"Key Scientific Drivers Behind Probiotic and Prebiotic Applications"
International Symposium of the International Scientific Association of Probiotics and Prebiotics
June 5-6, 2018, Furama Riverfront Hotel, Singapore

The Targets for Prebiotic Therapy

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UK

Organised by: ISAPP International Scientific Association of Probiotics and Prebiotics
In affiliation with: Singapore Society for Microbiology and Biotechnology
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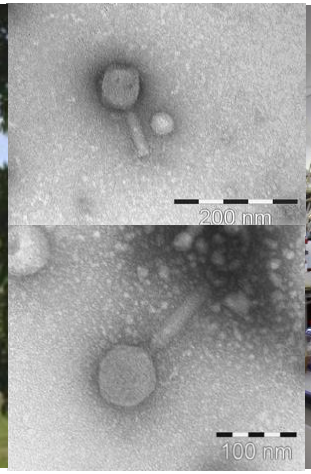
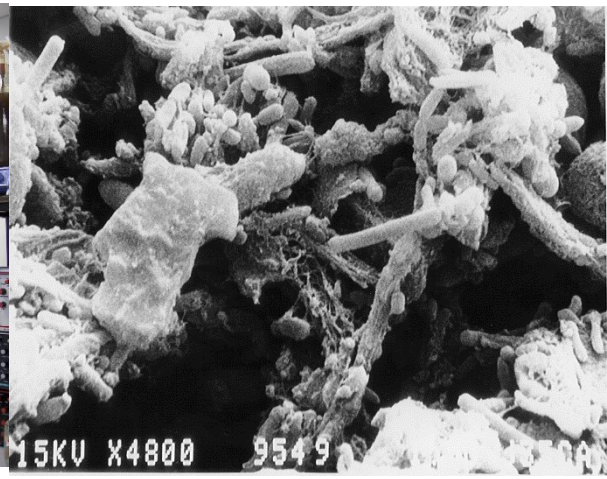


The emergence of prebiotics

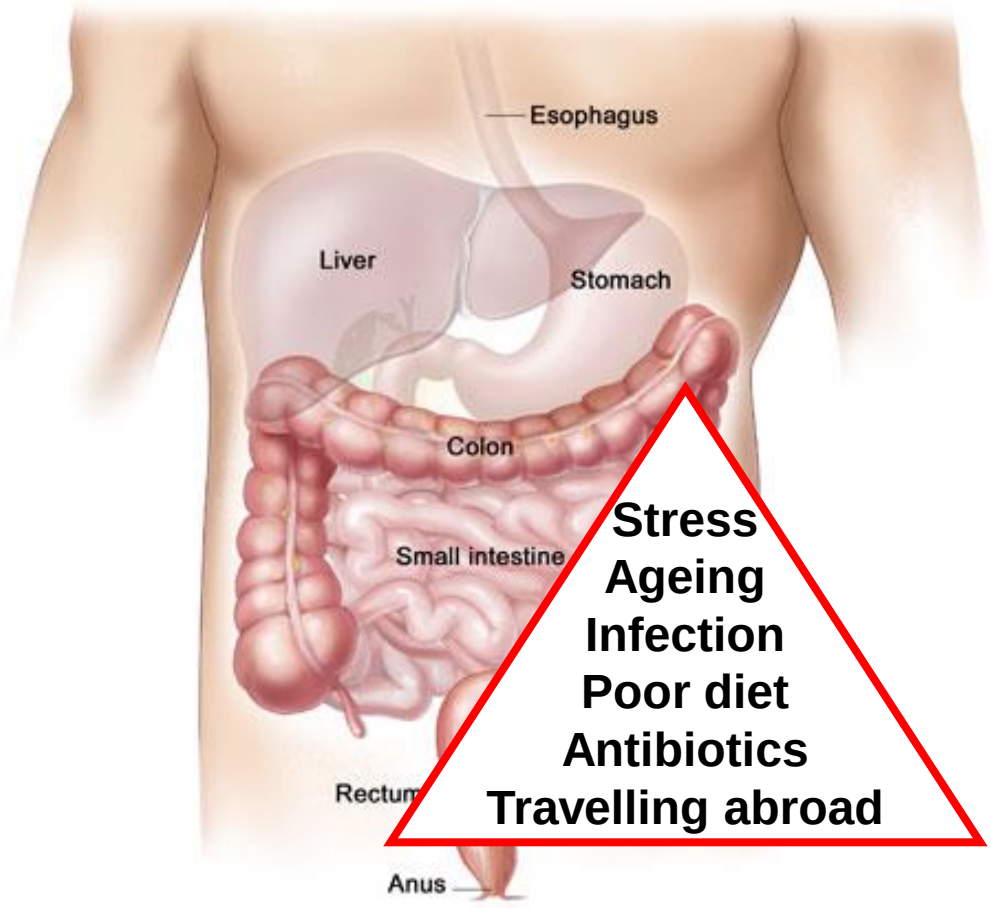
Glenn Gibson

ISAPP Singapore June 5th 2018

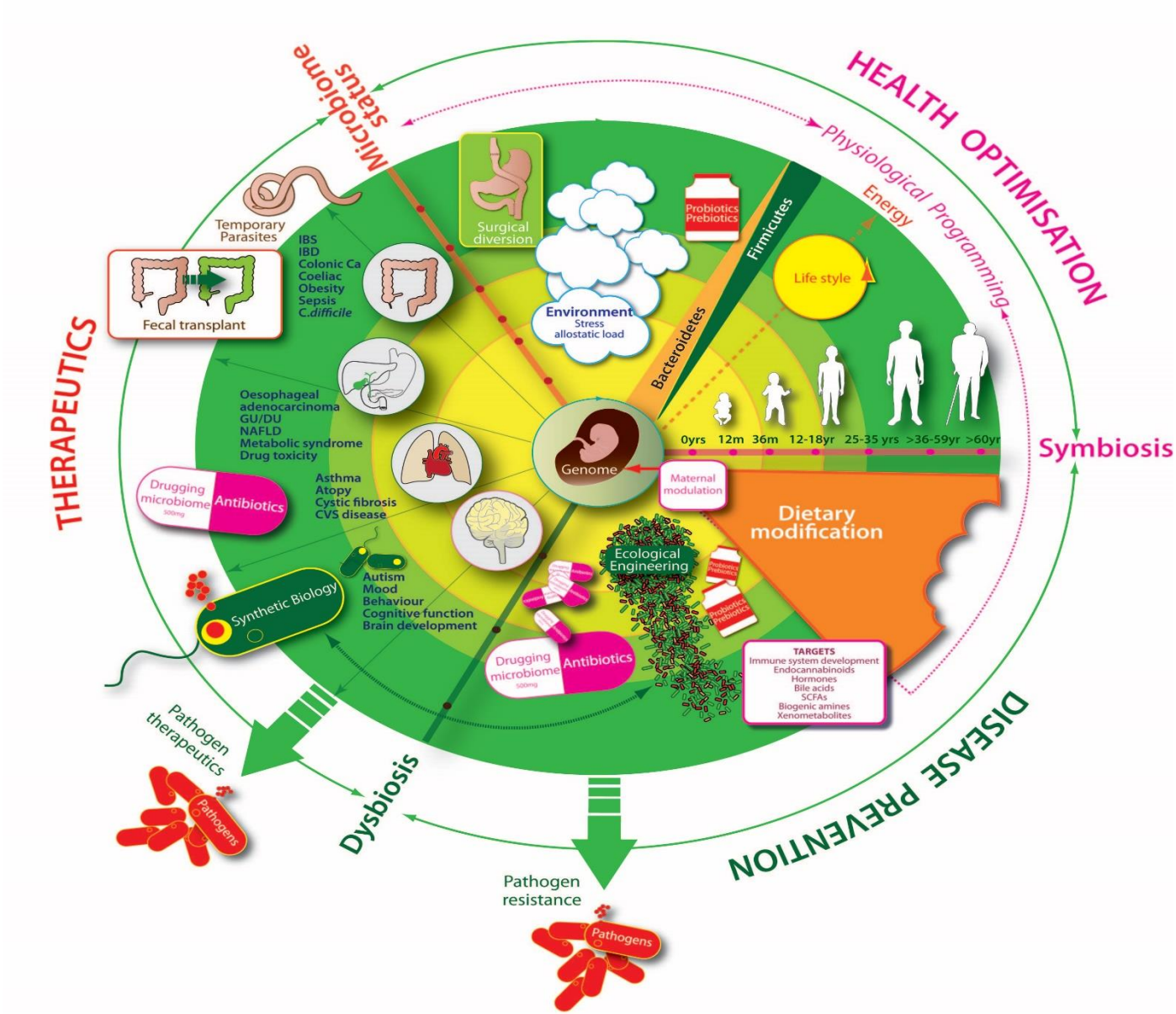
Past

Gut bacteria can be compromised

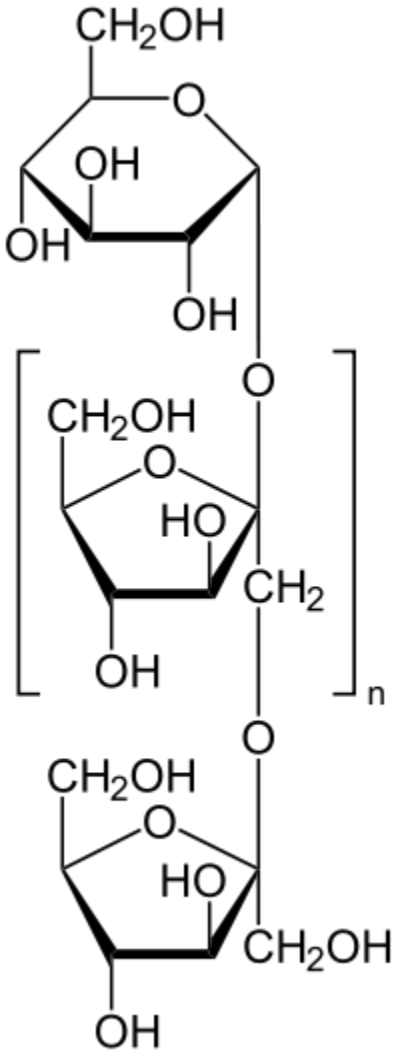
Compromised gut health & immunity



Therapeutic modulation



Inulin-derived fructans



Inulin

$[Fru\beta2\rightarrow1]_nFru\beta2\leftrightarrow1\alpha Gl$

c

n = 1 – 50

Inulinase

Oligofructose

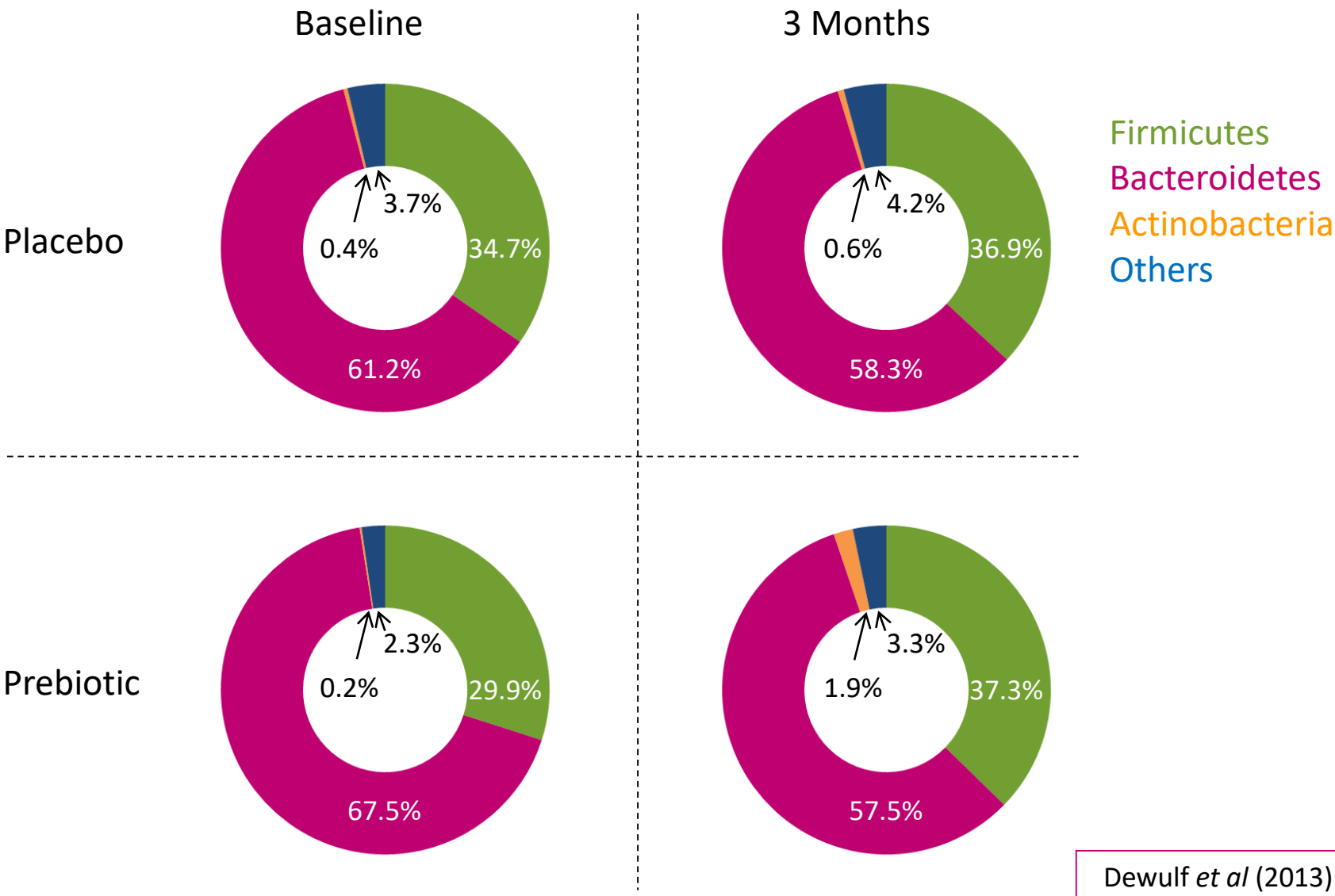
$[Fru\beta2\rightarrow1]_nFru$

$[Fru\beta2\rightarrow1]_nFru\beta2\leftrightarrow1\alpha Gl$

c

n = 1-5

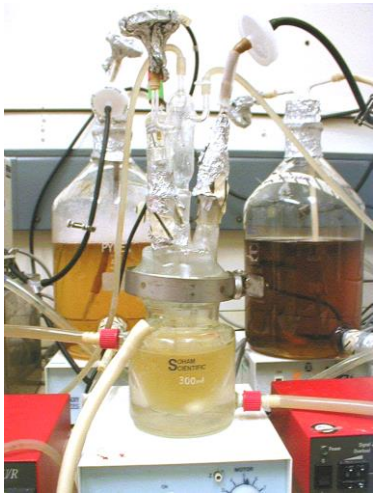
HITChip analysis – phylum level



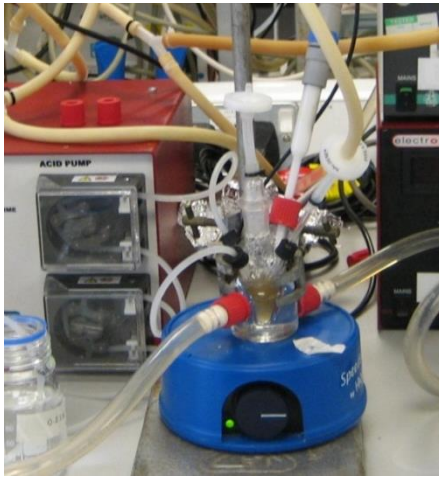
Dewulf *et al* (2013) *Gut* 62: 1112-1121

Present

Bioactivity testing

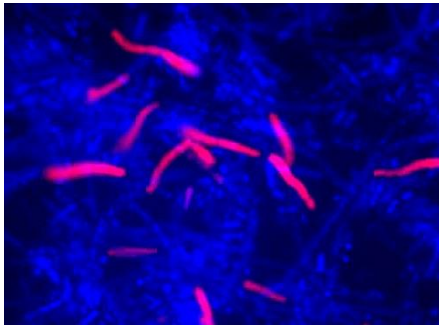


Batch cultures

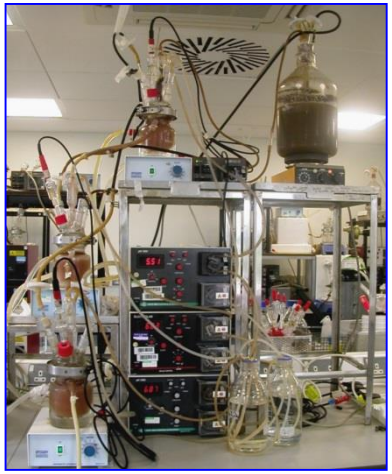


Micro
batch cultures

Metabolite
analysis



Molecular
microbiology
methods

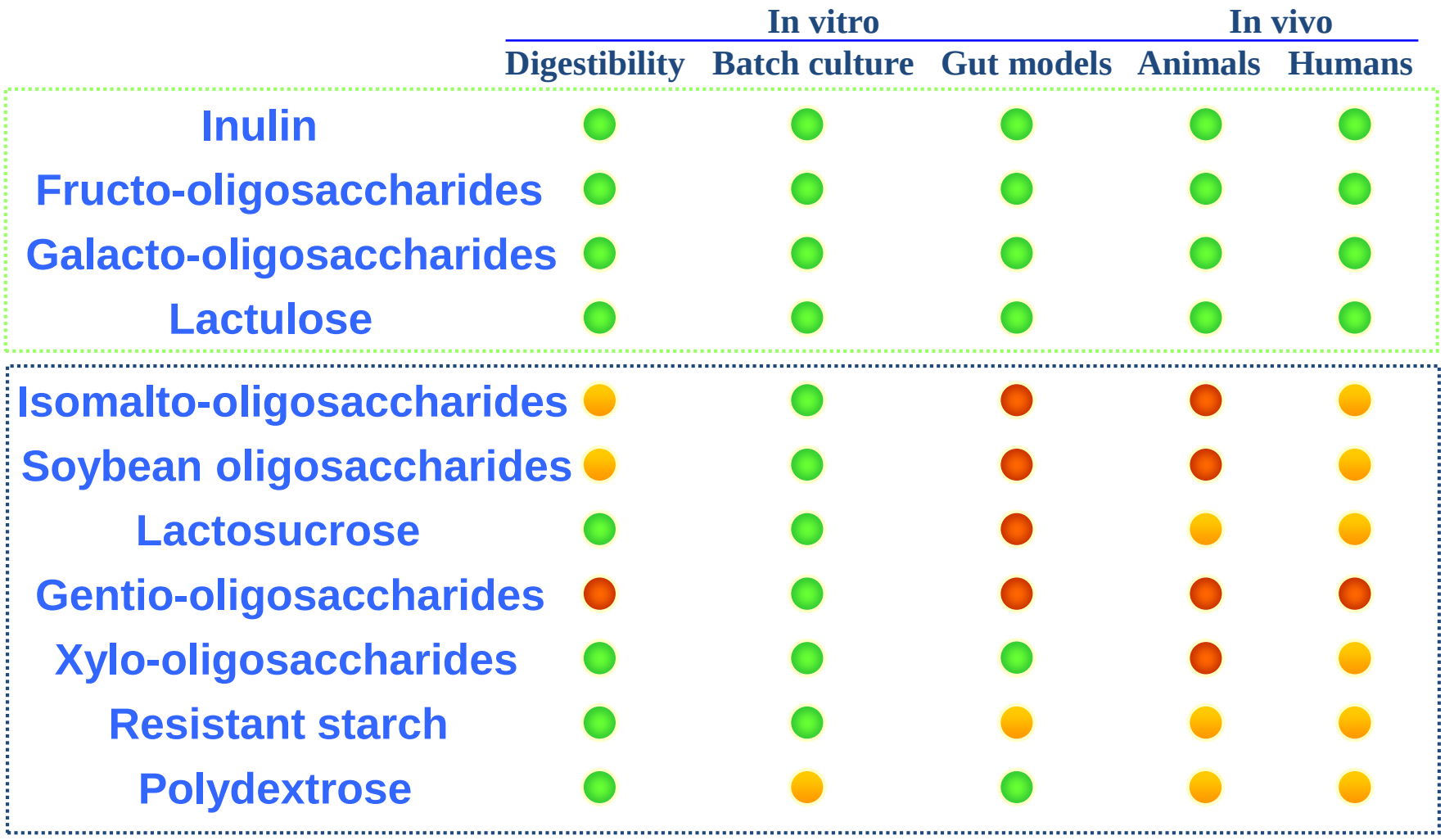


Gut models

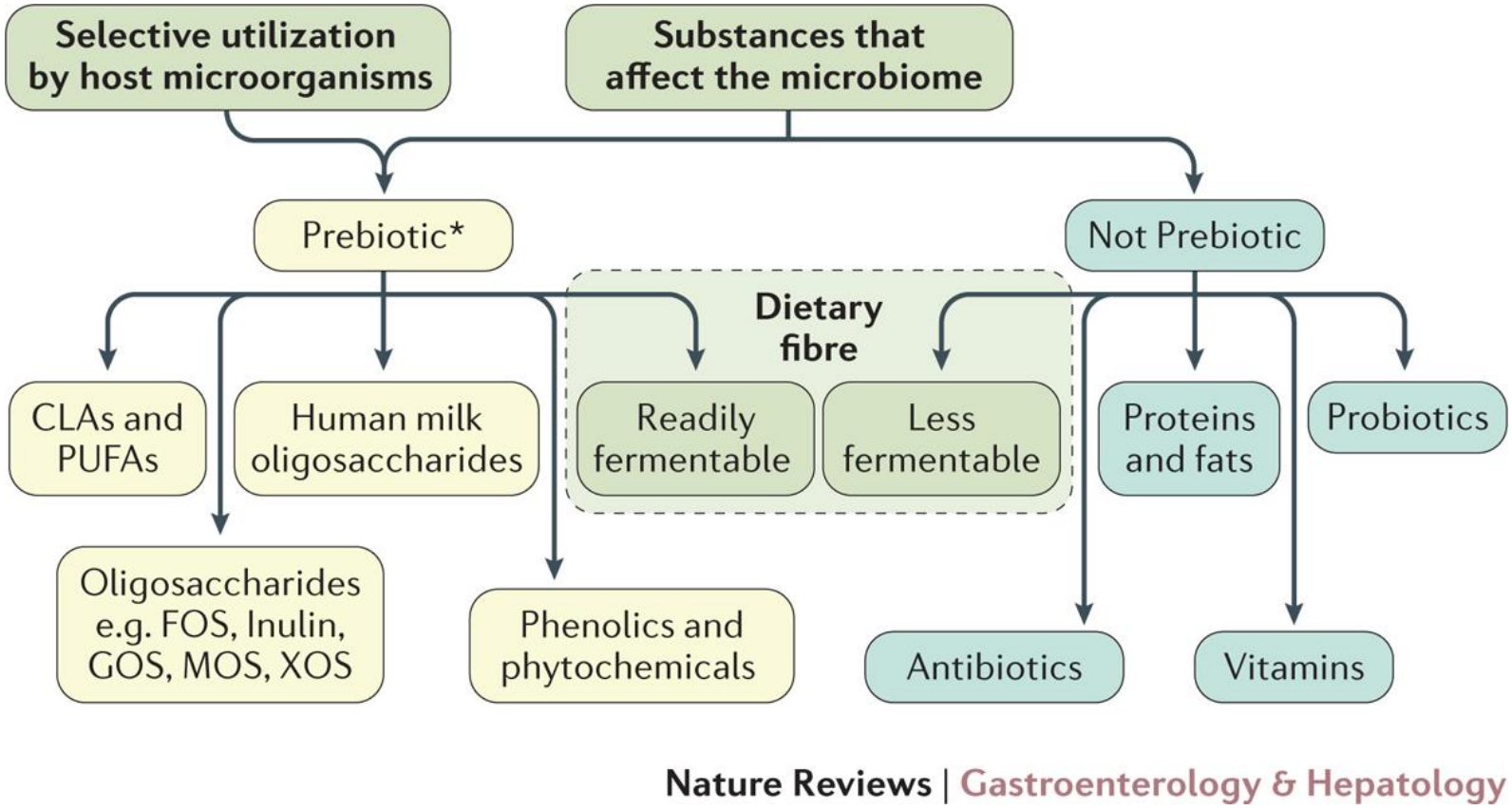
Human studies

Metabonomics

Reported prebiotic oligosaccharides



Distinguishing what is considered a prebiotic within the proposed definition



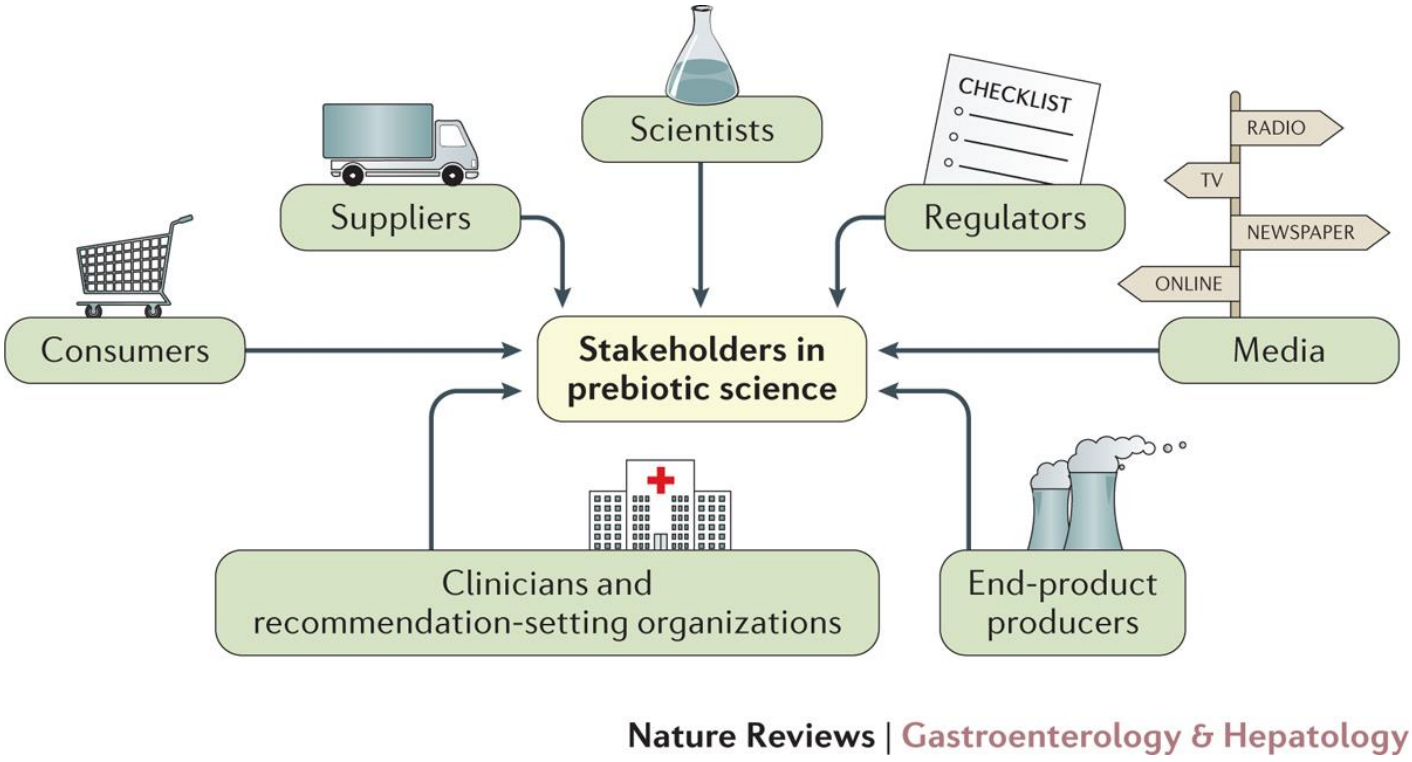
Gibson, G. R. *et al.* (2017) The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics *Nat. Rev. Gastroenterol. Hepatol.* doi:10.1038/nrgastro.2017.75

Table 1 | **Health end points targeted in human trials of orally administered prebiotics**

Health end point	Prebiotic used
Metabolic health: overweight and obesity; type 2 diabetes mellitus; metabolic syndrome and dyslipidaemia; inflammation	Inulin, GOS, FOS
Satiety	FOS
Stimulation of neurochemical-producing bacteria in the gut	GOS
Improved absorption of calcium and other minerals, bone health	Inulin, FOS
Skin health, improved water retention and reduced erythema	GOS
Allergy	FOS, GOS
IBD	Inulin, lactulose
Urogenital health	GOS
Bowel habit and general gut health in infants	GOS, FOS,
Infections and vaccine response	FOS, GOS, polydextrose
Necrotizing enterocolitis in preterm infants	GOS, FOS
IBS	GOS
Traveller's diarrhoea	GOS
Constipation	Inulin
Immune function in elderly individuals	GOS

FOS, fructooligosaccharides; GOS, galactooligosaccharides.

Stakeholders with an interest in prebiotic science



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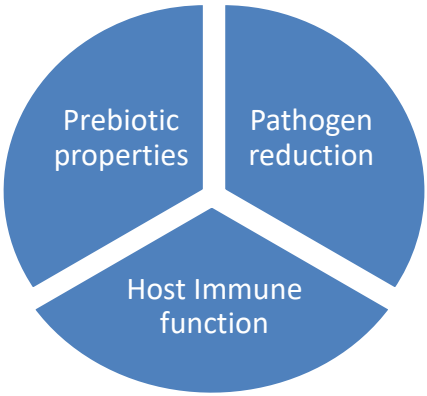
How may prebiotics work?



Selective proliferation of beneficial bacteria

faecal bulking → **improved bowel function**

Stimulate growth

B-GOS

bifidobacteria

Colonisation resistance

Pathogens

reduce exogenous and endogenous intestinal infection

Direct effect on invasion of GI pathogens

block adhesion

M cell

colonocytes

Direct effect on host epithelium

Immunomodulation

IL-10

IL-6

Anti-inflammatory

Suppress IBD inflammation

dendritic cell

Phagocytosis

Nk cell activity

Pathogen/viruses protection

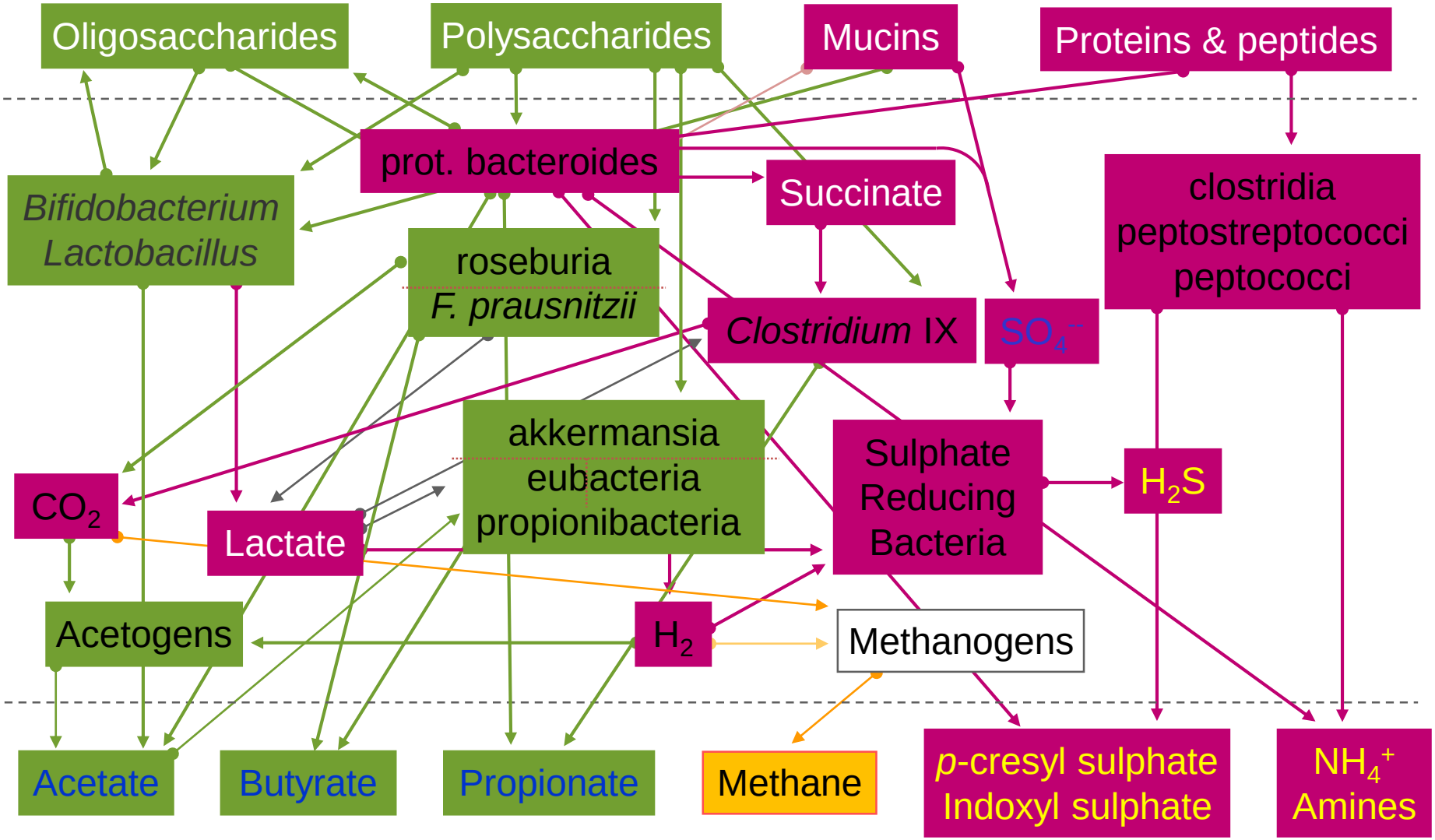
lamina propria

Possible future

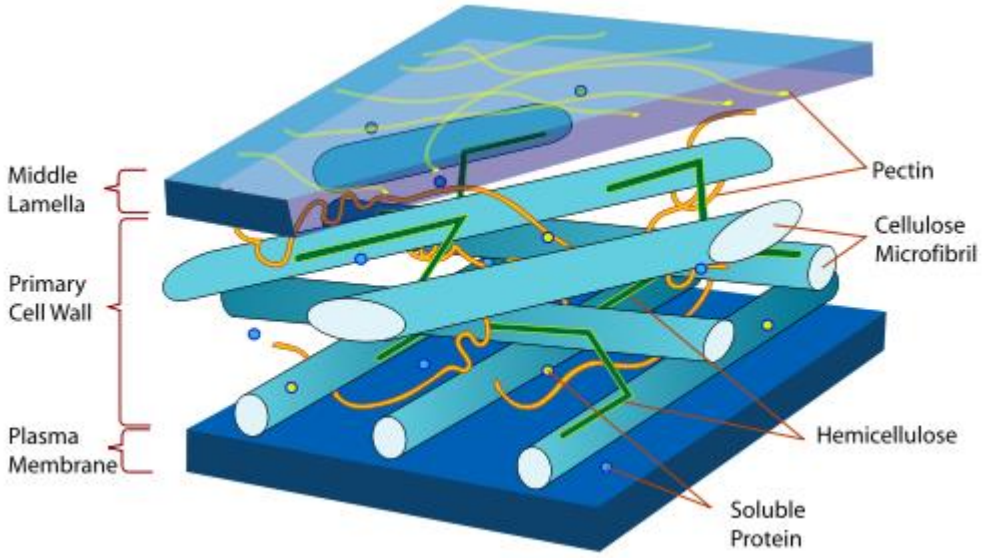
Beyond usual prebiotic effects

- Virulence attenuation
- Distal colon
- Encapsulation
- Anti-adhesive influences
- New targets
- Waste-stream use
- Synbiotics, including species changes
- Food quality aspects and functionality

Prebiotics – expanded diversity



Potential prebiotics from biomass



Pectins

- Citrus
- Apple
- Potato

Xylans

- Corn cob
- Wheat
- Oil palm

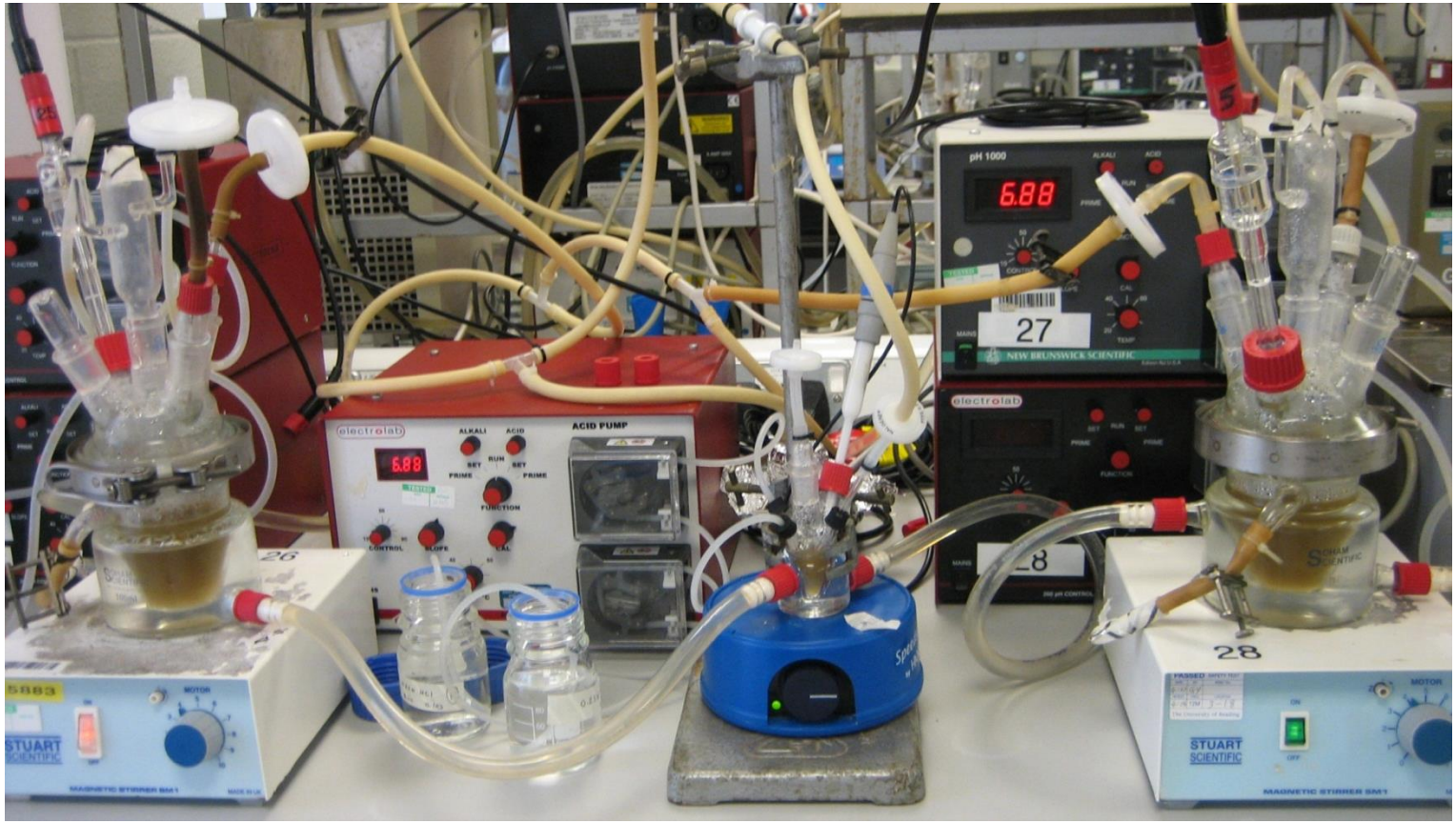
β-glucans

- Oat
- Barley

β-mannans

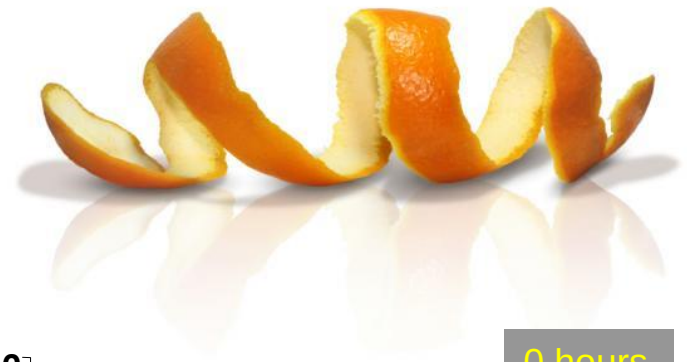
- Coffee

Microscale fermenter

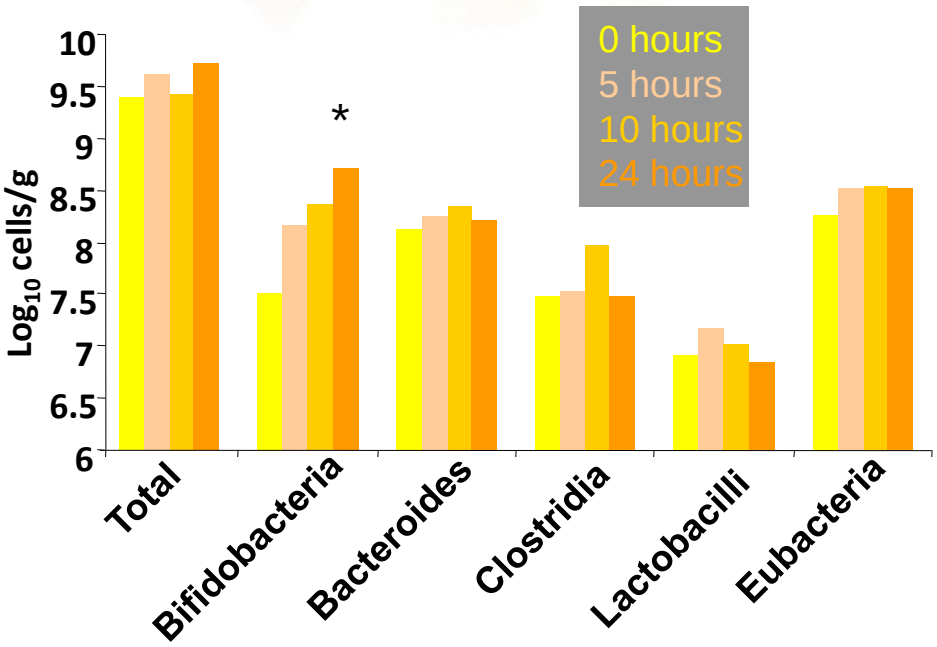


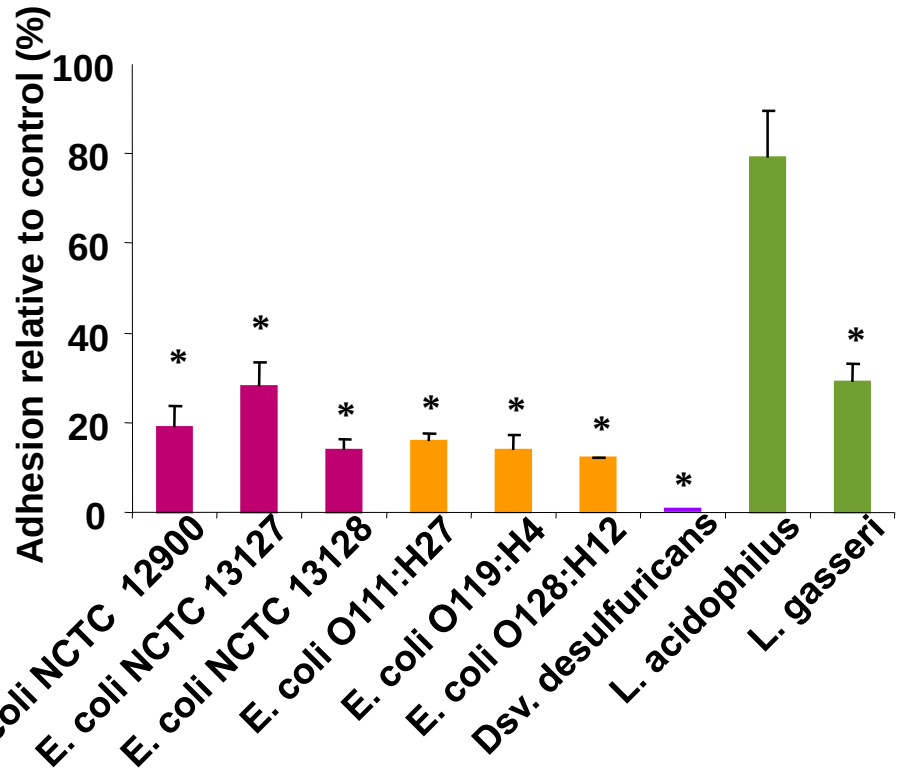
- 5ml working volume
- Stirred, anaerobic, pH-& temperature-controlled
- 50 mg test carbohydrate
- Bacteriology

Prebiotics from pectins



Pectin-derived oligosaccharides from orange peel wastes



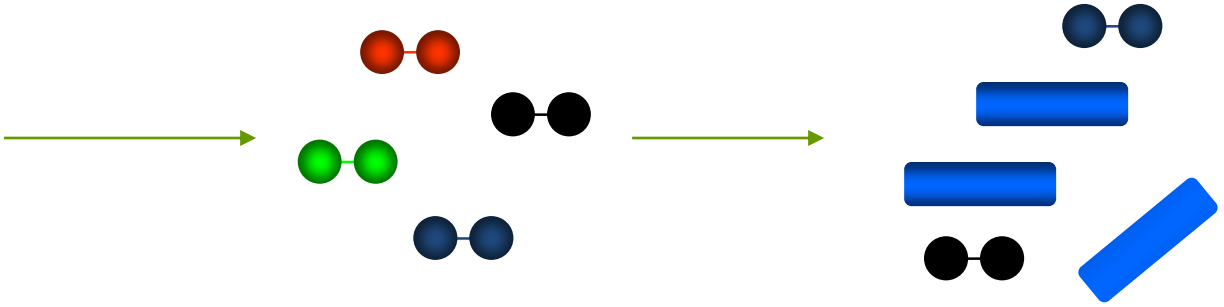


Species-targeted prebiotics

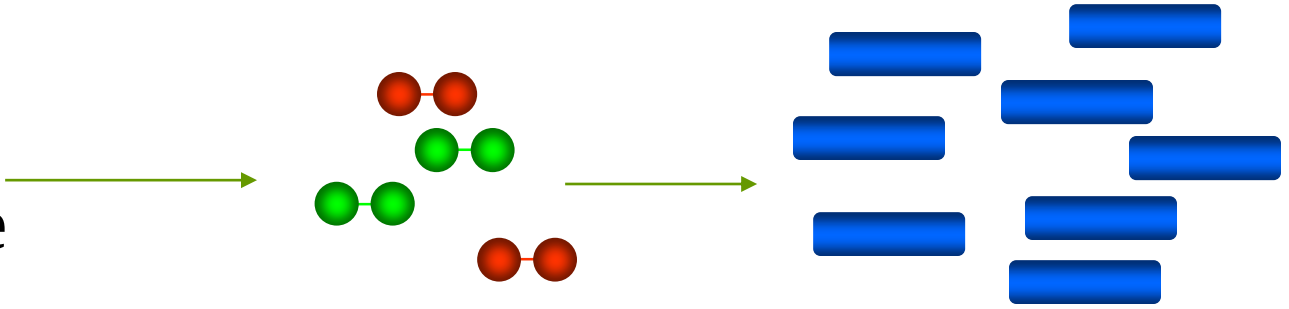
- Existing prebiotics act at the genus level
- It may be desirable to stimulate individual species
- For example, *B. infantis* has more powerful anti-microbial activity than *B. breve:* same for certain lactobacilli
- In theory, any lac or bif can be used to manufacture a prebiotic

Novel GOS - synthesis

Industrial β-galactosidase



Probiotic β-galactosidase



Probiotic-targeted GOS

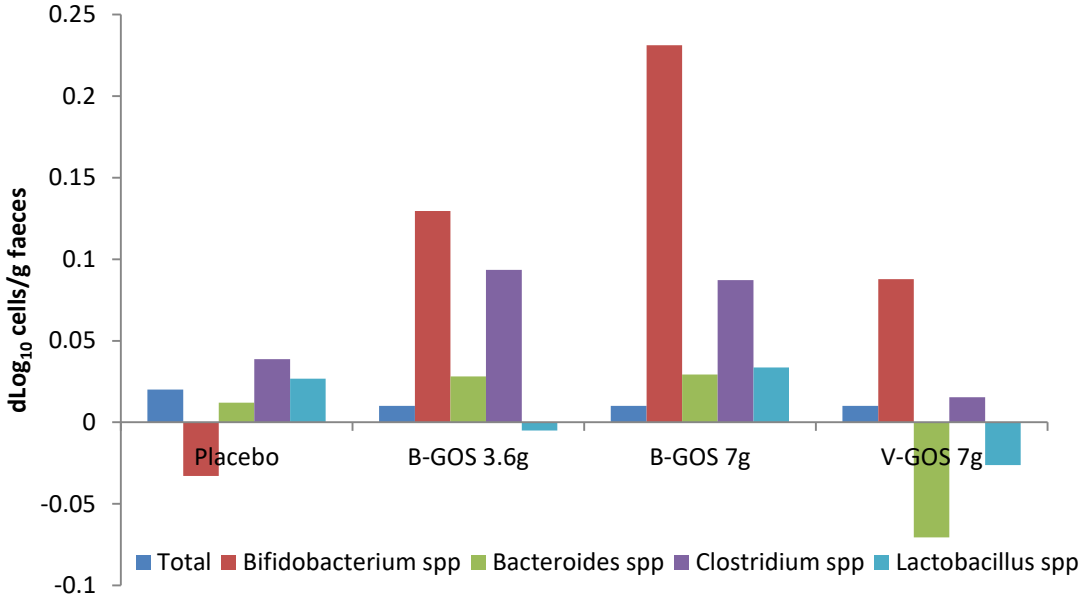
Probiotic	1	2	3	4	5
B. bifidum	1.05	0.76	0.79	0.73	1.05
B. pseudolongum	0.69	0.66	0.99	0.64	0.69
B. angulatum	0.89	0.96	0.71	0.91	1.27
B. infantis	0.98	1.20	0.73	0.99	0.95
B. adolescentis	0.48	0.48	0.81	0.83	1.01

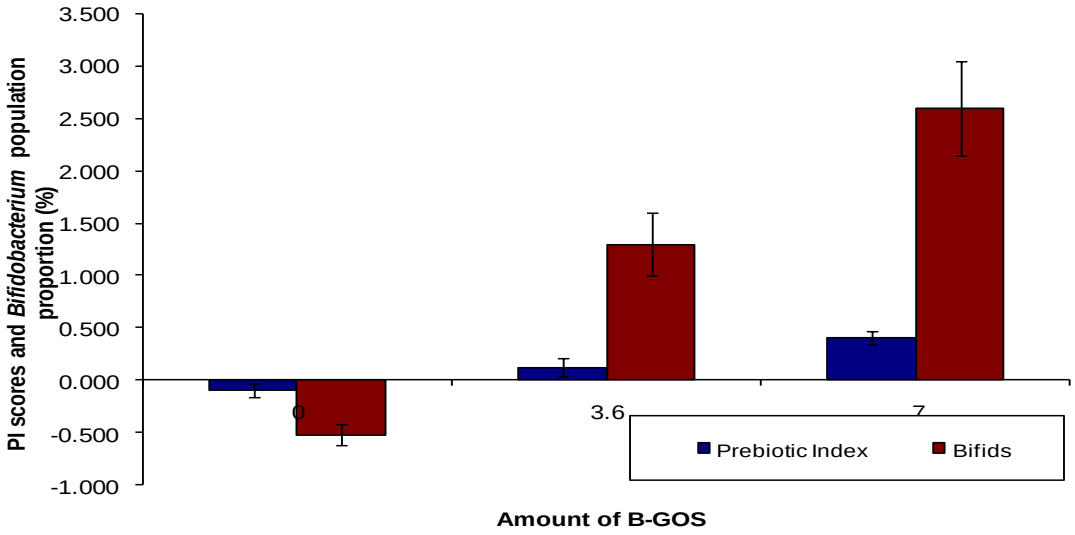
1: *B. bifidum* GOS
2: *B. infantis* GOS
3: *B. pseudolongum* GOS
4: *B. adolescentis* GOS
5: *B. angulatum* GOS

Healthy human volunteer study

- Double blinded, placebo controlled study of cross over design, with 30 healthy adult volunteers
- GOS was bifidogenic at a daily intake of 1.37g of active ingredient

- The bifidogenicity and prebiotic effect of GOS follows a dose response relationship
- The prebiotic value of GOS was attributed solely to bifidogenicity

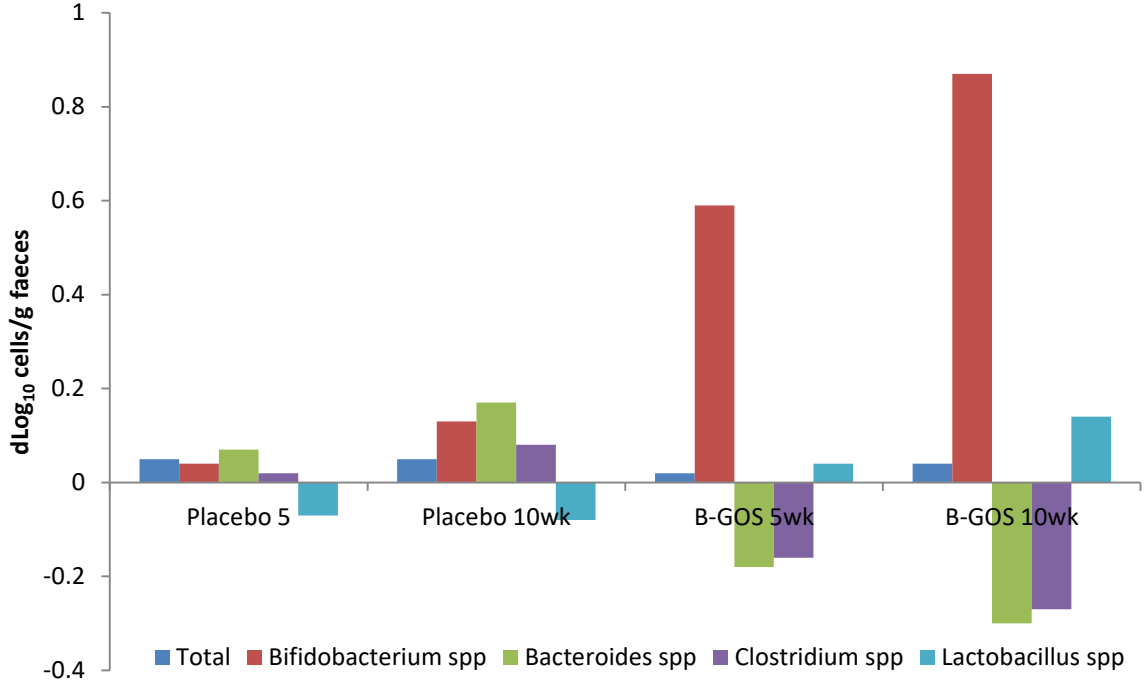




Effect of GOS on the colonic microbiota of the elderly

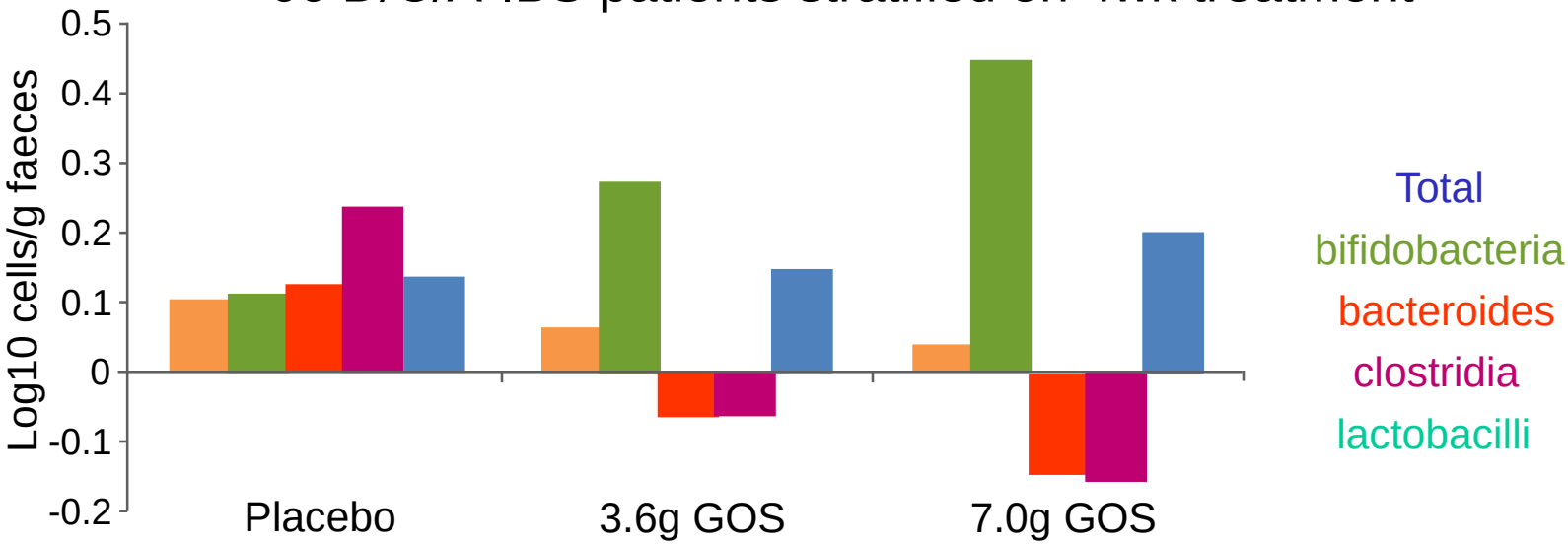
- Double blinded randomised, cross-over placebo controlled study
- 60 volunteers over 60 years old
- Two treatments (Placebo vs GOS) for 5 months to assess the effects on the colonic microflora by FISH

- Significant increase in the bifidobacterial numbers after 5 wks of intake followed by a further significant increase after another 5 wks.
- At the end of the 10 wks treatment, the bifidobacterial ratio of the elderly subjects was similar to that of healthy adults



Irritable bowel syndrome

Single blinded randomised placebo controlled study
66 D/C/A-IBS patients stratified on 4wk treatment

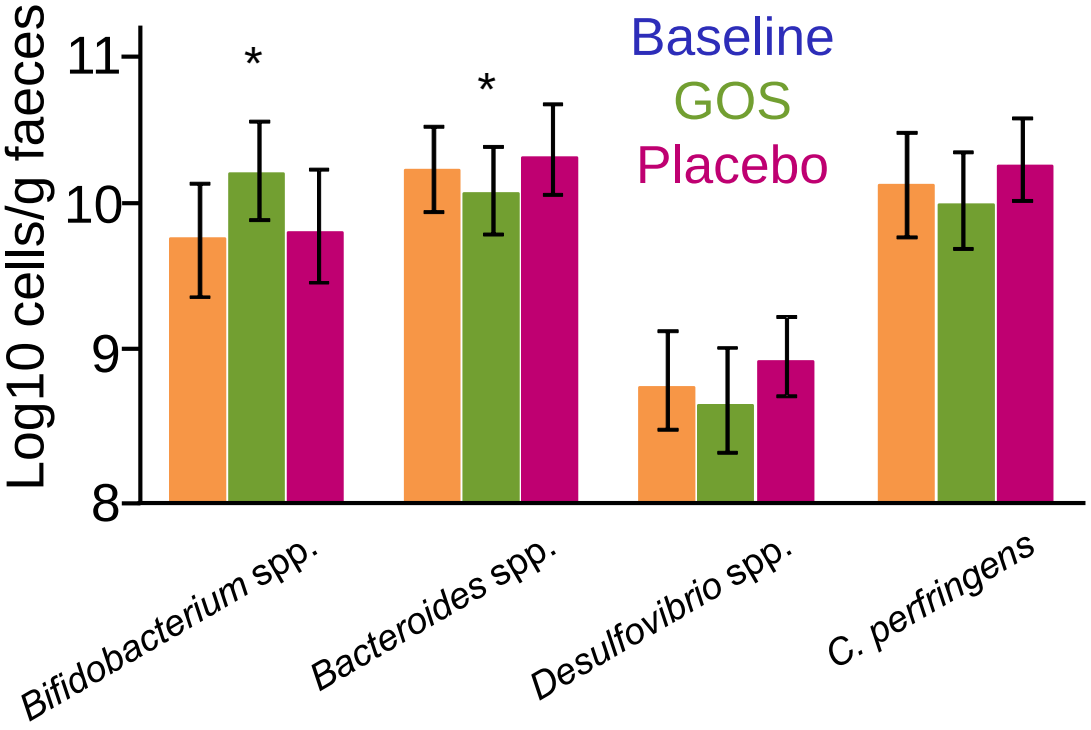


Significant improvements seen in:

- stool consistency
- flatulence
- bloating
- subjective global assessment
- composite score of symptoms
- anxiety

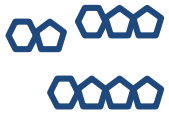
Metabolic syndrome

- 45 overweight adults with ≥3 metabolic syndrome risk factors
- 12 week cross over study feeding GOS or placebo



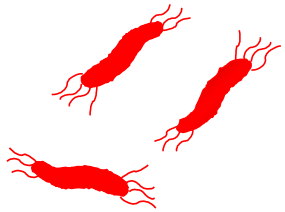
No significant changes in:
Atopobium spp
Lactobacillus spp
Clostridium coccoides/E. rectale
E. cylindroides
E. hallii
Clostridium cluster IX
Faecalibacterium prausnitzii
beta-proteobacteria

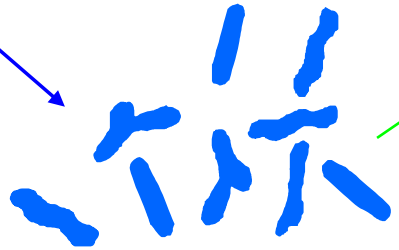
Synbiotics



prebiotics

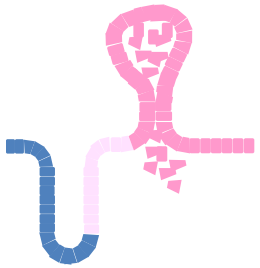
Increased antimicrobial activity

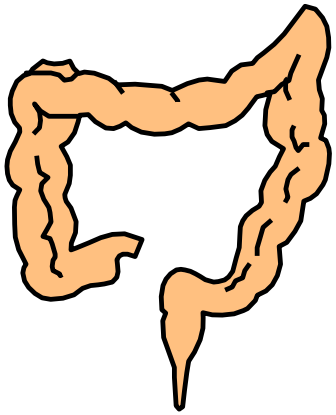




probiotics

Adjuncts for improved therapy





Increased bioactivity

Increased survival

Acknowledgements

- Prof Bob A Rastall
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