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PREVENTING CHRONIC DISEASES *VIA* GUT MICROBIOTA:

THE USE OF PREBIOTIC FIBERS, FROM SCIENTIFIC DEMONSTRATION TO MARKETING COMMUNICATION

CAROLINE PERREAU & CLÉMENTINE THABUIS

ROQUETTE NUTRITION AND HEALTH R&D

27TH OF SEPTEMBER 2022

ADEBIOTECH

ROQUETTE: A LEADER WITH A PURPOSE

Ambition

Unlocking the potential of nature to offer the best ingredients for **food, nutrition and health markets**.

8,000+
Employees

25
Industrial sites

90
Years of industrial and operational excellence

100+
Countries served by a global commercial network

€3.9bn
Turnover

300
R&D workforce

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AGENDA

1. Chronic diseases and gut microbiota
2. NUTRIOSE®, a good candidate to increase insulin sensitivity and thus to prevent diabetes
3. Gluconic acid to boost immune response and decrease antibiotics use in farms
4. How to put a new ingredient on the market and communicate on its health benefits?

- Novel food process
- Communication on the health benefits

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THE GUT MICROBIOTA: A MARKER OF HOST HEALTH

frontiers in
CELLULAR AND INFECTION MICROBIOLOGY

REVIEW ARTICLE
published: 09 August 2012
doi: 10.3389/fcimb.2012.00104

The function of our microbiota: who is out there and what do they do?

Noora Ottman[1], Hauke Smidt[1], Willem M. de Vos[1,2] and Clara Belzer[1]*

[1] *Laboratory of Microbiology, Wageningen University, Wageningen, Netherlands*
[2] *Department of Basic Veterinary Medicine and Department of Bacteriology and Immunology, University of Helsinki, Helsinki, Finland*

SCIENCE AND POLITICS OF NUTRITION

Role of the gut microbiota in nutrition and health

Ana M Valdes and colleagues discuss strategies for modulating the gut microbiota through diet and probiotics

Microbiome refers to the collective genomes of the micro-organisms in a particular environment, and microbiota is the community of micro-organisms themselves (box 1). Approximately 100 trillion micro-organisms (most of them bacteria, but also viruses, fungi, and protozoa) exist in the human gastrointestinal tract[1,2]—the microbiome is now best thought of as a virtual organ of the body. The human genome consists of about 23 000 genes, whereas the microbiome encodes over three million genes producing thousands of metabolites, which replace many of the functions of the host,[1,3] consequently influencing the host's fitness, phenotype, and health.[2]

Box 1: Glossary

- *Microbiome*—the collective genomes of the micro-organisms in a particular environment
- *Microbiota*—the community of micro-organisms themselves
- *Microbiota diversity*—a measure of how many different species and, dependent on the diversity indices, how evenly distributed they are in the community. Lower diversity is considered a marker of dysbiosis (microbial imbalance) in the gut and has been found in autoimmune diseases and obesity and cardiometabolic conditions, as well as in elderly people
- *Operational taxonomic unit*—a definition used to classify groups of closely related organisms. DNA sequences can be clustered according to their similarity to one another, and operational taxonomic units are defined based on the similarity threshold (usually 97% similarity) set by the researcher
- *Colonocytes*—epithelial cells of the colon
- *Germ-free animals*—animals that have no micro-organisms living in or on them
- *Short chain fatty acids*—fatty acids with two to six carbon atoms that are produced by bacterial fermentation of dietary fibres

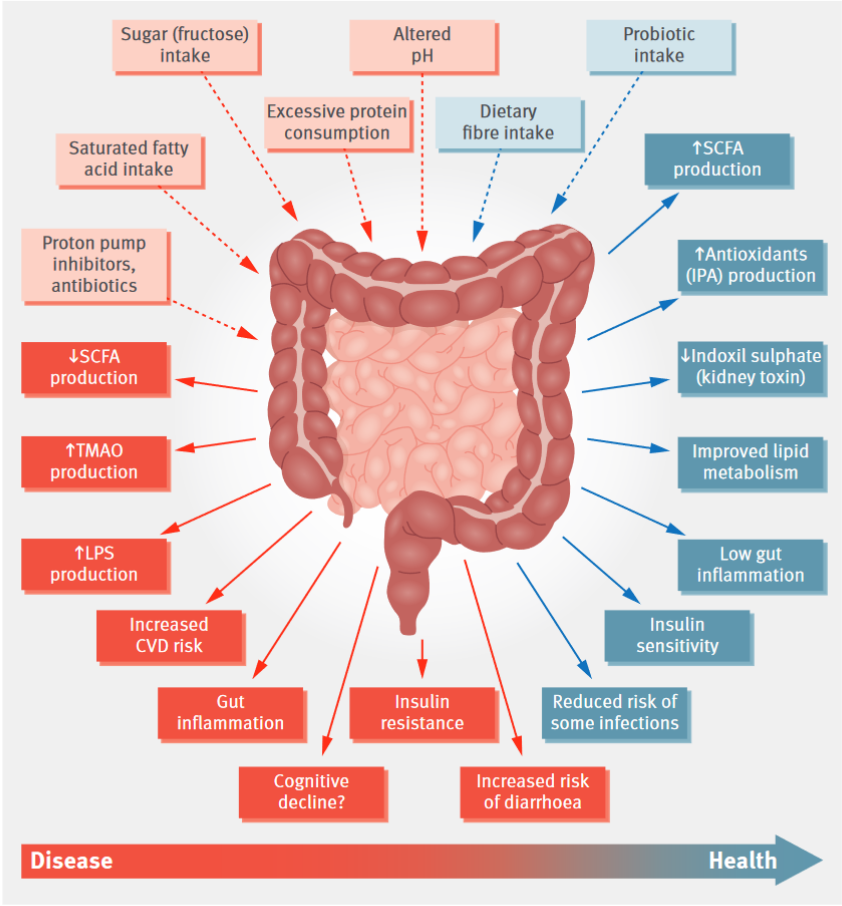

Fig 1 | Schematic representation of the role of the gut microbiota in health and disease giving some examples of inputs and outputs. CVD=cardiovascular disease; IPA=indolepropionic acid; LPS=lipopolysaccharide; SCFA=short chain fatty acids; TMAO=trimethylamine N-oxide

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THE GUT MICROBIOTA & BLOOD GLUCOSE MANAGEMENT

frontiers in Endocrinology

REVIEW
published: 30 January 2019
doi: 10.3389/fendo.2019.00029

Impact of Gut Microbiota on Host Glycemic Control

*Céline Gérard and Hubert Vidal**

Univ Lyon, CarMeN Laboratory, INSERM U1060, INRA U1397, INSA Lyon, Université Claude Bernard Lyon1, Oullins, France

Diabetologia (2018) 61:810–820
https://doi.org/10.1007/s00125-018-4550-1

ARTICLE

Aberrant intestinal microbiota in individuals with prediabetes

Kristine H. Allin[1,2] · Valentina Tremaroli[3,4] · Robert Caesar[3,4] · Benjamin A. H. Jensen[5] · Mads T. F. Damgaard[5] · Martin I. Bahl[6] · Tine R. Licht[6] · Tue H. Hansen[1] · Trine Nielsen[1] · Thomas M. Dantoft[7] · Allan Linneberg[7,8] · Torben Jørgensen[7,9,10] · Henrik Vestergaard[1,11] · Karsten Kristiansen[5] · Paul W. Franks[12,13,14] · the IMI-DIRECT consortium · Torben Hansen[1,15] · Fredrik Bäckhed[3,4,16] · Oluf Pedersen[1,17]

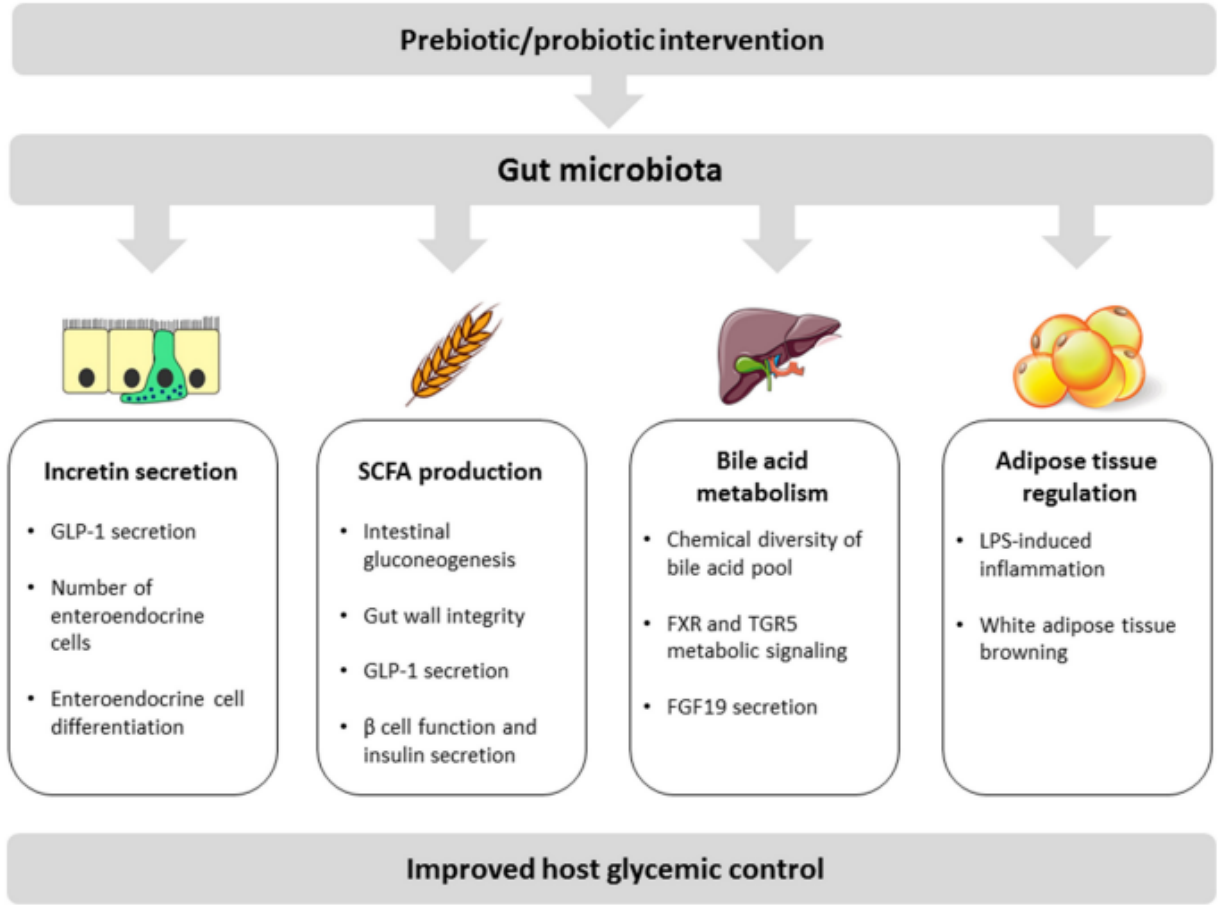
Received: 7 September 2017 / Accepted: 13 December 2017 / Published online: 29 January 2018

ARTICLE

doi:10.1038/nature11450

A metagenome-wide association study of gut microbiota in type 2 diabetes

Junjie Qin[1]*, Yingrui Li[1]*, Zhiming Cai[2]*, Shenghui Li[1]*, Jianfeng Zhu[1]*, Fan Zhang[3]*, Suisha Liang[1], Wenwei Zhang[1], Yuanlin Guan[1], Dongqian Shen[1], Yangqing Peng[1], Dongya Zhang[1], Zhuye Jie[1], Wenxian Wu[1], Youwen Qin[1], Wenbin Xue[1], Junhua Li[1], Lingchuan Han[3], Donghui Lu[3], Peixian Wu[3], Yali Dai[3], Xiaojuan Sun[2], Zesong Li[2], Aifa Tang[2], Shilong Zhong[4], Xiaoping Li[1], Weineng Chen[1], Ran Xu[1], Mingbang Wang[1], Qiang Feng[1], Meihua Gong[1], Jing Yu[1], Yanyan Zhang[1], Ming Zhang[1], Torben Hansen[5], Gaston Sanchez[6], Jeroen Raes[7,8], Gwen Falony[7,8], Shujiro Okuda[7,8], Mathieu Almeida[9], Emmanuelle LeChatelier[9], Pierre Renault[9], Nicolas Pons[9], Jean-Michel Batto[9], Zhaoxi Zhang[1], Hua Chen[1], Ruifu Yang[1,10], Weimou Zheng[1], Songgang Li[1], Huanming Yang[1], Jian Wang[1], S. Dusko Ehrlich[9], Rasmus Nielsen[6], Oluf Pedersen[5,11,12], Karsten Kristiansen[1,13] & Jun Wang[1,5,13]



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THE GUT MICROBIOTA & LOW-GRADE INFLAMMATION

microorganisms

MDPI

Review

Probiotics and Prebiotics for the Amelioration of Type 1 Diabetes: Present and Future Perspectives

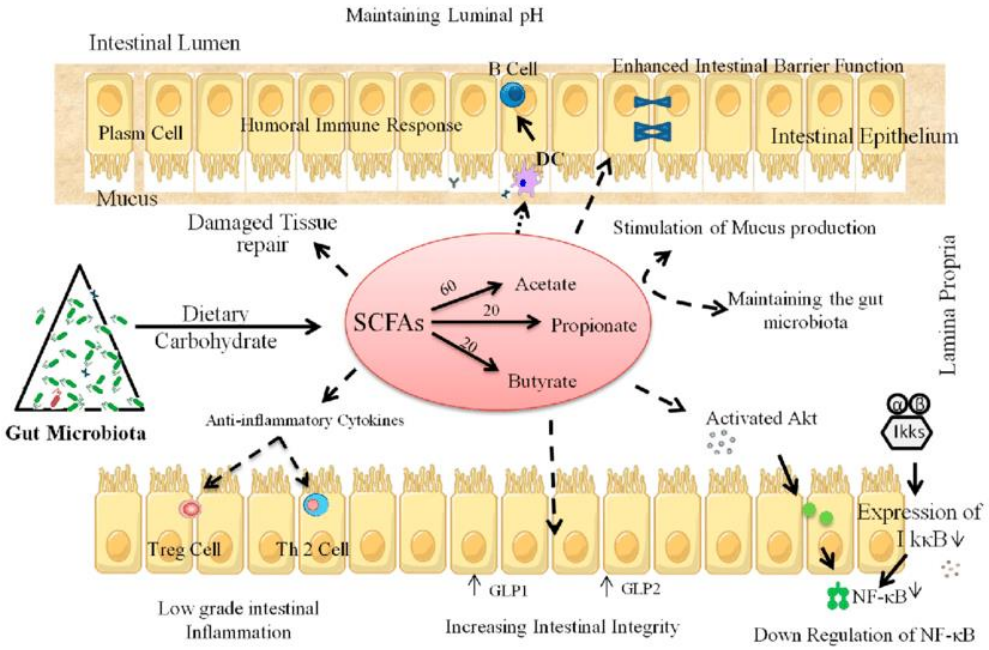
Sidharth Mishra [1,3], Shaohua Wang [1], Ravinder Nagpal [1], Brandi Miller [1], Ria Singh [1], Subhash Taraphder [3] and Hariom Yadav [1,2,*]

1 Department of Internal Medicine-Molecular Medicine, Centre for Diabetes, Obesity and Metabolism, Wake Forest School of Medicine, Winston-Salem, NC 27101, USA; spmishra@wakehealth.edu (S.M.); shaowang@wakehealth.edu (S.W.); rnagpal@wakehealth.edu (R.N.); bcmiller@wakehealth.edu (B.M.); ria.singh@gmail.com (R.S.)

2 Department of Microbiology and Immunology, Centre for Diabetes, Obesity and Metabolism, Wake Forest School of Medicine, Winston-Salem, NC 27101, USA

3 Department of Animal Genetics and Breeding, West Bengal University of Animal and Fishery Science, Kolkata 700 037, India; subhash.taraphder@gmail.com

* Correspondence: hyadav@wakehealth.edu; Tel.: +1-336-713-5049



Gut microbiota

OPEN ACCESS

Original research

Gut microbiota composition reflects disease severity and dysfunctional immune responses in patients with COVID-19

Yun Kit Yeoh [1,2], Tao Zuo [2,3,4], Grace Chung-Yan Lui,[3,5] Fen Zhang,[2,3,4] Qin Liu,[2,3,4] Amy YL Li,[3] Arthur CK Chung,[2,3,4] Chun Pan Cheung,[2,3,4] Eugene YK Tso,[6] Kitty SC Fung,[7] Veronica Chan,[6] Lowell Ling,[8] Gavin Joynt,[8] David Shu-Cheong Hui,[3,5] Kai Ming Chow [3], Susanna So Shan Ng,[3,5] Timothy Chun-Man Li,[3,5] Rita WY Ng,[1] Terry CF Yip,[3,4] Grace Lai-Hung Wong [3,4], Francis KL Chan [2,3,4], Chun Kwok Wong,[9] Paul KS Chan,[1,2,10] Siew C Ng [2,3,4]

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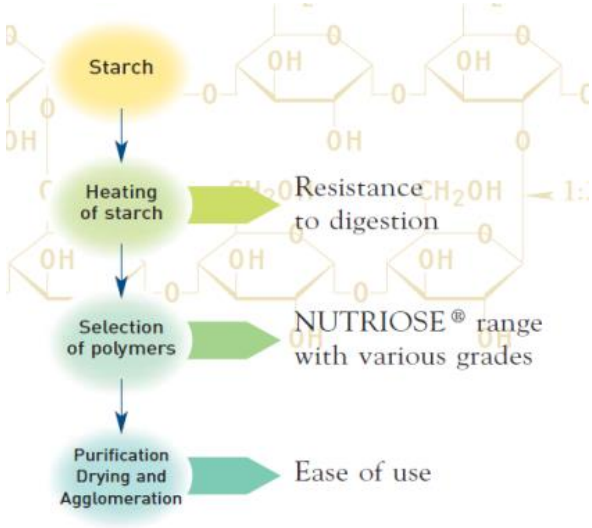
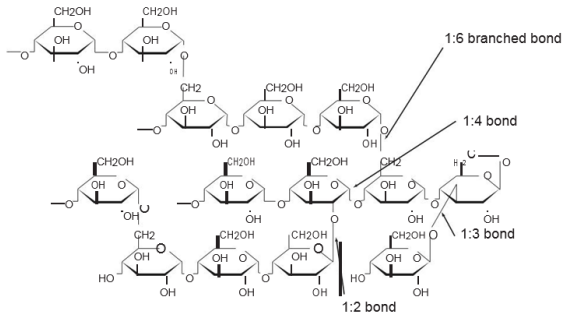
NUTRIOSE® SOLUBLE FIBER

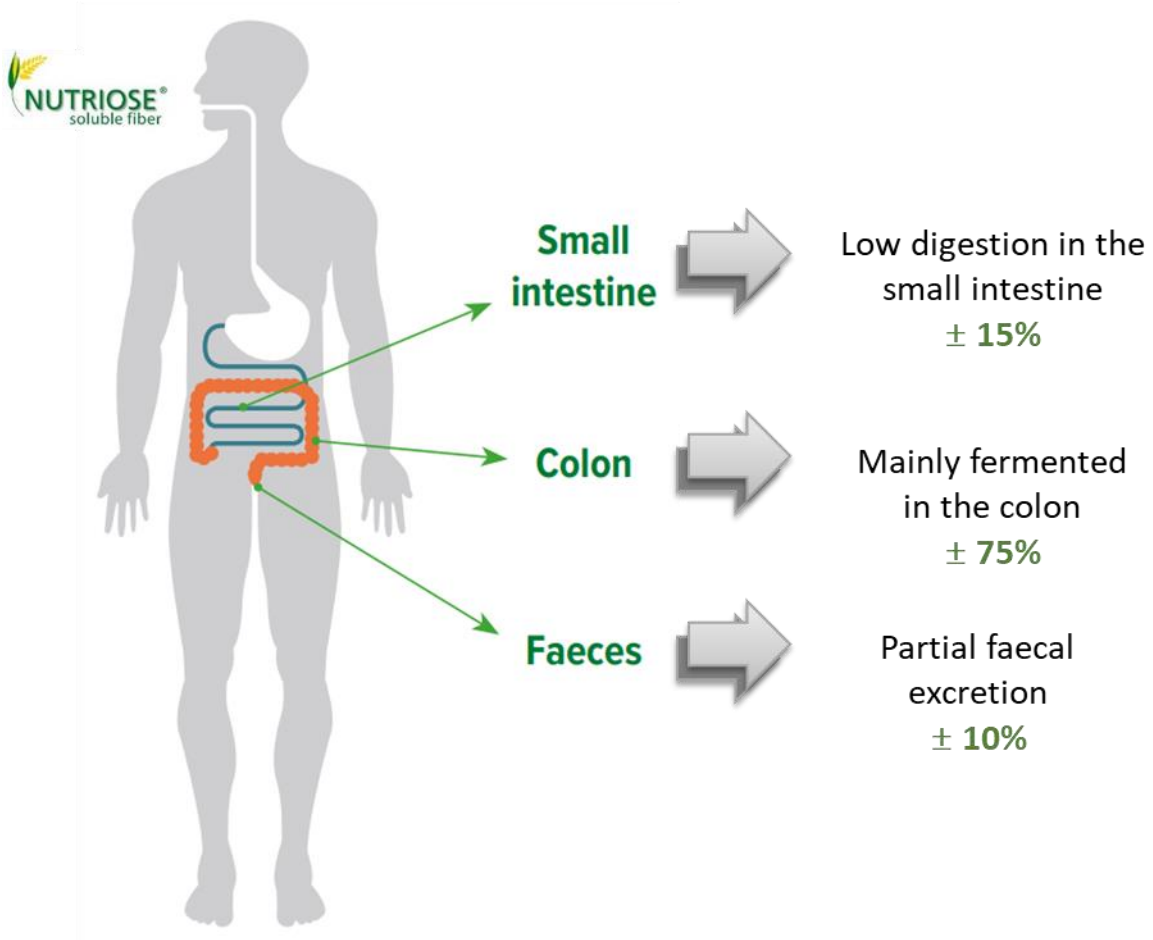
A SPECIFIC PROCESS FOR A SPECIFIC FIBER



OSIDIC LINKAGES NOT HYDROLYSED BY DIGESTIVE ENZYMES



THE METABOLIC FATE



Pasman *et al.* (2006); van den Heuvel *et al.* (2005); van den Heuvel *et al.* (2004)

4 HEALTH BENEFITS SUPPORTED BY CLINICAL STUDIES

NUTRIOSE® soluble fiber

BLOOD GLUCOSE MANAGEMENT

Glycaemic response
Blood glucose control

GUT HEALTH

Tolerance
Prebiotic - microbiota
Intestinal balance

SUSTAINED ENERGY RELEASE

Colonic fermentations
Physiologic/metabolic energy

SATIETY

Satiety
Weight management

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GUT HEALTH

THE STUDY OBJECTIVES

Investigate the effects of **14g/day NUTRIOSE®** for **28 days** in humans on **satiety, metabolic parameters** and **microbiota**

THE STUDY DESIGN

- Chronic, randomized, cross over study
- Setting up in the UK (**University of Reading**)

THE POPULATION

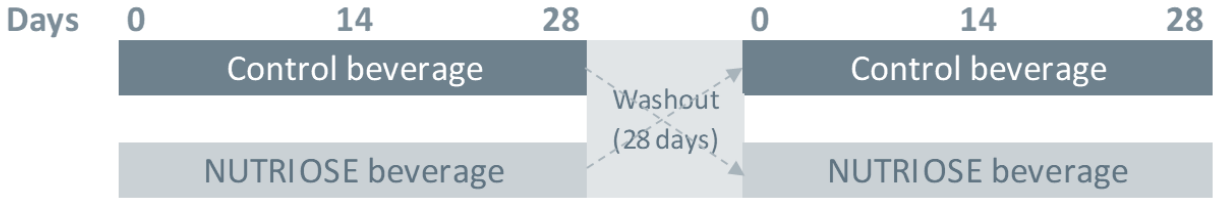
Volunteers

20 normal weight volunteers
(21.0-24.9 kg/m²)

16 overweight volunteers
(24.9-30.0 kg/m²)

- Aged 22-55 y
- Usual daily dietary fibre intake: 16g/day

Unit Study days

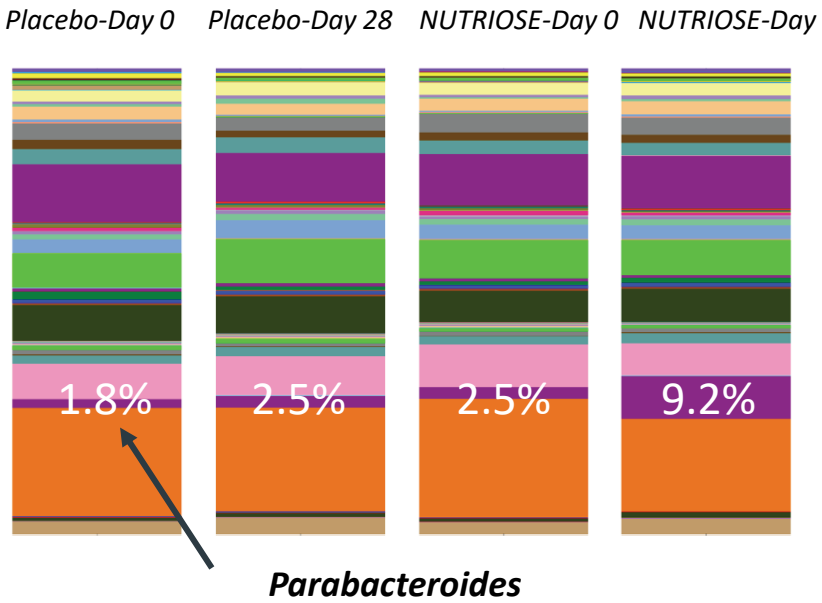


- Outcomes: Appetite evaluation, Fecal microbiota, blood glucose measurements after an orange juice intake

Hobden *et al.* (2021), Guérin-Deremaux et *al*. (2019) (poster)

GUT HEALTH

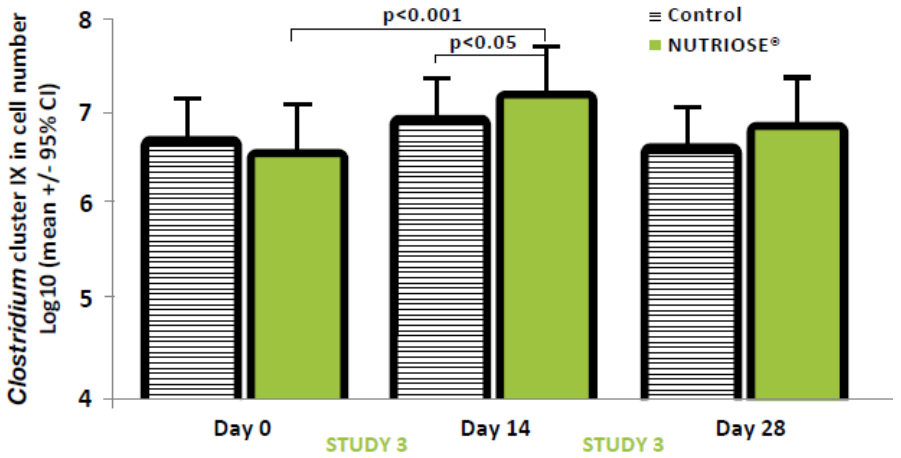
NUTRIOSE® INDUCES A POSITIVE IMPACT ON THE OVERALL GUT ECOSYSTEM IN HUMANS AND EXERTS POTENTIAL METABOLIC HEALTH BENEFITS



Parabacteroides

= a *Bacteroides* subgroup of the phylum *Bacteroidetes*

Relative abundance using faecal 16SrRNA sequencing



FISH technics: Clostridium cluster IX [(+)]

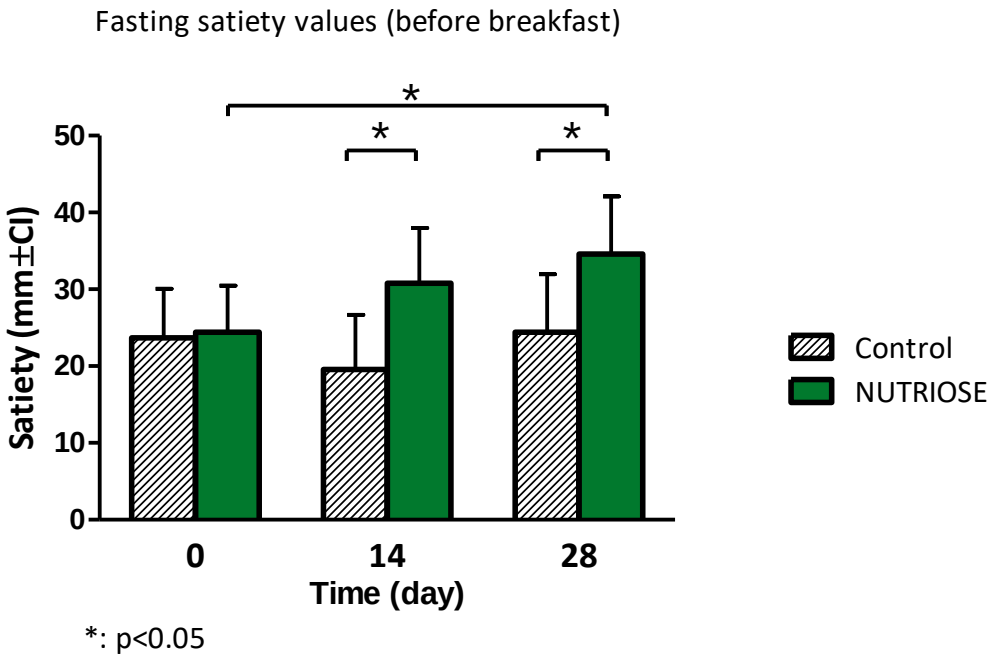
- Significant increase in the relative abundance of *Parabacteroides* genus, a saccharolytic genus
- Significant increase in *Clostridium cluster 9 group*, a propionate producing bacterial group

[+]: Selenomonas, Mitsuokella, Megamonas, Magasphaera, Veillonella

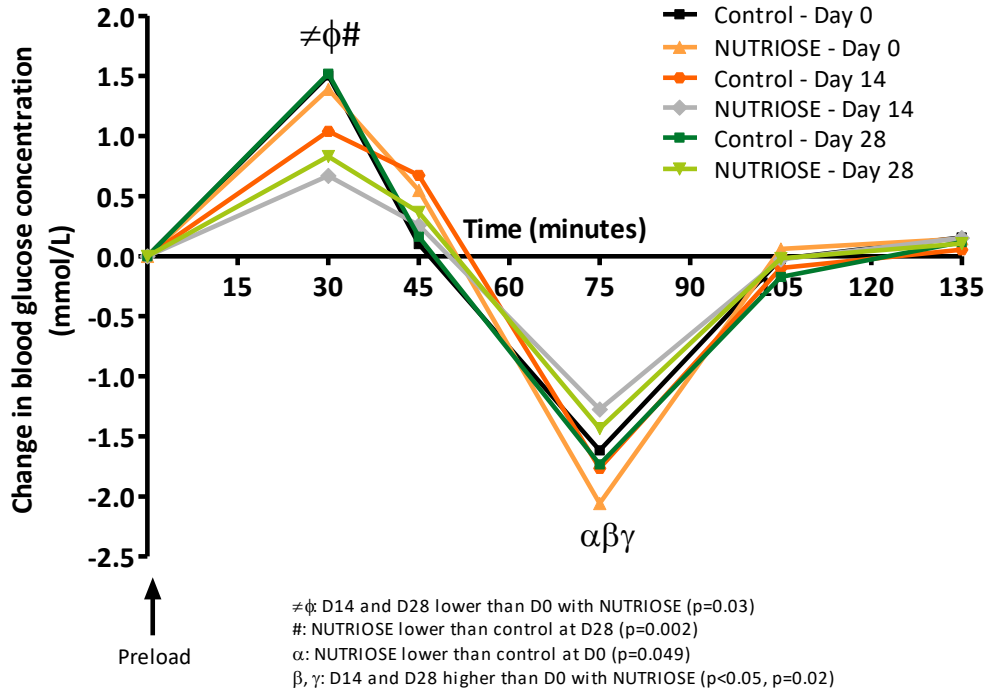
Guérin-Deremaux et *al*. (2019) (poster)

BLOOD GLUCOSE MANAGEMENT

NUTRIOSE® HAS A LOWERING EFFECT ON LONG TERM POST PRANDIAL GLUCOSE AND ON CALORIC INTAKE AND WEIGHT MANAGEMENT IN HUMANS



Fasting satiety ratings in the latter postprandial phase



Changes in blood glucose concentrations following intake of a carbohydrate-preload

- Increase in fasting satiety and postprandial satiety and fullness (data not shown)
- No measured impact in caloric intake

- Reduction of the overall postprandial glucose rise after a carbohydrate-preload administration
- Long term biological effects beyond a simple reduction in glycaemic carbohydrates

Hobden *et al.* (2021), Guérin-Deremaux et *al*. (2018) (poster)

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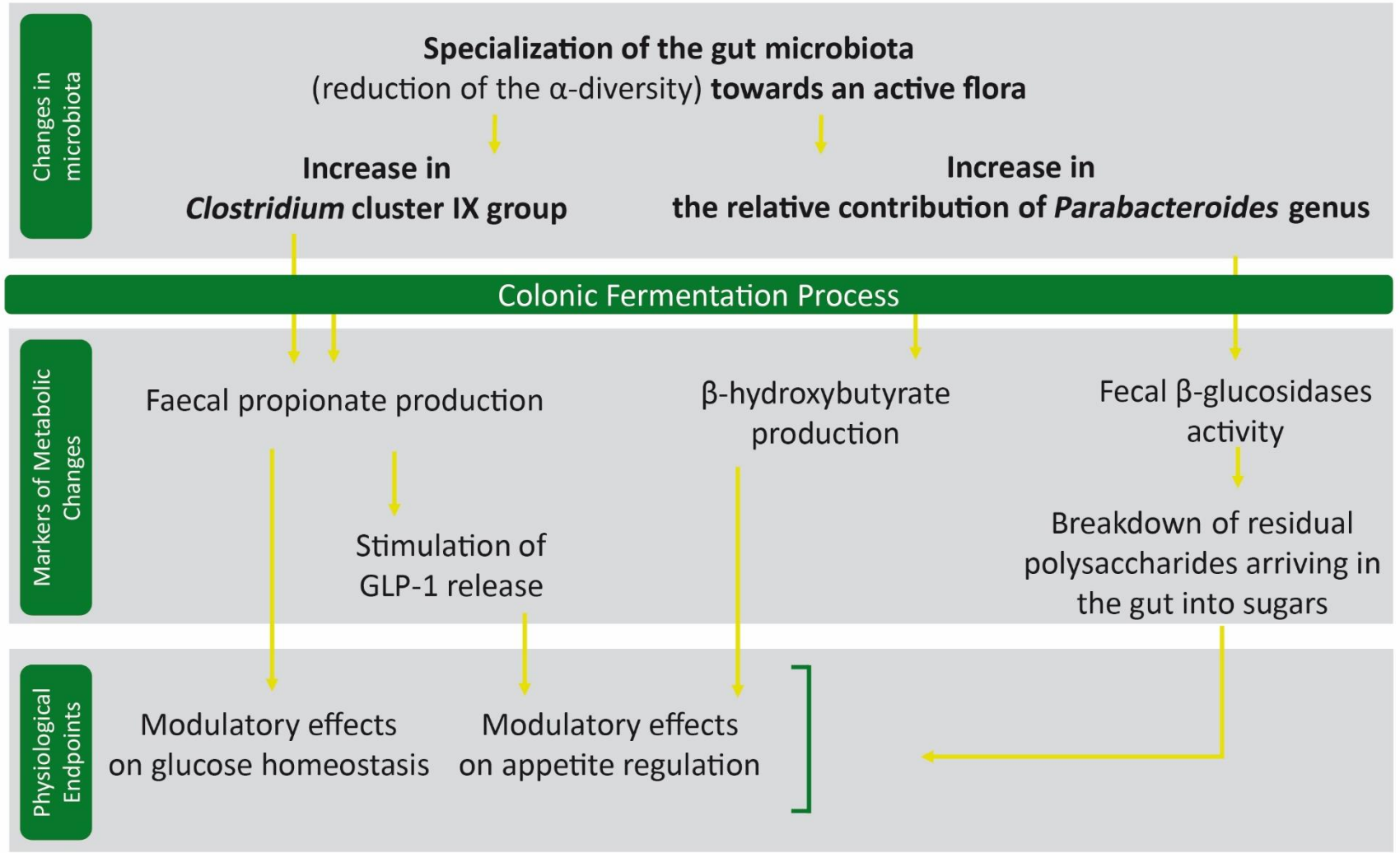


GUT HEALTH: GLUCONEOGENESIS, THE PUTATIVE MECHANISM OF ACTION

THE HEALTH BENEFITS OF NUTRIOSE® MAY BE EXPLAINED BY A CENTRAL ROLE OF INTESTINAL GLUCONEOGENESIS / THE GUT-BRAIN AXIS

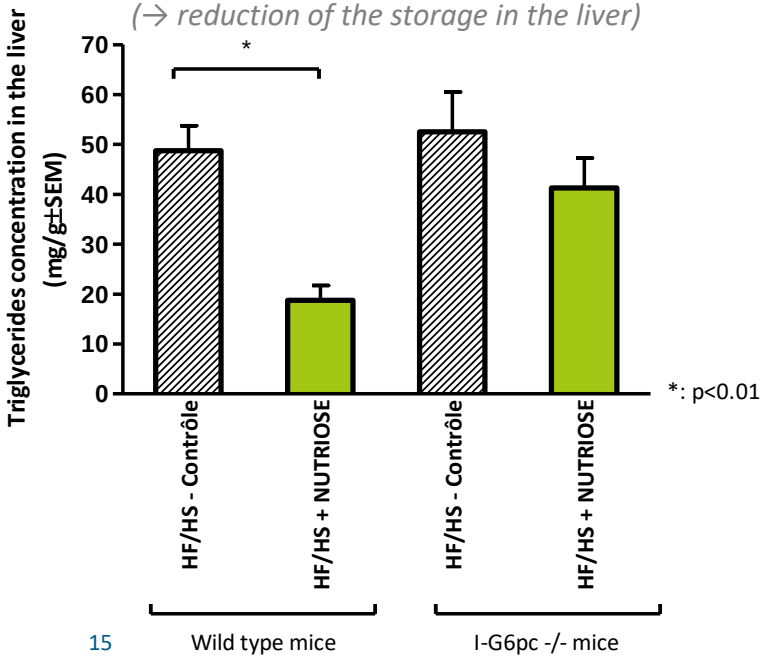
METHODOLOGY:

- Wild type mice and I-G6pc -/- mice (no intestinal glucose production = no gluconeogenesis) – France
- 3-week study period
- High fructose/High sucrose (HF/HS) diet supplemented with 10% NUTRIOSE®
- Blood parameters, Tissue weight, Fecal microbiota, SCFA

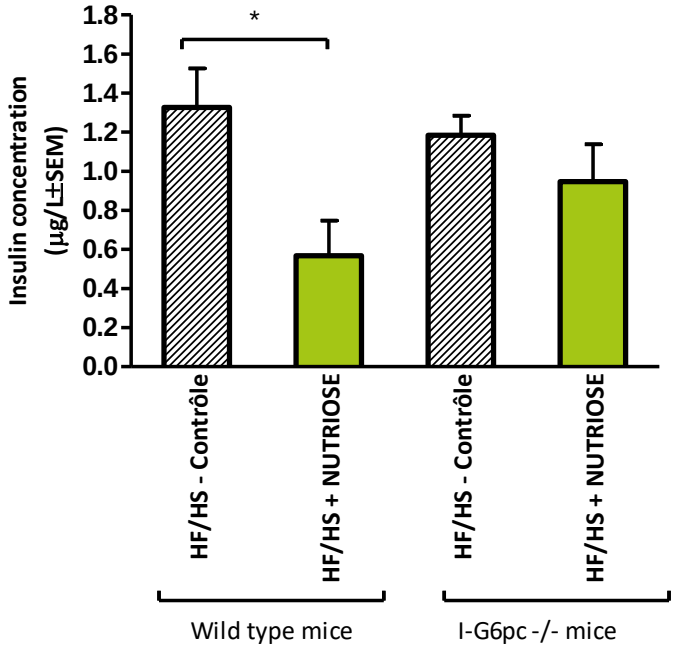
- Modulation of some parameters (triglycerides, insulin and other) and in gene expression (data not shown) in wild type mice only suggesting the role of intestinal gluconeogenesis
- Fecal microbiota modulation
- Increase in caecal butyrate (data not shown)

Intestinal gluconeogenesis may explain the clinical outcomes like satiety and blood glucose management

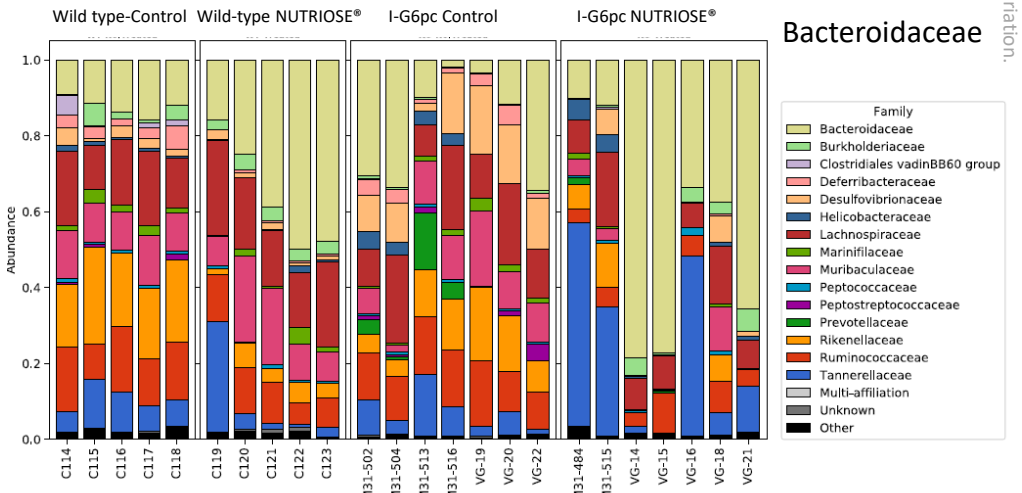
Triglycerides concentration in the liver
(→ reduction of the storage in the liver)



Plasma insulin concentration



Bacteria composition at the family level



Data not published - pending

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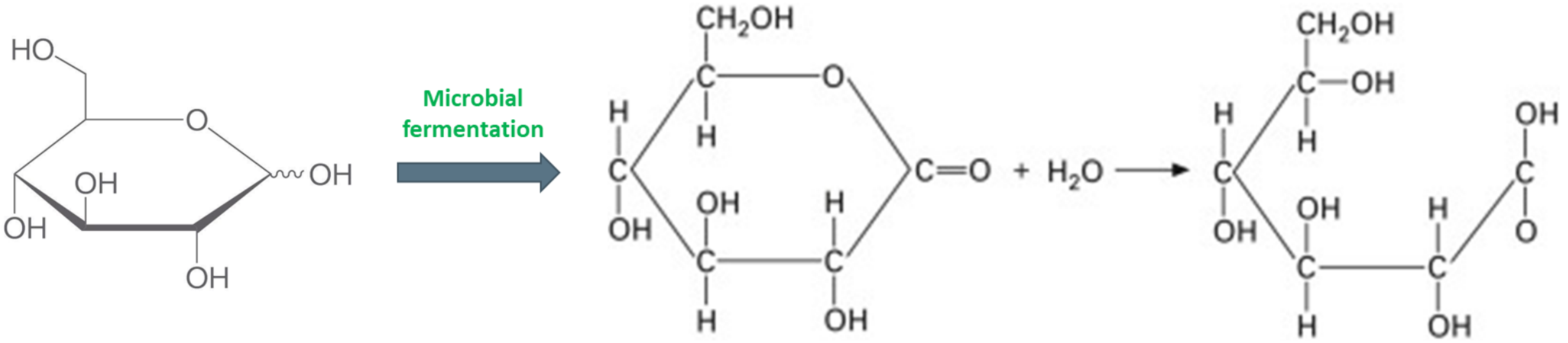
GDL & GUT HEALTH

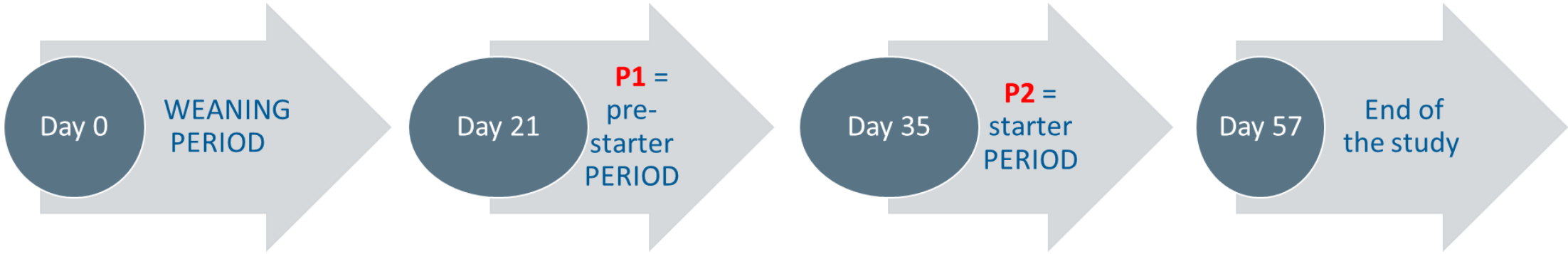


D/L-Glucose | Glucono-δ-Lactone (GDL) | Gluconic Acid (GA)

- Nutritional value can be added to glucose syrup using **microbial fermentation**
- GDL is used as a food stabilizer
- According to literature, GA is **poorly absorbed in the upper part of the GI** and can be converted **into butyrate by gut microbiota**
- Gluconic acid **prebiotic properties** were investigated in the present study

GDL & GUT HEALTH

Objective: to evaluate **the effect of a dietary Sodium Gluconate or Gluconic Acid supplementation** on weaning **performances and intestinal health in piglets** during the **nursery period**.



Significant impact on the main parameters of **zootechnical performance**:
- feed intake at the end of the **P1 & P2**
- **apparent digestibility** at the highest dose

Positive impact on **immune status**:
- significant decrease in blood lymphocytes indicating **lower infection levels**
- **lower antibiotic use**

IMPACT on **gut microbiota:**
- impact on **specific bacteria** (*Lactobacillus, F. prausnitzii*…) ➔ increase in **butyrate producers**
- **higher butyric acid** for both doses

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HOW TO PUT A NEW "PRODUCT" ON THE MARKET?

For European regulation -> within each company, an evaluation of a novel food dossier of an ingredient is usually done by a **committee gathering marketing, scientific and regulatory experts**

TRADITIONAL FOOD

No specific dossier

Evaluation of **human consumption** to **significant degree within the Union** of the ingredient or assessment of equivalence to another ingredient identified **before 15 May 1997** and taking into account these specific points (not exhaustive):

- food with a new or intentionally modified molecular structure,
- isolated from or produced from a plant or a variety of the same species
- production process already used or not

NOVEL FOOD

Any food that was not used for human consumption to a **significant degree within the Union before 15 May 1997**, and that falls under at least one of the 10 categories.

Novel food dossier

https://food.ec.europa.eu/system/files_en?file=2016-10/novel-food_guidance_human-consumption_en.pdf

HOW TO COMMUNICATE ON SCIENCE IN EUROPE?

B2B communication

RECOMMANDATIONS

- Ensure the communication does not relate to a product intended for the final consumer
- Remain **proportionate** and do not be misleading
- Remain **factual** (e.g. clinical studies data, scientific literature…)
- As we speak to professional, the vocabulary must be **scientific** and **technical**
- Use of **disclaimers*** when the health benefits of the ingredients are not yet approved/evaluated by regulatory organizations

Scientific communication

SCIENTIFIC PEER-REVIEWED PAPER
POSTER
SCIENTIFIC PRESENTATION
TECHNICAL MEETING WITH CUSTOMERS
WEBINARS

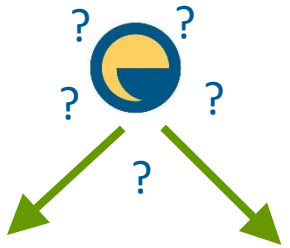
Health claims

APPROVED HEALTH CLAIMS or GENERIC HEALH CLAIMS

Must refer to the exact approved health claim/wording and the conditions of use.

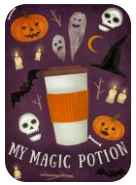
B2C communication

Roquette is NOT able to provide its customers with risk assessments on their final products. We can only support them.



RECIPE OF THE FINAL PRODUCT?

(NUTRIOSE® = JUST ONE INGREDIENT AMONG OTHERS)



LEVEL OF RISK THAT THE B2C COMPANY IS WILLING TO TAKE?

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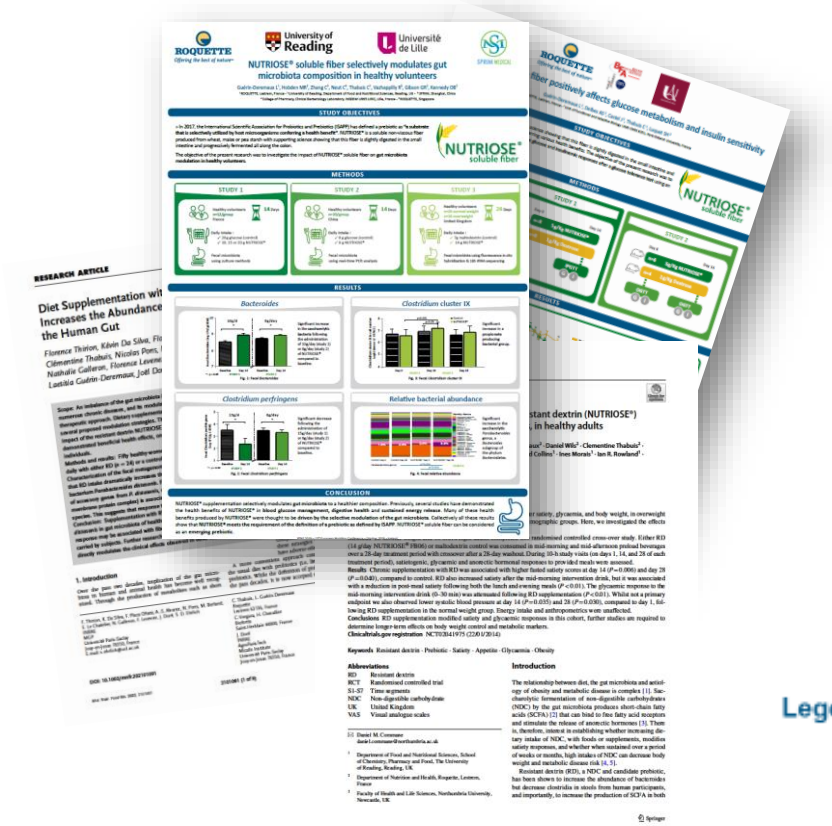
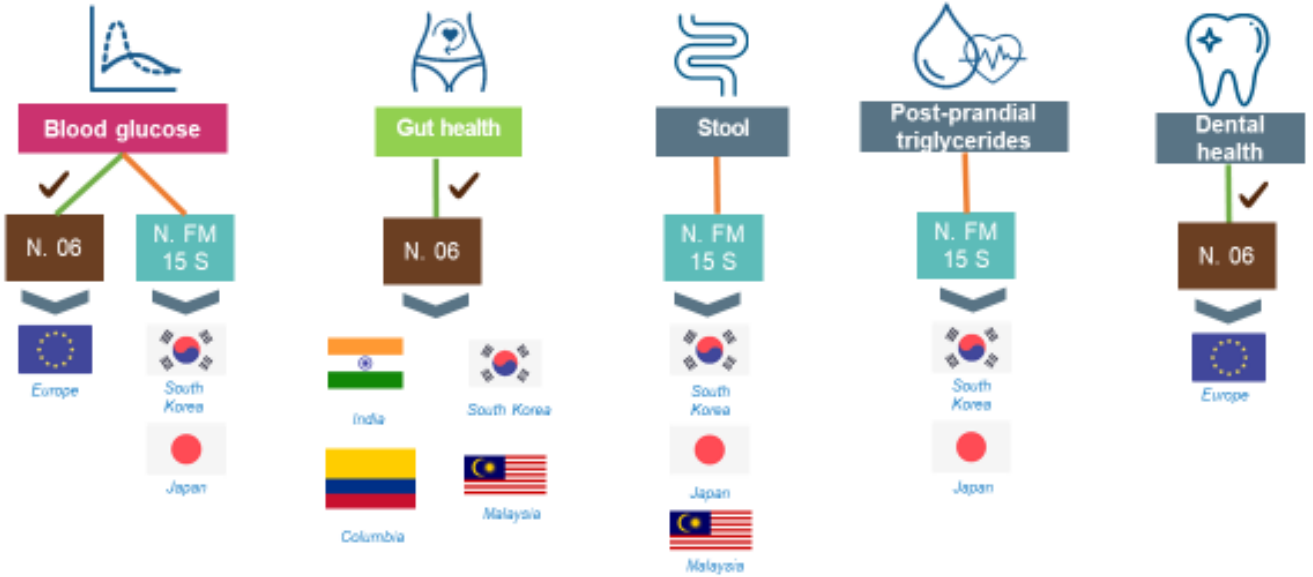
NUTRIOSE® – HEALTH BENEFITS AND CLAIMS

Scientific communication



Health claims



Legend

N. 06 — NUTRIOSE®06

N. FM 15 S — NUTRIOSE® FM 15 S

✓ Proven health benefits: Roquette proprietary **clinical evidence**

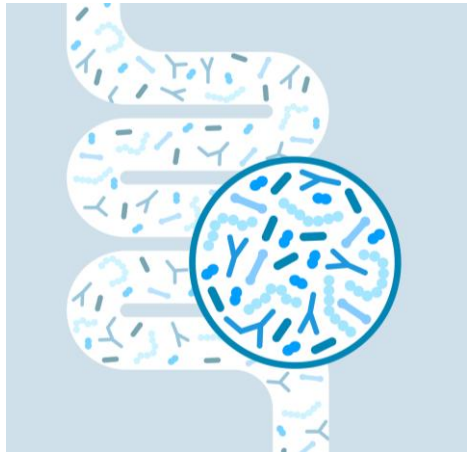
Accessible health-related claims by country

The examples given are suggestions, associated with more or less regulatory risk. A decision about whether a wording is acceptable or not may need to be made on a case-by-case basis. Front of pack claims are the responsibility of the responsible for the product marketing / placing on the market.

CONCLUSION

- The **gut microbiota** is a marker of **host health**.

  Microbiota **dysbiosis** <-> **Diseases**



- Thanks to its short- and long-term impact on **blood glucose management**, **NUTRIOSE®** can be a good candidate to **increase insulin sensitivity** and thus to **prevent diabetes**.
  - Microbiota modulation and gluconeogenesis -> putative mechanism of action
- **Gluconic acid** can **boost immune response** and **decrease antibiotics** use in farms
- Before putting a new product on the market -> **evaluation of novel food dossier**
- B2B communication allow **factual communication** between two professionals, before evaluation of B2C communication with approved health claims in Europe.

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