Université catholique de Louvain UCL

Louvain Drug Research Institute

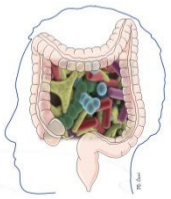
Metabolism and Nutrition research group

Brussels, Belgium

Modulation of the gut microbiota by prebiotics or probiotics: impact on metabolic syndrome

Prof. Patrice D. Cani

Research Associate FRS-FNRS

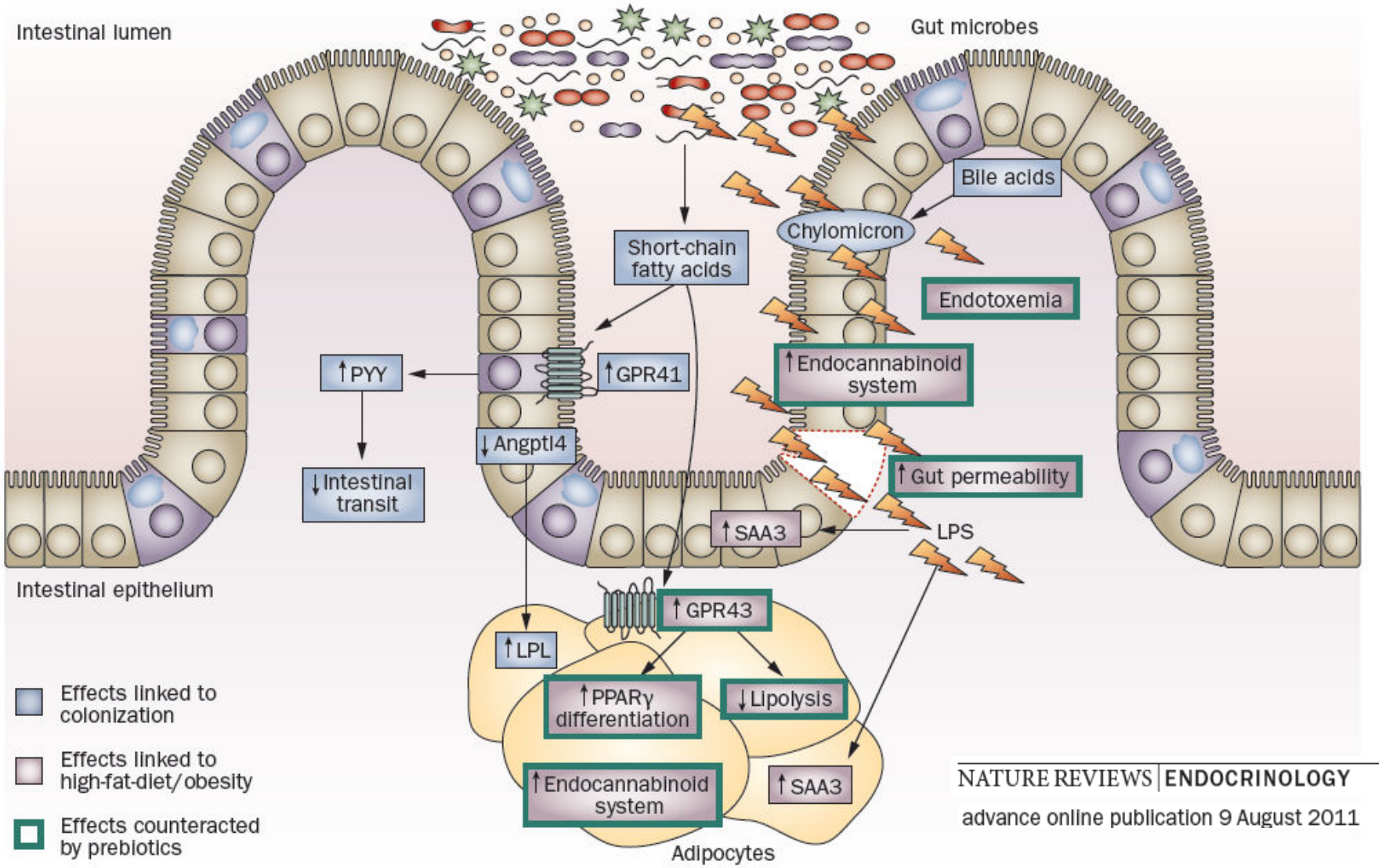


Metabolism & Nutrition

http://www.uclouvain.be/en-269734.html

fnrs LA LIBERTÉ DE CHERCHER

Targeting gut microbiota in obesity



NATURE REVIEWS | ENDOCRINOLOGY
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Nathalie M. Delzenne, Audrey M. Neyrinck, Fredrik Bäckhed and Patrice D. Cani

More than 15 years ago….

Dietary Modulation of the Human Colonic Microbiota: Introducing the Concept of Prebiotics

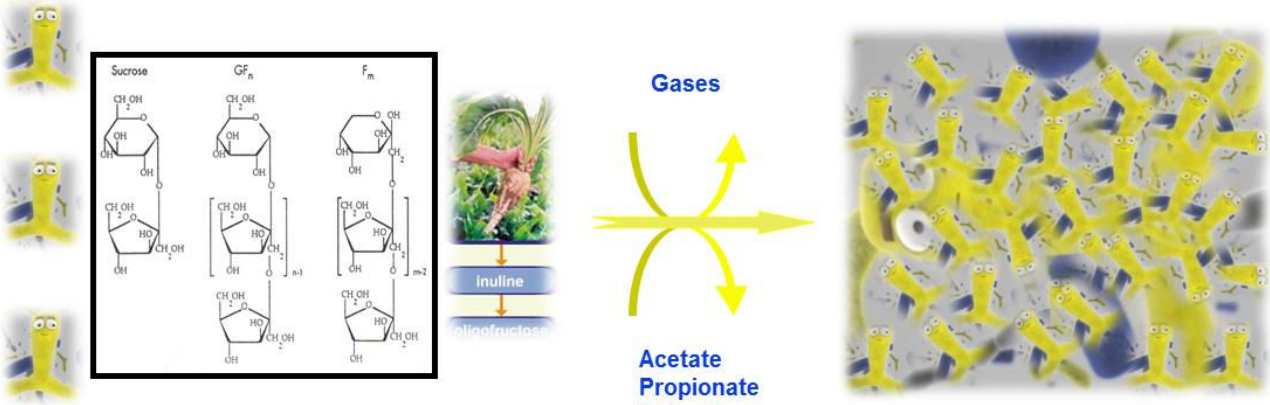
GLENN R. GIBSON AND MARCEL B. ROBERFROID[1]

MRC Dunn Clinical Nutrition Centre, Cambridge, United Kingdom and
**Unité de Biochimie Toxicologique et Cancérologique, Département des Sciences Pharmaceutiques, Université Catholique de Louvain, Brussels, Belgium*


Gibson and Roberfroid, *J. Nutr 1995*

- ✓ **Prebiotics such as oligofructose (OFS) reproducibly increase gut bifidobacteria**

Increased Bifidobacterium spp.



15 years later….
Another level of complexity!

Gut microbiota analysis by using high-throughput methods (Pyrosequencing, Phylogenic microarrays and qPCR)

- **102** Taxa are significantly affected
- **16** Displayed a > 10-fold change

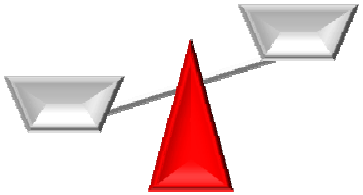
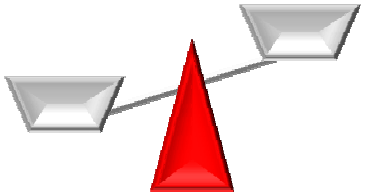
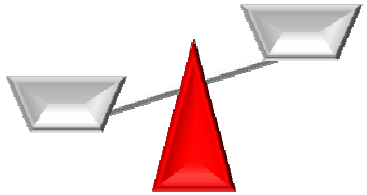
ORIGINAL ARTICLE

Responses of Gut Microbiota and Glucose and Lipid Metabolism to Prebiotics in Genetic Obese and Diet-Induced Leptin-Resistant Mice

Amandine Everard,[1] Vladimir Lazarevic,[2] Muriel Derrien,[3] Myriam Girard,[2] Giulio M. Muccioli,[4] Audrey M. Neyrinck,[1] Sam Possemiers,[5] Ann Van Holle,[5] Patrice François,[2] Willem M. de Vos,[3,6] Nathalie M. Delzenne,[1] Jacques Schrenzel,[2,7] and Patrice D. Cani[1]

Diabetes Publish Ahead of Print, published online September 20, 2011

Non exhaustive targets of prebiotic-induced microbiota modulation

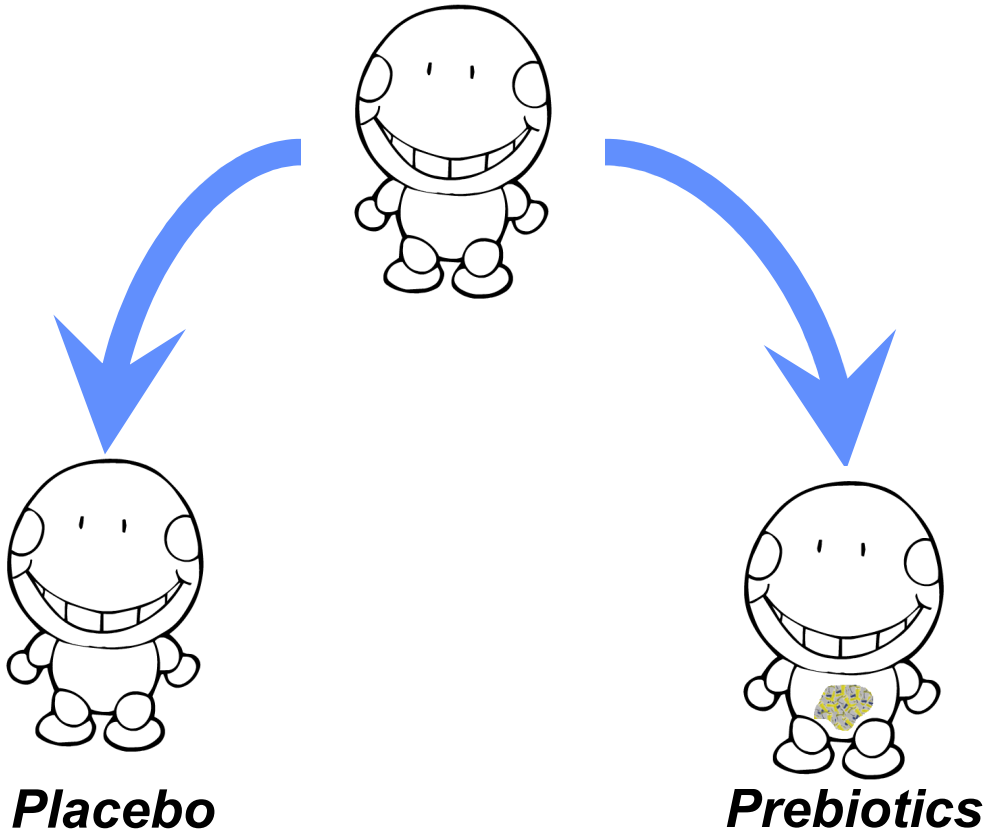
Energy homeostasis	Glucose & Lipid metabolism	Low grade inflammation
		
↘ Fat mass	↗ glucose tolerance	↘ Plasma LPS
↗Muscle mass	↗Insulin sensitivity	↗ Gut barrier
↘ Body weight	↘Hepatic steatosis	↘ Inflammation
↘ Food intake	↘Plasma lipids	

Cani and Delzenne *Pharmacology & Therapeutics* 2011
Delzenne and Cani Annu Rev Nutr 2011
Delzenne et al Nature Reviews Endocrinology 2011

NEW ↗ Leptin sensitivity

Everard et al *Diabetes 2011*

Gut microbiota and appetite regulation: impact of prebiotics



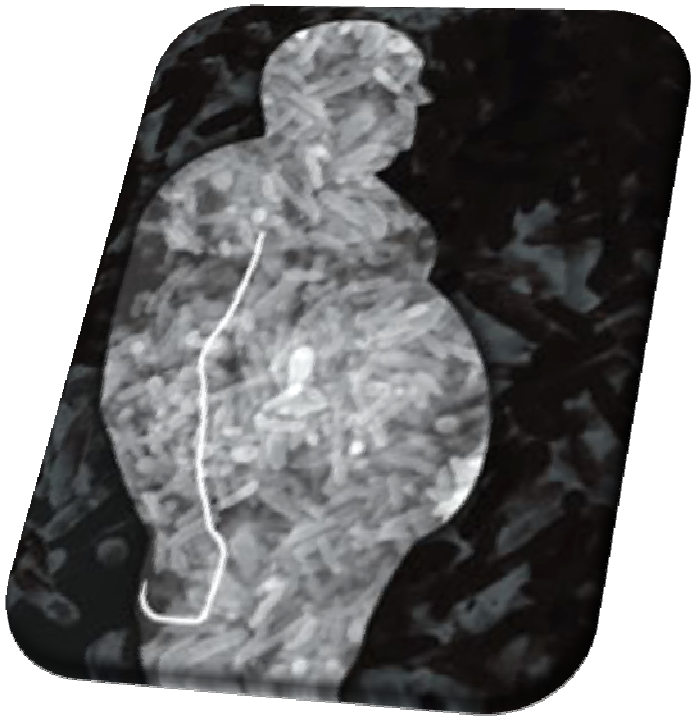
In healthy subjects

↘ Energy intake
↘ Hunger
↗ Satiety
↗ PYY
↗ GLP-1
↗ PP

↘ Glycemia

Cani et al *Eur J Clin Nutr* 2006
Cani et al *Am J Clin Nutr* 2009
Verhoef et al *Brit J Nutr* 2011

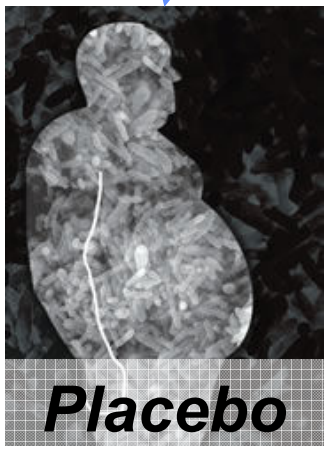
In obese humans?

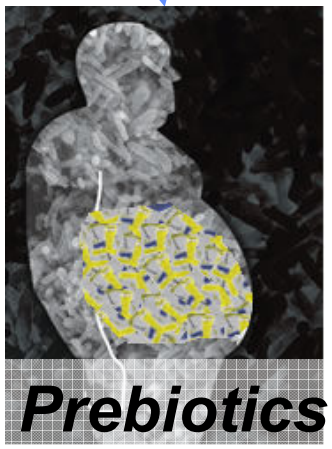


Prebiotics reduce food intake and visceral fat

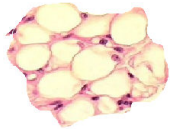
48 obese patients
12 weeks, prebiotics 20g/d

In obese subjects





↘ Body weight



↘ Fat mass

↘ Hunger
↗ Satiety
↗ PYY

↘ Energy intake

↘ Glycemia

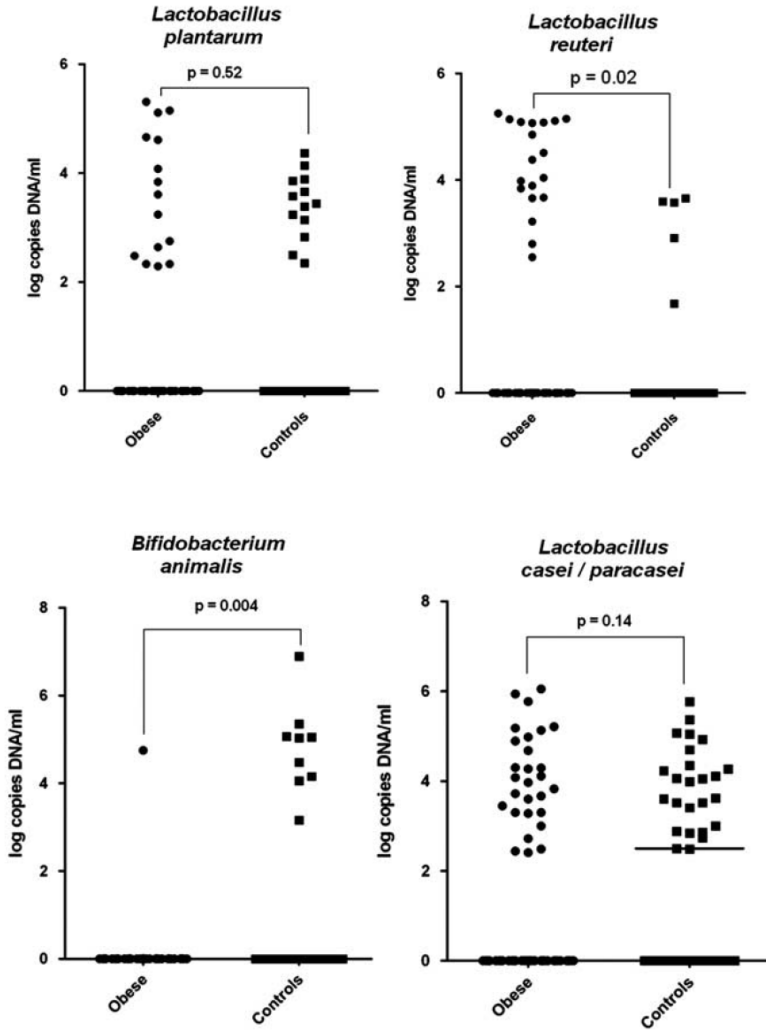
Parnell and Reimer *Am J Clin Nutr* 2009

Lactobacilli are not all associated with obesity!!!

Table 4 Results of *Bifidobacterium animalis*, *Lactococcus lactis* and seven *Lactobacillus* species-specific quantitative PCR

	Obese (n = 64)	*Controls* (n = 43)	P
Presence of targeted taxa[a]			
L. acidophilus	0 (0%)	0 (0%)	—
L. casei/paracasei	24 (37.5%)	24 (55.8%)	0.047
L. fermentum	11 (17.2%)	9 (20.9%)	0.40
L. gasseri	21 (32.8%)	9 (20.9%)	0.13
L. plantarum	14 (21.9%)	12 (27.9%)	0.31
L. reuteri	16 (25.0%)	4 (9.3%)	0.03
L. rhamnosus	11 (17.2%)	9 (20.9%)	0.40
Lactococcus lactis	55 (85.9%)	34 (79.1%)	0.25
Bifidobacterium animalis	1 (1.6%)	7 (16.3%)	0.007

[a]Values expressed as number (percentage). Fisher's exact test.



Probiotics and obesity

Microbiota	Study design	*n*	Duration	Treatment	Results
Probiotics					
Lactobacillus acidophilus NCFM[75]	Randomized, double-blind intervention	45 individuals with glucose intolerance and/or diabetes mellitus	4 weeks	Probiotic (10^{10} CFU/day) versus SiO_2/lactose (placebo)	Systemic inflammation upon LPS challenge in both groups Probiotics prevented loss of insulin sensitivity observed in the placebo group
Lactobacillus gasseri SBT2055[76]	Randomized, multicenter, double-blind, placebo-controlled intervention	87 individuals with a BMI of 24.2–37.0 kg/m^2 and visceral adiposity	12 weeks	Fermented milk with probiotics (10^{11} CFU/day) or without probiotics (placebo)	Reduced body weight, BMI, waist and hip circumference, visceral and subcutaneous fat mass in the probiotic versus the placebo group

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No intervention studies showing obesity features available until now!!

« Take home messages »

Further studies are needed!

-Prebiotics impact energy homeostasis

-Prebiotics changes gut microbiota in a complex fashion

-Lactobacillus are involved in energy homeostasis, but a careful analysis is mandatory before any conclusions