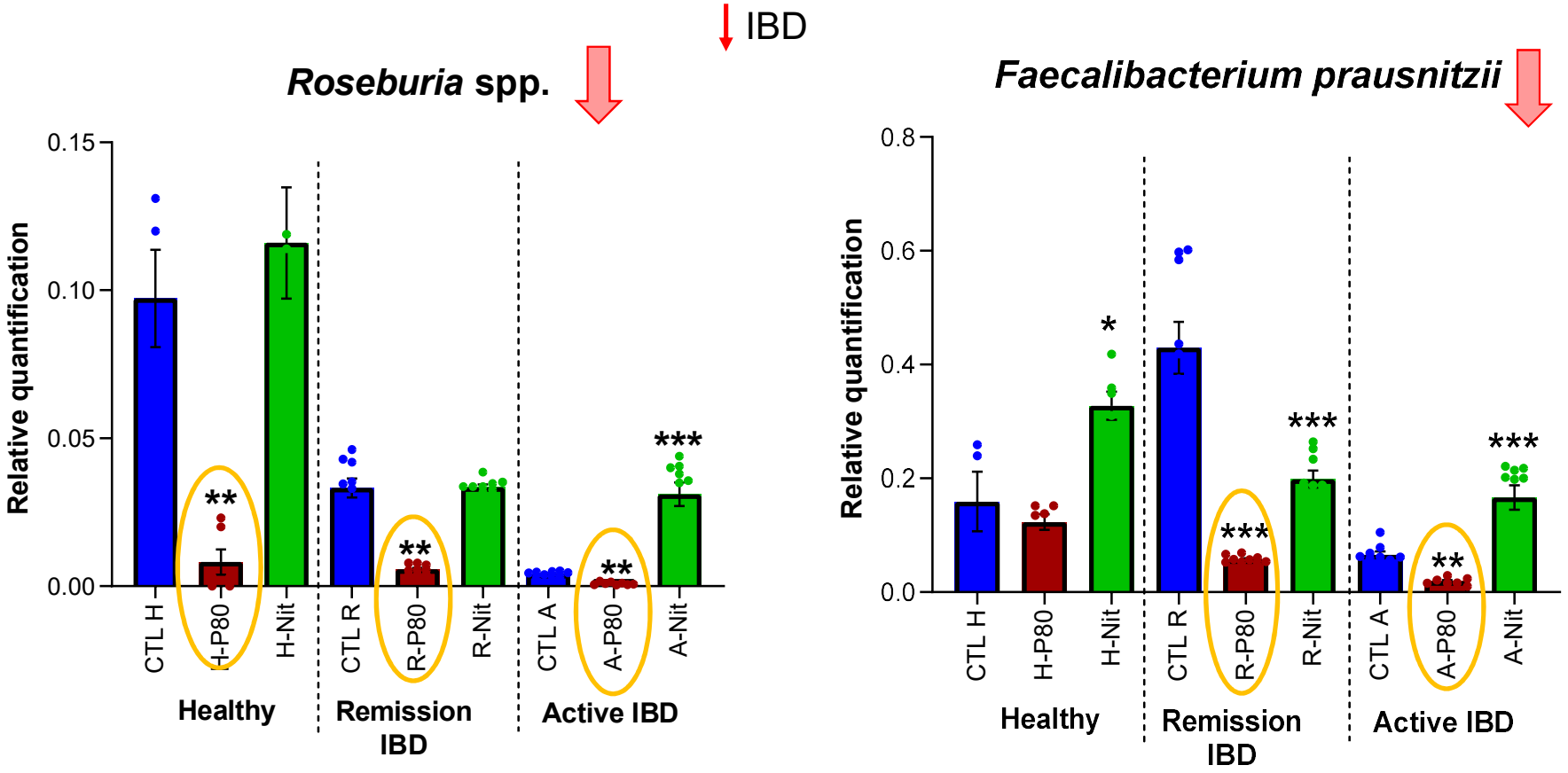


Polysorbate 80: ↓ *Roseburia* spp.

Results – Butyrate producers



Polysorbate 80: ↓ *Roseburia* spp.
↓ *F. prausnitzii* in IBD patients

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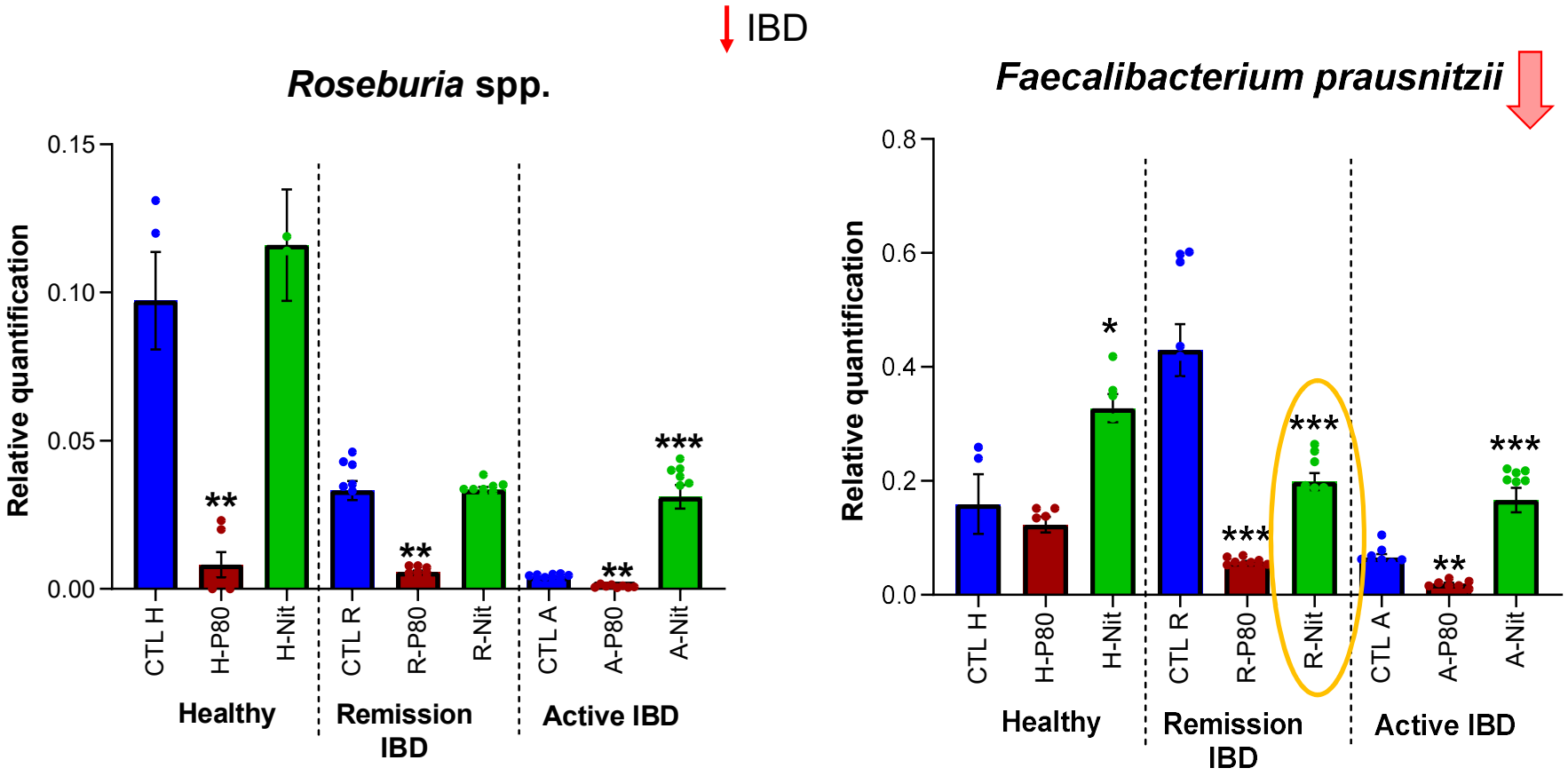
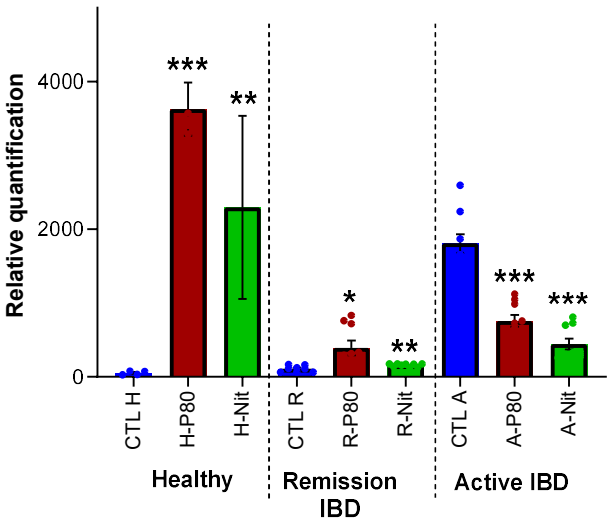


Sodium nitrite: ↓ *F. prausnitzii* in R

Results – IBD related bacteria

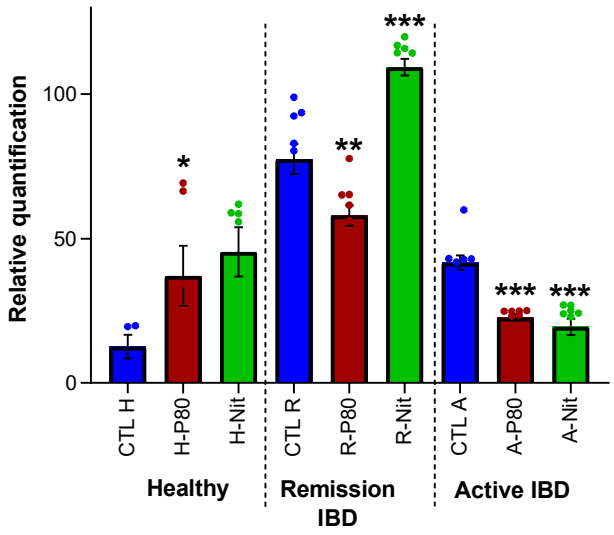
IBD ↑

***Enterococcus* spp.**



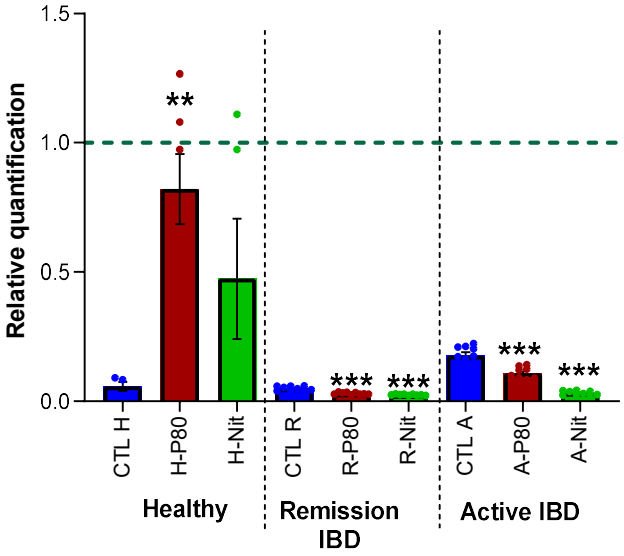
IBD ↑

***Escherichia/Shigella* spp.**



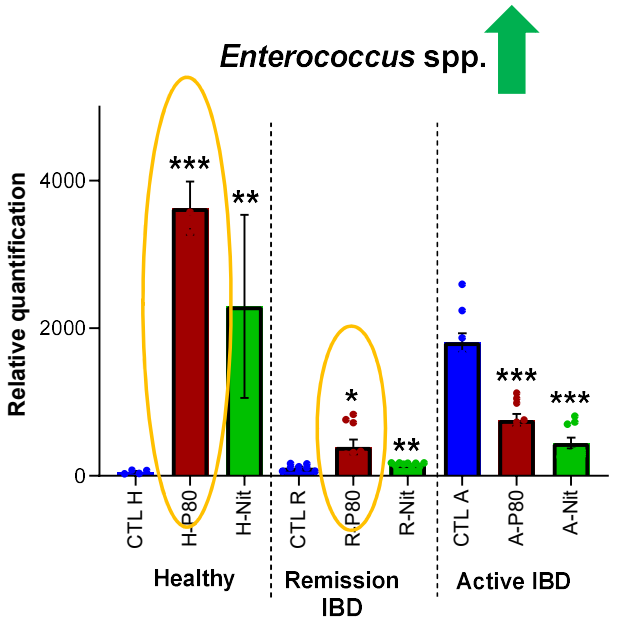
IBD ↓

Akkermansia muciniphila



Results – IBD related bacteria

IBD ↑



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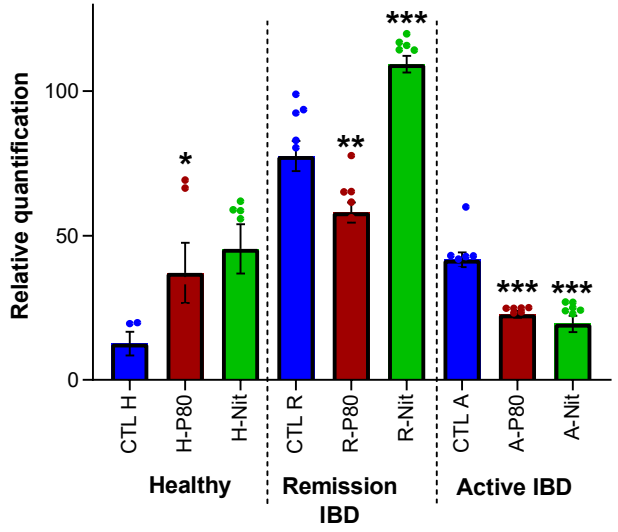

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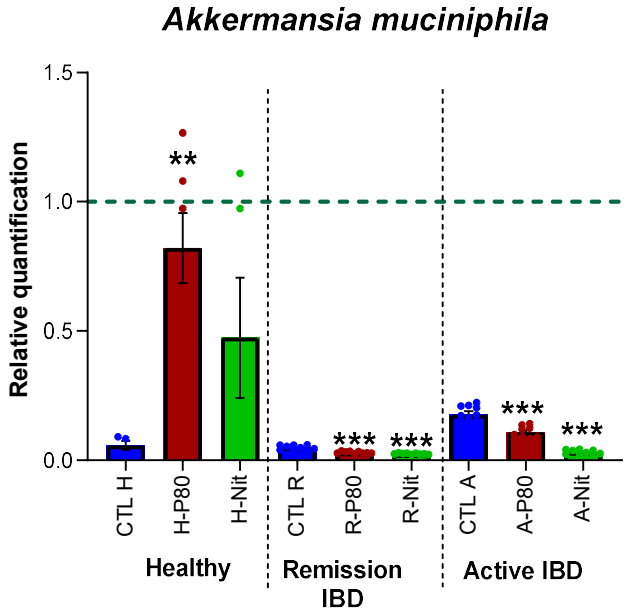

Polysorbate 80: ↑ *Enterococcus* spp. in H & R

Results – IBD related bacteria

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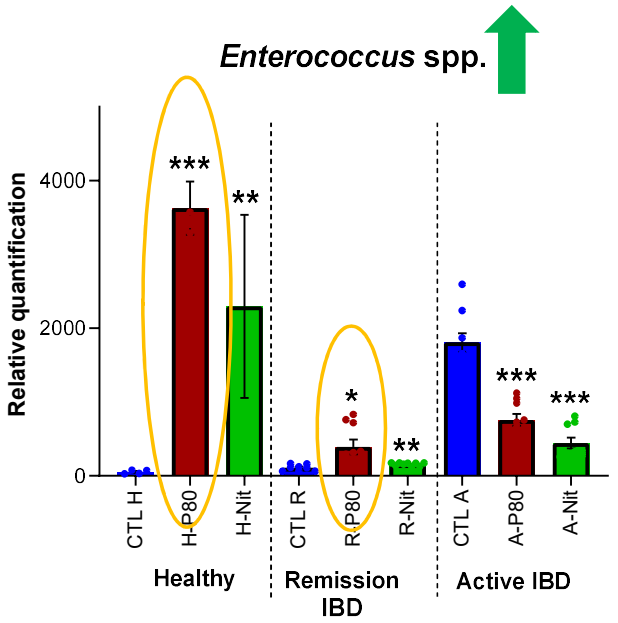

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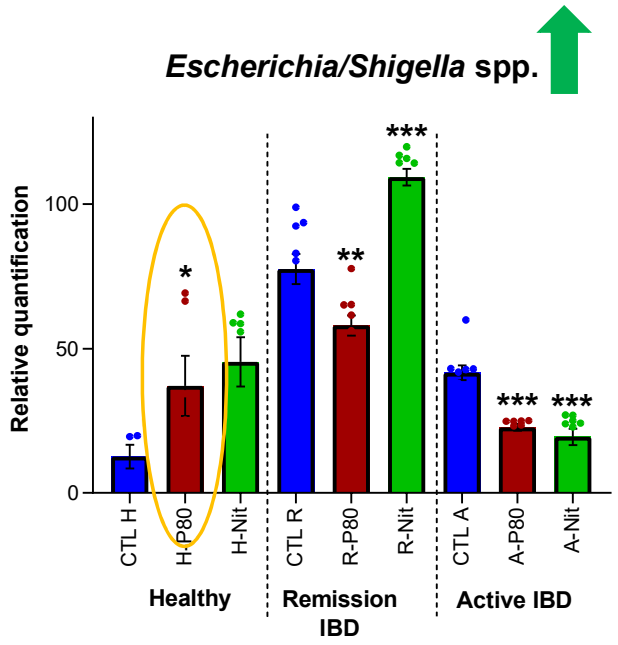

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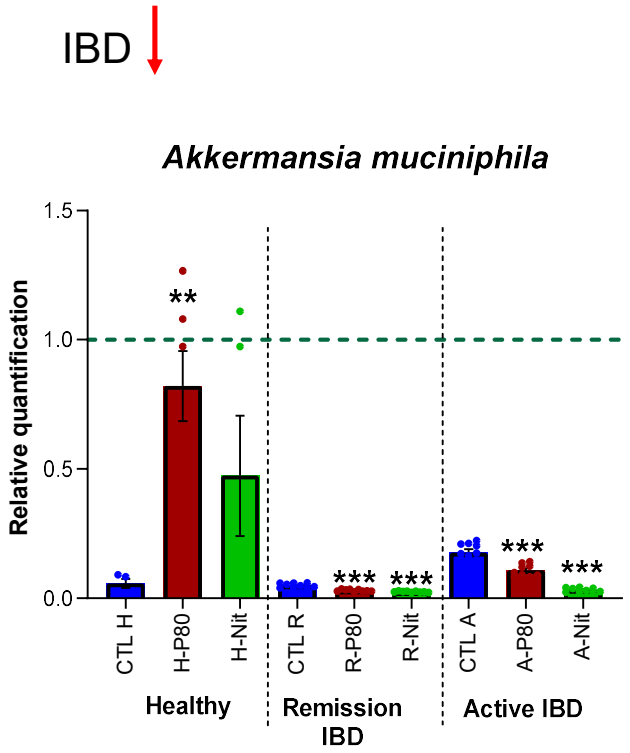

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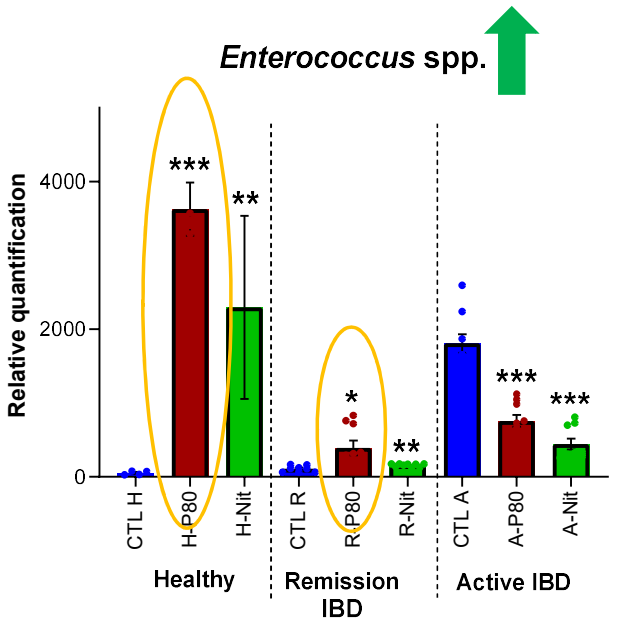

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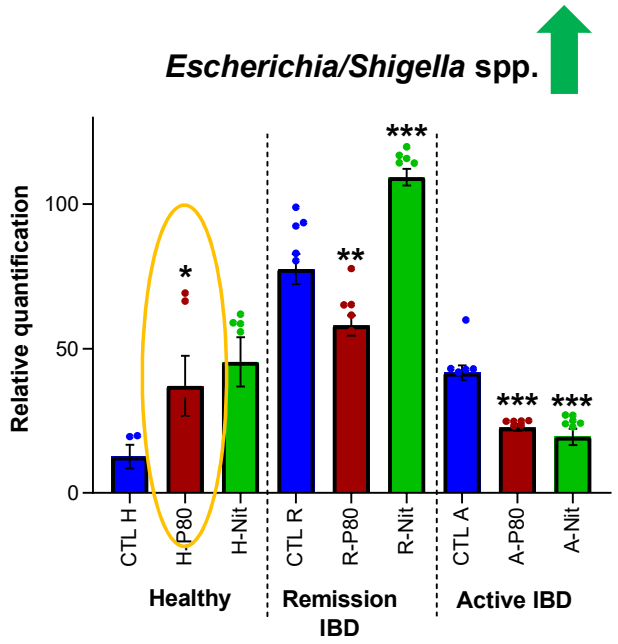

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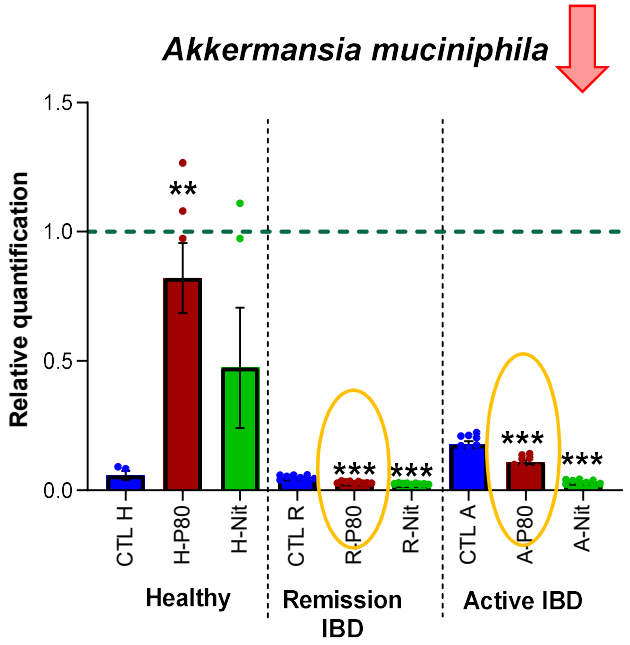

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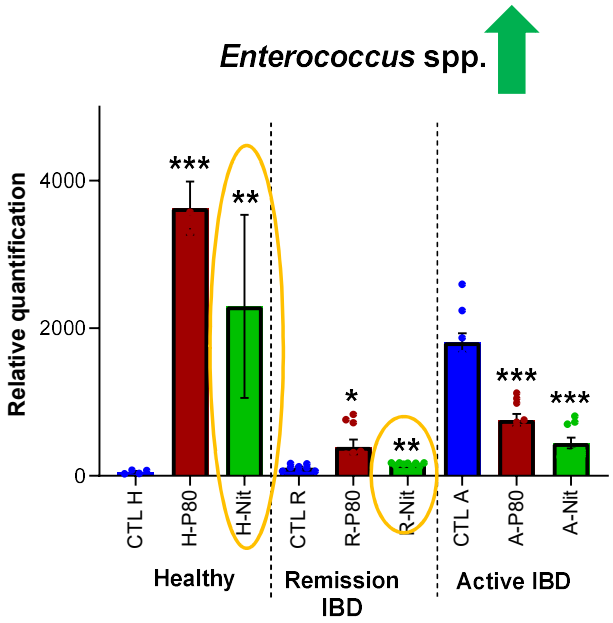

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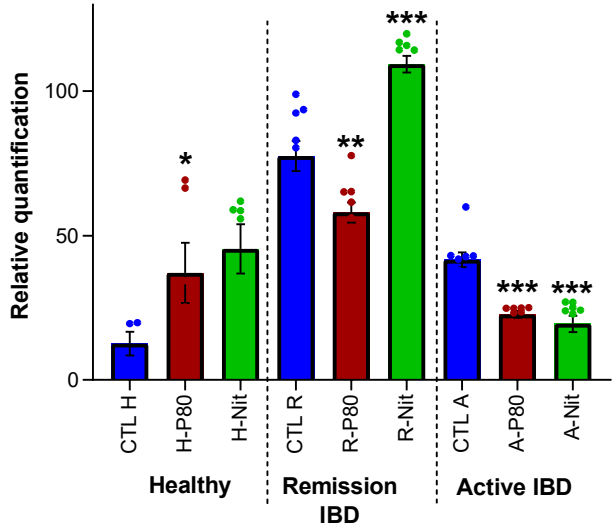

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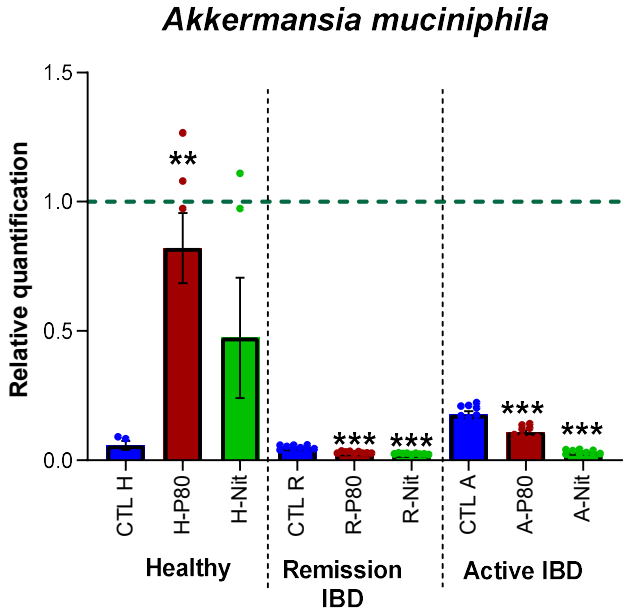

Sodium nitrite: ↑ *Enterococcus* spp. in H & R

Results – IBD related bacteria

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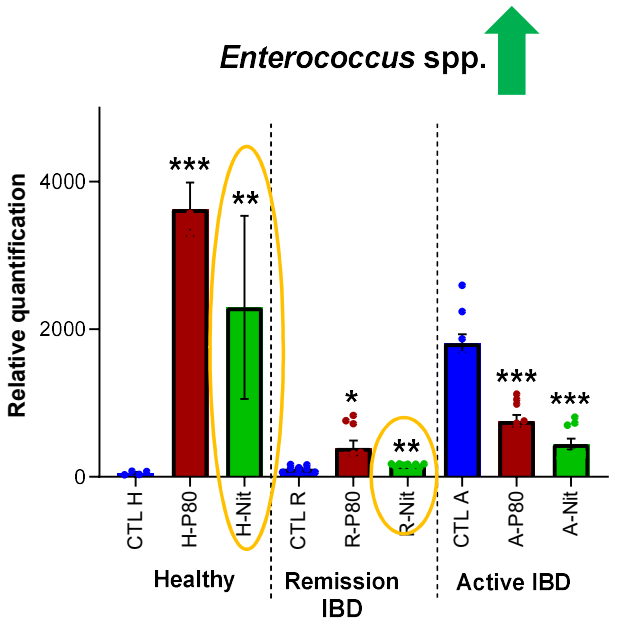

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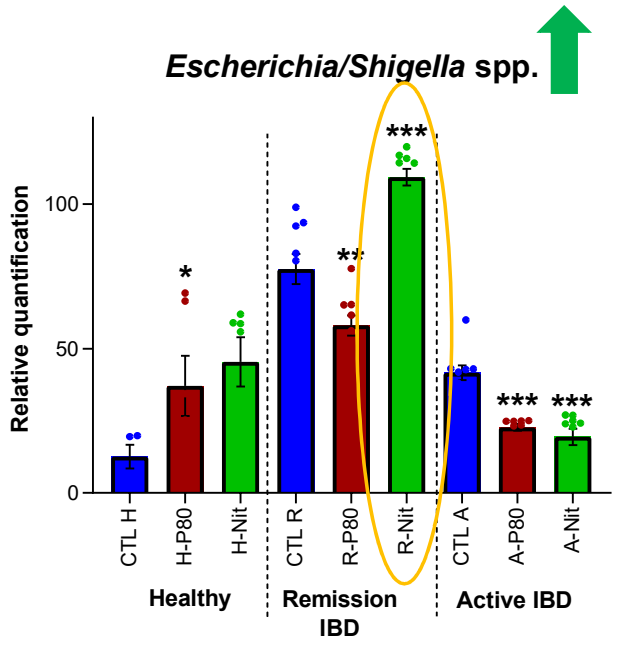

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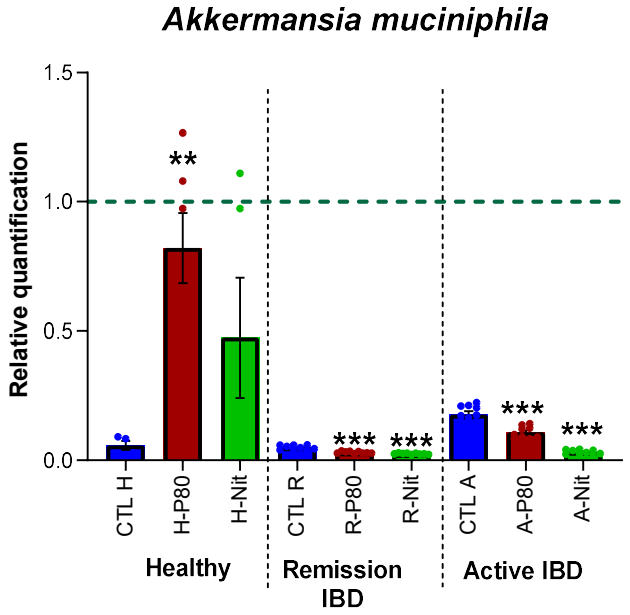

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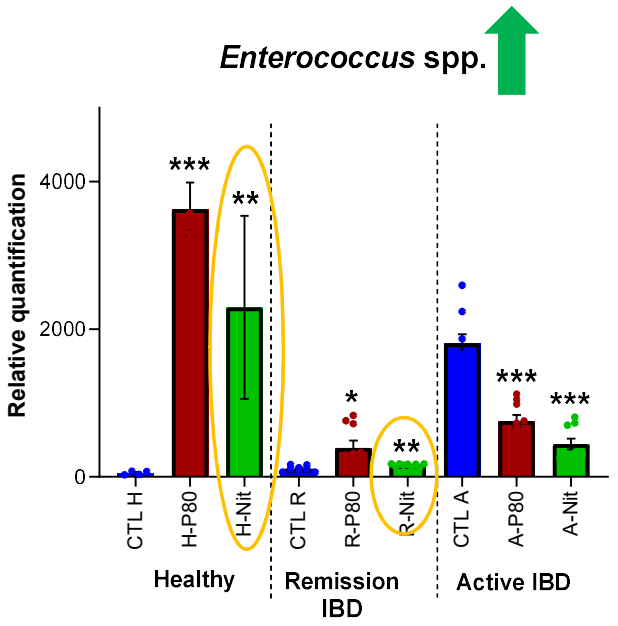

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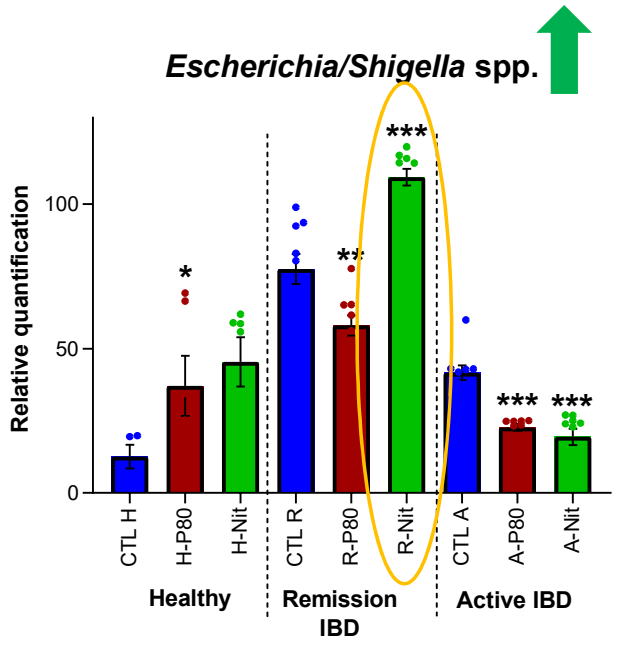

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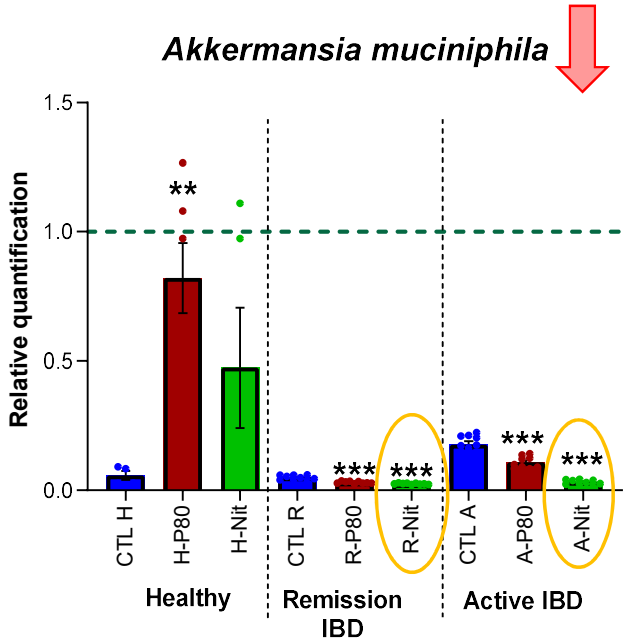

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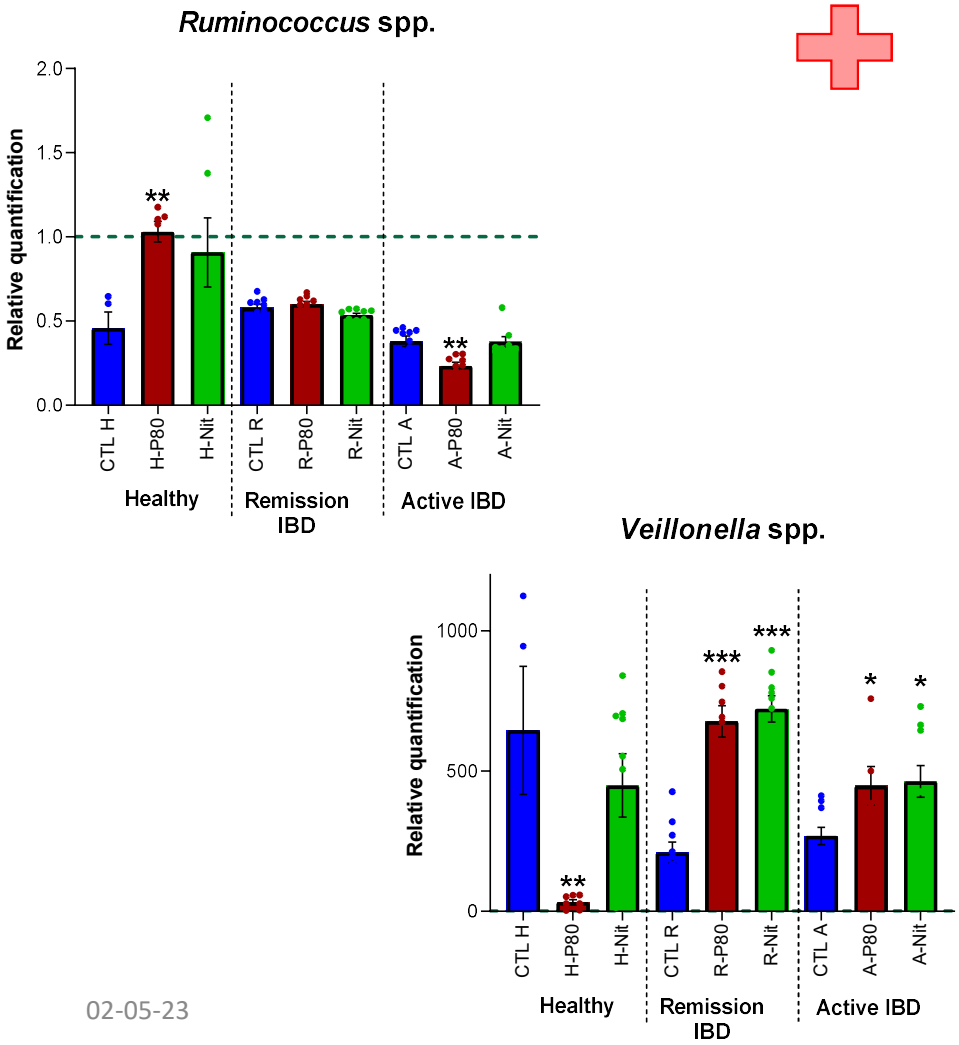
Results – Fibrosis related bacteria



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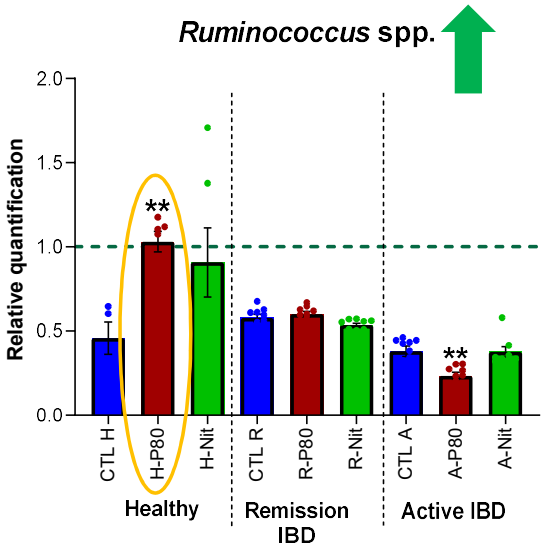
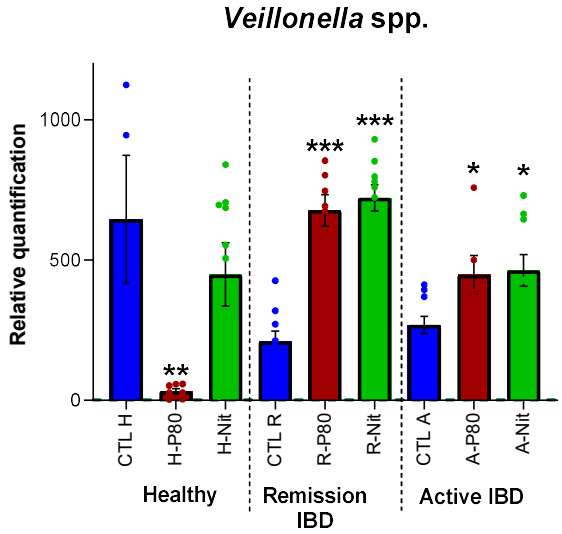
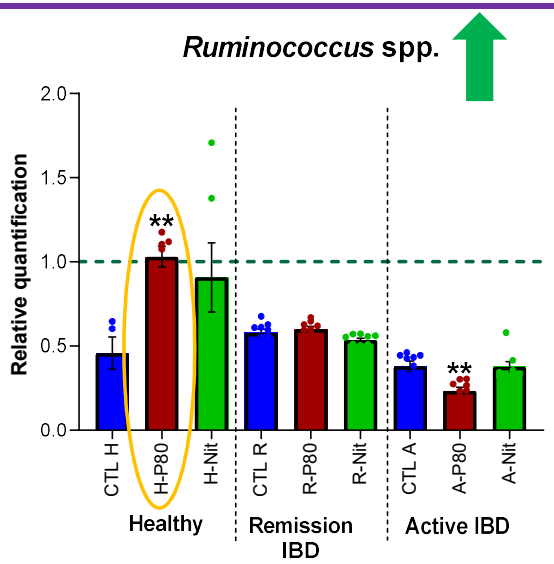


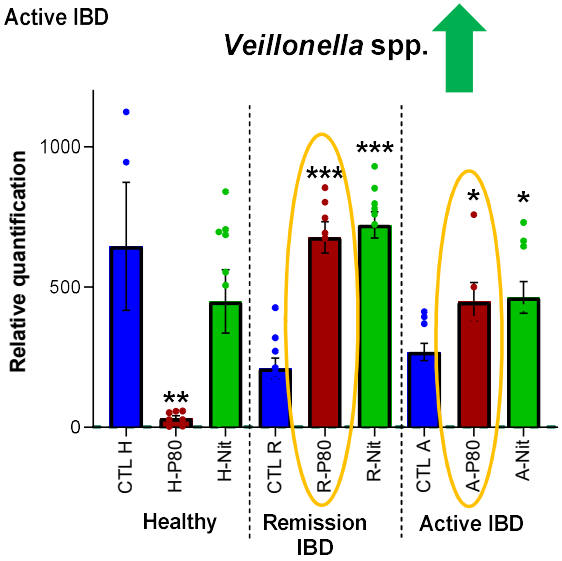
P80: *Ruminococcus* spp. in H



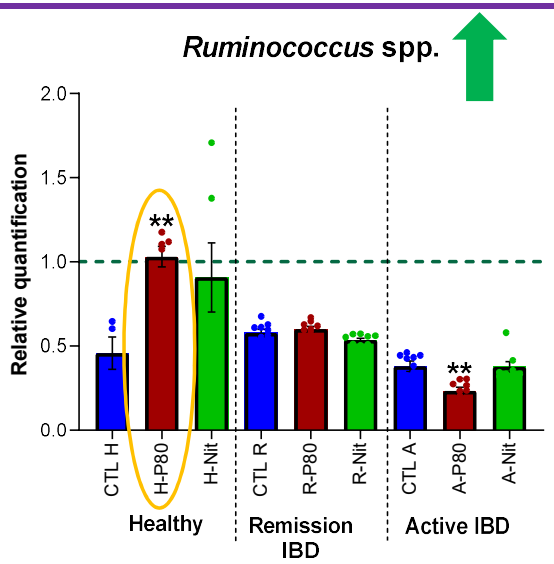
Results – Fibrosis related bacteria

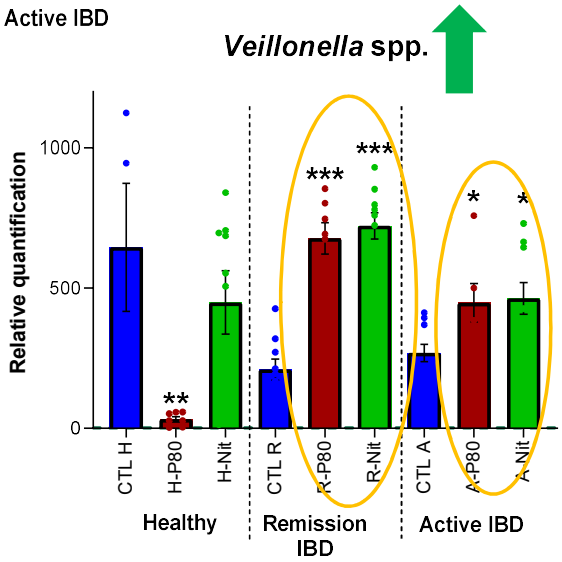


P80: *Ruminococcus* spp. in H
↑ *Veillonella* spp. In IBD patients



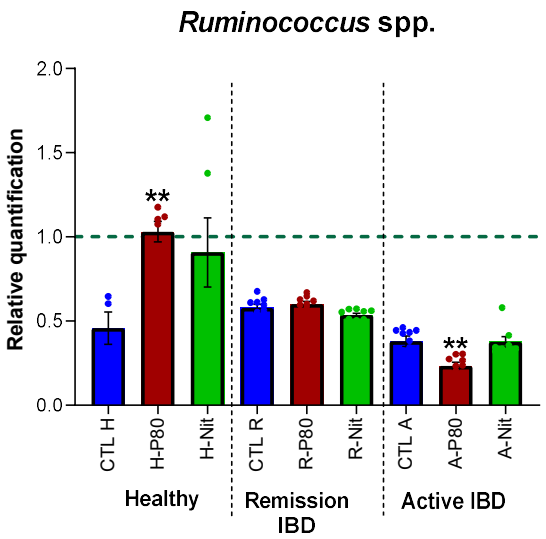
Results – Fibrosis related bacteria

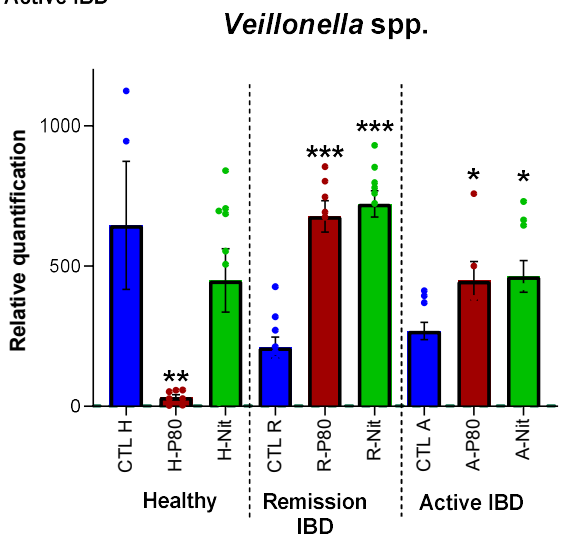


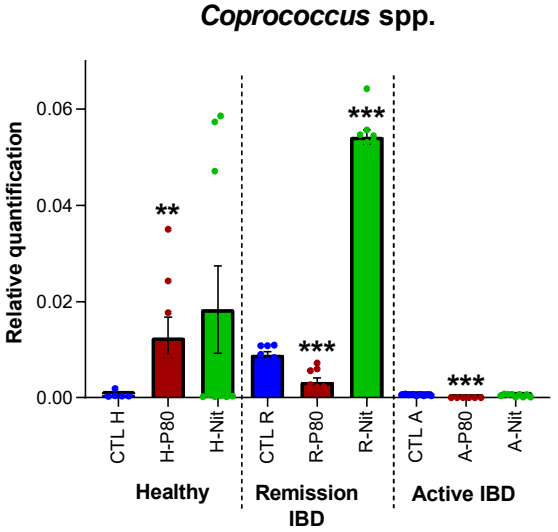


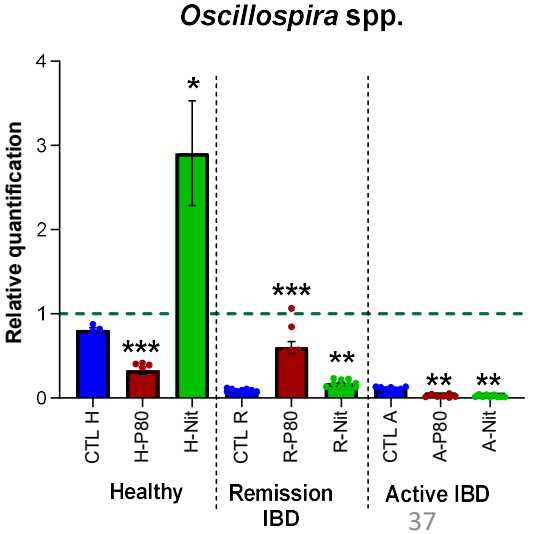
P80: *Ruminococcus* spp. in H
↑ *Veillonella* spp. in IBD patients
Nit: ↑ *Veillonella* spp. in IBD patients

Results – Fibrosis related bacteria

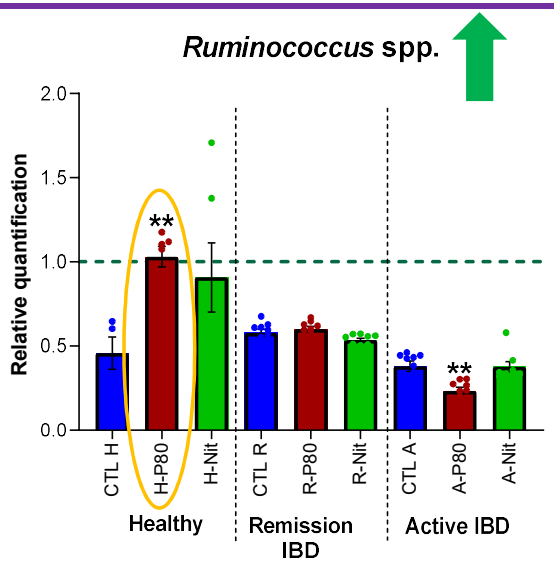




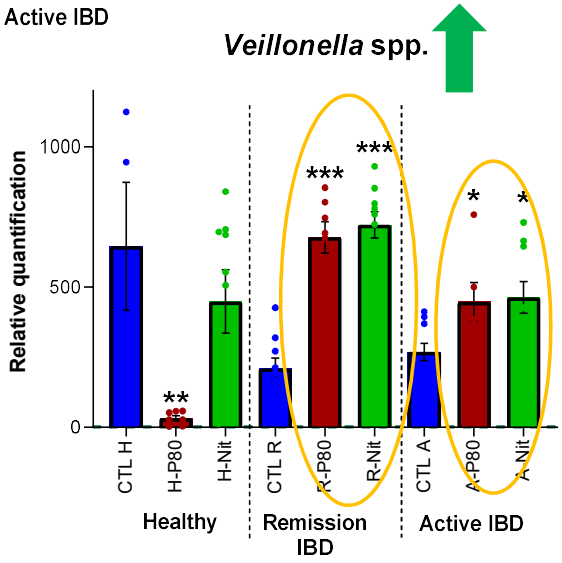


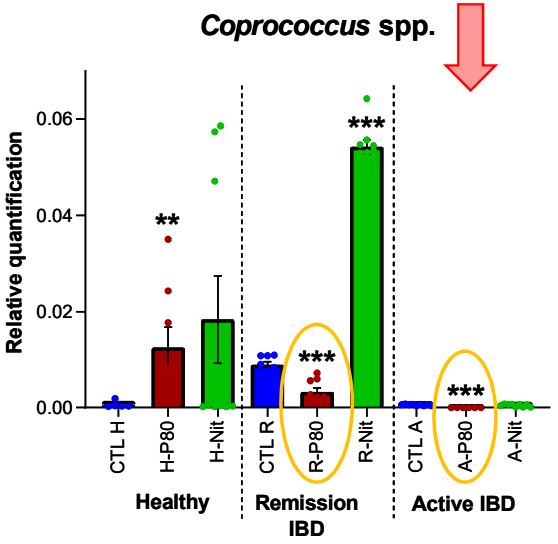


Results – Fibrosis related bacteria

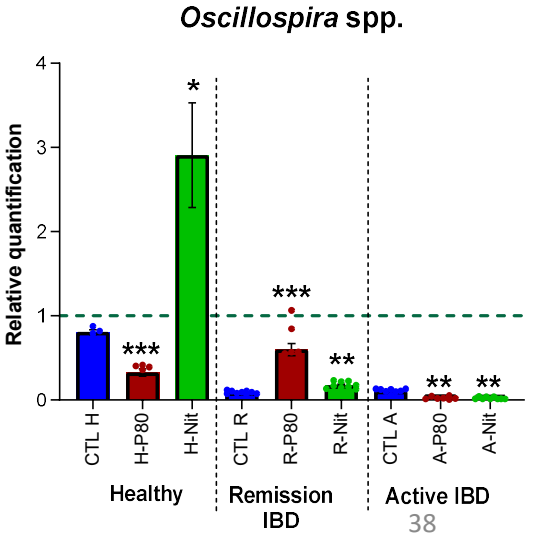


P80: *Ruminococcus* spp. in H
↑ *Veillonella* spp. in IBD patients
Nit: ↑ *Veillonella* spp. in IBD patients

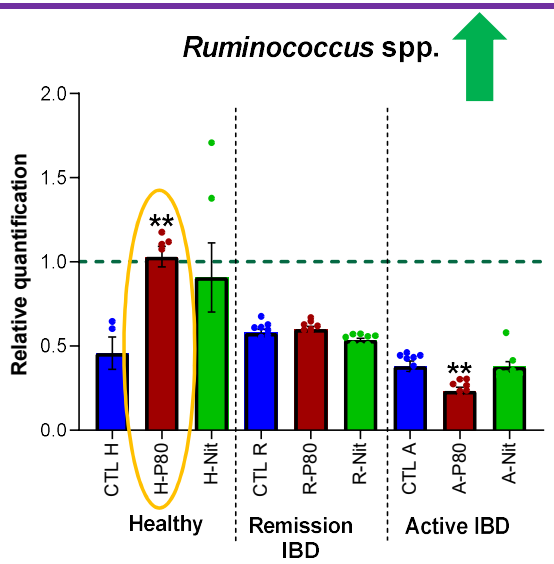


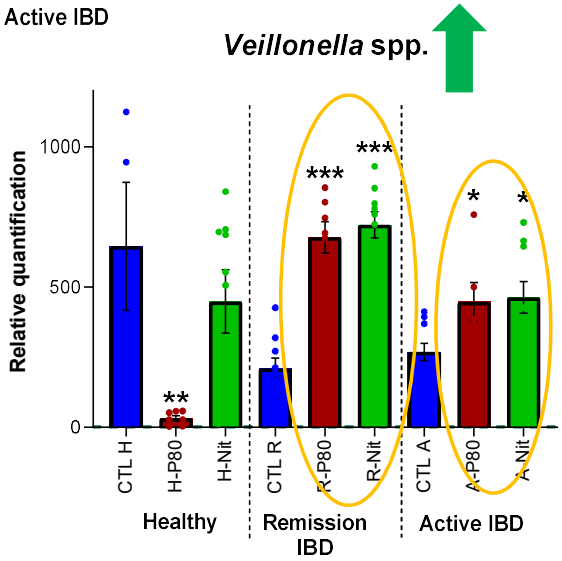


P80: ↓ *Coprococcus* spp. in IBD patients

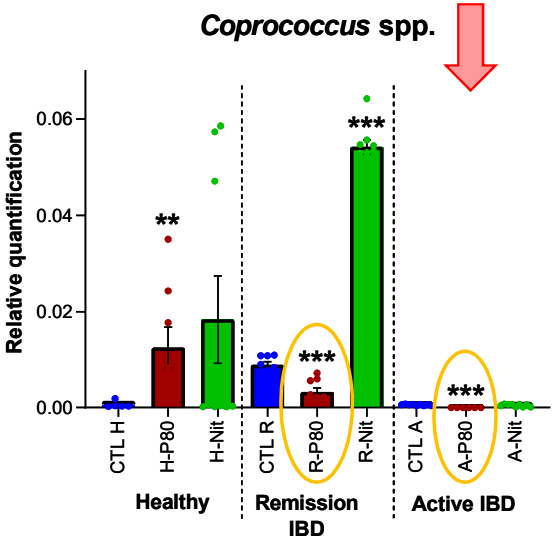


Results – Fibrosis related bacteria

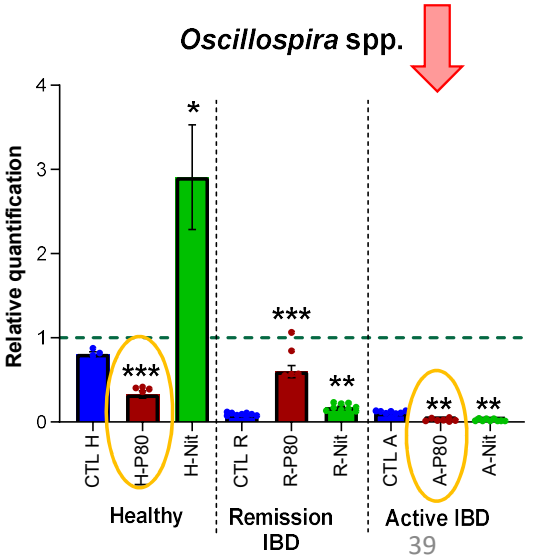




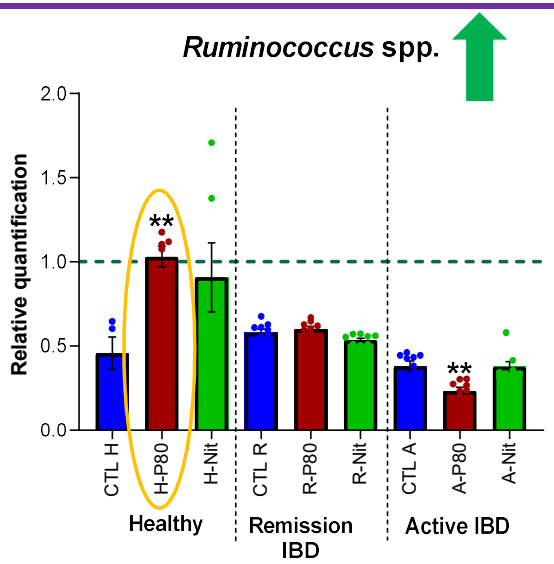
P80: *Ruminococcus* spp. in H
↑ *Veillonella* spp. in IBD patients
Nit: ↑ *Veillonella* spp. in IBD patients

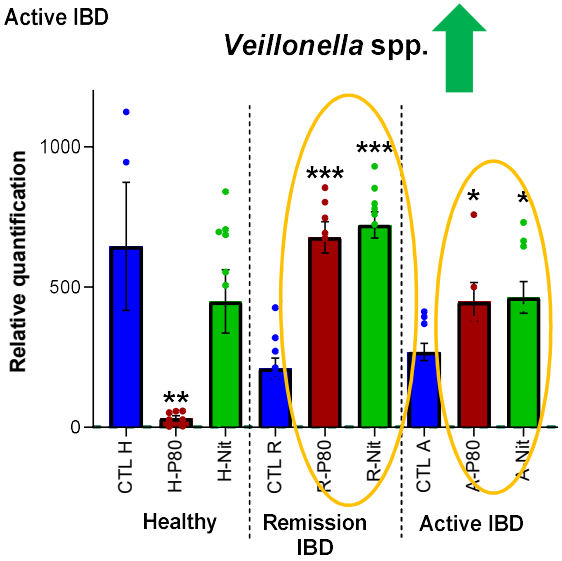


P80: ↓ *Coprococcus* spp. in IBD patients
↓ *Oscillospira* spp. in H and A

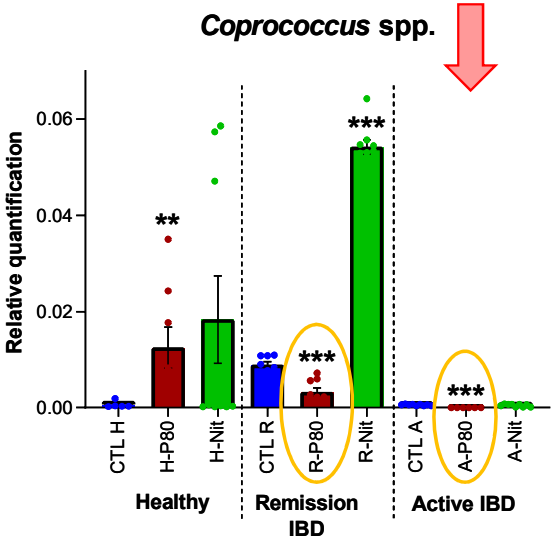


Results – Fibrosis related bacteria



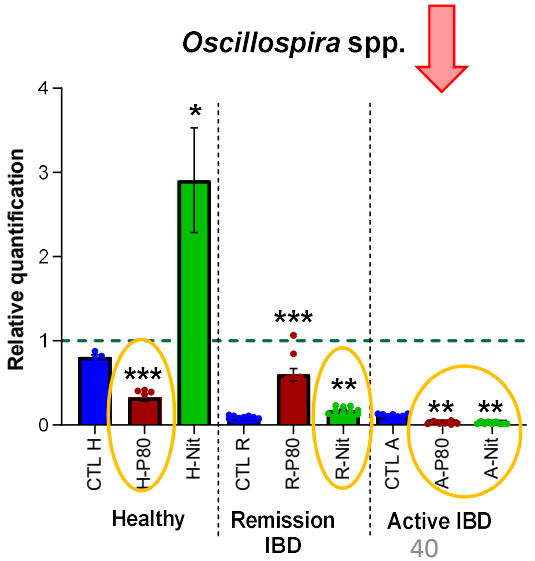


P80: *Ruminococcus* spp. in H
↑ *Veillonella* spp. in IBD patients
Nit: ↑ *Veillonella* spp. in IBD patients

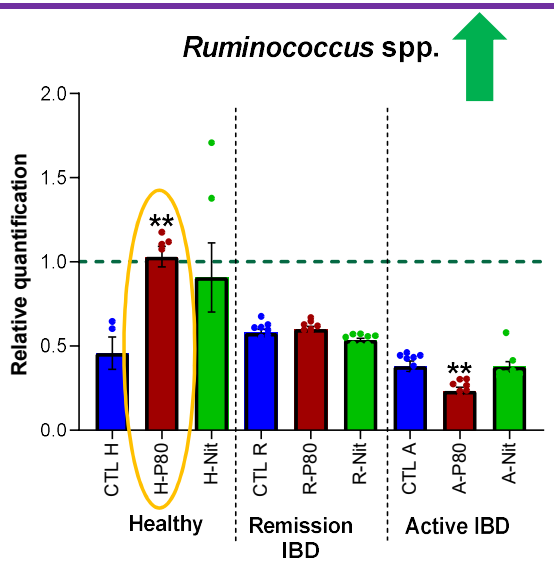


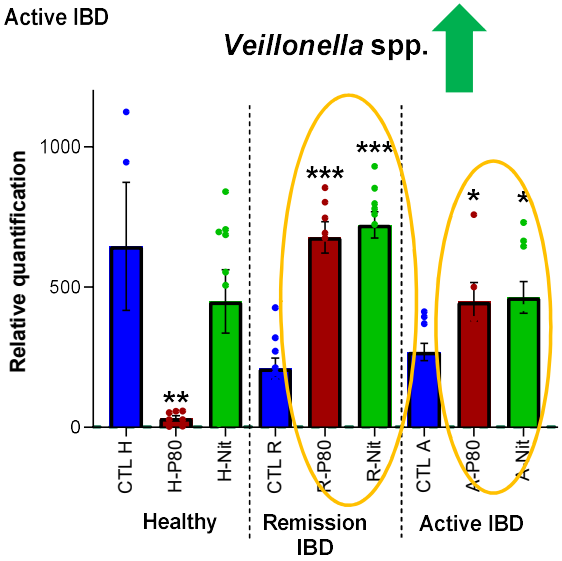
P80: ↓ *Coprococcus* spp. in IBD patients
↓ *Oscillospira* spp. in H and A

Nit: ↓ *Oscillospira* spp. in IBD patients

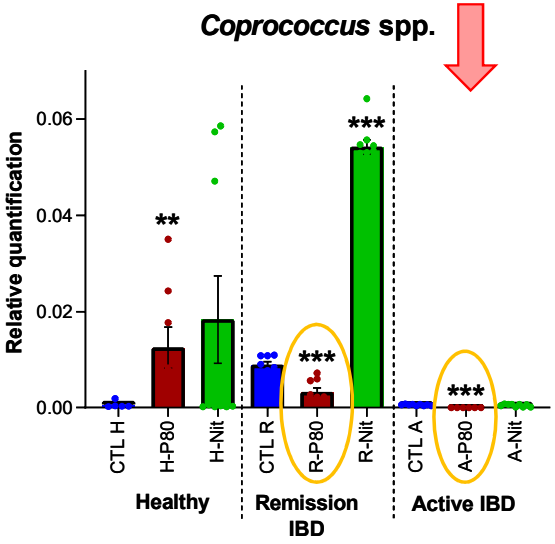


Results – Fibrosis related bacteria



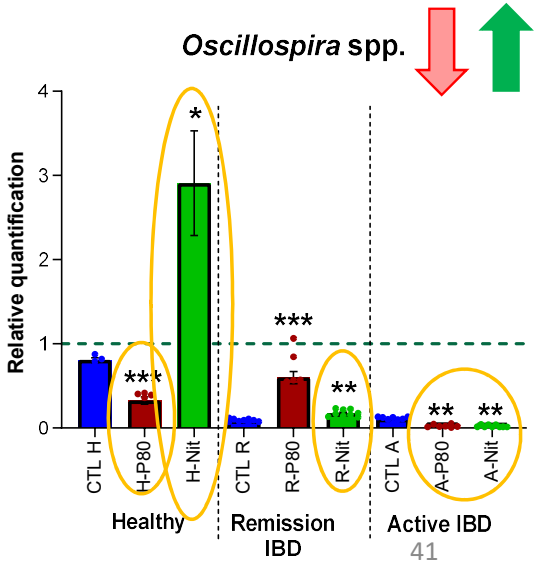


P80: *Ruminococcus* spp. in H
↑ *Veillonella* spp. in IBD patients
Nit: ↑ *Veillonella* spp. in IBD patients



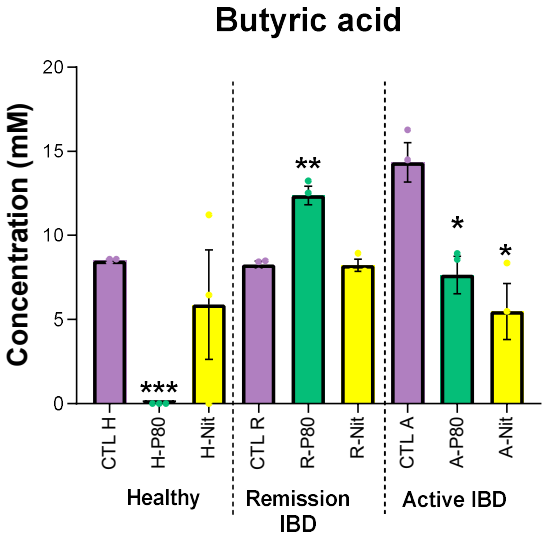
P80: ↓ *Coprococcus* spp. in IBD patients
↓ *Oscillospira* spp. in H and A

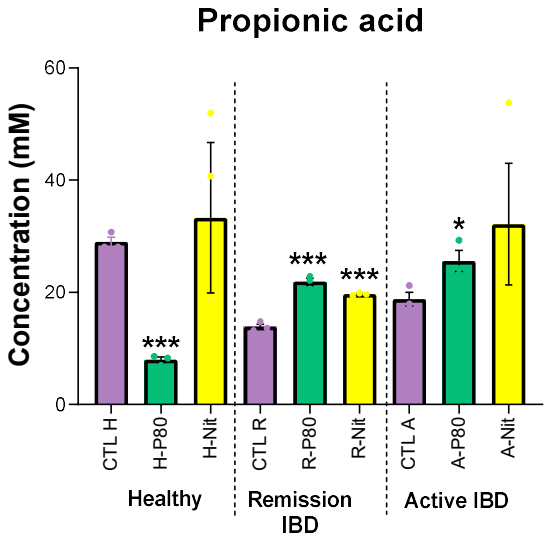
Nit: ↓ *Oscillospira* spp. in IBD patients
↑ *Oscillospira* spp. in H

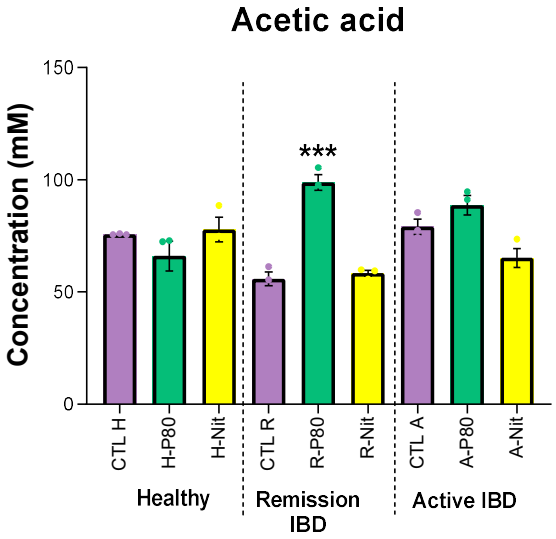


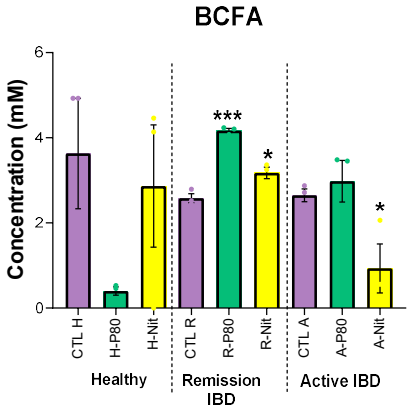
Results – SCFA production

IBD ↓



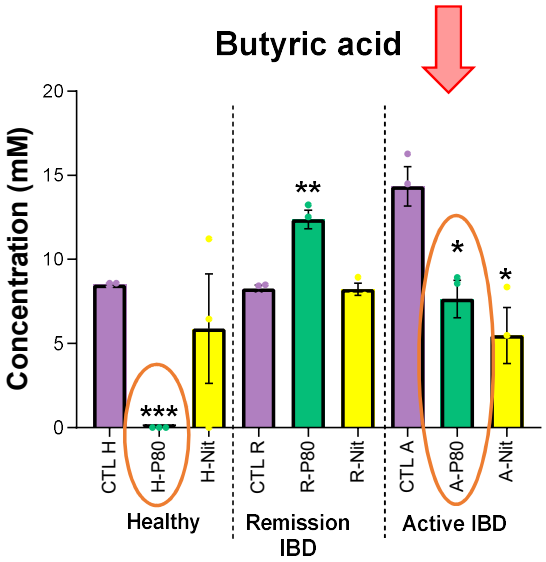


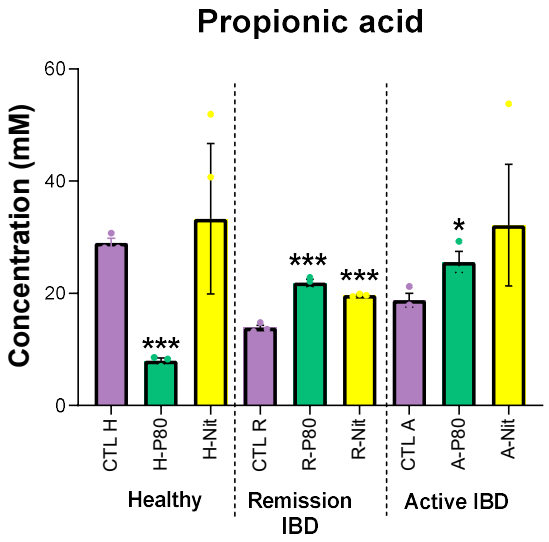


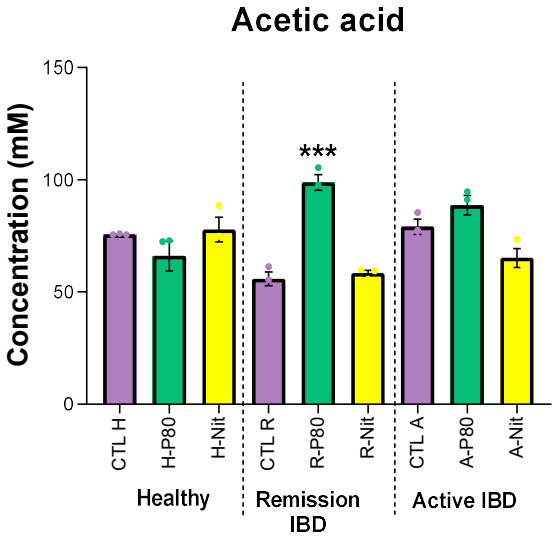


Results – SCFA production

IBD ↓

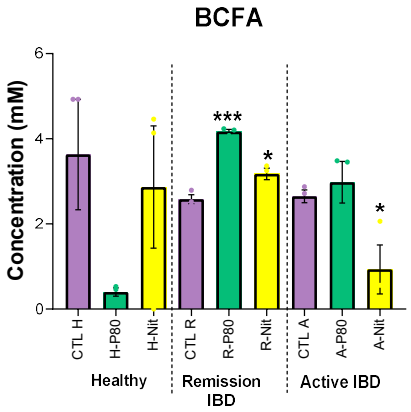






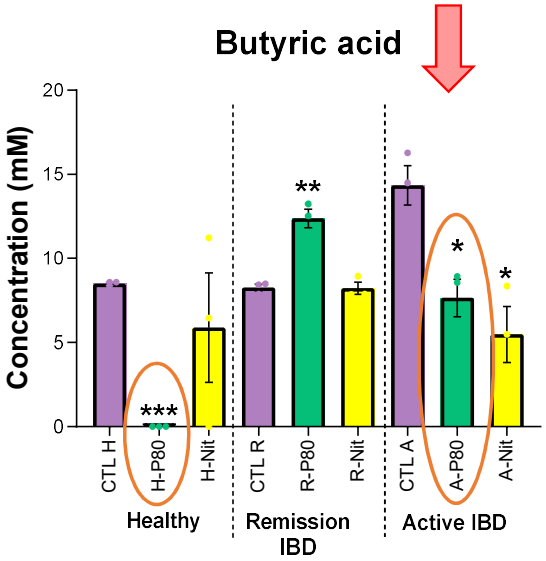
P80: ↓Butyrate in H and A

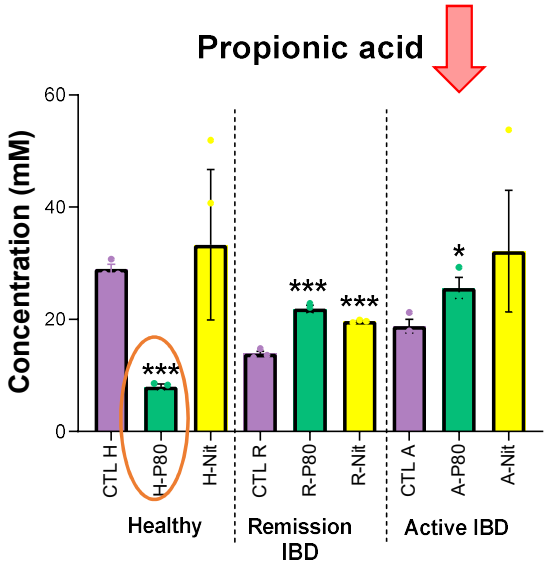
↓*Roseburia, Oscillospira*

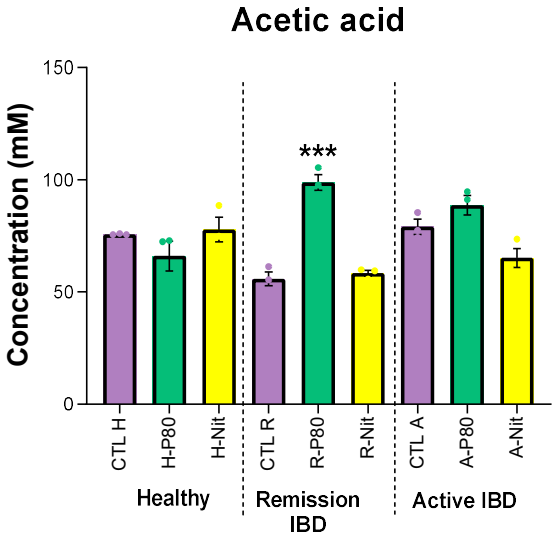


Results – SCFA production

IBD ↓





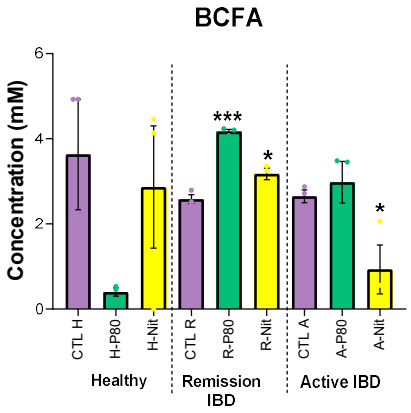


P80: ↓Butyrate in H and A

↓*Roseburia, Oscillospira*

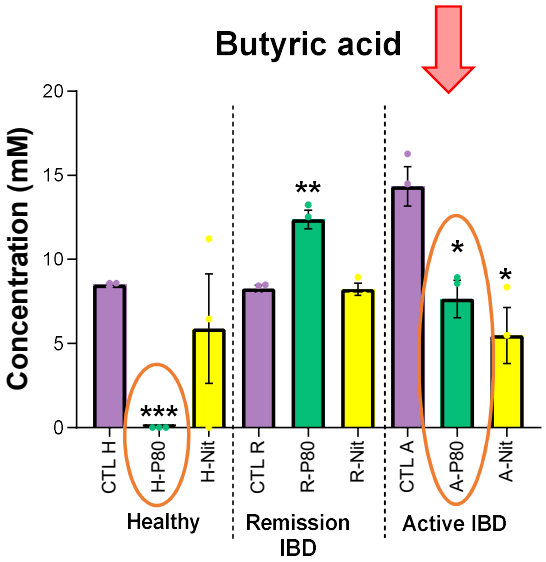
P80: ↓Propionate in H

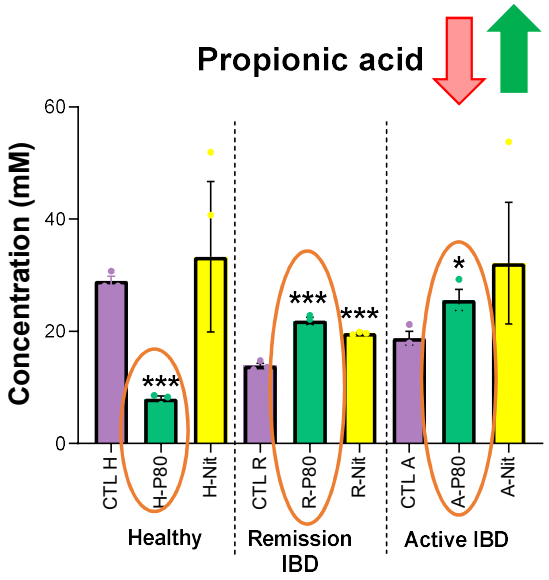
↓*Veillonella*

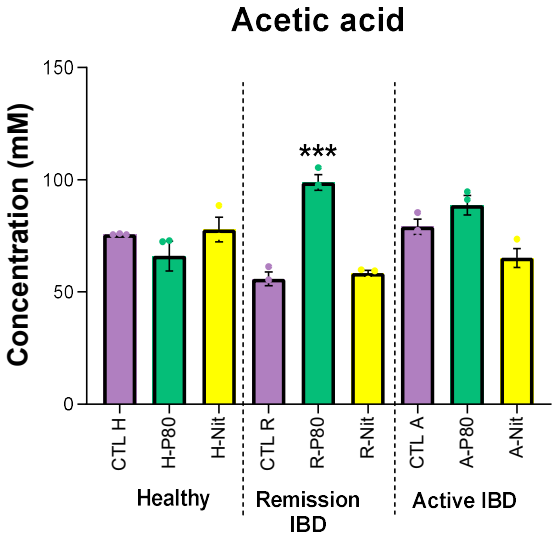


Results – SCFA production

IBD ↓





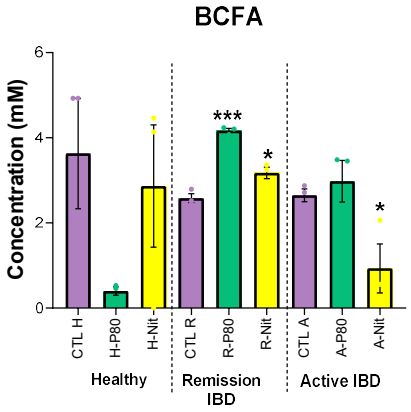


P80: ↓Butyrate in H and A

↓*Roseburia, Oscillospira*

P80: ↓Propionate in H

↓*Veillonella*

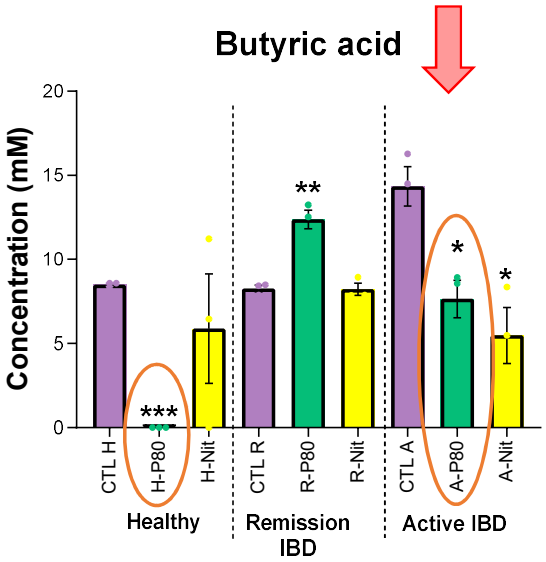


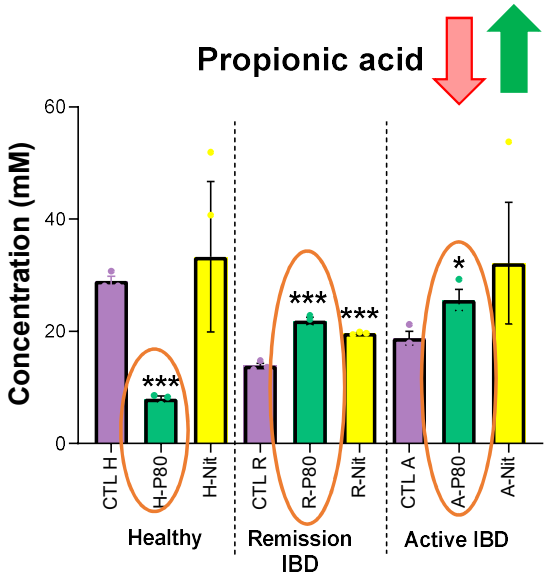
P80: ↑Propionate in IBD

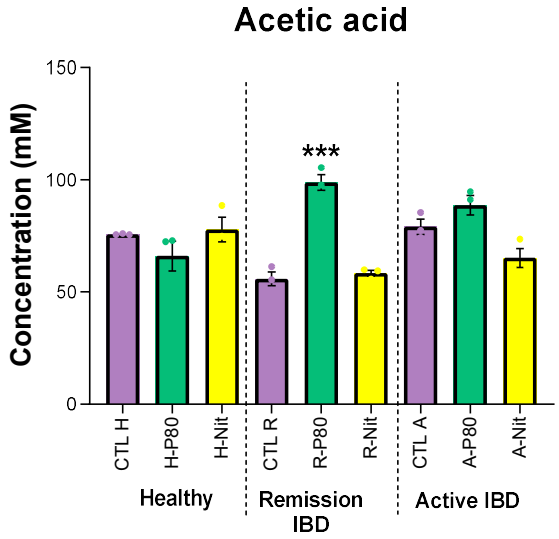
↑*Veillonella*

Results – SCFA production

IBD ↓





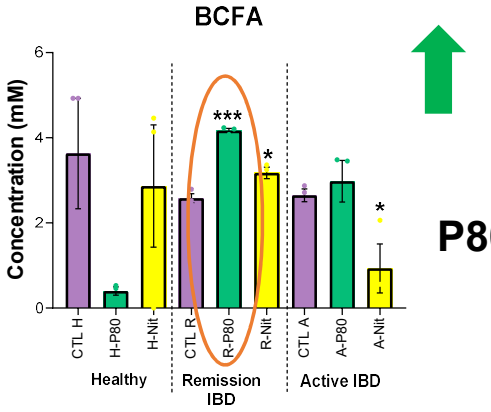


P80: ↓Butyrate in H and A

↓*Roseburia, Oscillospira*

P80: ↓Propionate in H

↓*Veillonella*



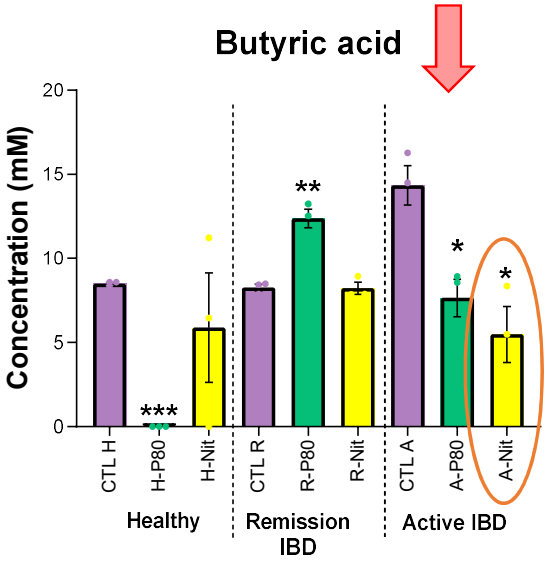
P80: ↑Propionate in IBD

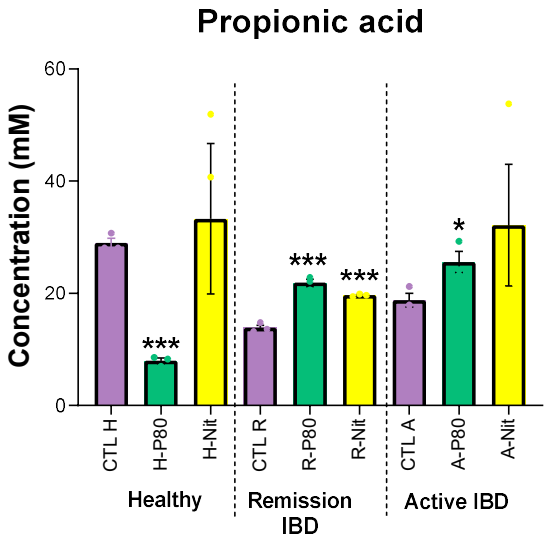
↑*Veillonella*

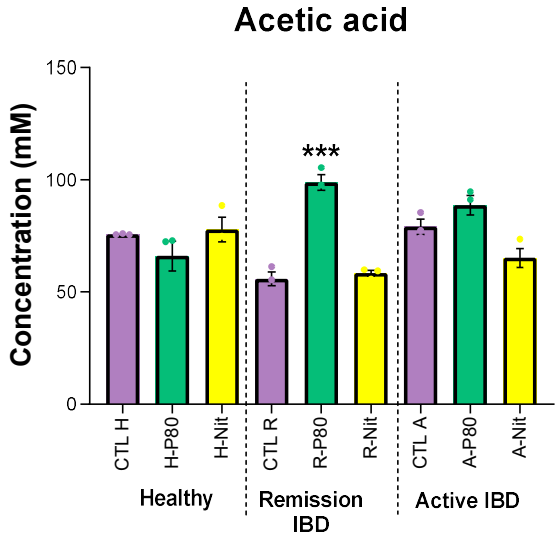
P80: ↑ BCFA in R

Results – SCFA production

IBD ↓

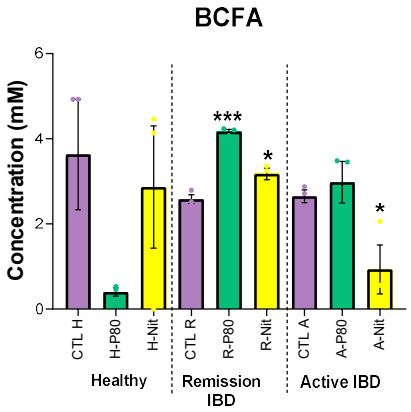






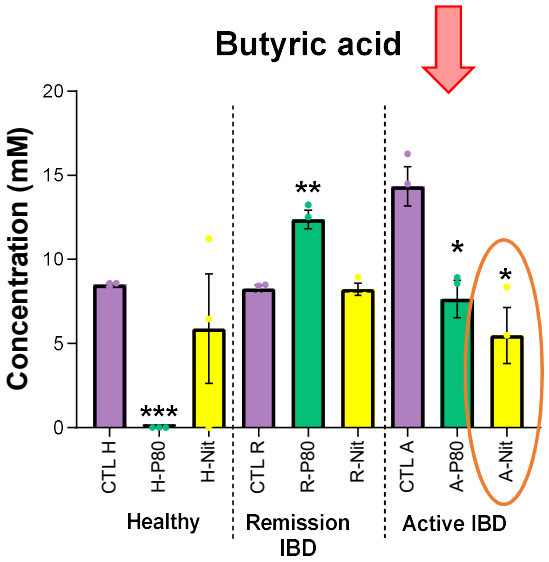
Nit: ↓Butyrate in H and A

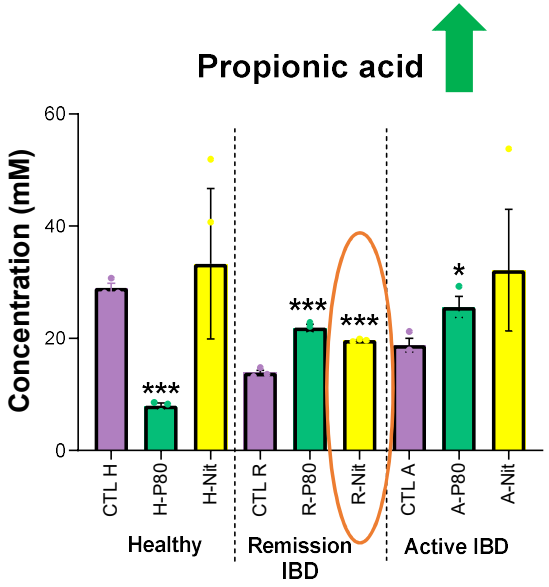
↓*Roseburia, Oscillospira, F. prausnitzii, Coprococcus, Ruminococcus*

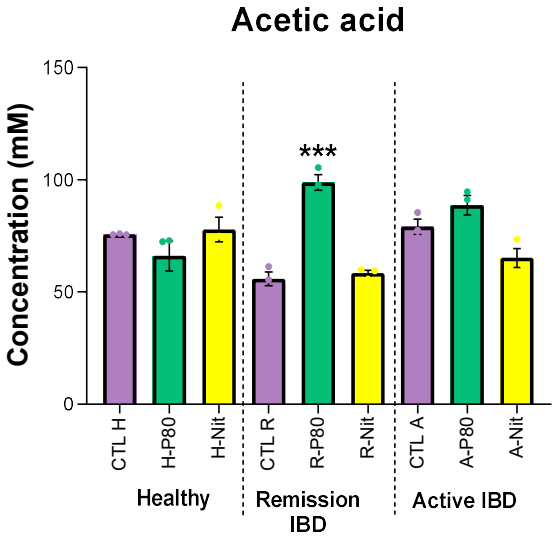


Results – SCFA production

IBD ↓





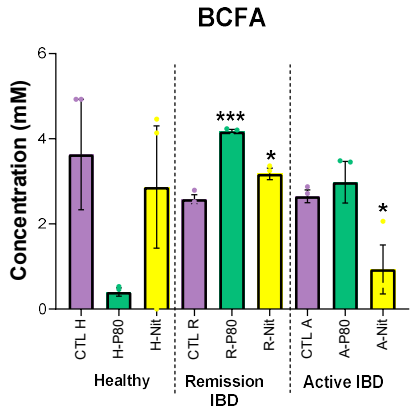


Nit: ↓Butyrate in H and A

↓*Roseburia, Oscillospira, F. prausnitzii, Coprococcus, Ruminococcus*

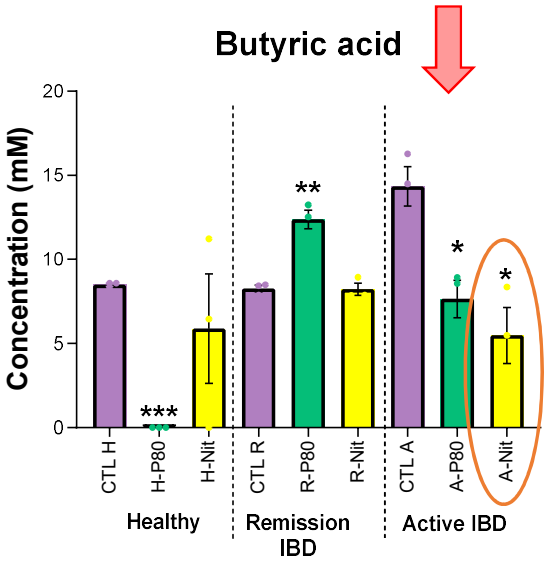
Nit: ↑Propionate in R

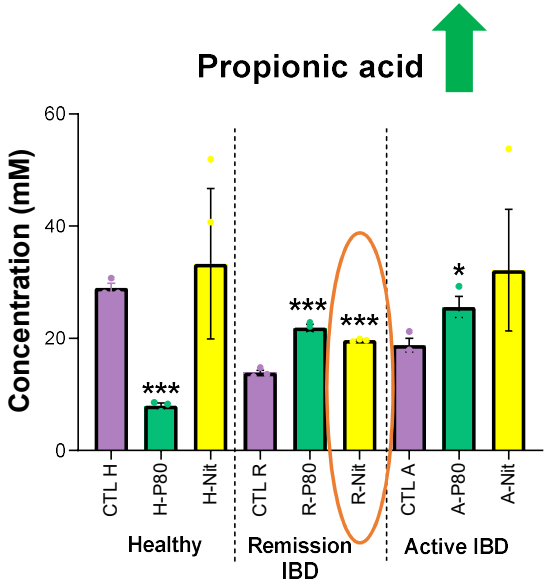
↑*Veillonella*

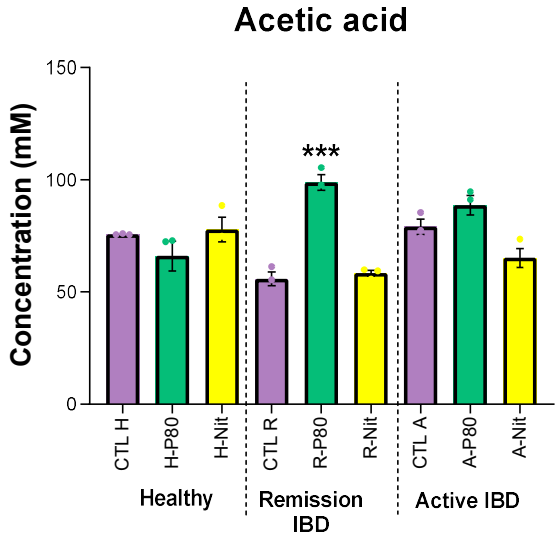


Results – SCFA production

IBD ↓





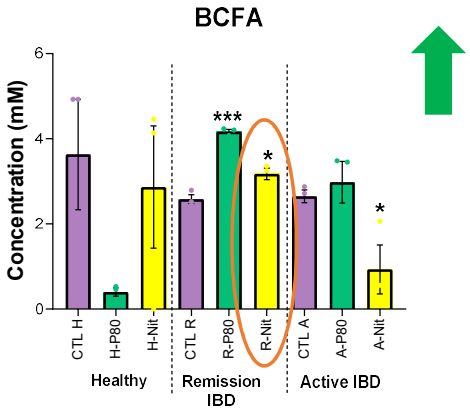


Nit: ↓Butyrate in H and A

↓*Roseburia, Oscillospira, F. prausnitzii, Coprococcus, Ruminococcus*

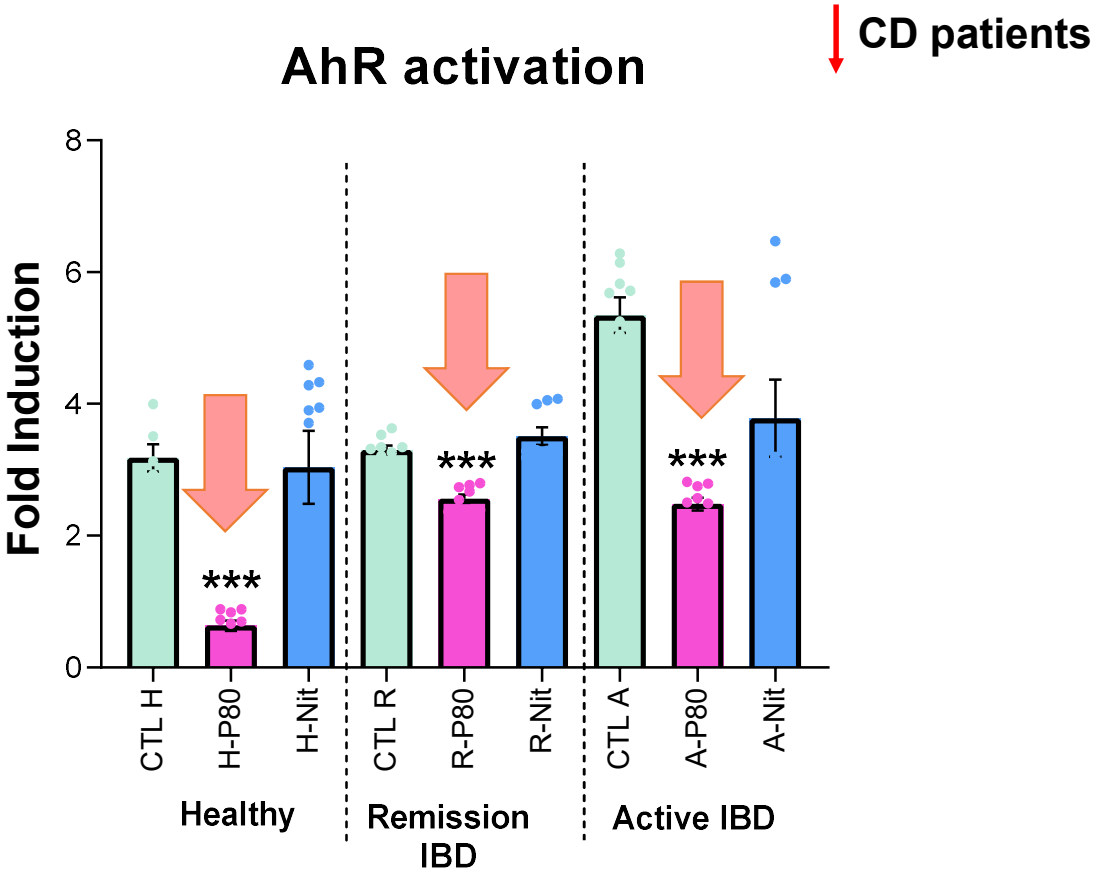
Nit: ↑Propionate in R

↑*Veillonella*

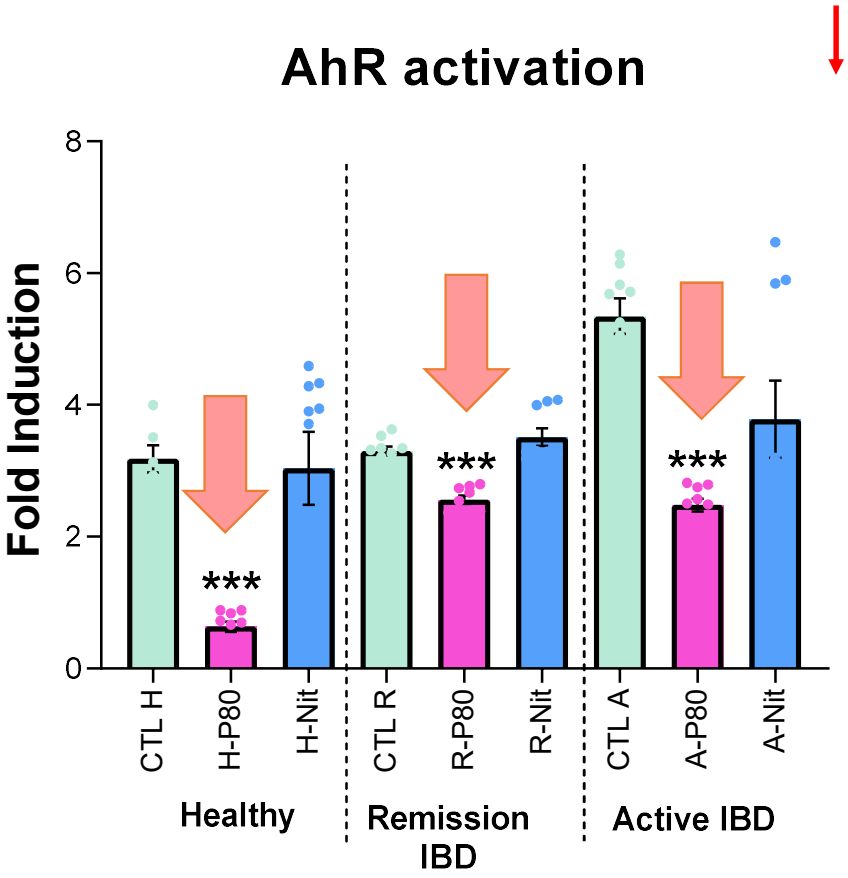


Nit: ↑ BCFA in R

Results – Microbial derived AhR agonist

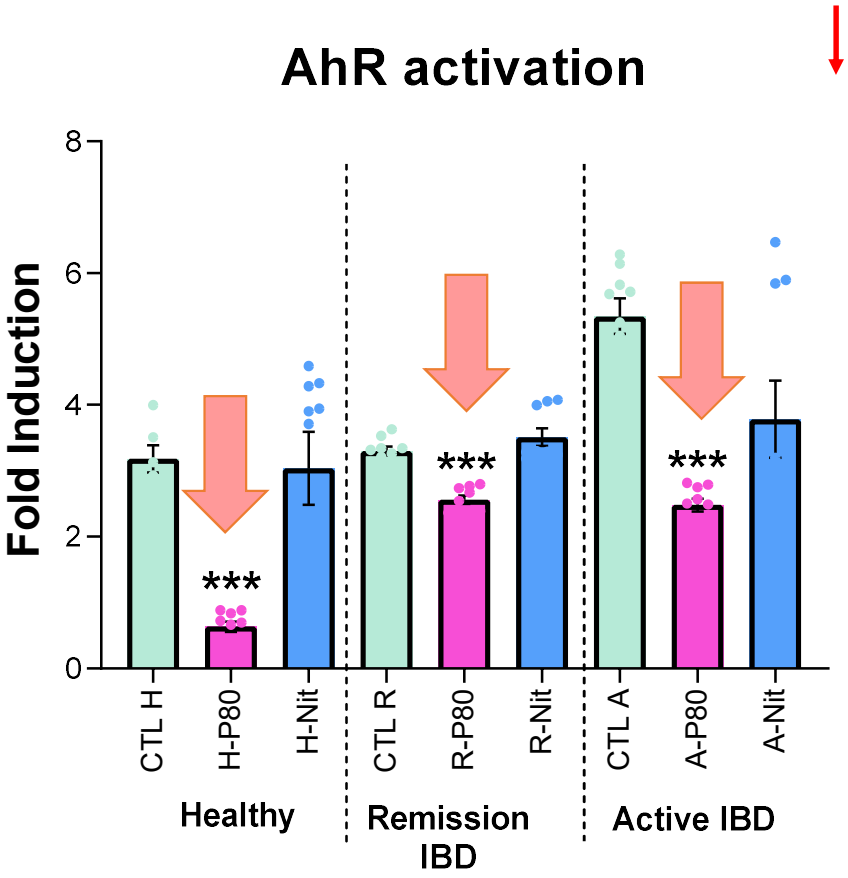


Results – Microbial derived AhR agonist



Polysorbate 80: ↓ AhR activation in all donors

Results – AhR activation

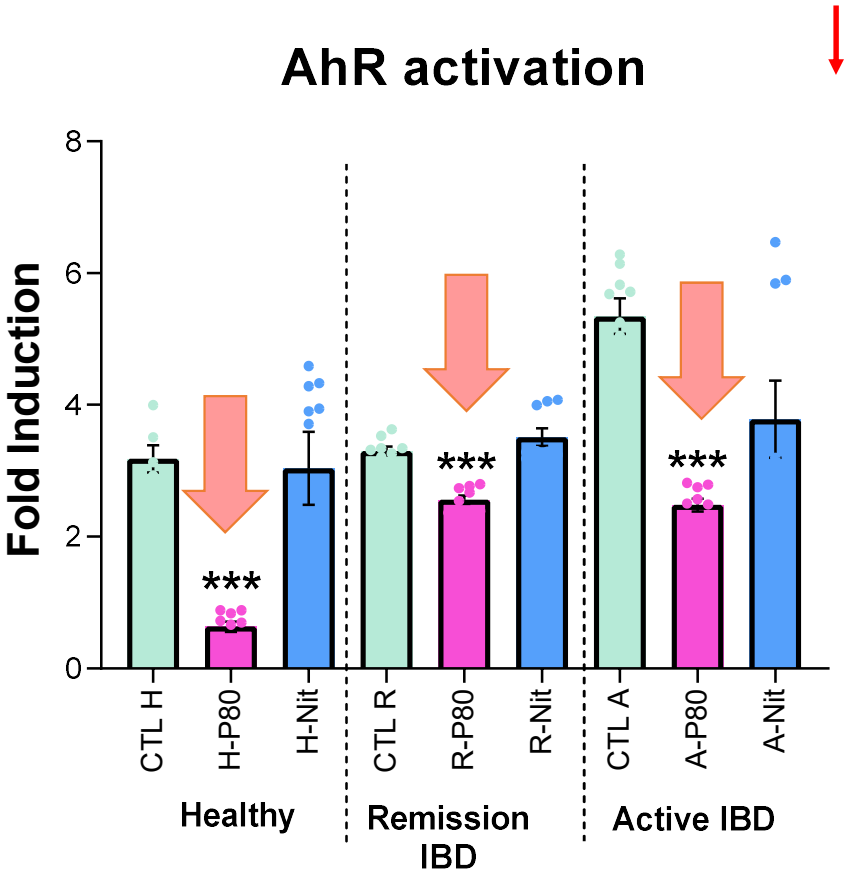


CD patients

Polysorbate 80: ↓ AhR activation in all donors

Production pro – inflammatory cytokines
Collagen synthesis

Results – AhR activation



Polysorbate 80: ↓ AhR activation in all donors

Production pro – inflammatory cytokines
Collagen synthesis

Epithelial barrier function
Production of anti – inflammatory cytokines
Mucus production
Antimicrobial peptides

Discussion

Polysorbate 80

- Strong effects in H and IBD patients
- ↓butyrate – producing bacteria → ↓SCFA (butyrate)
- ↑ IBD related bacteria (*Enterococcus*, *Escherichia /Shigella)*
- Fibrosis related bacteria: ↑*Veillonella* → ↑ propionate production
- Fibrosis related bacteria: ↓ *Coprococcus & Oscillospira*
- ↓ AhR activation

Discussion

Polysorbate 80

- Strong effects in H and IBD patients
- ↓butyrate – producing bacteria → ↓SCFA (butyrate)
- ↑ IBD related bacteria (*Enterococcus*, *Escherichia /Shigella)*
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- Fibrosis related bacteria: ↓ *Coprococcus & Oscillospira*
- ↓ AhR activation

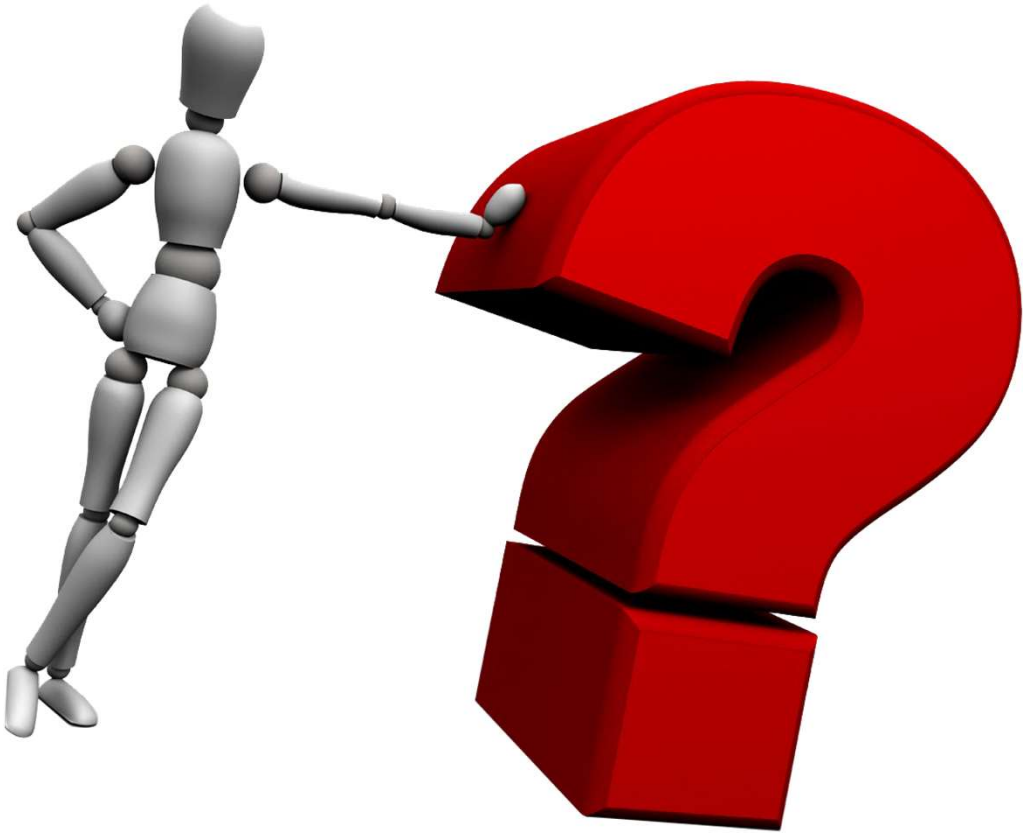
Sodium nitrite

- Effects mainly in IBD patients
- ↓F/B ratio
- ↓ *A. muciniphila*
- Fibrosis related bacteria: ↑*Veillonella* and ↓ *Coprococcus & Oscillospira*
- ↓SCFA (butyrate)

Take home message

- The effect of food additives observed on healthy intestinal microbiota can not be extrapolated to individuals having an altered microbiota as in IBD pathology
- Interactions Food additives – Gut microbiota – SCFA production in IBD patients need to be further studied
- Food additives affect AhR activation (influence inflammation pathways)
- Importance of single donor studies (inter – individual differences)

Questions & Answers time



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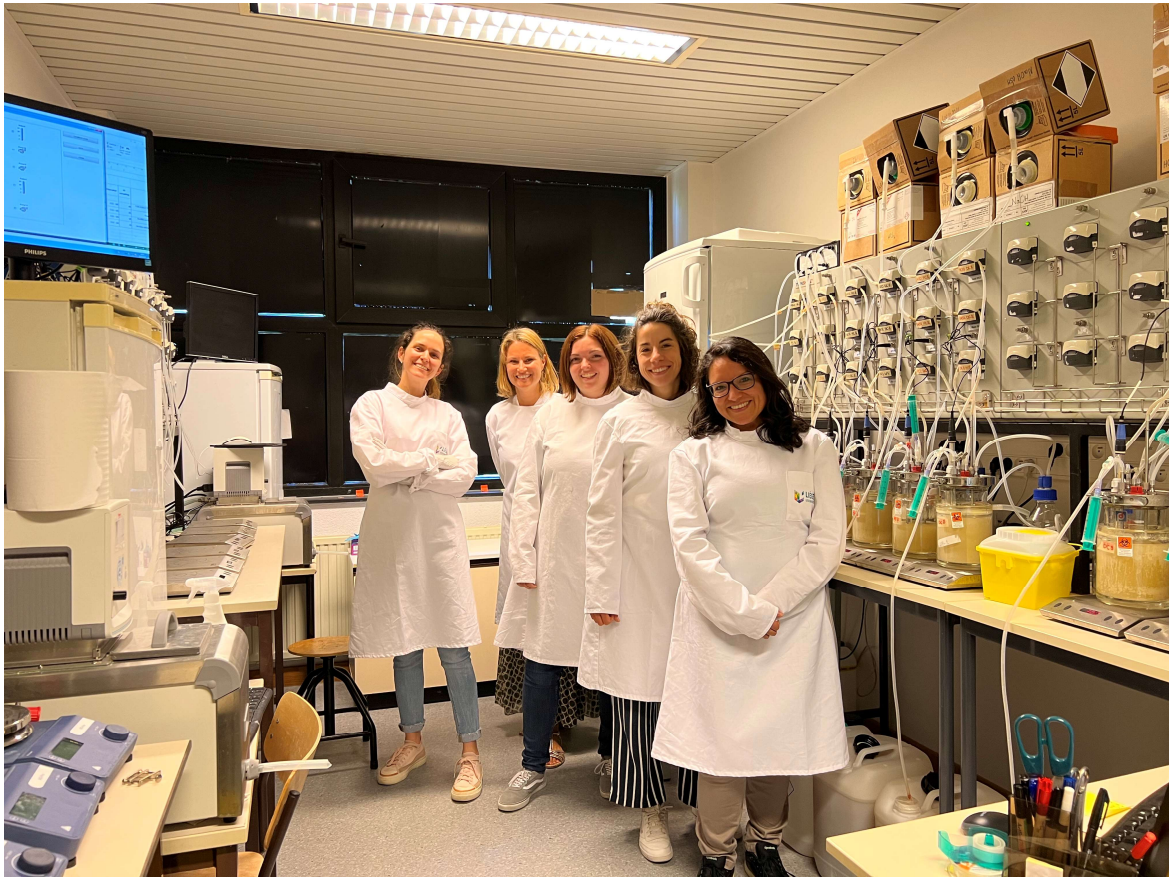

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