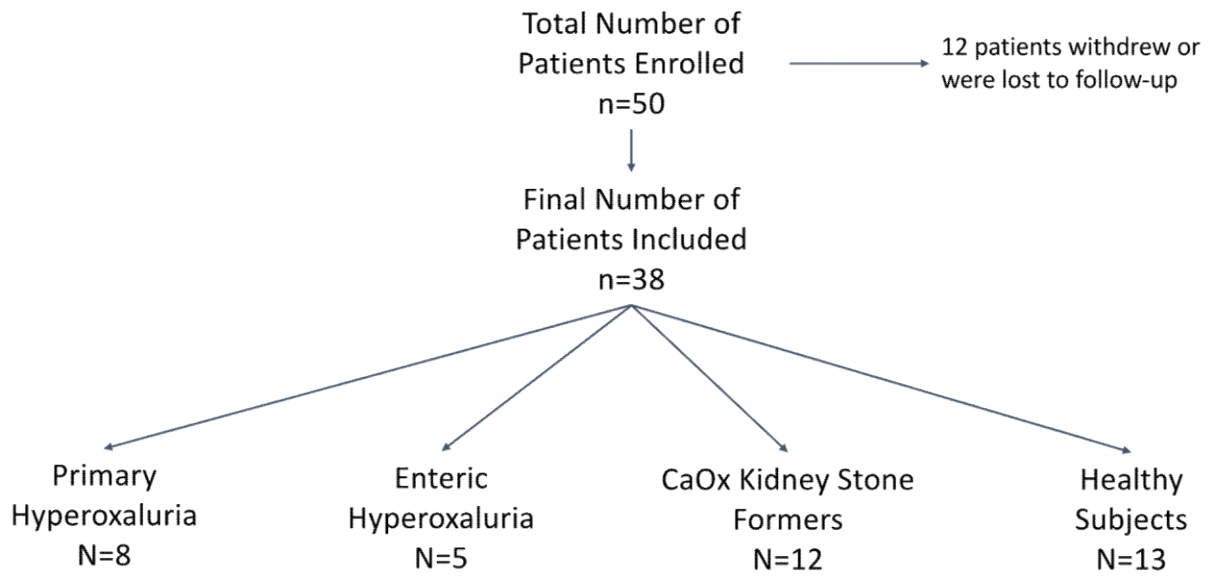
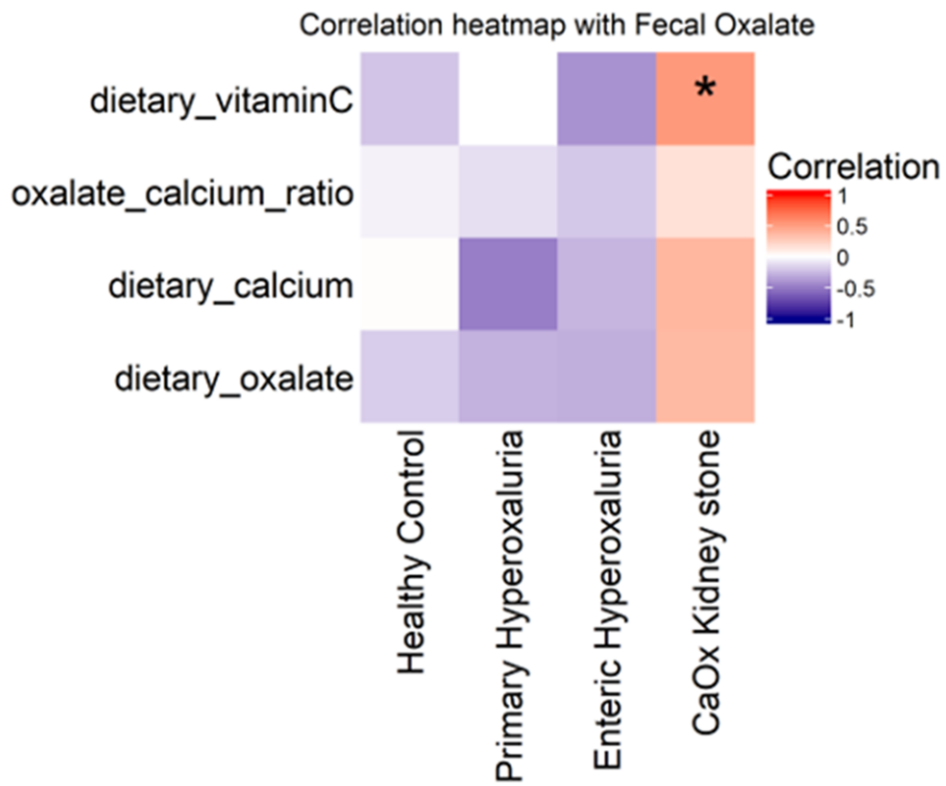


Supplementary Figure 1: Study enrolment by clinical group.

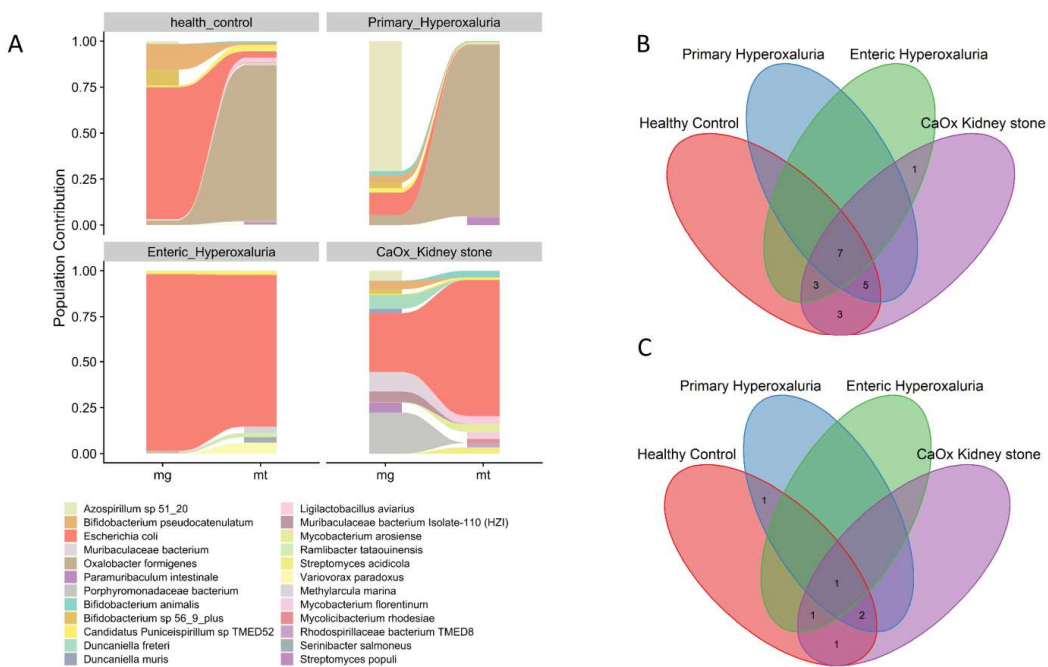


Supplementary Figure 2: Correlation between dietary component and fecal oxalate



This correlation vary between different subgroups. The Pearson correlation coefficient is used. * pvalue < 0.1

Supplementary Figure 3: Population Level Contribution of the OXC ODE

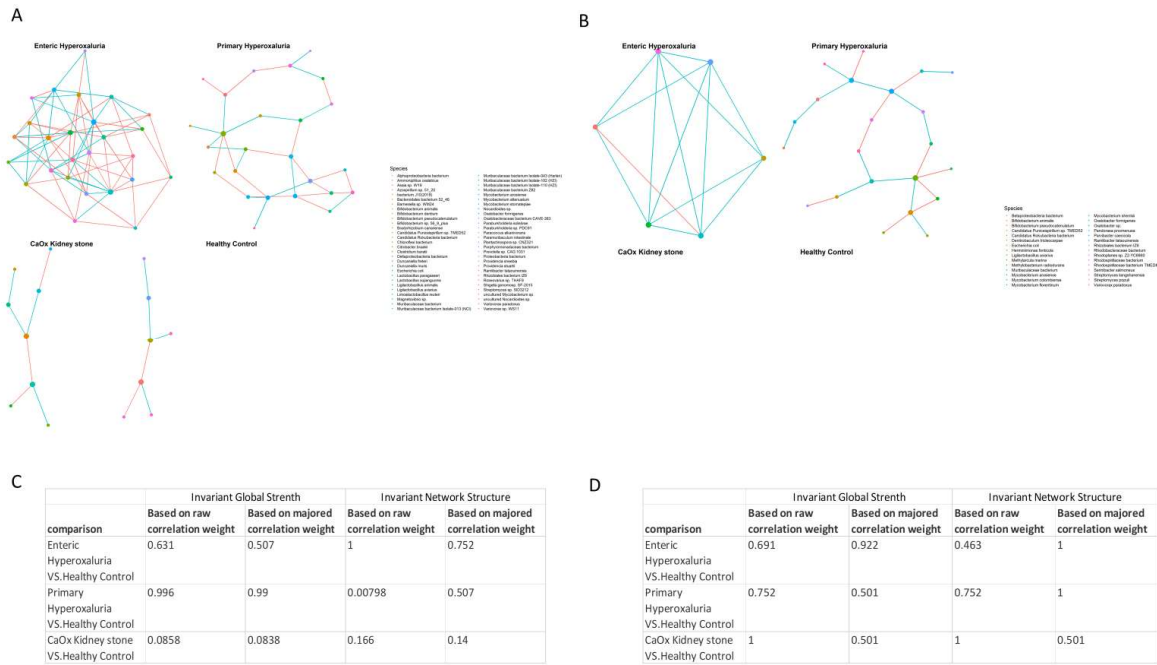


Panel A: Population Level Contribution based on OXC metagenomic (MTG) and metatranscriptomic (MTT) level of activity

Panel B: Gamma diversity of the oxalobiome based on MG_OXC

Panel C: Gamma diversity of the oxalobiome based on MT_OXC

Supplementary Figure 4: Oxalate-Degrading Bacterial Network based on OXC Levels



Panel A: Oxalate-degrading bacterial interaction network based on the MTG abundance of OXC

Panel B: Oxalate-degrading bacterial interaction network based on the MTT abundance of OXC

Panel C: Network comparison in the MTG based OXC networks

Panel D: Network comparison in the MTT based OXC networks

A correlation cut-off of 0.2 is used for graphical representation. Red edge is a

negative correlation and a blue edge is a positive correlation. Network comparisons are summarized

in a table of p-values, using two metrics with two types of comparison, one involving the raw

correlation value and the other a majored value.

Supplementary Tables

Supplementary Table	1	24h Urinalysis
Supplementary Table	2	Group comparisons of clinical outcomes: PH vs HC
Supplementary Table	3	Group comparisons of clinical outcomes: EH vs HC
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Supplementary Tables 7 to 10 : node betweenness and degree for every species involved in the network

Supplementary Table	7	MTG_FRC_EH
Supplementary Table	8	MTG_FRC_PH
Supplementary Table	9	MTT_FRC_EH
Supplementary Table	10	MTT_FRC_PH

Abbreviations

MTG	Metagenomics Dataset
MTT	Metatranscriptomics Dataset
OXC	Oxalyl-CoA decarboxylase
FRC	Formyl-CoA: oxalate CoA transferase
PH	Primary Hyperoxaluria
EH	Enteric Hyperoxaluria
CKS	CaOx Kidney stone Formers
HC	Healthy controls

Supplementary Table 1

Condition	EH	CKS	PH	ANOVA p-value
24 hr urine volume (L/24 hr)	1.64	2.53	4.48	0.01
24 hr calcium results (mg/24 hr)	111	185.67	135.99	0.27
24 hr citrate results (mg/24 hr)	526.98	493	399.29	0.73
24 hr potassium results (mmol/24 hr)	53.6	51.1	82	0.15
24 hr sodium results (mmol/24 hr)	168.8	147.11	184.57	0.61
pH level	5.92	6.22	6.3	0.43
CaOx SS	2.38	3.65	3	0.56

Supplementary Table 2

Group comparisons of clinical outcomes: Primary Hyperoxaluria vs Healthy Control

	HC (N=13)	PH (N=8)	P-value
Age			
Mean (SD)	39.1 (11.8)	33.0 (13.6)	0.316
Median [Min, Max]	34.0 [24.0, 58.0]	29.0 [21.0, 63.0]	
Sex			
Female / Male	7 (53.8%) / 6 (46.2%)	6 (75.0%) / 2 (25.0%)	0.4
Ethnicity			
Hispanic or Latino	2 (15.4%)	0 (0%)	0.505
not Hispanic or Latino	11 (84.6%)	8 (100%)	
Race			
White	11 (84.6%)	6 (75.0%)	0.713
More than one / unknown / unreported	2 (15.4%)	1 (12.5%)	
American Indian	0 (0%)	1 (12.5%)	
Height			
Mean (SD)	166 (10.5)	170 (4.60)	0.325
Median [Min, Max]	168 [151, 186]	169 [166, 176]	
Missing	1 (7.7%)	2 (25.0%)	
Weight			
Mean (SD)	70.4 (13.7)	72.3 (8.40)	0.71
Median [Min, Max]	73.7 [46.0, 94.3]	71.6 [61.2, 84.8]	
Missing	1 (7.7%)	2 (25.0%)	
BMI			
Mean (SD)	25.2 (3.43)	24.9 (1.76)	0.809
Median [Min, Max]	25.4 [19.9, 31.5]	25.0 [22.2, 27.6]	
Missing	1 (7.7%)	2 (25.0%)	
dietary_calcium			
Mean (SD)	1160 (629)	1320 (464)	0.535
Median [Min, Max]	1010 [541, 2520]	1290 [666, 1970]	
Missing	1 (7.7%)	1 (12.5%)	
dietary_oxalate			
Mean (SD)	236 (316)	333 (323)	0.537
Median [Min, Max]	134 [103, 1230]	159 [110, 967]	
Missing	1 (7.7%)	1 (12.5%)	
oxalate_calcium_ratio			
Mean (SD)	0.228 (0.233)	0.250 (0.196)	0.828
Median [Min, Max]	0.132 [0.0721, 0.853]	0.118 [0.0805, 0.579]	
Missing	1 (7.7%)	1 (12.5%)	
dietary_vitaminC			
Mean (SD)	80.4 (37.6)	152 (61.5)	0.0225
Median [Min, Max]	71.5 [41.1, 173]	155 [39.5, 233]	
Missing	1 (7.7%)	1 (12.5%)	
fecal_Oxalate			
Mean (SD)	0.240 (0.0944)	0.998 (0.140)	<0.001
Median [Min, Max]	0.261 [0.106, 0.421]	1.01 [0.785, 1.18]	
oxalate_urine			
Mean (SD)	31.9 (7.73)	99.9 (57.0)	0.0118
Median [Min, Max]	34.4 [12.2, 39.7]	80.8 [64.0, 235]	

Supplementary Table 3

Group comparisons of clinical outcomes: Enteric Hyperoxaluria vs Healthy Control

	EH (N=5)	HC (N=13)	P-value
Age			
Mean (SD)	55.6 (14.5)	39.1 (11.8)	0.0623
Median [Min, Max]	53.0 [39.0, 72.0]	34.0 [24.0, 58.0]	
Sex			
Female / Male	4 (80.0%) / 1 (20.0%)	7 (53.8%) / 6 (46.2%)	0.596
Ethnicity			
not Hispanic or Latino	5 (100%)	11 (84.6%)	1
Hispanic or Latino	0 (0%)	2 (15.4%)	
Race			
White	5 (100%)	11 (84.6%)	1
More than one / unknown / unreported	0 (0%)	2 (15.4%)	
Height			
Mean (SD)	167 (7.82)	166 (10.5)	0.993
Median [Min, Max]	163 [160, 177]	168 [151, 186]	
Missing	0 (0%)	1 (7.7%)	
Weight			
Mean (SD)	99.4 (19.6)	70.4 (13.7)	0.0252
Median [Min, Max]	104 [67.7, 121]	73.7 [46.0, 94.3]	
Missing	0 (0%)	1 (7.7%)	
BMI			
Mean (SD)	35.7 (5.88)	25.2 (3.43)	0.0127
Median [Min, Max]	38.0 [25.6, 40.4]	25.4 [19.9, 31.5]	
Missing	0 (0%)	1 (7.7%)	
dietary_calcium			
Mean (SD)	1250 (426)	1160 (629)	0.757
Median [Min, Max]	1150 [851, 1850]	1010 [541, 2520]	
Missing	1 (20.0%)	1 (7.7%)	
dietary_oxalate			
Mean (SD)	331 (275)	236 (316)	0.587
Median [Min, Max]	222 [143, 736]	134 [103, 1230]	
Missing	1 (20.0%)	1 (7.7%)	
oxalate_calcium_ratio			
Mean (SD)	0.275 (0.232)	0.228 (0.233)	0.736
Median [Min, Max]	0.176 [0.130, 0.620]	0.132 [0.0721, 0.853]	
Missing	1 (20.0%)	1 (7.7%)	
dietary_vitaminC			
Mean (SD)	133 (152)	80.4 (37.6)	0.544
Median [Min, Max]	68.8 [33.5, 359]	71.5 [41.1, 173]	
Missing	1 (20.0%)	1 (7.7%)	
fecal_Oxalate			
Mean (SD)	0.932 (0.117)	0.240 (0.0944)	<0.001
Median [Min, Max]	0.914 [0.813, 1.12]	0.261 [0.106, 0.421]	
oxalate_urine			
Mean (SD)	62.5 (12.7)	31.9 (7.73)	0.00357
Median [Min, Max]	59.0 [47.5, 79.2]	34.4 [12.2, 39.7]	

Supplementary Table 4

Group comparisons of clinical outcomes: CaOx Kidney stone vs Healthy Control

	CKS (N=12)	HC (N=13)	P-value
Age			
Mean (SD)	47.5 (13.8)	39.1 (11.8)	0.117
Median [Min, Max]	51.0 [25.0, 67.0]	34.0 [24.0, 58.0]	
Sex			
Male			
Ethnicity			
Hispanic or Latino	1 (8.3%)	2 (15.4%)	1
not Hispanic or Latino	11 (91.7%)	11 (84.6%)	
Race			
More than one / unknown / unreported	2 (16.7%)	2 (15.4%)	1
White	10 (83.3%)	11 (84.6%)	
Height			
Mean (SD)	174 (8.62)	166 (10.5)	0.0625
Median [Min, Max]	175 [162, 186]	168 [151, 186]	
Missing	0 (0%)	1 (7.7%)	
Weight			
Mean (SD)	83.5 (21.2)	70.4 (13.7)	0.0875
Median [Min, Max]	78.0 [52.2, 120]	73.7 [46.0, 94.3]	
Missing	0 (0%)	1 (7.7%)	
BMI			
Mean (SD)	27.2 (5.43)	25.2 (3.43)	0.294
Median [Min, Max]	25.9 [19.4, 39.6]	25.4 [19.9, 31.5]	
Missing	0 (0%)	1 (7.7%)	
dietary_calcium			
Mean (SD)	1300 (742)	1160 (629)	0.626
Median [Min, Max]	1190 [494, 3020]	1010 [541, 2520]	
Missing	0 (0%)	1 (7.7%)	
dietary_oxalate			
Mean (SD)	212 (167)	236 (316)	0.821
Median [Min, Max]	190 [49.7, 619]	134 [103, 1230]	
Missing	0 (0%)	1 (7.7%)	
oxalate_calcium_ratio			
Mean (SD)	0.184 (0.144)	0.228 (0.233)	0.59
Median [Min, Max]	0.141 [0.0532, 0.553]	0.132 [0.0721, 0.853]	
Missing	0 (0%)	1 (7.7%)	
dietary_vitaminC			
Mean (SD)	156 (129)	80.4 (37.6)	0.0729
Median [Min, Max]	129 [14.0, 371]	71.5 [41.1, 173]	
Missing	0 (0%)	1 (7.7%)	
fecal_Oxalate			
Mean (SD)	0.742 (0.192)	0.240 (0.0944)	<0.001
Median [Min, Max]	0.687 [0.434, 1.12]	0.261 [0.106, 0.421]	
oxalate_urine			
Mean (SD)	33.8 (12.2)	31.9 (7.73)	0.655
Median [Min, Max]	34.8 [12.3, 52.0]	34.4 [12.2, 39.7]	

Supplementary Table 5

q-value across 6 pairwise comparisons based on BH correction

		EH vs. PH	EH vs. CKS	EH vs. HC	PH vs. CKS	PH vs. HC	CKS vs. HC
	Age	0.105	0.322	0.125	0.105	0.322	0.176
	Sex	1	0.509	0.715	0.509	0.642	0.642
	Ethnicity	1	1	1	1	1	1
	Race	1	1	1	1	1	1
Body Measures	Height (cm)	0.48	0.329	0.993	0.414	0.48	0.329
	Weight (kg)	0.1	0.211	0.1	0.198	0.71	0.175
	BMI	0.038	0.055	0.038	0.303	0.809	0.353
Nutritional Data	Dietary Calcium (mg)	0.939	0.939	0.939	0.939	0.939	0.939
	Dietary Oxalate (mg)	0.991	0.881	0.881	0.881	0.881	0.985
	Ox/Ca Ratio	0.859	0.859	0.859	0.859	0.859	0.859
	Dietary Vitamin C	0.919	0.919	0.919	0.919	0.135	0.219
Outcomes	Fecal Oxalate (uM/mg)	0.383	0.034	3.82E-05	0.004	2.02E-07	1.40E-06
	Urinary Oxalate (mg/24hr)	0.134	0.011	0.011	0.02	0.02	0.655

Supplementary Table 6

Gamma diversity - Venn Diagram Taxa

	FRC	MTG	OXC	FRC	MTT	OXC
EH:PH	Betaproteobacteria bacterium RIFCSPLOWO2_12_FULL _68_20	NA	NA	NA	NA	NA
EH:CKS	NA	Paramuribaculum intestinale	NA	NA	NA	NA
EH:HC	NA	NA	NA	NA	NA	NA
PH:CKS	NA	NA	NA	NA	NA	NA
PH:HC	Filomicrobium sp.	NA	Betaproteobacteria bacterium RIFCSPLOWO2_02_FULL _62_17; Muribaculaceae bacterium; Muribaculaceae bacterium Z82	Oxalobacter formigenes		
CKS:HC	Adlercreutzia mucosicola; Azospirillum brasilense; Bifidobacterium magnum; Ligilactobacillus aviarius; Muribaculaceae bacterium Isolate-002 (NCI); Paraburkholderia megapolitana; Streptomyces violaceusniger	Ligilactobacillus aviarius; Mycobacterium arosiense; Streptomyces sp. SID3212	NA	Ligilactobacillus aviarius		
EH:PH:CKS	Pseudonocardia kunmingensis	NA	Ammoniphilus oxalaticus	NA		
EH:PH:HC	Acidobacteria bacterium; Starkeya novella; Sulfobacillus acidophilus	NA	NA	NA	NA	NA

	FRC	MTG	OXC	FRC	MTT	OXC
EH:CKS:HC	Actinophytocola sp.;					
	Bacteroides sp. CAG:927;					
	mine drainage					
	metagenome;					
	Paramuribaculum					
	intestinale;					
	Porphyromonadaceae	Muribaculaceae				
	bacterium;	bacterium;				
	Pseudonocardiaceae	Porphyromonadaceae				
	bacterium;	bacterium; Prevotella sp.				
Streptomyces sp. AZ1-7	CAG:1031		NA		Escherichia coli	
				Azospirillum sp. 51_20;		
				Betaproteobacteria		
				bacterium;		
				Betaproteobacteria		
				bacterium UKL13-2;		
				Bifidobacterium		
				pseudocatenulatum;		
				Candidatus		
Bifidobacterium	Ammoniphilus			Entotheonella factor;		
pseudocatenulatum;	oxalaticus; Azospirillum			Ephemera danica;		
Bifidobacterium sp.	sp. 51_20;			Oxalobacter formigenes;		
56_9_plus; Kribbella	Bifidobacterium			Porphyromonadaceae		
flavida; Lentzea deserti;	pseudocatenulatum;			bacterium; Providencia	Bifidobacterium	
Muribaculaceae	Bifidobacterium sp.			rettgeri;	animalis;	
bacterium; Providencia	56_9_plus;			Rhodospirillaceae	Mycobacterium	
stuartii; Streptomyces	Deltaproteobacteria			bacterium	arosiense	
luteus	bacterium					
PH:CKS:HC						

Supplementary Table 7

MG_FRC_EH

Species	Node Betweenness	Node Degree
Ligilactobacillus animalis	50.385	22
Pseudonocardiaceae bacterium	49.231	21
Caballeronia grimmiae	48.676	24
Actinophytocola sp.	47.121	24
Streptomyces scopuliridis	42.035	20
Halopolyspora algeriensis	40.626	20
Limosilactobacillus mucosae	38.008	18
Paraburkholderia caballeronis	36.043	19
Nonomuraea polychroma	33.761	19
Alphaproteobacteria bacterium	33.148	17
Streptomyces sp. AZ1-7	32.721	20
bacterium D16-34	32.709	18
Nocardiopsis sinuspersici	30.919	17
Bifidobacterium dentium	29.941	18
Kibdelosporangium sp. MJ126-NF4	29.814	19
Afipia sp. 64-13	27.244	15
Starkeya novella	26.994	17
Oxalobacter formigenes	26.287	18
Bacteroides sp. CAG:927	26.208	14
Porphyromonadaceae bacterium	24.911	15
Pigmentiphaga sp. NML080357	24.376	15
Burkholderiales bacterium	24.334	15
Amycolatopsis suaedae	24.239	16
Paraburkholderia sp. SOS3	23.754	16
Mycobacterium sp. SWH-M5	23.631	16
Sulfobacillus acidophilus	23.171	17
Barnesiella sp. WM24	22.059	15
Enterobacter cancerogenus	21.841	14
Thermostaphylospora chromogena	21.289	15
Cupriavidus basilensis	20.904	16
Pandoraea thiooxydans	20.783	15
Betaproteobacteria bacterium RIFCSPLOWO2_12_FULL_68_20	20.702	14
Roseovarius sp. A-2	20.072	13
mine drainage metagenome	19.904	13
Nonomuraea terrae	19.746	16
Muribaculaceae bacterium Isolate-036 (Harlan)	19.084	13
Cupriavidus sp. OV038	18.958	14
Inquilinus limosus	18.860	14
Candidatus Entotheonella factor	18.178	15
Cupriavidus gilardii	17.443	12
Azospirillum sp. 51_20	17.141	14
Mycolicibacterium sp. P9-64	16.186	13
Providencia rettgeri	15.802	13
Mycobacterium sherrisii	15.518	14
bacterium MnTg02	15.263	13
Mycobacterium sp. BK086	14.775	12
Streptomyces sp. 8K308	14.161	12
Bradyrhizobium huanghuaihaiense	13.781	13
Acidobacteria bacterium	13.746	12

Pseudonocardia kunmingensis	13.552	12
Escherichia coli	12.741	14
Candidatus Muproteobacteria bacterium RBG_16_60_9	12.571	9
Deltaproteobacteria bacterium	12.529	11
Streptomyces glauciniger	12.506	12
Gammaproteobacteria bacterium	11.279	11
Bifidobacterium pseudolongum	11.185	12
Bifidobacterium sp.	10.795	12
Paramuribaculum intestinale	9.135	8
alpha proteobacterium BAL199	9.061	11
Streptomyces populi	7.013	12
Betaproteobacteria bacterium	6.148	9

Supplementary Table 8

MG_FRC_PH

Species	Node Betweenness	Node Degree
Cupriavidus basilensis	214.571	14
Lentzea guizhouensis	155.302	12
Labrys okinawensis	153.866	11
Pandoraea thiooxydans	135.922	11
Bifidobacterium sp. 56_9_plus	135.181	10
Pseudonocardia kunmingensis	112.028	10
Streptomyces glauciniger	110.537	10
Cupriavidus sp. OV038	105.632	9
Acrocarpospora macrocephala	99.763	8
Caballeronia glebae	99.292	7
Azorhizobium caulinodans	97.551	9
Nonomuraea terrae	79.294	7
Streptomyces luteus	77.998	7
Alphaproteobacteria bacterium	75.355	8
Sulfobacillus acidophilus	75.211	5
Chloroflexi bacterium	71.307	9
Muribaculaceae bacterium Isolate-036 (Harlan)	69.820	8
Bifidobacterium sp.	67.908	7
Muribaculaceae bacterium Z82	63.266	7
Alphaproteobacteria bacterium MarineAlpha3_Bin4	59.248	8
Betaproteobacteria bacterium RIFCSPLOWO2_12_FULL_68_20	58.176	6
Deltaproteobacteria bacterium	56.305	6
Nocardiopsaceae bacterium YIM 96095	53.187	8
Bifidobacterium pseudocatenulatum	52.204	7
Caballeronia grimmiae	51.893	7
Cupriavidus gilardii	49.216	7
Streptomonospora sp. M2	48.445	6
Ammoniphilus oxalaticus	44.581	6
Providencia huaxiensis	44.453	6
Kribbella flavida	43.554	7
Rhodospirillales bacterium	41.072	5
Pseudaestuariaiivita atlantica	38.776	7
Gammaproteobacteria bacterium	38.329	6
Lentzea deserti	36.672	4
Nocardiopsis sinuspersici	35.086	6
Nonomuraea sp. C10	34.982	6
Limosilactobacillus reuteri	28.408	6
Limosilactobacillus equigenerosi	27.792	6
Magnetovibrio sp.	27.715	6
Providencia stuartii	26.022	5
Bifidobacterium pseudolongum	25.567	5
Bifidobacterium animalis	24.921	5
Oxalobacter formigenes	22.883	4
Methylobacterium sp. B4	21.419	6
Pigmentiphaga sp. NML080357	19.664	6
Bifidobacterium cuniculi	19.242	5
Xanthobacter tagetidis	19.067	5
bacterium D16-34	14.114	3
Usitatibacter palustris	13.838	4

Escherichia coli	13.361	4
Bradyrhizobium huanghuaihaiense	11.304	3
Actinoplanes sp. ATCC 53533	10.971	3
Filomicrobium sp.	7.575	3
Mycobacterium sherrisii	7.416	3
Azospirillum sp. 51_20	6.331	3
Acidobacteria bacterium	5.665	3
Candidatus Paraburkholderia sp. 4M-K11	5.541	3
Betaproteobacteria bacterium	5.450	3
Mycobacterium sp. SWH-M5	4.335	3
Mangrovibacter sp. MFB070	2.729	2
Amycolatopsis suaedae	1.912	2
Gemmatimonadetes bacterium	1.350	2
Muribaculaceae bacterium	0.425	2
Caballeronia calidae	0.000	1
Starkeya novella	0.000	1

Supplementary Table 9

MT_FRC_EH

Species	Node Betweenness	Node Degree
Collimonas fungivorans	0.533	7
Escherichia coli	0.367	6
Ammoniphilus oxalaticus	0.367	6
Hyphomicrobiales bacterium	0.200	5
Streptomyces sp. 8K308	0.200	6
Cupriavidus basilensis	0.167	5
Streptomyces phaeoluteigriseus	0.167	5

Supplementary Table 10

MT_FRC_PH

Species	Node Betweenness	Node Degree
Oxalobacter formigenes	169.705	9
Adlercreutzia muris	153.511	6
Ephemera danica	145.255	7
Acidobacteria bacterium RIFCSPLOWO2_02_FULL_67_21	144.806	7
Streptomyces hainanensis	87.375	8
Rhodospirillales bacterium URHD0017	75.558	5
Betaproteobacteria bacterium UKL13-2	72.422	4
Ancylobacter rudongensis	69.657	7
Mesorhizobium camelthorni	69.464	4
Betaproteobacteria bacterium RIFCSPLOWO2_12_FULL_64_23	63.669	4
Labrys okinawensis	62.961	5
Muribaculaceae bacterium Z82	61.660	4
Amycolatopsis saalfeldensis	59.712	5
Betaproteobacteria bacterium RIFCSPLOWO2_02_FULL_63_19	58.742	5
Bifidobacterium pseudocatenulatum	58.338	3
Muribaculaceae bacterium	57.345	5
Escherichia coli	56.652	5
Streptomyces sp. IB201691-2A2	53.226	6
Caballeronia hypogeia	52.694	4
Betaproteobacteria bacterium RIFCSPLOWO2_02_FULL_62_17	52.440	4
Azospirillum sp. 51_20	51.172	5
Methylobacterium sp. AMS5	50.829	5
Nocardiopsis flavescens	50.279	4
Bacteroides sp. CAG:927	49.506	4
Acidobacteria bacterium	40.570	4
Rhizobiales bacterium 62-47	40.542	4
Massilia umbonata	36.627	4
Providencia rettgeri	35.322	5
Betaproteobacteria bacterium	30.763	4
Rhizobiales bacterium 12-68-15	27.438	3
Gammaproteobacteria bacterium	25.098	4
Candidatus Entothionella factor	25.047	3
Polynucleobacter paneuropaeus	22.010	4
Betaproteobacteria bacterium RIFCSPLOWO2_12_FULL_65_14	21.304	2
Acidobacteria bacterium RIFCSPLOWO2_12_FULL_67_14b	18.960	2
Cupriavidus nantongensis	18.076	3
Cupriavidus basilensis	14.267	3
Paramuribaculum intestinale	11.388	3
Ligilactobacillus animalis	9.708	2
Porphyromonadaceae bacterium	7.337	2
Paracoccus saliphilus	7.167	2
Rhodospirillaceae bacterium	6.429	4
Rhodospirillales bacterium	6.376	2
Usitatibacter rugosus	5.408	2
Proteobacteria bacterium	4.483	2
Bifidobacterium criceti	3.700	2
Bifidobacterium pseudolongum	0.000	2
Silicimonas algicola	0.000	1
Ammoniphilus oxalaticus	0.000	2