Supplementary Materials

Table S1 Research using different sequencing approaches.

Reference	Subjects	Approaches	Condition	Main findings
Shen *et al.* [1]	Wild-type (WT) and APPswe/PS1dE9 (APP/PS1) transgenic (Tg) Alzheimer's disease (AD) mice	16S amplicon sequencing	AD	The abundance of *Helicobacteraceae* and *Desulfovibrionaceae* at the family level and *Odoribacter* and *Helicobacter* at the genus level were significantly higher, while *Prevotella* abundance was significantly lower in APP/PS1 mice than in WT mice.
Zhuang *et al.* [2]	AD patients and healthy controls	16S amplicon sequencing	AD	The composition of the gut microbiota *Bacteroides*, *Actinobacteria*, *Ruminococcus*, *Lachnospiraceae*, and *Selenomonadales* differed between AD patients and controls.
Minter *et al.* [3]	Different drug delivery time of combinatorial antibiotic (ABX)	16S amplicon sequencing	AD	Early postnatal ABX treatment resulted in long-term alteration of gut microbial genera, predominantly expansion

	treatment in APP/PS1 mice			of *Lachnospiraceae* and reduction of S24-7.
Sun *et al.* [4]	Male APP/PS1 transgenic mice and matched WT mice treated with or without prebiotic fructooligosaccharides (FOS)	16S amplicon sequencing	AD	FOS reversed the altered microbial composition in the Tg group: increased *Proteobacteria*, *Helicobacteraceae* and *Desulfovibrionaceae*, and decreased *Lactobacillus*.
Parikh *et al.* [5]	Mice homozygous for apolipoprotein E 2 (APOE2), APOE3, or APOE4, and familial AD mutations	16S amplicon sequencing	AD	APOE alleles constitute a major genetic risk factor for AD. The relative abundance of multiple bacterial taxa was significantly different as a function of APOE genotype.
Scheperjans *et al.* [6]	Parkinson's disease (PD) patients and control subjects	16S amplicon sequencing	PD	The abundance of *Prevotellaceae* in feces of PD patients was reduced compared to controls.
Aho *et al.* [7]	PD patients and control subjects	16S amplicon sequencing	PD	Specific bacterial taxa differed between patients and controls, such as *Roseburia*, *Prevotella*, and *Bifidobacterium*.
Li *et al.* [8]	PD patients and healthy volunteers	16S amplicon sequencing	PD	Compared to healthy controls, putative cellulose- degrading bacteria from the genera *Blautia*, *Faecalibacterium*, and

				Ruminococcus were significantly decreased and putative pathobionts from the genera *Escherichia*/*Shigella*, *Streptococcus*, *Proteus*, and *Enterococcus* were significantly increased in PD patients.
Qian *et al.* [9]	PD patients and their healthy spouses	16S amplicon sequencing	PD	*Clostridium IV*, *Aquabacterium*, *Holdemania*, *Sphingomonas*, *Clostridium XVIII*, *Butyricicoccus*, and *Anaerotruncus* were enriched in the feces of PD patients.
Lin *et al.* [10]	PD patients and age-matched controls	16S amplicon sequencing	PD	The abundance of *Lachnospiraceae* was reduced and *Bifidobacteriaceae* was enriched in PD patients.
Lin *et al.* [11]	PD patients and age- and gender-matched controls	16S amplicon sequencing	PD	Increased relative abundance of *Verrucomicrobia*, *Mucispirillum*, *Porphyromonas*, *Lactobacillus*, and *Parabacteroides* in PD *vs* controls.
Mertsalmi *et al.* [12]	PD patients and controls	16S amplicon sequencing	PD	PD patients with IBS-like symptoms had lower abundance of *Prevotella* bacteria.

Keshavarzian *et al.* [13]	PD patients and healthy controls	16S amplicon sequencing	PD	Compared with PD, butyrate-producing bacteria from the genera *Blautia*, *Coprococcus*, and *Roseburia* were significantly increased in feces of controls and bacteria from the genus *Faecalibacterium* were significantly increased in the mucosa of controls.
Pietrucci *et al.* [14]	PD patients and healthy controls	16S amplicon sequencing	PD	Compared to healthy controls, the presence of the Lactobacillaceae, Enterobacteriaceae, and Enterococcaceae families were significantly higher, while Lachnospiraceae were significantly reduced in feces from PD patients.
Radulescu *et al.* [15]	WT and bacterial artificial chromosome model of HD (BACHD) Tg mice	16S amplicon sequencing	HD	Compared to WT mice, both 3- and 6 -month-old BACHD mice showed decreased abundance of *Prevotella* and *Bacteroides* at the genera level.
Park *et al.* [16]	Individuals living in urbanized town communities (UTC) and longevity village communities (LVC)	16S amplicon sequencing	Aging	Anti-inflammatory bacteria *Faecalibacterium spp.* *EF402172_s*, and *EF404388_s* were only detected in LVC, which may play an important role in preserving residents'

				health in LVC.
Smith *et al.* [17]	Male and female mice in control and acarbose treatment groups at each of three study sites	16S amplicon sequencing	Aging	This study suggested a role of the gut microbiota in the longevity-enhancing properties of acarbose.
Haran *et al.* [18]	Nursing home elders	Metagenomics sequencing	AD	The microbiome of AD elderly showed a lower proportion and prevalence of bacteria with the potential to synthesize butyrate, as well as higher abundances of taxa that are known to cause pro-inflammatory states.
Bedarf *et al.* [19]	Early stage, Levodopa-naïve PD patients and age-matched controls	Metagenomics sequencing	PD	*Akkermansia muciniphila* and unclassified *Firmicutes* were increased, while *Prevotella copri* and *Eubacterium biforme* were decreased in PD samples. Functional analyses of the metagenomes revealed metabolic differences in microbiota in PD involving ß-glucuronate and tryptophan metabolism.
Vulevic *et al.* [20]	Elderly volunteers assigned to two groups: one with placebo (maltodextrin)	Metabolite analysis	Aging	B-GOS led to increases in *Bifidobacteria*, which correlated with increased lactic acid in fecal fluid.

	and the other with Bimuno-galacto-oligosaccharides mixture (B-GOS)			
Gutiérrez-Díaz *et al.* [21]	Healthy mature volunteers from Asturias region (North Spain)	Metabolite analysis	Aging	Subjects on a Mediterranean diet presented greater fecal concentrations of benzoic and 3-hydroxyphenylacetic acids, and higher levels of *Clostridium cluster XVIa* and *Faecalibacterium prausnitzii*.
Conte *et al.* [22]	Caucasian volunteers divided into four groups: young subjects, elderly controls, elderly centenarians' offspring, and centenarians	Metabolite analysis	Aging	The existence of age-related differences in the pattern of fecal volatile organic compounds (VOCs) like formic acid and butyl ester contributes to explaining the complex biology of human aging and longevity. VOCs could be considered as promising markers to evaluate aging and longevity.
Brasili *et al.* [23]	Adult (3 months old) and aged (16 months old) mice received an oral supplementation of 2 probiotics or	Metabolite analysis	Aging	The probiotics induced in both adult and aged mice higher 4-hydroxyphenylacetate and lower xylose in treated mice compared with controls, while valerate was higher in treated

	phosphate-buffered saline daily for 30 days			adult mice and lower in treated aged mice than in controls.
		16S amplicon sequencing		Microbial diversity was lower in healthy mice than in AD mice, but stable over time.
Fujii *et al.* [24]	Mice transplanted with feces from AD patients or from healthy people	Metabolite analysis	AD	Nervous system-related metabolites, including taurine, γ-aminobutyrate, and valine, were significantly deficient in feces from mice transplanted with feces from AD patients compared with mice transplanted with feces from healthy people.
		16S amplicon sequencing		A trend of higher *Prevotella* at ages 20 and 24 weeks in MP mice than in age-matched LC samples.
Ghaisas *et al.* [25]	MitoPark (MP) model mice with PD and their littermate controls (LCs)	Metabolite analysis	PD	An increase in sterol absorption in 20-week-old MP mice compared to LCs supports the notion that this increased absorption may be a response to the rapid weight loss in MP mice after age 16 weeks, which corresponded to PD

				progression and severity.
Vemuri *et al.* [26]	Young and aging mice both fed with normal chow and probiotic chow containing *Lactobacillus acidophilus DDS-1*	16S amplicon sequencing	Aging	*DDS-1* increased *Akkermansia muciniphila* and *Lactobacillus spp*., and reduced the abundance of *Proteobacteria spp*..
		Metabolite analysis		*DDS-1* resulted in improvement of metabolic phenotype in the aging mice, involving amino-acid metabolism, protein synthesis and metabolism, carbohydrate metabolism, and butanoate metabolism.
Shenghua *et al.* [27]	22-month-old natural aging model divided into a model group and a FufangZhenzhuTiaoZhi (FTZ) group; two-month-old young mice as control	16S amplicon sequencing	Aging	FTZ treatment restored the intestinal microbiome disorders in aging mice, such as decreased beneficial butyrate-producing bacteria and increased harmful bacteria
		Metabolite analysis		FTZ treatment partially reversed fecal metabolite abnormalities, like linoleic acid, glycerophospholipid, α-linolenic acid, biosynthesis of unsaturated fatty acids, and

				glycerolipid metabolism.
Tuikhar *et al.* [28]	Centenarians (~100 years) and young adults (25–45 years) from a region with high centenarian prevalence (>6 centenarians/10,000 citizens) and young adults from a nearby region with low centenarian prevalence (<1 centenarian/10,000 citizens)	16S amplicon sequencing	Aging	There was a higher species richness and biodiversity in the family *Ruminococcaceae* in centenarians.
		Metabolite analysis		In centenarians, there was a higher level of compounds with neuro-pharmacological properties like GABA and imidazole 4-acetic acid, as well as azole compounds with antifungal and amebicidal activity, and lower levels of cyclohexanecarboxylic acid as an environmental contaminant in fecal extracts.

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