Supplemental Tables

Table S1: Demographic information of PD patients (N=6) and HC (N=6).

ID	Age	Gender	Race	BMI	PD Duration (Years)	UPDRS*	HY STAGE**	Bowel Habit Score***	Bristol Stool Scale	L-Dopa Dosage Strength	L-Dopa Dosage Frequency****	Medications
PD1	73	Female	Caucasian	27	12	40	2	1	3	25/100	4.5	None
PD2	63	Male	Caucasian	27	2	35	2	3	3	25/100	3	None
PD3	57	Female	Caucasian	18	22	21	2	0	2	25/100	10	None
PD4	55	Male	Caucasian	24	6	27	2	3	3	25/100	8	325mg aspirin daily
PD5	57	Male	Caucasian	24	2	27	2	0	4	None	None	Sertraline 150 mg daily and bupropion XL 300 mg daily
PD6	58	Male	Caucasian	24	4	17	2	1	3	None	None	None
Control1	42	Male	Caucasian	25	-	-	-	-	-	-	-	None
Control2	41	Female	African American	28	-	-	-	-	-	-	-	None
Control3	72	Male	Caucasian	24	-	-	-	-	-	-	-	81mg aspirin daily
Control4	70	Female	Caucasian	23	-	-	-	-	-	-	-	81 mg aspirin daily
Control5	57	Female	Caucasian	22	-	-	-	-	-	-	-	None
Control6	53	Female	Caucasian	25	-	-	-	-	-	-	-	Fluoxetine 20 mg; levothyroxine; methylphenidate 5 mg

*Unified Parkinson Disease Rating Scale, **Hoehn and Yahr Stage, ***Gastrointestinal Symptom Bowel Habit Score: low to high constipation occurrence (0-10): constipation requiring treatment with score of greater than 5; Bristol Stool Scale is a diagnostic medical tool designed to classify the form of human feces into seven categories: Type 1 is severe constipation, type 2 is mild constipation, types 3 and 4 are ideal stools as they are easy to defecate while not containing excess liquid, type 5 lacks fiber, and types 6 and 7 indicate diarrhea; ****Total Number of L-Dopa Tablets consumed per day, BMI = Body Mass Index, PD = Parkinson's disease, (-) = data not collected. Age, gender and BMI did not differ significantly between PD and HC cases. No Probiotics or Antibiotics were taken. PD patients recruited for this study had no clinically significant constipation based on either their Bristol Stool Score (majority scored 3-4) or structured questionnaire - where patients were asked to rate (0=no difficulty; 10=most severe difficulty) regarding their difficulty in Bowel Habit Score [constipation] and none rated difficulty more than 3. Indeed, the only patient who's Bristol Stool Score was 2, rated his Bowel Habit Score as 0. Also, none of the patients took laxatives. We specifically selected these patients to exclude these potential confounding factors.

Table S2. Human study correlations between leaky gut (Percent Sucralose) and other factors.

	Correlations with Percent Sucralose Excretion	*P*-Value	Pearson R
Demographics	Age of Subjects	0.6211	0.159
	BMI of Subjects	0.0809	-0.523
Barrier Impairments	ZO-1 Scoring	0.1777	-0.417
Endotoxin	LBP Levels in Plasma	0.4433	-0.274
Cell Counts	Number of TLR4+ Cells	0.3170	0.316
	Number of CD3+ Cells	0.1219	0.471
Gene Expression	CLD1	0.1152	0.530
	IFNB1	0.0545	0.623
	IFNG	0.0715	0.592
	IL17A	0.0528	0.626
	IL1B	**0.0299**	0.682
	CCL5	0.0702	0.594
	CCR5	**0.0249**	0.698
	IRAK2	0.0817	0.576
	TOLLIP	**0.0231**	-0.704
	TLR4	**0.0305**	0.680
	DSG3	0.0586	0.615
	IL7R	**0.0354**	0.666
	IL8	0.1168	0.528

Table S3. Human study correlations between intestinal barrier dysfunction (ZO-1 scoring data) and other factors.

	Correlations with Percent Sucralose Excretion	*P*-Value	Pearson R
Demographics	Age of Subjects	0.740	-0.107
	BMI of Subjects	0.700	-0.124
Endotoxin	LBP Levels in Plasma	**0.003**	0.831
Cell Counts	Number of TLR4+ Cells	0.142	-0.450
	Number of CD3+ Cells	0.149	-0.442
Gene Expression	CLD1	0.053	-0.626
	IFNB1	**0.014**	-0.741
	IFNG	**0.034**	-0.670
	IL17A	**0.025**	-0.698
	IL1B	**0.016**	-0.734
	CCL5	**0.008**	-0.777
	CCR5	**0.019**	-0.721
	IRAK2	**0.012**	-0.755
	TOLLIP	0.068	0.598
	TLR4	**0.042**	-0.649
	DSG3	**0.0003**	-0.905
	IL7R	**0.009**	-0.769
	IL8	0.090	-0.563

Table S4. List of Log2FoldChange individual short-chain-fatty-acid (SCFA) genera with decreased abundance between healthy control and Parkinson's disease human subjects in both the sigmoid mucosa and feces.

Mucosa Genus SCFA	**Log2FC**	**Abundance Mean, *HC***	**Abundance Mean, *PD***
Dorea	**-2.458917197**	280.4	51
Lachnospira	**-0.789294951**	60.2	34.8
Faecalibacterium	**-0.746547421**	632.8	377.2
Blautia	**-0.40729844**	603.2	454.8
Coprococcus	**-0.372754773**	79.2	61.2
f_Lachnospiraceae.Other	**-0.297115401**	51.4	41.8
f_Lachnospiraceae.g_Unclassified	**-0.295107112**	564	459.7
Roseburia	**-0.171450856**	189.2	168
Feces Genus SCFA	**Log2FC**	**Abundance Mean, *HC***	**Abundance Mean, *PD***
Roseburia	**-1.839383776**	300.6	84
Anaerostipes	**-1.230297619**	24.4	10.4
f_Lachnospiraceae;g_Other	**-0.808270628**	78.8	45
Blautia	**-0.787669034**	666	385.8
Faecalibacterium	**-0.629819571**	1071.4	692.4
Coprococcus	**-0.588685587**	116.4	77.4
f_Lachnospiraceae.g_Unclassified	**-0.450692995**	609	445.6
Lachnospira	**-0.38766106**	34.8	26.6

N=6 subjects/group. (f) = family or (g) = genus taxonomic level. (HC) = healthy control; (PD) = Parkinson's disease. Log2FC = log2 fold change: (abundance mean PD/ abundance mean HC). SCFA = short chain fatty acid.

Table S5. Group analysis of similarity (ANOSIM) results for cecum mucosa and cecum content.

Comparisons	**Taxonomic level**	**Global *R***	***P*-value**
Cecum Mucosa			
WT.Vehicle vs. WT.Rotenone	Genus	0.664	**0.001**
TLR4KO.Vehicle vs. TLR4KO.Rotenone	Genus	0.760	**0.001**
WT.Vehicle vs. TLR4KO.Vehicle	Genus	0.580	**0.001**
WT.Rotenone vs. TLR4KO.Rotenone	Genus	0.364	**0.001**
Cecum Content			
WT.Vehicle vs. WT.Rotenone	Genus	0.512	**0.001**
TLR4KO.Vehicle vs. TLR4KO.Rotenone	Genus	0.870	**0.001**
WT.Vehicle vs. TLR4KO.Vehicle	Genus	0.531	**0.001**
WT.Rotenone vs. TLR4KO.Rotenone	Genus	0.206	**0.012**

P-value = $P < 0.05$; Global *R* comparison was based on ANOSIM performed within the software package Primer7; *P*-values were calculated based on a permutational analysis, employing 999 permutations; square-root transformation.