INTERNATIONAL SYMPOSIUM ON IBD RESEARCH
FUNDED BY PATIENTS' ORGANISATIONS

“BUTYRATE PRODUCING BACTERIA AS PROBIOTIC TREATMENT IN IBD”

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Butyrate producing bacteria as probiotic treatment in IBD

**Human gut microbiota**

*In vitro* model to study the gut microbiota: M-SHIME

*In vitro* characterization of novel butyrate producing bacteria
Butyrate producing bacteria as probiotic treatment in IBD

Human gut microbiota

Composition
Function
Importance in IBD

*In vitro* model to study the gut microbiota: M-SHIME

*In vitro* characterization of novel butyrate producing bacteria
Our body is a microbial bioreactor

(Scientific American, June 2012)
Difference between mucosal & luminal microbiota

(Van den Abbeele et al., 2011, FEMS microbiology reviews, 35:681-704; LabMET)
Gut microbiota are responsible for our well-being

**Balanced**
- Energy from indigestible carbohydrates
- Vitamins K and B
- Beneficial metabolites
- Gut immune system

**Unbalanced**
- Pathogens: *Salmonella, Listeria*
- Diabetes
- Obesity
- Inflammatory Bowel Diseases
Gut microbiota play a role in etiology of IBD

**INTERNATIONAL SYMPOSIUM ON IBD RESEARCH FUNDED BY PATIENTS ORGANISATIONS – ROADMAP**

**HOST FACTORS**
- Susceptibility genes

**ENVIRONMENTAL FACTORS**
- Smoking, stress, appendectomy, ...

**MICROBIOTA: DYSBIOSIS**
- **Phylogenetic changes**
  - ↓ Firmicutes
  - ↓ Bacteroidetes
- **Altered functionality**
  - ↓ Butyrate production
  - ↑ Sulfate reducing capacity ($^\circ$ $H_2S$)

* Sokol et al., 2006; Sokol et al., 2009; Levine et al., 1998
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SHIME & M-SHIME

Study with UC microbiota

Therapeutic value of butyrate producing bacteria

*In vitro* characterization of novel butyrate producing bacteria
SHIME
Simulator of the Human Intestinal Microbial Ecosystem

Pancreatic juice

\[ N_2 \]

SHIME feed

Stomach

Small intestine

Colon ascendens
pH = 5.6 – 5.9
Res. time = 20h

Colon transversum
pH = 6.1 – 6.4
Res. time = 32h

Colon descendens
pH = 6.6 – 6.9
Res. time = 24h

Pancreatic juice

\[ N_2 \]

SHIME feed

Stomach

Small intestine

Colon ascendens
pH = 5.6 – 5.9
Res. time = 20h

Colon transversum
pH = 6.1 – 6.4
Res. time = 32h

Colon descendens
pH = 6.6 – 6.9
Res. time = 24h
Validation studies:

Molly et al., 1993, Microbiology and Biotechnology, 39, 254-258 (LabMET)
Possemiers et al., 2006, Journal of nutrition, 136, 1862-1867 (LabMET)
Van den Abbeele et al., 2010, AEM, 76, 5237-5246 (LabMET)
M- SHIME simulates luminal AND mucosal part of the human intestinal microbial ecosystem
M- SHIME simulates luminal AND mucosal part of the human intestinal microbial ecosystem

Validation study:
Van den Abbeele et al., 2012, ISMEJ, accepted (LabMET)
M-SHIME study for evaluation colonization efficiency of microbial communities: HV vs. UC

6 healthy individuals (HV)

6 ulcerative colitis patients (UC)

Difference in colonization of M-SHIME?
Microbial community in UC produces more acetate and less butyrate.

(Vermeiren et al., 2012, FEMS microbiology ecology, 79:685-696; LabMET)
Microbial community in UC produces more acetate and less butyrate

Healthy UC

UC

↓ Butyrate producing bacteria

Roseburia spp.

Faecalibacterium prausnitzii

↑ Sulfide production

(Vermeiren et al., 2012, FEMS microbiology ecology, 79:685-696; LabMET)
Carbohydrate fermentation is disturbed

Pryde et al. (2002)
Butyrate has beneficial effects on the gut function

- Inhibits pro-inflammatory pathways
- Strengthens mucosal barrier

• Is the main energy source for colonocytes

Mucus layer
Epithelial cells
RESEARCH PROJECT
Butyrate producing bacteria as probiotics in IBD

• Isolation of butyrate producing bacteria

• Evaluation of novel isolates

• Stimulation of butyrate production \textit{in situ}

Metabolite analysis
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*Butyricicoccus pullicaecorum*

Assessment of gastrointestinal behavior
Butyricicoccus pullicaecorum is a good candidate for probiotic use in IBD

• High production of butyrate

• Butyricicoccus species are decreased in the fecal microbiota of IBD patients (UC & CD) *

• B. pullicaecorum reduces the severity of colitis in a rat model for inflammation*

* (Eeckhaut V., Cleynen I., De Preter V., Machiels K., Vermeire S., 2012, Belgian week gastroenterology, poster)
What is a good probiotic?

- Survives stomach (acid stress)
- Survives small intestine (bile salt stress)
- Colonizes the lower gastrointestinal tract (ileum & colon)
Monitoring survival during passage of stomach and small intestine

B. pullicaecorum
(7 log CFU/mL)

Variation
digestive parameters
pH (2 – 6)
fed/fasted
O₂ (0% - 6%)
[bile salts]
**B. pullicaecorum** is able to survive the passage of the stomach and small intestine.
Colonization efficiency & metabolic activity under lower gastrointestinal conditions
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*Mucosal butyrate producing bacteria guardians for human health*

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M-SHIME a tool to study the complex gut microbiota

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*Butyricicoccus pullicaeorum* is a good candidate to use as probiotic in IBD
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Like
Acknowledgments

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