Table S2A: Effects of prebiotics in Colorectal Cancer

Prebiotic	**Effects**	**Model**	**Reference**
Inulin and GOS	In situ production of SCFA Significant increases of *Bifidobacterium* spp.	Animal	10
GOS	Significant increase in beneficial populations, such as *Bifidobacterium* spp.; 56.9% increase in propionate production Increase of Bacteroidetes and reduction of Firmicutes populations Reduction of the genus *Desulfovibrio* spp. Increase in the genus *Phascolarctobacterium*	Animal	12
Inulin	Increase in situ production of SCFA (propionic acid and butyric acid) Increase of Bacteroidetes and Prevotellaceae Reduction of the Firmicutes Increase of the genus *Blautia* Increase in fecal mass Reduction (49.9%) in the number of colon polyps	Animal	11
COS	Reduction of *Escherichia* spp., *Shigella* spp., *Enterococcus* spp. and *Turicibacter* Increase of *Akkermansia* spp., butyrate producing bacteria and *Cladosporium* spp.	Animal	13
FOS (25%) XOS (25%) polydextrose (25%) Resistant dextrin (25%)	Improvement of serum immunological indicators Significant increase in levels of igG and igM, igG, igA, total B lymphocytes and T cells Increased level of transferrin Reduction of Bacteroidetes Increase of *Bifidobacterium* spp. and *Enterococcus* spp. Increase of harmless strains of *Escherichia* specie	Human	53
FOS + *Bifidobacterium longum*	Increased of SCFA in feces Suppression of rotting bacteria in feces Suppression of *Bacteroides fragilis* enterotoxin	Human	14
Acacia gum + *Lactiplantibacillus plantarum*	Reduction of TNF-α levels due to the anti-inflammatory activity of acacia gum Reduction of β-glucuronidase levels	Animal	15

Yacon	Improved intestinal permeability Increased production of epithelial mucus Increased antioxidant activity Reduction of TNF Increased SCFA levels Increased production of antibacterial defensins and anti-inflammatory cytokines, mainly IL-10	Animal	16
Jabuticaba seeds + *Lactobacillus delbrueckii* subsp.*bulgaricus*	Increase of Bacteroidetes Reduction of Firmicutes Reduction of β-glucoronidase, β-glucosidase, galactosidase, mucinase and nitroreductase (bacterial metabolizing enzymes), and consequent reduction in the incidence of colon cancer Growth inhibition of *Bacteroides*, *Clostridium* and *Propionibacterium* spp. Increase of *Lactobacillus* and *Bifidobacterium* spp.	Animal	17
JP	Significant decrease in Firmicutes/Bacteroidetes ratio Strong activity in the regulation of dysbiosis and maintenance of microbial balance Increased SCFA production	Animal	18
NVPS	Reduction in the number and size of tumors Reduction in the incidence of CRC Reduced Firmicutes/Bacteroidetes ratio Increase in SCFA producing genera, including butyric producers (*Butyricicoccus*, *Butyrivibrio* and *Butyricimonas*) and acetic acid (*Lachnospiraceae* UCG 001, *Lachnospiraceae* UCG 006 and *Blautia*)	Animal	19
Dextran	Production of SCFA with an anti-inflammatory action	Animal	20

Table S2B: Effects of prebiotics in neurovegetative diseases and cognitive functions

Prebiotic	Effects	Model	Reference
Cognitive Functions			
Inulin + *Bifidobacterium animalis* subsp. *lactis*	Improvements in scores of the neurocognitive index domain (overall cognitive function, overall attention, cognitive flexibility, and executive functions) Reduction of some inflammation markers	Human	23
Polydextrose	Better performances in sustained attention Increased abundance of *Ruminoclostridium* 5	Human	24
Stress			
Prebiotic fruits and vegetables, fermented foods	Improvement of perceived stress in adults	Human	21
FOS and GOS	Increase of *Bifidobacterium* spp. No clear effect on the markers of stress and inflammation	Human	22
Anxiety and Depression			
ALAC+ sodium butyrate	Relieve the symptoms of anxiety Reduction of intestinal inflammation Reduction of the immobility time Increased preference of sucrose, thereby reducing anhedonia.	Animal	25
Galactosylsucrose	Improvement of self-efficacy for patients with depression	Human	26
Autism			
GOS + *Limosilactobacillus reuteri* and *Bifidobacterium longum*	Increased survival of probiotics Increased levels of Firmicutes, *Akkermansia*, *Blautia* and *Actinobacter* Reduction of Bacteroides and Verrucomicrobia Increased concentrations of SCFA Reduction of constipation, diarrhea and pain Improvement in terms of lethargy, irritability and stereotypes	In vitro fermentation model: SHIME (Simulator of Human Intestinal	27

		Microbial Ecosystem)	
B-GOS	Increased amounts of creatinine, creatine, dimethyl-cine, dimethylanine, carnitine, citrate, adipate and trimethylamine-N-oxide in children's urine with ASD Reduction of amino acid and lactate levels Improvement of abdominal pain	Human	28
B-GOS	Significant increase of bifidobacteria, *Rosburia*, *Bacteroides*, *Atopobium*, *Faecalibacterium prausnitzii*, *Sutterella* spp.; rectal *Eubacterium* Reduction of Veillonellaceae Increased of acetate and lactate	Human	29
B-GOS combined with a casein and gluten free diet	Improvement in sociality and behavioural traits Increased of *Faecalibacterium prausnitzii* and *Bacteroides* spp.	Human	30
ALAC+ sodium butyrate	Improvement of sociability and memory Reduction of intestinal inflammation Increased mobility Reduction of repetitive behavior	Animal	25
Inulin + oligofructose	Improvement of intestinal permeability Improvement of the behavioral field (reduction of repetitive behaviors)	Animal	95
Schizophrenia			
Green leafy vegetables, high-fibre fruit, whole grains	Improvement of cardio-metabolic profile in schizophrenia spectrum disorders	Human	31
Parkinson			
Inulin, resistant starch, resistant maltodextrin, rice bran	Beneficial biological changes in the microbiota, SCFA, inflammation, and neurofilament light chain Reduction of the markers of inflammation (plasma zonulin and stool calprotectin)	Human	32

Table S2C: Effects of prebiotics in intestinal diseases

Prebiotic	Effects	Model	Reference
Inflammatory Bowel Disease			
Inulin	Increased level of indigenous lactobacilli; Reduction of the pH of the colon; Reduction of the mucosal inflammation and lower scores of histological damage	Animal	33
Inulin + FOS	Reduction in intestinal inflammation Increased levels of intestinal bifidobacteria and lactobacilli; Decrease in mucosal proinflammatory cytokines	Animal	34
Resveratrol	Increased levels of *Bifidobacterium* and *Lactobacillus* Lower amounts of *E. coli* and Enterobacteriaceae	Animal	35
Inulin + FOS + *Bifidobacterium*	Reduction in intestinal inflammation and in the intestinal TNF and IL-1a levels	Human	36
fructans of inulin type	Increase in colon butyrate production and improvement of colitis	Human	37
Inulin + FOS	Improved clinical symptoms and increased level of *Bifidobacterium*	Human	38
FOS	Reduction of the HBI score Increased fecal *Bifidobacterium* concentrations Increase of the percentage of IL-10–positive DCs.	Human	39
Irritable Bowel Disease			
scFOS	Reduction of anxiety scores Increase of Bifidobacteria population	Human	42
GOS	Increase in the number of Bifidobacteria relief of flatulence, abdominal pain, and discomfort symptoms	Human	44
Enteric Syndrome			

GOS + Bifidobacteriaceae	Intestinal increase of bifidobacterial and lactic acid bacteria Improved renal function	Animal	47
EPS + *Leuconostoc mesenteroides*	Growth stimulation of bifidobacteria, *Lactobacillus* spp. and SCFA Increase in antioxidant activity Stimulation of antioxidant activity Improvement of skin immunity	Animal	48
Inulin + *Lacticaseibacillus casei*	Increase in basophils and lactobacilli concentration Reduction of total coliform concentration in faeces Reduction of diarrheal phenomena Increased consistency of the faeces Reduction of serum cholesterol concentration	Animal	46
Catechins	Increase of *Lactobacillus* spp., *Bifidobacterium* spp., *Akkermansia* spp., *Roseburia* spp. and *Faecalibacterium* spp. Increased production of SCFA	Animal	45

Table S2D: Effects of prebiotics in Obesity

Prebiotic	**Effects**	**Model**	**Reference**
COS	Increased level of acetic acid, with reduction of propionic and butyric acid; *Bacteroides* increase in microbiota and reduction of Proteobacteria and Actinobacteria	Animal	49
FOS/GOS	Improvement of the microbiota dysbiosis Increased inflammatory cytokines	Animal	50
Flavanols: epi-gallocatechin, epigallocatechin gallate, epicatechin, epicatechin gallate	Increase of *Akkermansia*, *Roseburia* and *Bifidobacterium* Increased production of butyrate Improvement of intestinal barrier function Reduction of the Firmicutes/Bacteroidetes ratio Reduction of translocation of endotoxins	Animal	51
Decaffeinated Green and Black Tea (GT and BT) polyphenols	Inhibition of weight gain in mice fed a high-fat diet Firmicutes/Bacteroidetes ratio reduction α-amylase and α-glucosidase inhibition in saliva and small intestine Increased SCFA (acetate and propionate)	Animal	52
Aqueous extracts of tea	*Firmicutes* increase and decrease of Bacteroidetes Potential growth of *Akkermansia muciniphila*	Animal	53
Marc and cinnamon extracts	Improvement of blood sugar Reduction of fat mass increase Enrichment in Firmicutes Decrease in *Bacteroides* Reduction of hepatic steatosis	Animal	54
Inulin	Increase of actinobacteria Reduction of Clostridia Reduction of girmicutes (*B. obeum*, *E. ruminantium*, *B. obeum*, *B. luti*, *B. faecis*, *R. faecis*, *Oscillibacter* spp.) Growth stimulus of *Bacteroides* spp. (*B. uniformis*, *B. xilanisolveni*)	Animal	55
Vanillin and lignans	Reduction of Firmicutes Increase of Bacteroidetes and Verrucomicrobia Inhibition of lipopolysaccharide producing bacteria (LPS) Improved sensitivity to insulin	Animal	56

	Stimulation of SCFA production		
Cranberry extract	Reduction of intestinal triglyceride content Relief of intestinal inflammation and oxidative stress Increase of *Akkermansia* spp. Reduction of the weight gain	Animal	58
Apple Procyanidins	Increase of *Akkermansia muciniphila* Improved sensitivity to insulin Improvement in lipid catabolism	Animal	59
Resveratrol	Increase of *Lactobacillus* spp., *Akkermansia muciniphila* and *Bifidobacterium* spp. Improved sensitivity to insulin	Animal	60
Pterostilbene	Increase of *Akkermansia muciniphila* Improved sensitivity to insulin Increased production of butyrate and propionate	Animal	61
Catechins	Increase of *Roseburia* spp., *Lactobacillus* spp., *Bifidobacterium* spp. *Akkermansia* spp. *Faecalibacterium* spp.	Animal	45
Inulin-type fructans (ITF)	Growth stimulation of Bifidobacteria and *Faecalibacterium prausnitzii* Reduction of *Bacteroides intestinalis* and *Bacteroides vulgatus*	Human	62
Soy isoflavones	Increase of *Faecalibacterium* Reduction in blood lipid levels Improved immune function and intestinal permeability Attenuation of oxidative damage Increased fraction of beneficial bacteria producing SCFA (*Bacteroidetes* and Proteobacteria)	Animal	66
Pomegranate extract	Increase of *Bacteroides*, *Faecalibacterium*, *Butyricicoccus*, *Odoribacter* and *Butyricimonas* Reduction of *Parvimonas*, *Methanobrevibacter* and *Methanosphaera*	Animal	67
Pomegranate extract + syringaresinol	Reduction of serum LBP, therefore polyphenols could modulate metabolic endotoxaemia	Animal	68
Arctic berries	Relief of intestinal infiammation induced by a high-fat diet Reduction of hepatic steatosis Prevention of hyperinsulinemia	Animal	58

Pollen extract	Reduction of lipid accumulation in serum and liver Reduction of oxidative damage and inflammation Increase of *Bifidobacterium* spp.	Animal	70
Genistein	Reduction of weight gain Reduction of serum triglycerides Improvement of the glucose tolerance	Animal	71
Chicory inulin combined with a probiotic mixture (20 billion CFU; lactobacilli, bifidobacteria, *Bacillus*, *Streptococcus*, *Saccharomyces*)	Reduction of BMI, body weight, and waist and hip circumferences Reduced subclinical inflammation related to immunity	Human	65
Inulin-type fructan	Increase in *Bifidobacterium* content Reduction of fecal calprotectin Increase of rumenic and conjugated linolenic acid	Human	63
Galacto-mannans combined with *Bacillus coagulans*	Higher weight loss in patient of bariatric surgery Significant decrease of plasma triglycerides	Human	73
Bifidobacterium animalis subsp. *lactis* and FOS	Changes in serum metabolite profile related to a decrease in inflammation	Human	64
FOS, yeast β-glucans, silymarin extract	Reduction of cortisol with effect on sleep quality	Human	72
Resistant dextrin	Modification of satiety and glycaemic responses	Human	96

Table S2E: Effects of prebiotics in type-2 Diabetes and Metabolic Syndrome

Prebiotic	Effects	Model	Reference
Diabetes			
COS	Reduction of hyperglycemia, hyperlipidemia Prevention of obesity Histological improvement in the liver of T2DM mice Increased of Firmicutes, Bacteroidetes and Proteobacteria	Animal	74
COS	Reduction of BGL in diabetic mice; Increase of Actinobacteria, Lachnospiraceae and Corynebacteriaceae populations	Animal	75
ITF + *Lactobacillus* spp.	Reduction of BGL Reduction of FBG Reduction of the Firmicutes/Bacteroidetes ratio Increased of *Lactobacillus* spp., *Bacteroides*, *Phascolarctobacterium* and *Lachnoclostridium*	Animal	76
ITF	Increase in the intestinal level of Bifidobacteria Increased concentration of acetic and propionic acids Decrease of *Firmicutes* Slight increase of *F. prausnitzii*	Human	77
Resistant Dextrin and maltodextrin	Resistant dextrin improves sleep and QOL in obese women with type 2 diabetes Modulation of glycemia, metabolic endotoxemia and subsequently a decrease in biomarkers of inflammation and HPA axis activity	Human	79
Inulin-type fructans	Improvement incretin responses or glucose regulations	Human	97
Commercial prebiotic formula	Modulation of gut microbiota		80
Metabolic Syndrome			
NACOS	Promotion of insulin synthesis Improved glucose tolerance	Animal	81

NACOS	Inhibition of lipid accumulation in the liver Reduction of the Firmicutes/Bacteroidetes ratio Reduction of *Desulfovibrio* spp. Reduction of fasting blood sugar Increase of the *Lactobacillus*/*Enterococcus* ratio		82
Pro-anthocyanidins from grape seeds	Reduction of cecal butyrate Increase of *Bacteroides* and Proteobacteria Decrease in Firmicutes Significant increase of *Akkermansia muciniphila*	Animal	83
Pomegranate extract	Modulation of gut microbiota, depending also on the pharmacological therapy Reduction of lipopolysaccharide-binding protein	Human	84
Inulin, inulin+traditional Chinese medicine (TCM), or inulin+metformin	Inulin alone or combined with metformin or TCM altered specific gut microbiota taxa but not the general diversity Correlation of microbiota with lipids, uric acid, and glucose, with possible effects on MetS	Human	98

Table S2F: Effects of prebiotics in Osteoporosis and Immunity

Prebiotic	Effects	Model	Reference
Osteoporosis			
FOS	Increase in bone mass Increase of butyrate concentration in the colon	Animal	85
FOS/GOS	Improved calcium, phosphorus and magnesium absorption Reduction of bone loss in ovariectomy-induced rats	Animal	86
FOS and dried prunes	Improvement of bone mineral density Improvement in bone recovery	Animal	87
FOS	Increased *Lactobacillus* and *Bacteroides* population Increased calcium content in the femoral bone Decrease of the level of urinary deoxypyridinoline and serum high-sensitivity C-reactive proteins.	Animal	88
Soluble corn fiber	Variable impact on calcium absorption in pre-menopausal women due probably to gut microbiota alteration	Human	89
Soluble corn fiber, with and without calcium supplementation	Increase bone density after 6 months in preadolescent	Human	90
Immunity			
Syringaresinol	Reduction of the Firmicutes/Bacteroidetes ratio Increase of *Lactobacillus* and *Bifidobacterium* spp. Reduction of *Akkermansia* spp.; Reduction of serum level of LPS binding protein Improvement of humoral immunity	Animal	91
B-GOS	Significant increase in *Bifidobacteria, Lactobacillus* spp., *C. coccoide*, *Enterococcus* spp. Significant increases in phagocytosis and production of anti-inflammatory cytokine interleukin-10 (IL-10) Significant reduction in the production of proinflammatory cytokines (IL-6, IL-1beta and tumor necrosis factor alpha) Reduction of *Desulfovibrio* spp.	Human	92

Chicory inulin	Increase in the *Bifidobacterium* spp.	Human	93
GOS and FOS	Increased in bifidobacteria and butyrate	Human	94

List of abbreviations

1. **ADHD** = Attention Deficit Hyperactivity Disorder;
2. **ADOS-CSS** (Autism Diagnostic Observation Schedule – Calibrated Severity Score) = standard assessment tool in autism research;
3. **AN** = Anorexia Nervosa;
4. **ATEC** = Autism Treatment Evaluation Checklist;
5. **BDI** (Beck Depression Inventory) = depression assessment tool;
6. **BDNF** = brain-derived neurotrophic factor;
7. **BGL** = blood glucose levels;
8. **BMI** = Body Mass Index;
9. **CD** = Crohn's disease;
10. **CRP** = C-reactive protein;
11. **DCA** = secondary bile acid deoxycholic acid;
12. **DCs** = dendritic cells;
13. **FBG** = fasting blood glucose;
14. **FOS** = fructo-oligosaccharides;
15. **FPG** = fasting plasma glucose;
16. **FST** (Forced Swim Test) = rodent depression assessment test;
17. **GABA** = gamma-aminobutyric acid;
18. **HDL** = High Density Lipoprotein;
19. **IBS=** Irritable Bowel Disease;
20. **IBS-SSS=** Irritable Bowel Disease-Severity Scoring System;
21. **IL** = interleukin;
22. **ISI** = insulin sensitivity index;
23. **KYN** = Kynurenine
24. **LBP** = Lipopolysaccharide Binding Protein
25. **LDL** = low density lipoproteins;
26. **LPS** = lipopolysaccharide,
27. **MDS-UPDRS** (Movement Disorder Society-Unified Parkinson's Disease Rating Scale) = Parkinson's disease rating scale.
28. **Mice db/db** = mice homozygous for a defect in the leptin receptor;
29. **MMSE** (Mini mental State Examination) = cognitive status assessment tool;
30. **QOL** = Sleep quality and quality of life
31. **SCFA** = Short Chain Fatty Acids;
32. **scFOS** = short chain Fructo-oligosaccharide
33. **SNAP-IV** = ADHD assessment test;
34. **SNC** = Sympathetic nervous system;

35. **TNF** = Tumor Necrosis Factor;
36. **TRP** = Tryptophan;
37. **UC** = Ulcerative colitis.