



# PREBIOTIC COMPONENTS IN FOOD AND THEIR RELATION TO HUMAN HEALTH

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Winter school seminar 4



## ISSUES ADRESSED

- > What is a prebiotic?
- > How is the prebiotic effect demonstrated?
- > What is the relation and proposed mechanisms for effects on human health?
- > Conclusions

## THE DEFINITION OF A PREBIOTIC

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### › ORIGINAL DEFINITION

- › *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 improve host health*

Gibson & Roberfroid (1995)

### › UPDATED DEFINITION

- › *A selectively fermented ingredient that allows **specific changes**, both in the **composition** and/or activity in the **gastrointestinal** microflora, that confer benefits upon host well-being and health*

Roberfroid (2007)

## CRITERIA TO QUALIFY AS A PREBIOTIC

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1. Neither hydrolyzed, nor absorbed in the upper GI tract
2. Selectively fermented by one or a limited number of potentially beneficial bacteria in the colon
3. Alter the composition of the microbiota towards a healthier composition
4. Induce effects that are beneficial to the host health

Roberfroid (2007)

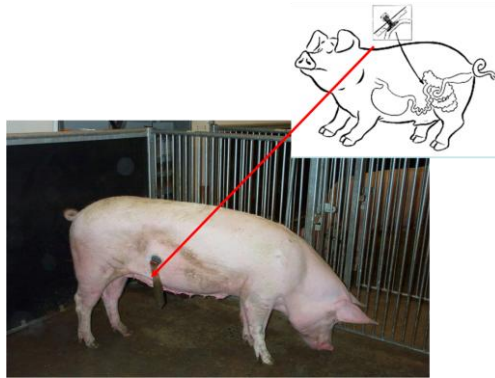


**Any food that reaches the colon is a prebiotic candidate**

## METHODS to assess prebiotics according to this definition

### 1. Non-digestibility

- > Germ-free or antibiotic-treated animals
- > Destructive or invasive methods (ileostomy, euthanasia)
- > Non-glycaemia/insulinaemia



## METHODS to assess prebiotics according to this definition

### 2. Fermentation

- > *In vitro* - batch- or continuous culture with single or mixed bacterial populations
- > *In vivo* - Euthanasia, faecal collection, breath test



## METHODS to assess prebiotics according to this definition

### 3. Selective stimulation of growth and/or activity

- > NOT pure cultures
- > Faecal or gut samples *in vitro* or *in vivo*
- > Qualitative or quantitative characterisation

**TABLE 1** Principal methodologies employed to enumerate colonic bacteria

Method	Advantages	Disadvantages
Classical culture and chemical characterization	Straight forward, relatively inexpensive, possibility of performing a large number of replicates.	Subjectivity, limited to culturable bacteria, selectivity of medium is ambiguous, metabolic plasticity of organisms may introduce error.
FISH	Applicable to unculturable as well as culturable bacteria, highly specific.	Availability of probes limited to known bacteria, time consuming.
PCR	Applicable to unculturable as well as culturable bacteria. High reliability, allows placement of previously unidentified bacteria.	Expensive, time consuming. Subject to bias in the PCR process.
Direct community analysis	Culture-independent. Applicable to elucidate the diversity of entire samples.	Subject to bias in the PCR process.
Denaturing/temperature gradient gel electrophoresis (D/TGGE)	Rapid. Applicable to both culturable and unculturable bacteria.	Qualitative rather than quantitative. Subject to bias in the PCR process.

Roberfroid (2007)

## COMPONENTS that qualify according to this definition

### > Clear scientific evidence

- > Inulin (FOS)
- > trans-galactooligosaccharides (TOS)

### > Preliminary/promising

- > Gluco-, isomalto-, xylo-, raffinose family-oligosaccharides
- > Lactosucrose, polydextrose

### > Sparse

- > Genti-, pectic-, manno-, melibiose-, N-acetylchito- oligosaccharides
- > Resistant starch and derivatives
- > Non-cellulosic polysaccharides
- > Germinated barley
- > Oligodextrans
- > Lactose, glutamine, lactoferrin-derived peptide

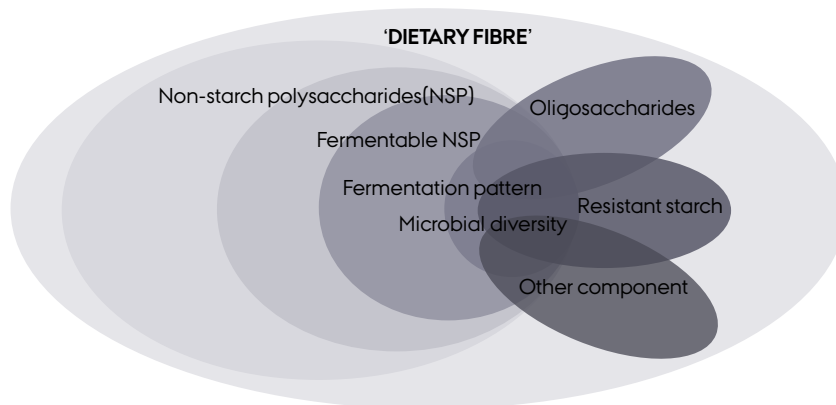


Roberfroid (2007)

## A MORE FLEXIBLE DEFINITION

'Potential substrates for bacterial inhabitants of the intestine'

Lim *et al.* (2005)



## Is it wise to broaden the definition?

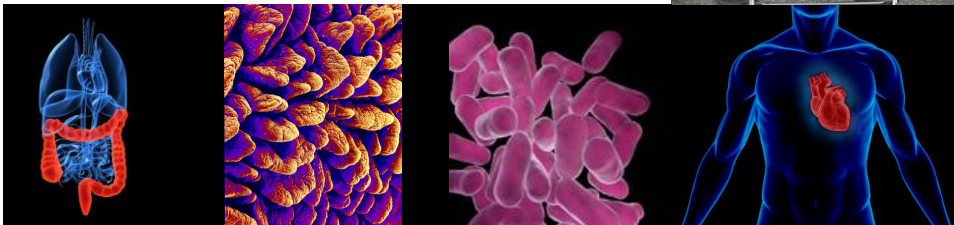
### DEFINITIONS and CRITERIA are IMPORTANT !

- > *Prebiotics are not always bifidogenic*
  - > Stimulation of other species may also have beneficial effects
- > *Bifidogenic factors are not always prebiotics*
  - > Only if the stimulation contribute to health and well-being
- > *Not all non-digestible carbohydrates are bifidogenic or prebiotics*
  - > NDCs may be prebiotic, bifidogenic, harmful or inert
- > *Is the prebiotic effect the most important health 'factor'?*
  - > NDC's may have beneficial effects on health not linked to the prebiotic effect

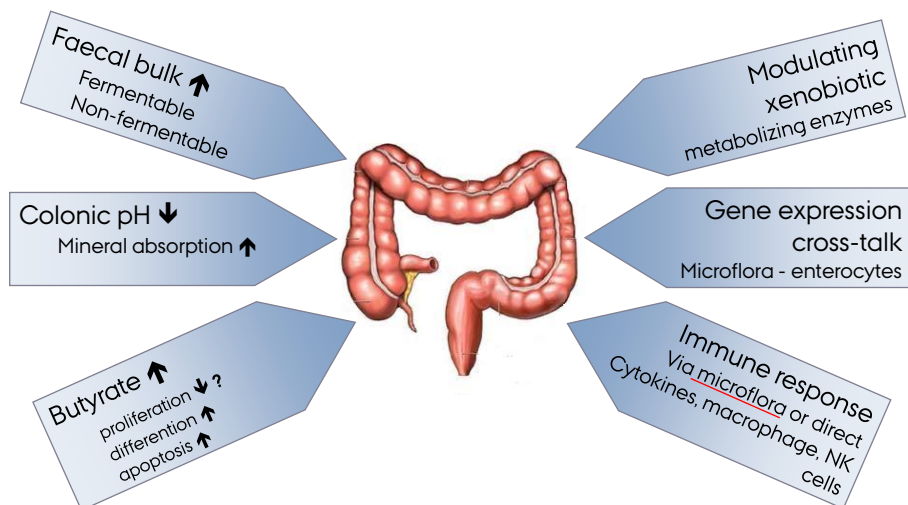
Modified from Food-Info.net

## EFFECTS ON HEALTH

- > 'Gut health'
- > Colon cancer
- > Obesity
- > Diabetes
- > Cardiovascular disease



## GUT HEALTH and COLON CANCER



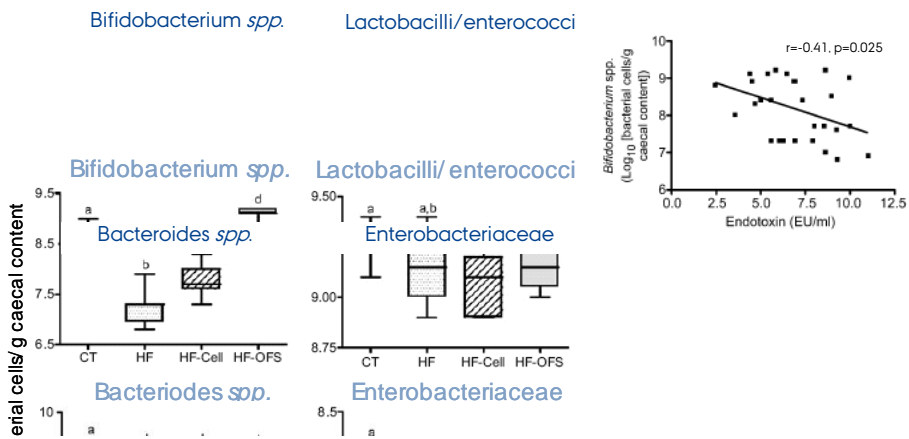
Lim *et al.* (2005)

## OBESITY

- > Increased energy efficiency
  - > SCFA are absorbed from the colon
- > FIAF (Fasting Induced Adipose Factor)
  - > Regulates fatty acid flux
  - > Expression depends on the microflora
- > TNF- $\alpha$  levels in blood correlates with bifidobacteria content

Delzenne *et al.* (2008)

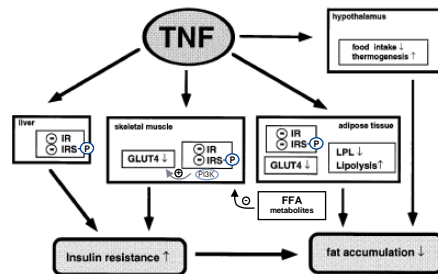
## RESTORATION of gut flora by FOS



From Cani *et al.* (2007)

## Type-2 DIABETES and CVD

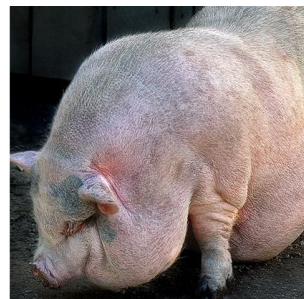
- > TNF- $\alpha$  is overexpressed in NIDDM patients and obese subjects
  - > Adipose tissue, muscle and circulating levels
- > TNF- $\alpha$  impairs insulin sensitivity
- > TNF- $\alpha$ , IL-6 and C-reactive protein (CRP) are risk markers of CVD
- > FOS feeding (Cani *et al* 2007)
  - > improved insulin sensitivity
  - > Better glucose tolerance
  - > Reduced proinflammatory cytokines (IL-1 $\alpha$ , IL-1 $\beta$ , IL-6)
  - > Improved barrier function?



Modified after Bulló-Bonet *et al.* (1999) and Quinn *et al.* (2008)

## HOW DO STUDIES IN ANIMALS CONTRIBUTE?

- > To understand underlying mechanisms
- > To study digestion and physiology under controlled conditions
- > Disease models



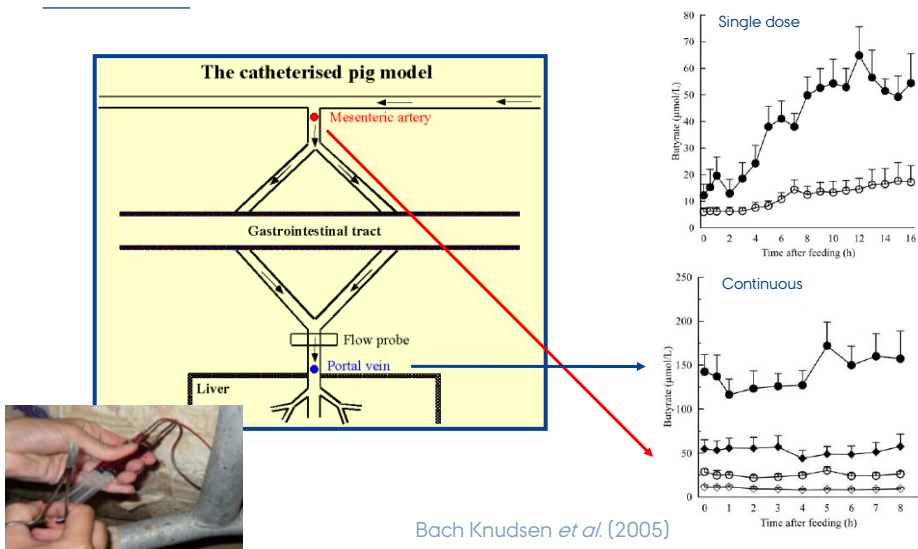
## BUTYRATE production in the pig colon is not due to beta-glucan

	mmol/kg digesta	Ratio Ace:Pro:But
Low DF	88	56.4:34.6:9.0
High fibre (HF) oat bran	151	53.3:33.3:13.3
HF soluble $\beta$ -glucan	111	56.6:33.3:10.1
HF insoluble residue	101	54.4:32.2:13.3

**BUT** betaglucan has beneficial effects on glucose- and cholesterol metabolism...

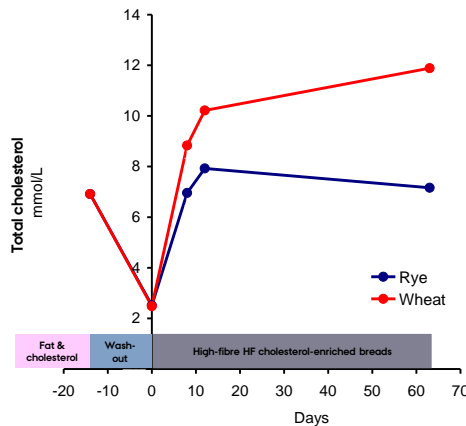
Bach Knudsen *et al.* (1993)

## RYE increases production and absorption of butyrate in pigs



Bach Knudsen *et al.* (2005)

## RYE decrease plasma cholesterol by mechanisms other than **propionate**



- > Propionate in gut contents did not increase (butyrate did)
- > No increase in total absorption of SCFA
- > Only a marginal increase in the ratio of propionate in hepatic portal blood
- > No effect on expression of HMG-CoA reductase (HMGR) in liver
- > Effects appear related to impaired absorption!

Lærke *et al.* (2008)

- > Both oats and rye are hypoglycaemic and hypocholesterolaemic
- > These studies suggest that arabinoxylans in oats and rye are responsible for the increase in butyrate production

**BUT does this make them prebiotic?**

## CONCLUSIONS

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- > Only 2 dietary sources – FOS and GOS - qualify as prebiotic according to Gibson/Roberfroids definition
- > A range of other NDC are fermented to varying degree
- > Prebiotics (and other fermentable CHO) can influence the 'quality' and/or activity of the gut microflora
- > Diet and microflora can affect systemic inflammatory status (e.g.TNF- $\alpha$ ) i models
- > Systemic TNF- $\alpha$  is overexpressed in obesity and type-2 diabetes and linked to insulin sensitivity
- > NDC's can beneficially affect health by other means than through prebiotic action

