

Introduction to prebiotics

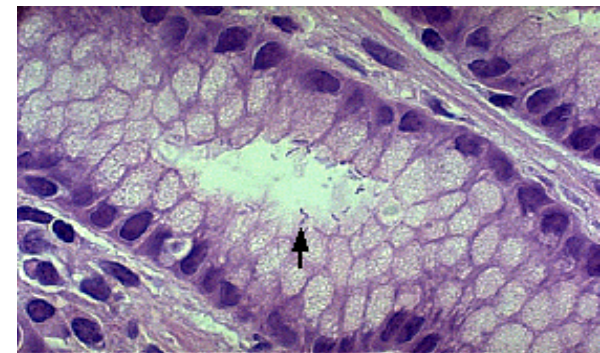
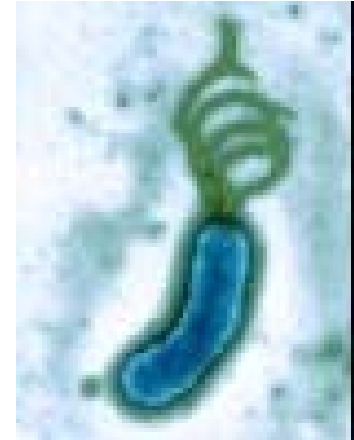
Glenn Gibson

Washington Workshop

February 10th 2011

Microflora of the stomach

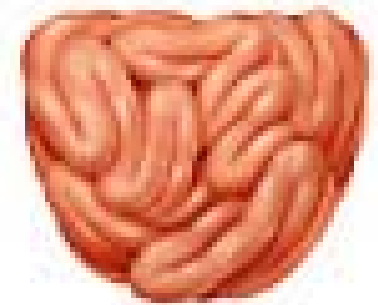
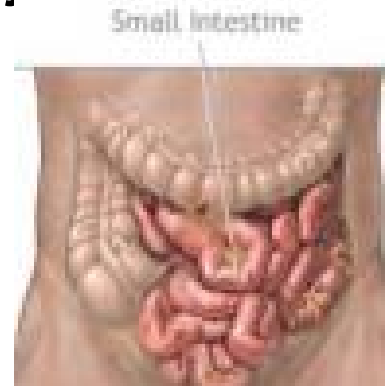
- Low pH
- Transit time ca. 30-60 minutes
- HCl + pepsin
- Colonisers need to invade the mucosal layer
- Numbers are low
- *H. pylori* is notorious



Microflora of the small intestine

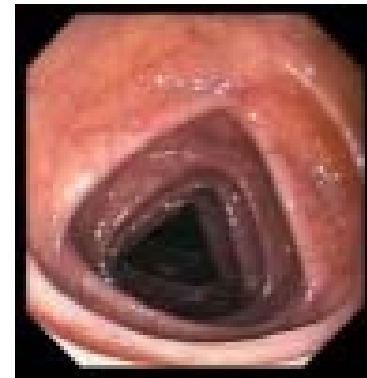


- Transit time is 2-4h
- The organ is a long narrow tube
- Bile salts and pancreatic secretions affect colonisation by the indigenous flora
- Typical numbers are around 1 million per mL contents. Varies jejunum to ileum

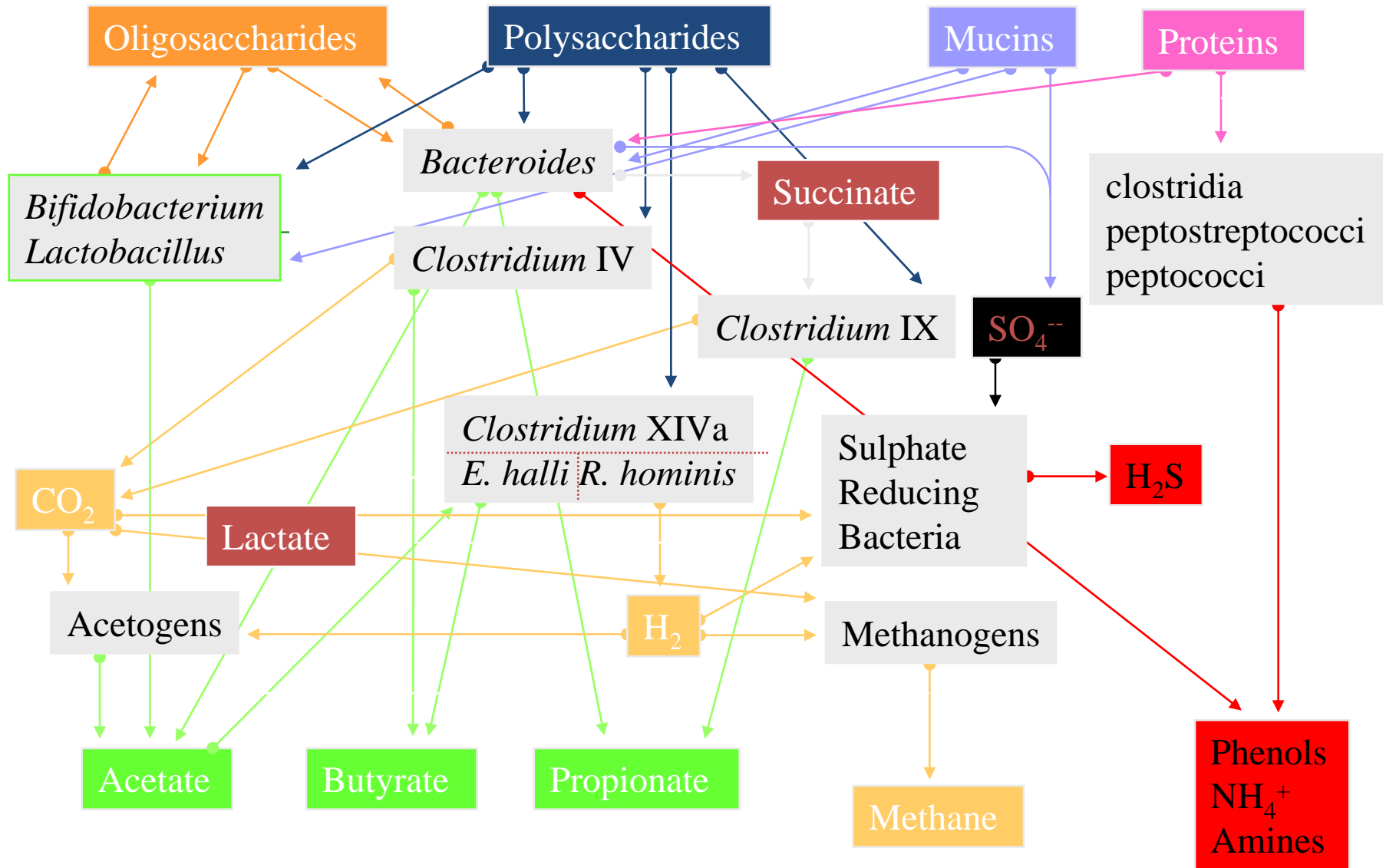


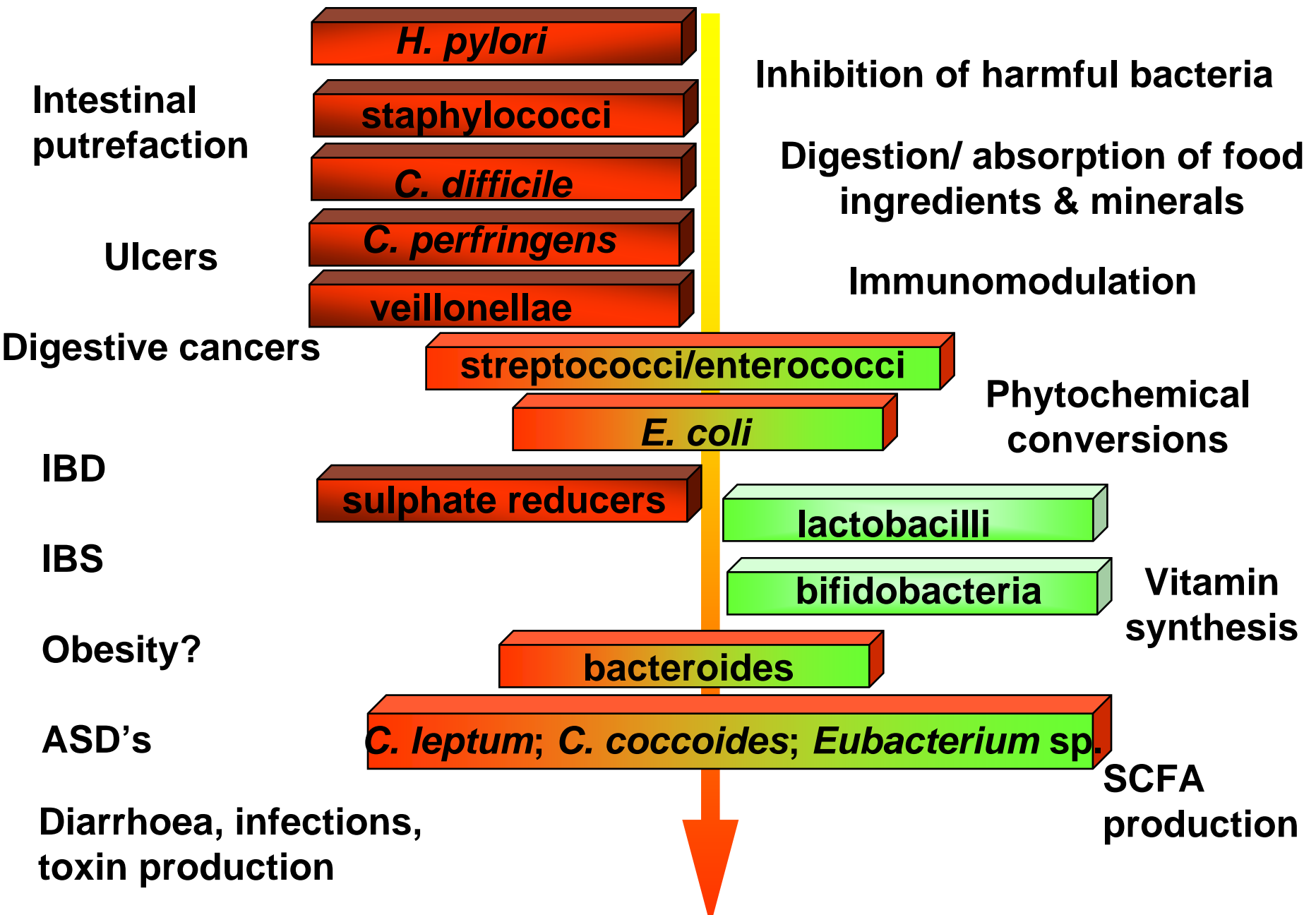
Microflora of the large intestine

- 150cm in length
- Typical transit time of 24-72h
- The most heavily colonised organ in the human body
- Antimicrobial intake, stress, poor diet and living conditions all affect the flora composition
- Up to 1000 species
- Most of the bacteria in your body (1,000,000,000,000,000) are here



The colonic ecosystem: major components





- bacteroides
- bifidobacteria
- lactobacilli
- clostridia
- veillonella
- acetogens
- enterococci
- staphylococci
- streptococci
- bacilli
- SRB
- methanogens
- roseburia
- faecalibacteria
- eubacteria
- peptococci
- peptostreptocci
- ruminococci



- dorea
- collinsella
- holdemania
- blautia
- parabacteroides
- alistipes
- coprococcus
- subdoligranulum
- butyrivibrio
- propionibacteria
- anaerotruncus
- saccharomyces
- *Penicillium*
- megasphaera
- selenomonas
- prevotella
- Yeasts
- fusobacteria



Prebiotic - Definitions

‘Non digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon and thus improves host health’ (1995)

‘A selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal microflora, that confers benefits upon host wellbeing and health’ (2004)

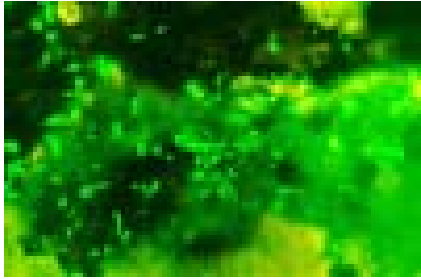
Prebiotics – Definition. 2010

- *A dietary prebiotic is a selectively fermented ingredient that results in specific changes, in the composition and/or activity of the gastrointestinal microbiota, thus conferring benefit(s) upon host health*

International Scientific Association for
Probiotics and Prebiotics.
IFIS FF Bulletin.

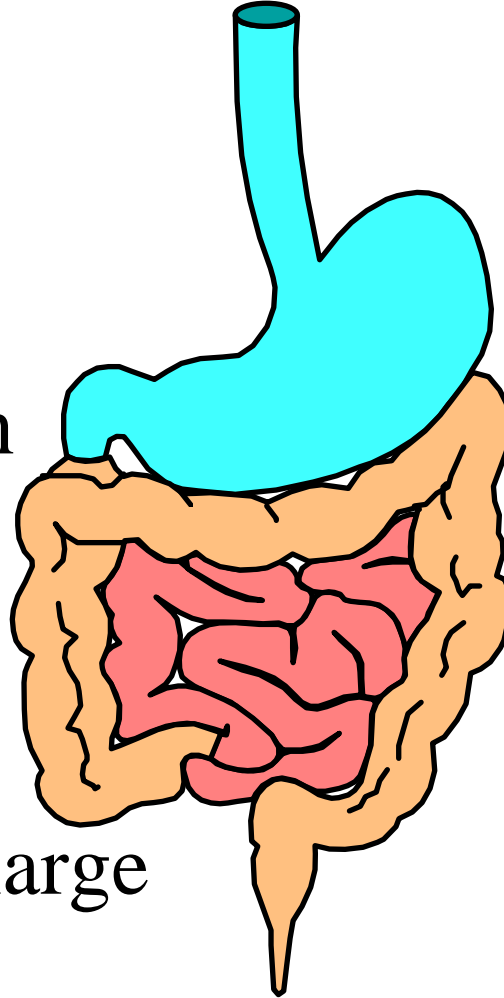


Prebiotics



3. selective fermentation

2. enters the large gut



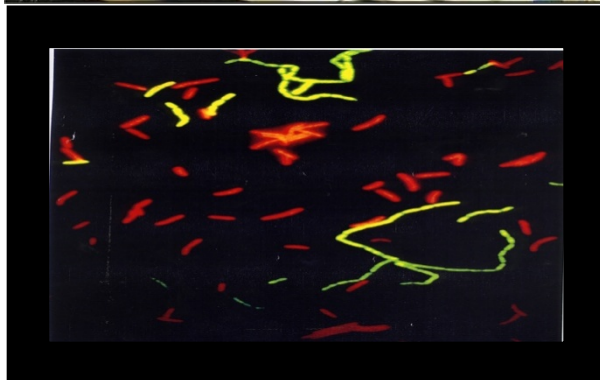
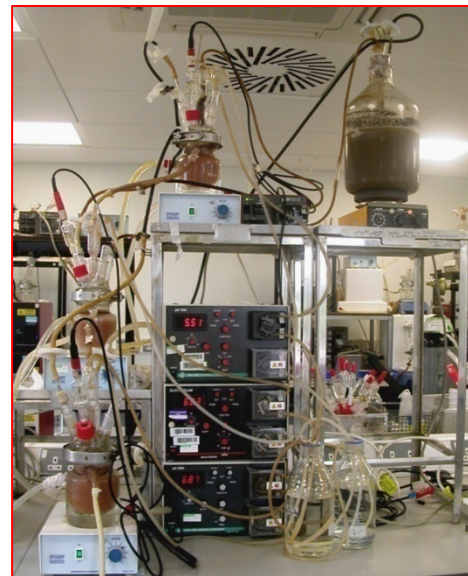
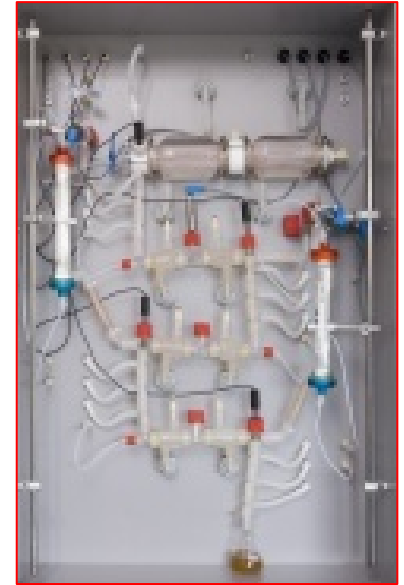
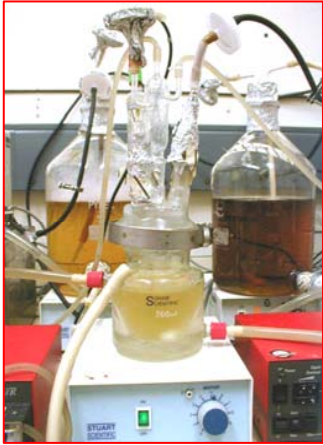
1. NDC and related ingredients



Prebiotic effects and the gut: testing

In vivo studies are essential to prove a prebiotic effect

In vitro tests allow comparative studies and eventually selection of ingredients showing a potential effect

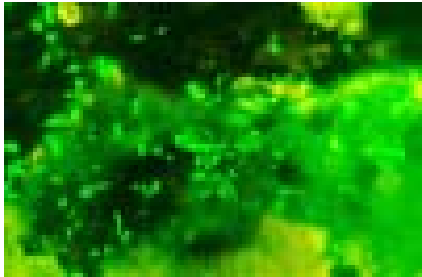


Prebiotic effects and the gut

Non-digestible carbohydrates with prebiotic effects selectively stimulate the growth of bacterial genera/species characterised exclusively, or preferably, by saccharolytic fermentation. This would be preferred to a proteolytic fermentation.



This is established for prebiotic effects favouring the growth of bifidobacteria and lactobacilli. Emerging genera are *Eubacterium*, *Faecalibacterium* and *Roseburia*, although more evidence is needed on their physiological properties



Where do we find prebiotics?

- Human breast milk is one source
- Manufactured forms (GOS, lactulose)
- Some occur naturally (e.g. inulin in asparagus, onion, artichoke, banana)
- OF derived from inulin



ISAPP definition:

A dietary prebiotic is a selectively fermented ingredient that results in specific changes, in the composition and/or acitivity of the gastrointestinal microbiota, thus conferring benefit(s) upon host health



All Suggested Prebiotics



- Inulin*
- Fructo-oligosaccharides (FOS)*
- Galacto-oligosaccharides (GOS)*
- Lactulose*
- Isomalto-oligosaccharides (IMO)
- Lactosucrose
- Polydextrose (PDX)
- Xylo-oligosaccharide (XOS)
- Mannan-oligosaccharides (MOS)
- Soybean oligosaccharide (SOS)
- Gluco-oligosaccharide (GIOS)
- GiOS
- AXOS
- Germinated barley foodstuffs
- Oligodextrans
- Gluconic acid
- Pectic-oligosaccharides
- Lactose
- Glutamine and hemicellulose rich substrates
- Resistant starch and its derivatives
- Oligosaccharides from melibiose
- Lactoferrin-derived peptide
- N-acetylchitooligosaccharides
- Isoflavonic phytoestrogens
- Various fibres and derivatives

* Meet criteria for classification

Some food products

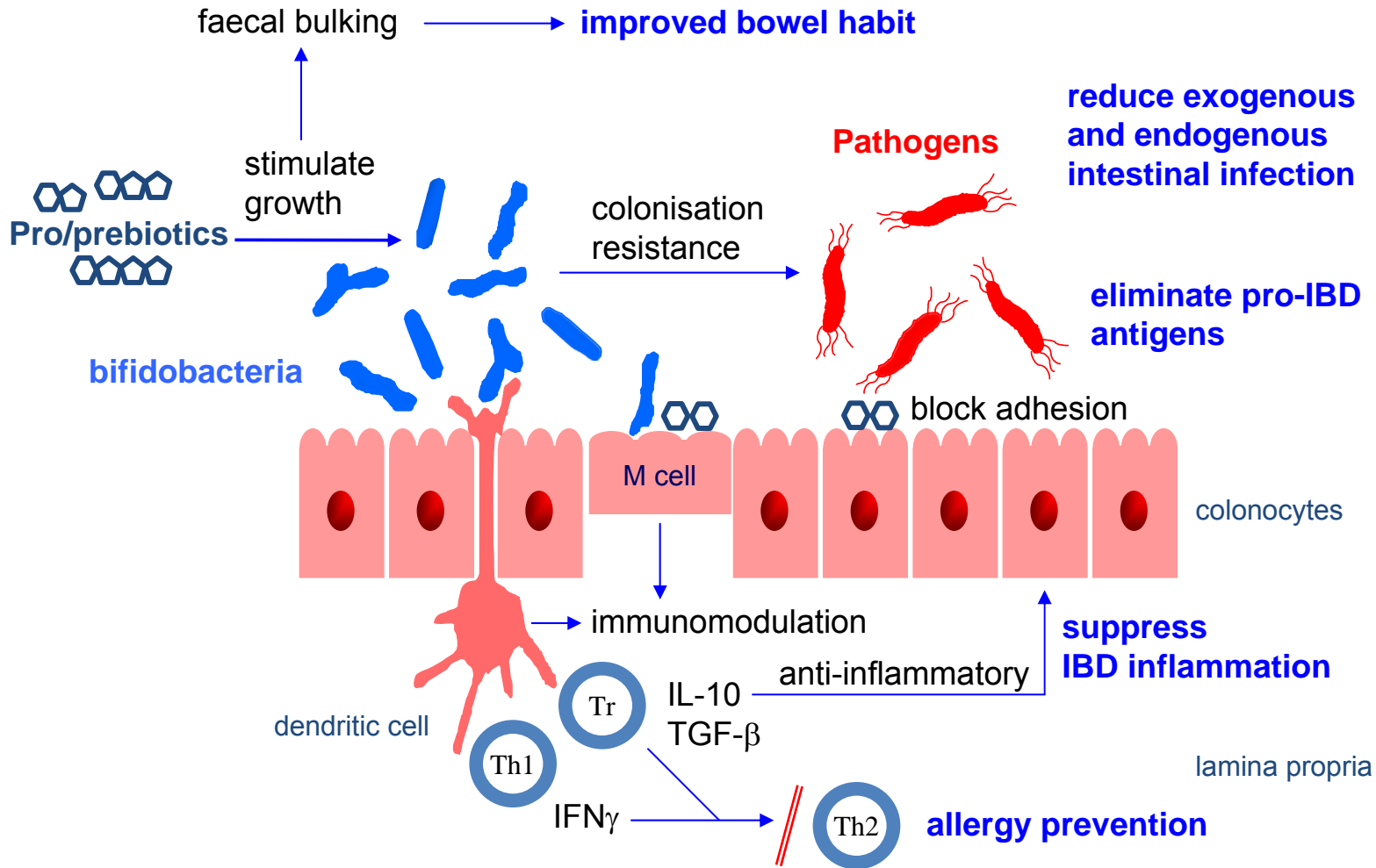


- Dairy products
- Beverages and health drinks,
- Spreads
- Infant formulae and weaning foods
- Cereals
- Bakery products
- Confectionery chocolates, chewing gum
- Savoury product, soups
- Sauces and dressings
- Meat products
- Dried instant foods
- Canned foods
- Food supplements
- Animal feeds
- Petfoods



Health benefits of prebiotics

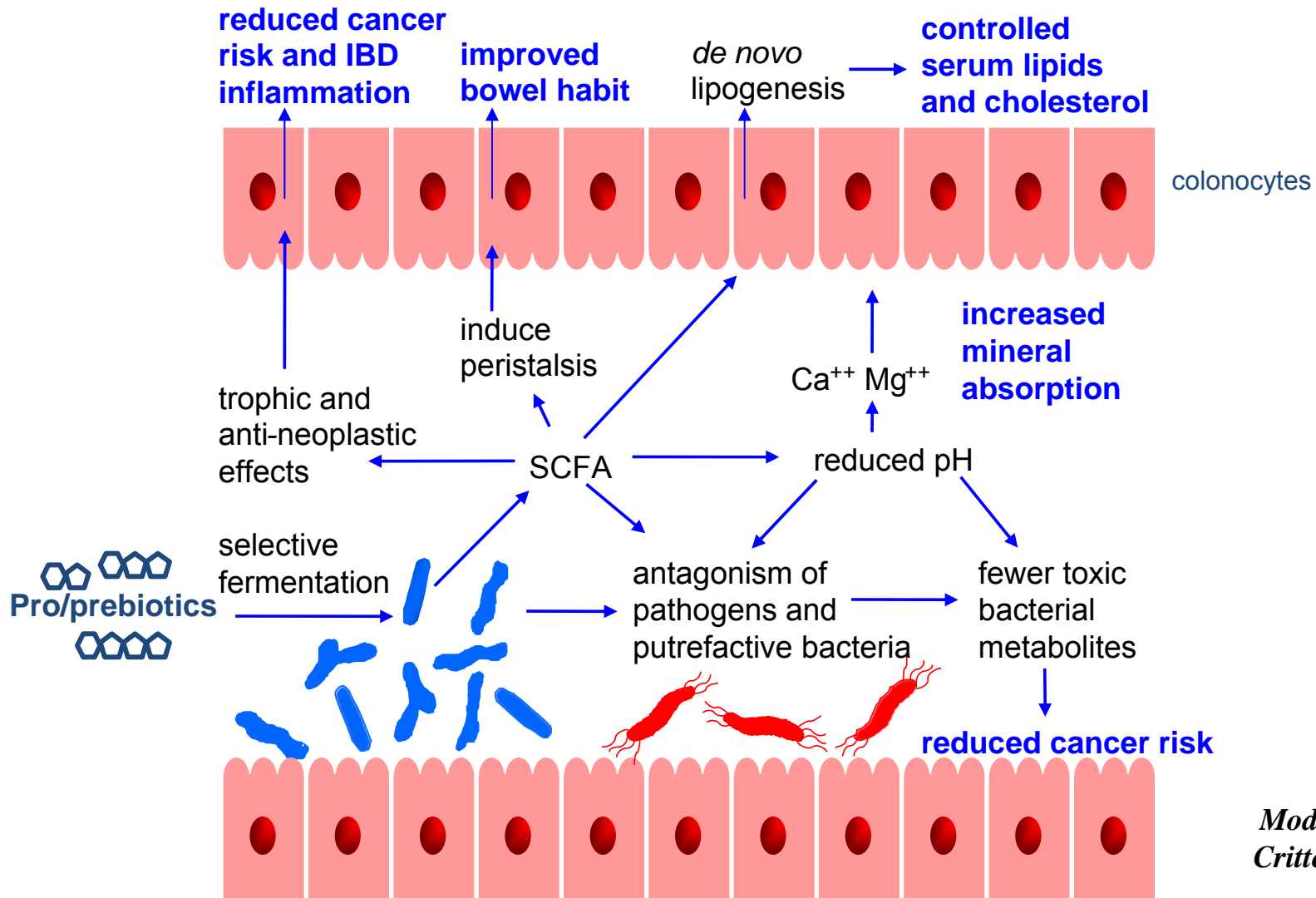
Proliferation of beneficial bacteria



Modified from Crittenden 2006

Health benefits of prebiotics

Beneficial microbial activities



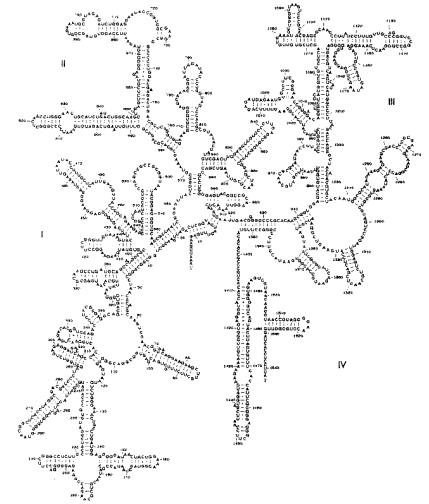
Modified from
Crittenden 2006

Current health aspect drivers

- **Bowel cancer****
- **IBD****
- **Pathogens*****
- **CDV***
- **Mineral availability ****
- **TD***
- **AAD***
- **IBS****
- **Atopic reactions**
- **Obesity**
- **ASD's**



The common link is microbial factors

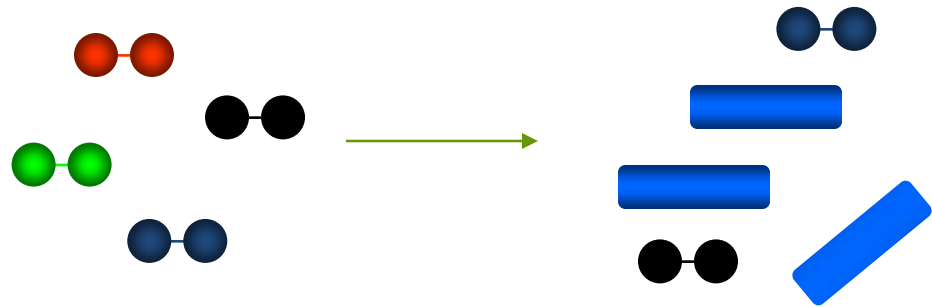


A new prebiotic GOS

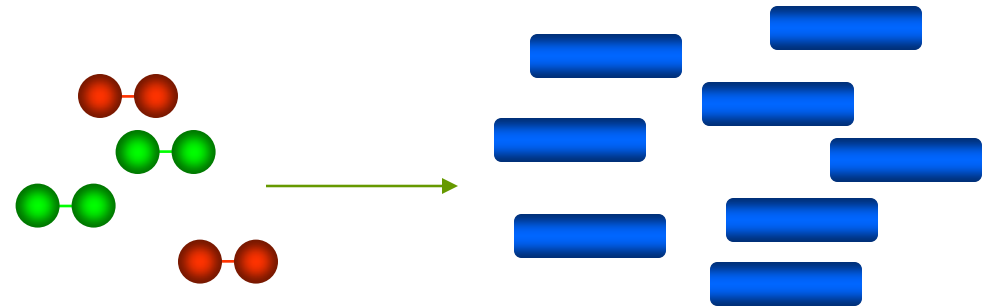


Novel GOS - synthesis

**Industrial
 β -galactosidase**



**Probiotic
 β -galactosidase**



Novel GOS - example

Oligomate 55

<i>L. acidophilus</i>	0.67
<i>B. longum</i>	0.56
<i>B. adolescentis</i>	0.54
<i>B. bifidum</i> BB-12	0.52
<i>L. plantarum</i>	0.46
<i>B. pseudolongum</i>	0.39
<i>B. angulatum</i>	0.37
<i>B. infantis</i>	0.36

B. angulatum oligo

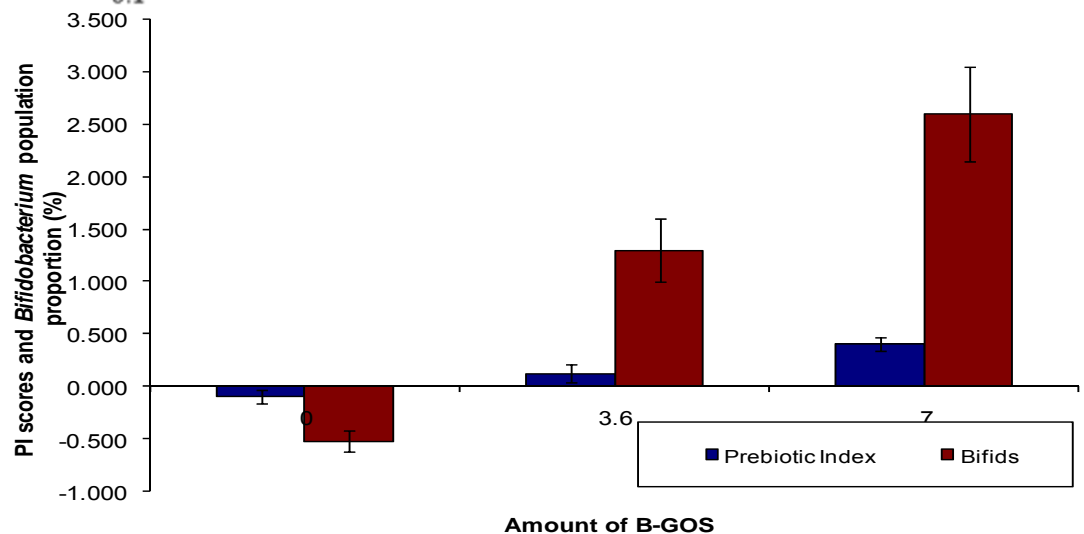
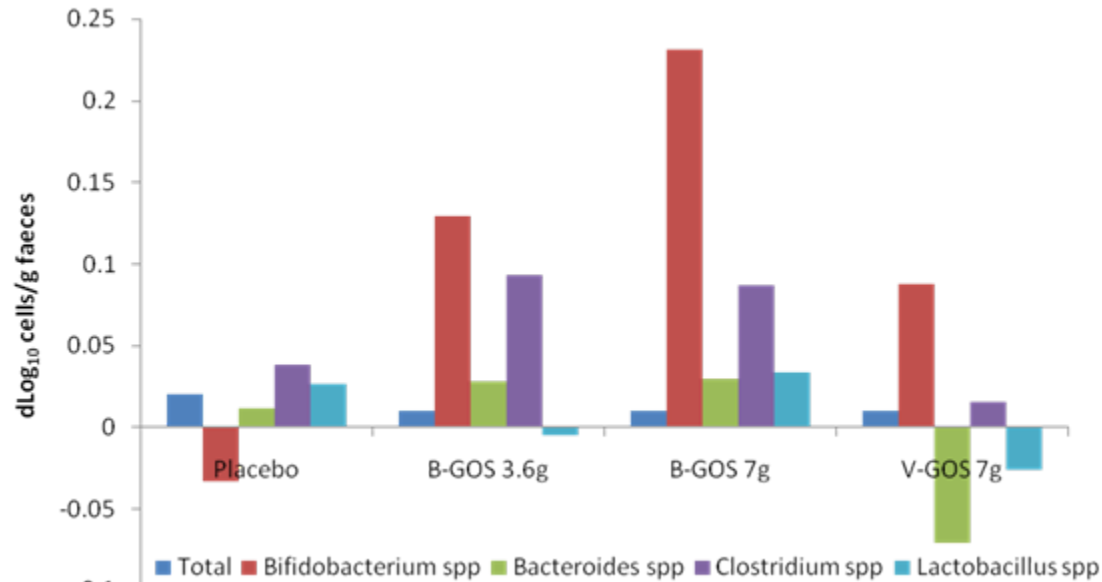
<i>B. angulatum</i>	0.52
<i>L. acidophilus</i>	0.38
<i>B. longum</i>	0.37
<i>B. infantis</i>	0.36
<i>B. pseudolongum</i>	0.35
<i>B. adolescentis</i>	0.32
<i>B. bifidum</i> BB-12	0.27
<i>L. plantarum</i>	0.26

Healthy human volunteer study

- Double blinded, placebo controlled study of cross over design, with 30 healthy adult volunteers

- The bifidogenicity and prebiotic effect of GOS follows a dose response relationship

- The prebiotic value of GOS was attributed solely to bifidogenicity



Depeint et al (2008) Am J Clin Nutr 87: 785-91

Effect of GOS on IBS sufferers

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

Baseline period 2 weeks

7 g Placebo

7 g Placebo

3.6 g Placebo

4 weeks

Washout period 2 weeks

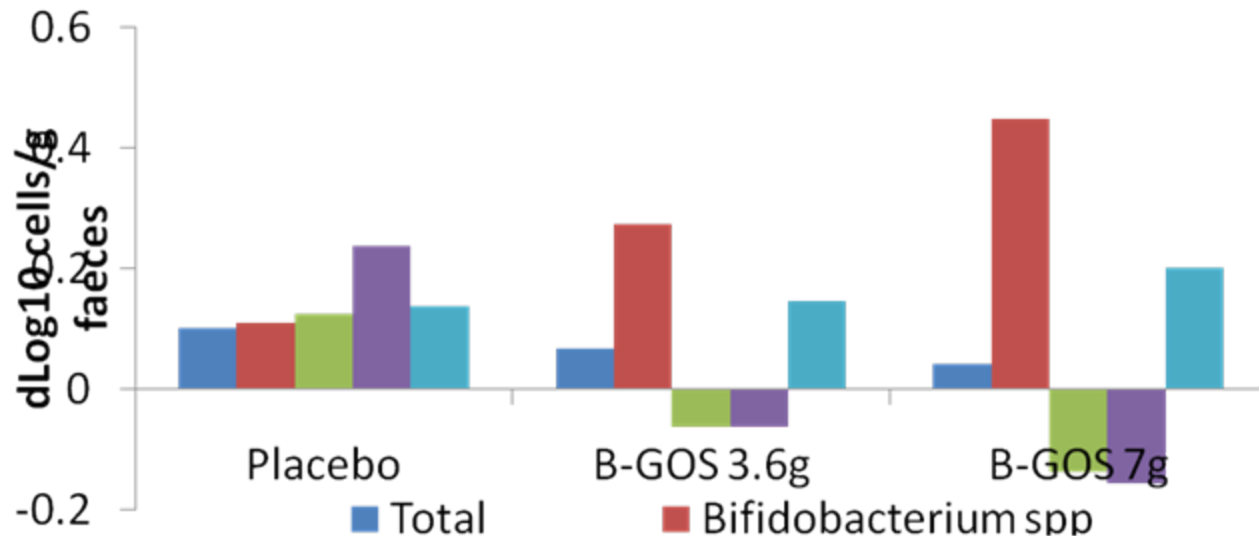
7 g Placebo

7 g GOS

3.6 g GOS

4 weeks

- Significant prebiotic effect at a daily intake of 1.37g of active GOS
- Concomitant effect on symptoms (D, C + A)

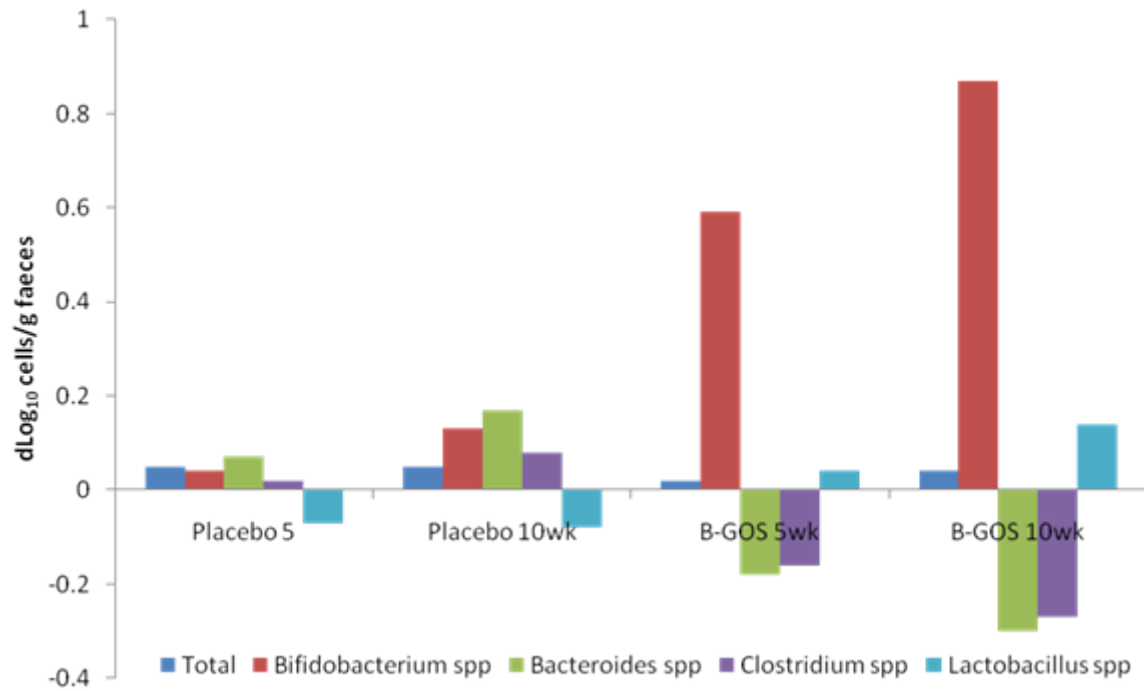


Effect of GOS on the colonic microflora of the elderly

- 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 bifidobacterial numbers after 5 wks of intake followed by a further significant increase after another 5 wks. After this, bifidobacteria levels were similar to that of healthy adults

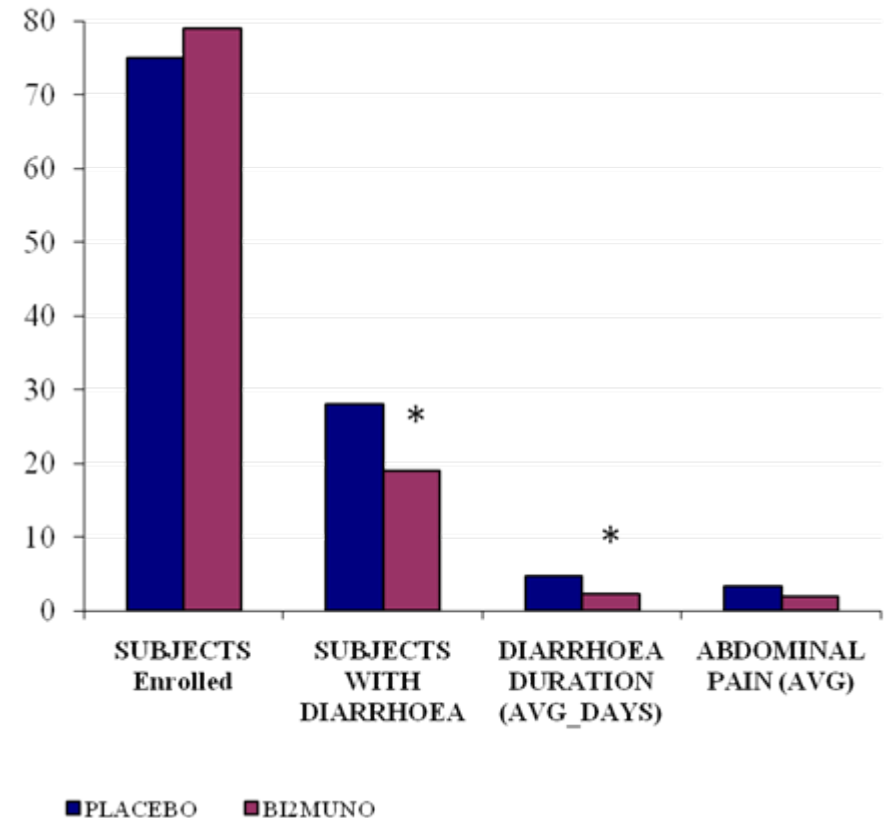
• Positive influence on pro vs anti-inflammatory cytokines and other immune markers



Vulevic et al (2008) Am J Clin Nutr 88: 1436-46

Efficacy of GOS in Traveller's Diarrhoea

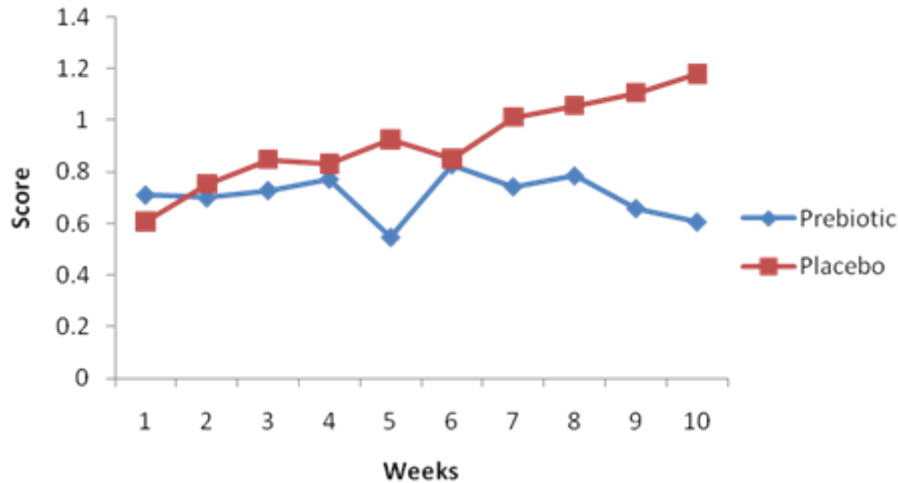
- Double blinded randomised placebo controlled study
- 160 volunteers travelling for at least 2 weeks to high or low risk countries
- Two groups in a parallel design (Maltodextrin vs GOS)
- Monitoring:
 - Frequency of bowel motions (number per day)
 - Nature of motions – semi-solid, watery, bloody
 - Impact of symptoms of Travellers' diarrhoea – graded as none, mild, moderate or severe
 - Presence or absence of abdominal pain
 - Presence or absence of vomiting



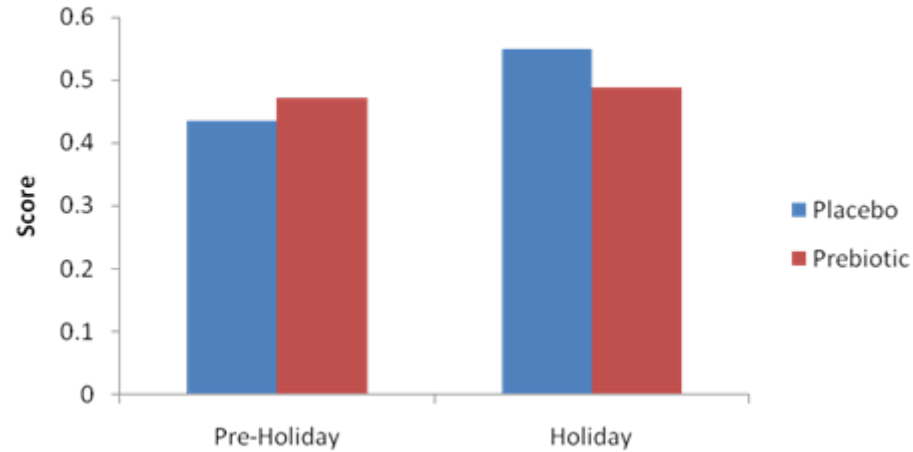
Drakoularakou et al (2010) Eur J Clin Nutr, 64, 146-152.

Effects on flatulence

Elderly Flatulence

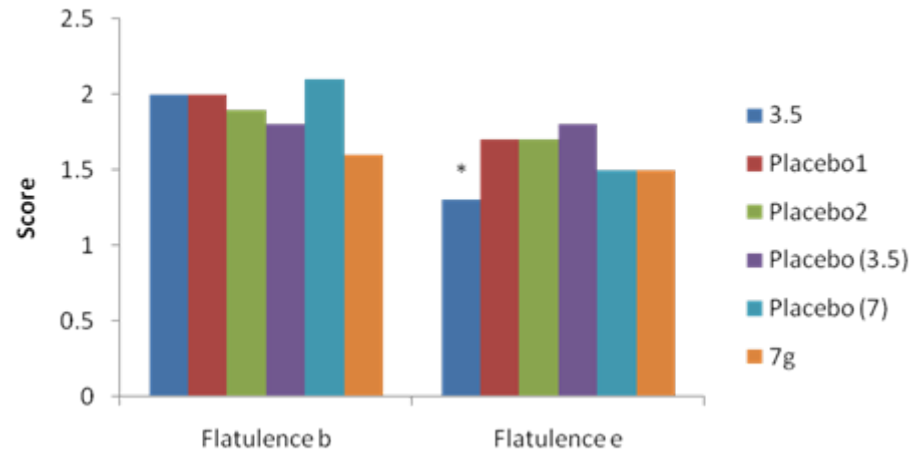


TD Flatulence



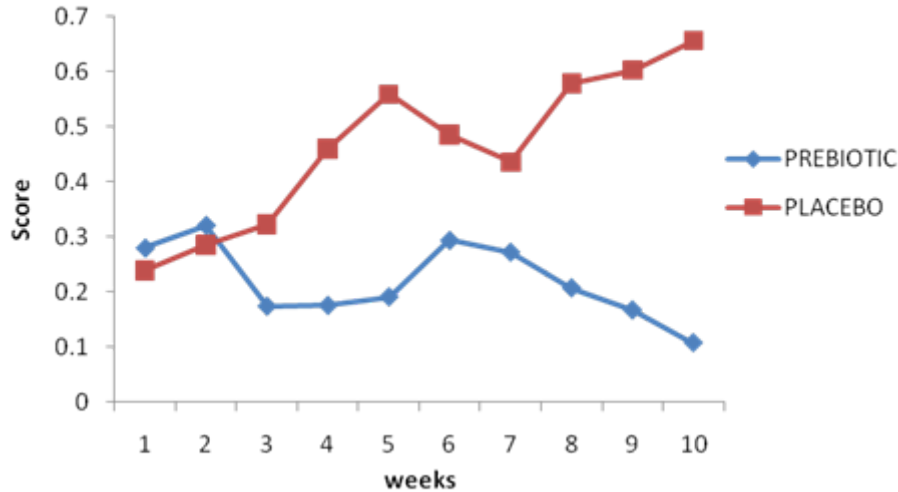
Fermentation of GOS by the colonic microflora did not cause increase in flatulence, probably because of the increased selectivity towards bifidobacteria (non gas producers)

IBS Flatulence

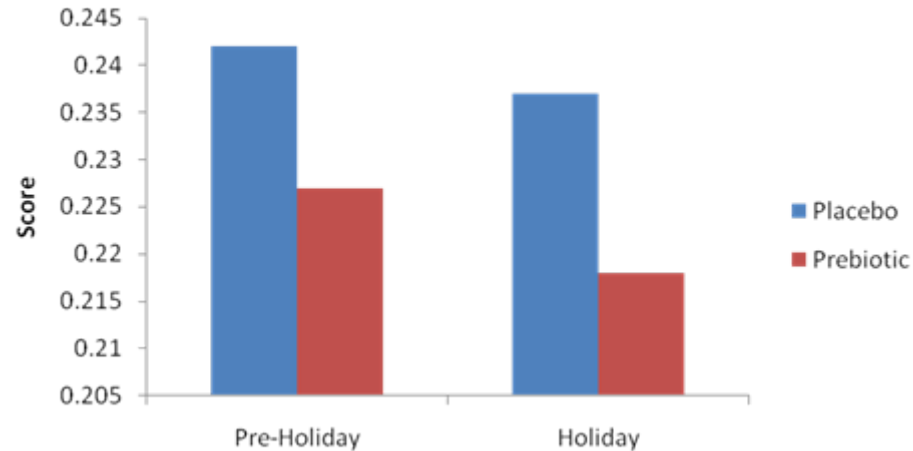


Effects on bloating

Elderly Bloating

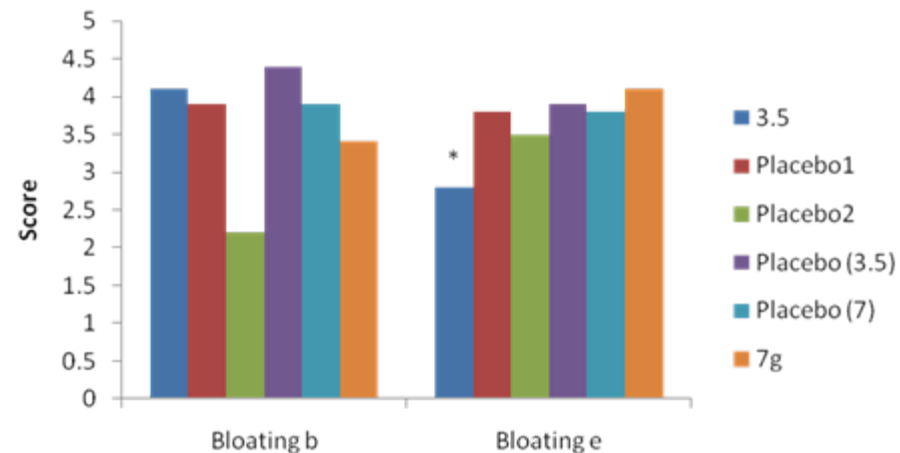


TD Bloating



Supplementation of GOS was seen to significantly reduce bloating in sufferers and reduce the bloated feeling of healthy subjects

IBS Bloating



Bloating – biggest complaint for UK women

1. Bloating (52%)
2. Double chin (42%)
3. Thunder thighs (41%)
4. Muffin top (31%)
5. Back fat (23%)
6. Small breasts (11%)
7. Thick ankles (6%)

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How to beat the bloat

Bloating is an uncomfortable problem suffered by many women. But, says Lambert, it can often be easy to remedy.

By Victoria Lambert

Published: 7:00AM GMT 15 Mar 2010

News that up to half of all probiotic supplements – which contain so-called "friendly" bacteria – are probably ineffective will be a blow to the thousands of women who take them to combat that dreaded female condition – bloating.

According to Glenn Gibson, a professor of food microbiology at Reading University, nearly 50 per cent of the probiotic yoghurts, powders and capsules sold in their millions every year simply do not have the minimum of 10 million bacteria per dose necessary to have any impact on our digestive systems.



Novel GOS - Summary

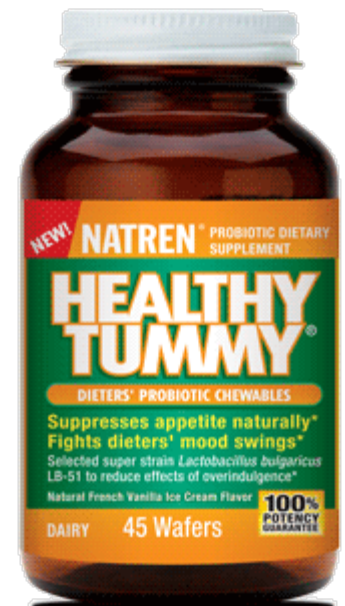
- Synthesised from enzymes in *B. bifidum*
- Has prebiotic GOS capacity
- Tested *in vitro*, pigs, humans
- Has anti-adhesive capacity
- Supplement + food product
- Tested in IBS, elderly, TD
- Athletes ongoing
- Military + metabolic syndrome planned
- Reduced bloating and flatulence



Pro and prebiotic benefits in other areas



I believe that I am in possession of a probiotic organism which I call, "The Gyrobacillum". The organism has been researched by my company, and as a result I also believe that it imparts the Power of Resurrection to its host. Please read the attached file which was originally formatted as a brochure in WordPerfect 8.



Recent prebiotic in vivo trials

Healthy: biscuits, wheat grain, bran cereals, fermented dairy drinks (x2), blackcurrant juice, novel GOS, chocolate, companion animals, pigs, TD, PDX, XOS, fruit shots, new inulin

Gut mediated disorders:

ulcerative colitis,
irritable bowel syndrome,
colorectal cancer,

peptic ulcers,
obesity,

ASD's

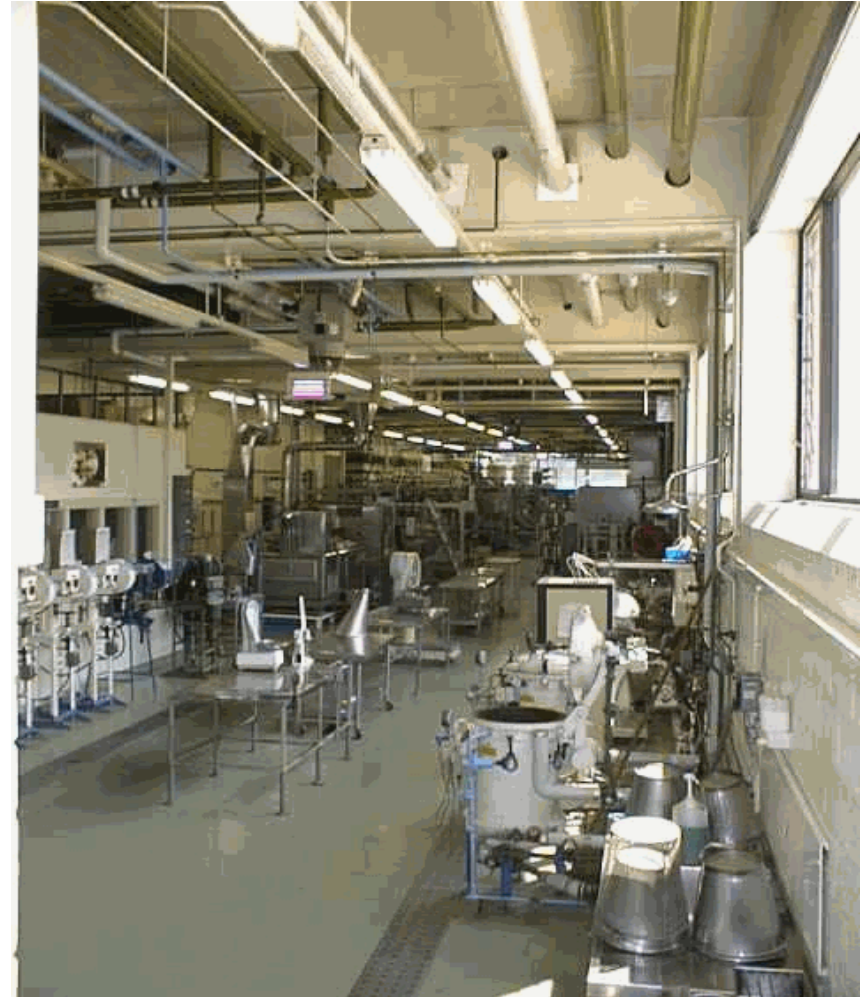
AAD,

(in conjunction with various UK hospitals)

Age related studies: infants (inc. longitudinal) and the elderly

Ongoing:

ASD's2, bread, sports



Metabonomics

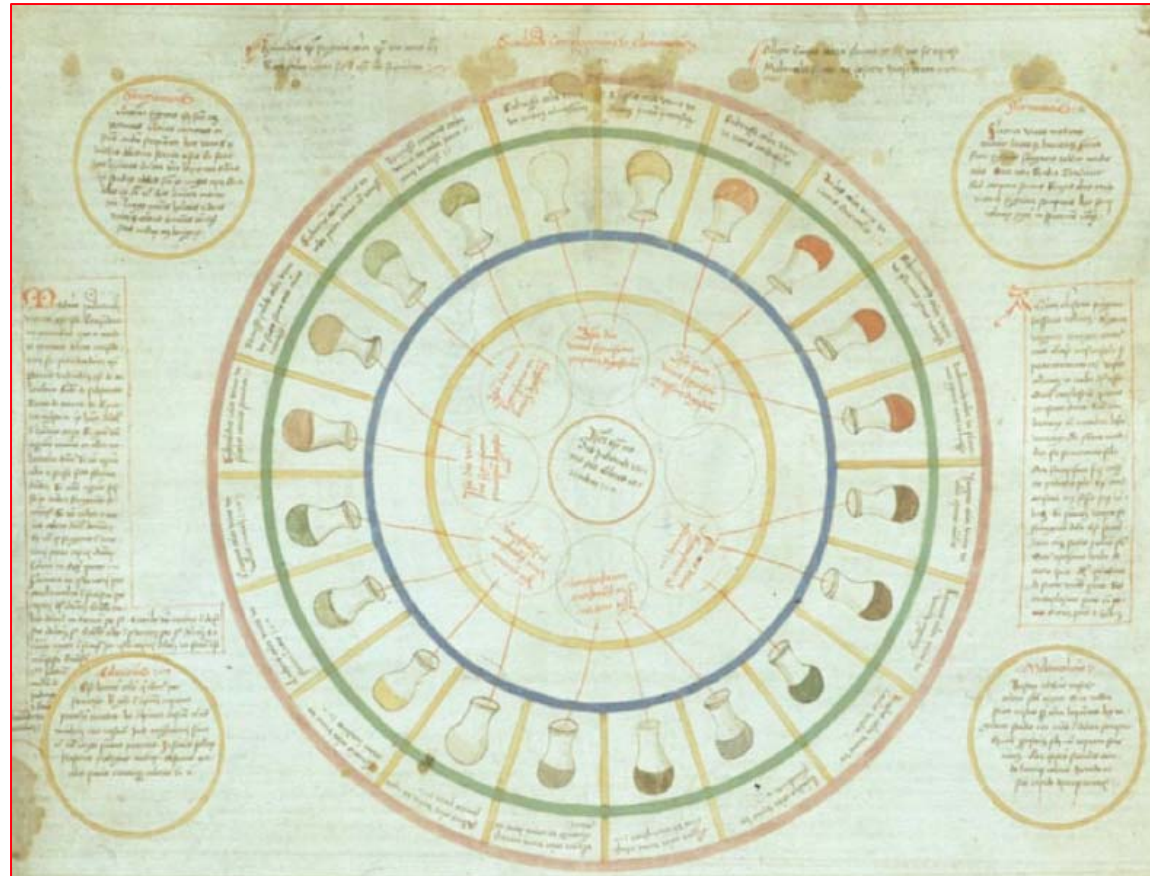
Jeremy K. Nicholson and John C. Lindon

(2008, Vol 43, 1054-1056)

Organisms often respond in complex and unpredictable ways to stimuli that cause disease or injury. By measuring and mathematically modelling changes in the levels of products of metabolism found in biological fluids and tissues, metabonomics offers fresh insight into the effects of diet, drugs and disease.

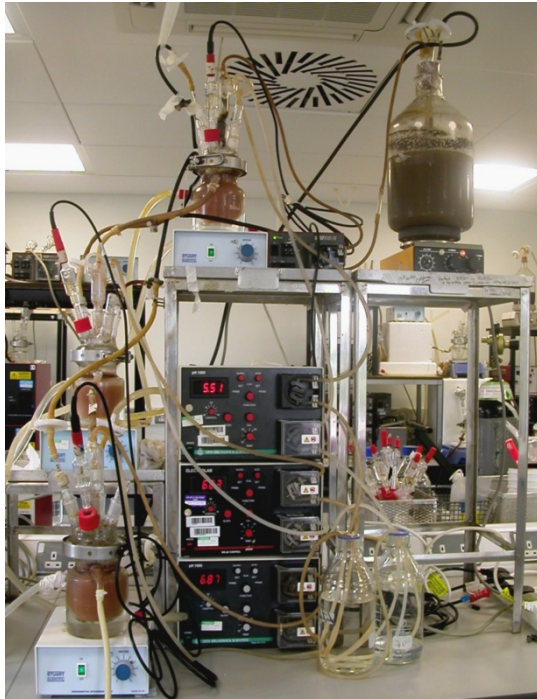
Figure 1 | Metabonomics of yore. This urine wheel was published in 1506 by Ullrich Pinder, in his book *Epiphania Medicorum*. It describes the possible colours, smells and tastes of urine, and uses them to diagnose disease.

The Metabolic Window on Systems Biology

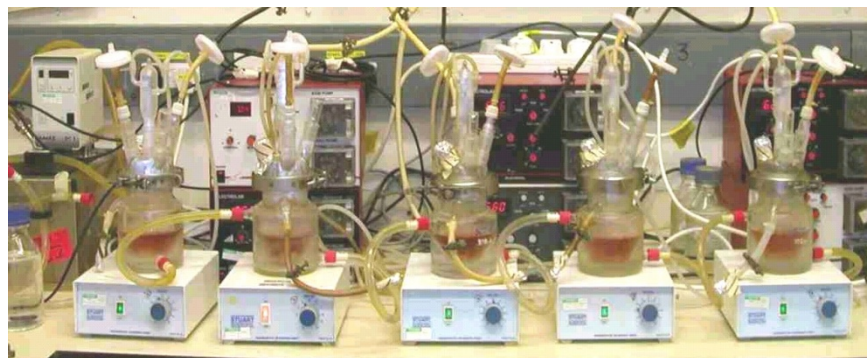
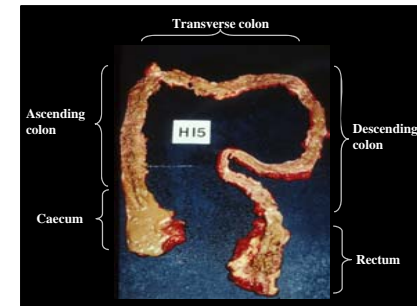


Metabolic profiling has a long history: The Urine Wheel

Prebiotic microflora modulation and metabolic effects



- *In vitro* gut models (batch, complex)
- Faecal microbiology (16S rRNA)
- Healthy subjects and patients
 - Biomarkers of disease
 - blood lipids
 - faecal water genotoxicity
 - immunology
 - Metabolite profiles – blood, urine, faeces (MS, NMR based metabonomics)



Aspects

- **Gut models**
 - Effect on metabolism by gut microbiota
 - Comprehensive view of microbiota possible
 - Useful for determining mechanisms
- **Health consequences of prebiotics**
 - Human studies with clear health outcomes
 - Models “rule out” (not in)
 - Metabonomics in human studies
- **Synbiotic and prebiotic development**
 - Waste materials as sources of prebiotics?
 - Manufacture and scale-up?
 - Economics?