Supplementary Material

Table S1. Epigenetic modifications induced by nutraceuticals in relation to obesity

Nutraceutical	Model	Effects	Targeted genes or pathways	Gut microbiota	miR	Study
Resveratrol	Humans	Modulation of mitochondrial activity	AMPK ↑ SIRT-1 ↑	*Bacteroidetes/Firmicutes ratio* ↑	miR-211-3p ↑ miR-1224 ↑ miR-539-5p ↑ miR-511-3p ↓	61, 63-70, 75, 78
	In vitro and animal models	Glucose homeostasis	CCAAT-C/EBPα ↓			
		decrease adipogenesis increase thermogenesis	UCP1 ↑ FNDC5 ↑	*Lactobacillus* ↑		
		Reducing of fat acumulation	SREBPs ↓	*Bifidobacterium* ↑		
		Stimulation of browning process	FIAF ↑			
		Reduction of body weight Reduction of subcutaneous adipose tissue Protection against sarcopenic obesity	LPL ↓ PKA/LKB1/AMPK ↑	*Enterococcus faecalis* ↓		
Curcumin	Humans			*Bacteroidaceae* ↑ *Prevotellaceae* ↓		
	In vitro and animal models	Antiadipogenic	C/EBPα ↓ KLF5 ↓ PPARγ ↓ aP2 ↓	*Rikenellaceae* ↑ *Anaerotruncus* ↓ *Exiguobacterium* ↑		
		Anti-inflammatory	MAPK ↑ STAT3 ↓ IL-1β ↓	*Helicobacter* ↓	miR-17-5p ↑	82, 83, 85-101
		Increase thermogenesis and energy expenditure	UCP1↑	*Shewanella* ↑ *Serratia* ↑		
		Reduces insulin resistance	STAT3 ↓	*Lactococcus* ↑ *Turicibacter* ↑ *Parasutterella genera* ↑		
Ginger	Humans In vitro and animal models	Antiadipogenic	C/EBPα ↓ PPARγ ↓ aP2 ↓ FAS ↓ AKT/GSK3 ↓	*Firmicutes/Bacteroidetes ratio* ↑ *Proteobacteria* ↑ *Ruminococcus* ↓	miR-21 ↓ miR-132 ↓	115-129 133, 136, 139
		Anti-inflammatory and hypoglycemic	TNFα ↓ IL6 ↓			
		Reduction of hepatic lipid accumulation	FGF2 ↑ CPT1 ↑ ACOX1 ↑ UCP1 ↑			
		Increase thermogenesis and energy expenditure, reduce body weight and waist circumferences				
Epigallocatechin-3-gallate (EGCG)	Humans In vitro and animal models	Antiobesity Increases lipolysis and lipid oxidation	AMPK ↑ HSL ↑	*Bacteroides* ↑ *Parasutterella* ↑	miR-1297 ↓ miR-373-3p ↓ miR-192-5p ↓	

					miR-1266-5p ↓ miR-595 ↓	
		Enhances basal metabolism	ATGL ↑	*Allobaculum* ↓		
		Decreases weight gain	ACOD2 ↑	*Roseburia* ↓		
		Decreases adipose tissue weight	PPARγ ↑	*Erysipelotrichacea* ↓		
		Decreases calorie intake	MCAD ↑	*Lachnospiraceae* ↓		
			UCP3 ↑	*Ruminococcaceae* ↓		
			NRF1 ↑	*Anaerotruncus* ↓		
			COX-2 ↓	*Odoribacter* ↓		
		Suppresses liver inflammation	iNOS ↓	*Enterorhadus* ↓		142-148 153-157
			DRP1 ↓	*Lachnospiracea* ↓		
		Amelioration of muscle autophagy in diabetes	Beclin1 ↓	*Akkermansia* ↑		
				Christensenellaceae ↑		
			PPARGα ↑	*Bifidobacterium* ↑		
		Improvement in insulin sensitivity and lipid profile		*Fusobacterium varium* ↓		
			GLUT4 ↑			
			LPL ↑	*Enterobacteriaceae* ↓		
				Bilophila ↓		
	Humans In vitro and animal models	Antiobesity induce body weight reduction	LEP ↓	*Akkermansia* ↑		
			PPARγ ↓	*Bacteroides*↑		
			C/EBP-α ↓	*Prevotella* ↑		
		Improves lipolysis in adipocytes	PPARα ↑	*Allobaculum* ↑		
			PGC-1α ↑	*Odoribacter* ↑		
		Increases energy expenditure	TRPV-1 ↓	*Coprococcus* ↑		
			ADIPOQ ↑	*SCFAs* ↑		
		Increases satiety	UCP1 ↑	Acetate concentrations ↑	mmu-let-7a-5p ↑	
			SIRT-1 ↑			
Capsaicin		Decreases the desire to eat	BMP8b ↑	Propionate concentrations ↑	mmu-let-7d-5p ↑	165-179
		Improves glucose intolerance	PGC-1α ↑		mmu-let7b-3p ↑	
			BDNF ↑	*Escherichia* ↓		
		Increases thermogenesis and improves cholesterol level	PRMD16 ↑	*Desulfovibrio* ↓		
			FOXC2 ↑	*Sutterella* ↓		
			NCOA1 ↑	*Helicobacter* ↓		
		Conversion of white/beige cells into brown adipocites	DIO2 ↑			
			SIRT1 ↑			
	Humans	Anti-obesity	PI3K/AKT activity ↓	*Firmicutes /Bacteroidetes ratio* ↑		
	In vitro and animal models	Reduces food intake	PPARγ ↓			
		Increases energy expenditure	UCP1 ↑	*Bifidobacterium spp* ↑ *Prevotella* ↑		
Caffeine		Anti-adipogenic Reduces adipocytes number	FAS ↓	*Porphyromonas* ↑		191-199 200, 201
			CCAAT-C/EBPα ↓			
			C/EBPβ ↓			
		Improves dyslipidemia	SREBP-1			
		Anti-inflammatory	TNFα ↓			
			MCP-1 ↓			
			IL-6 ↓			