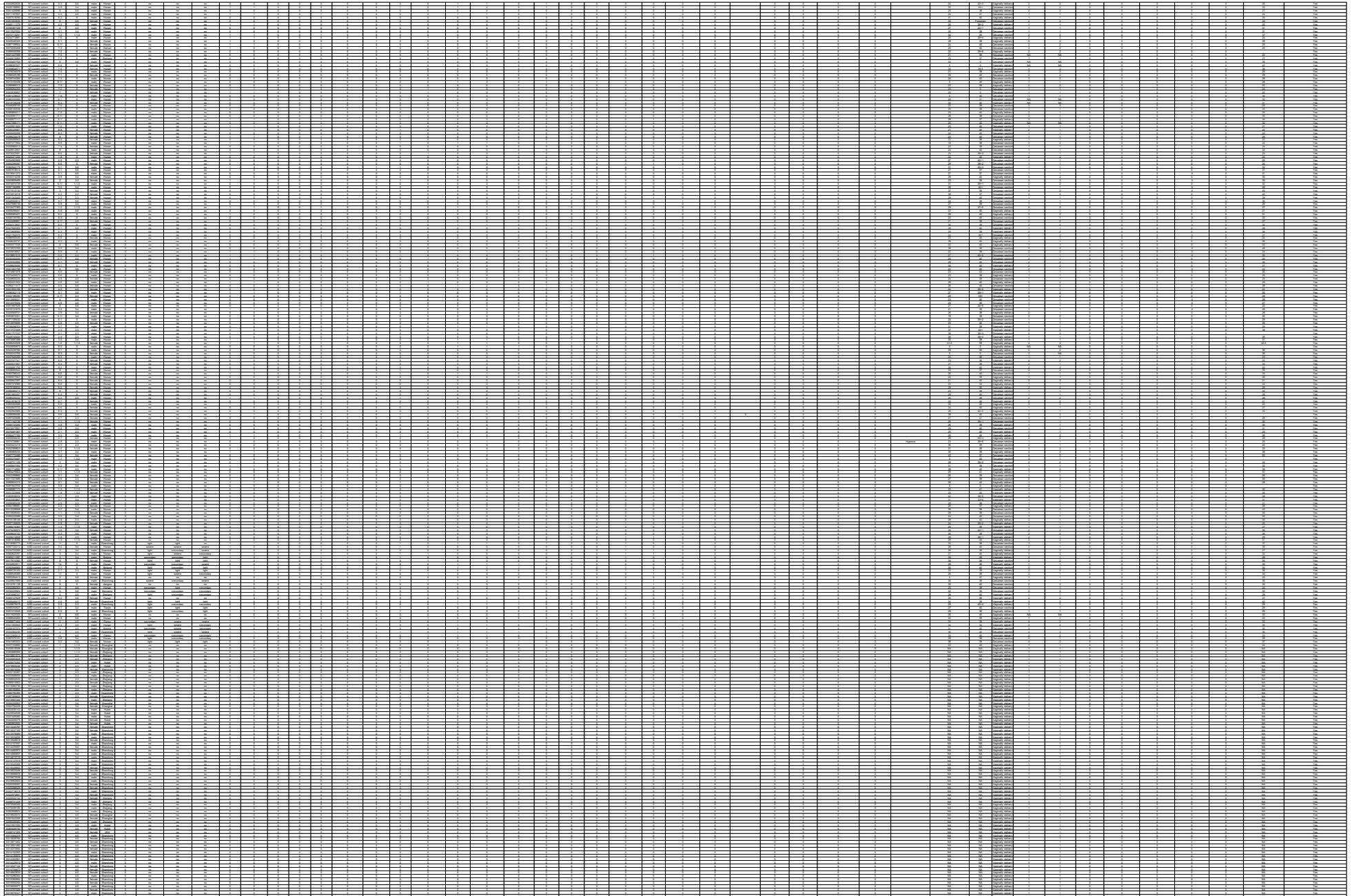
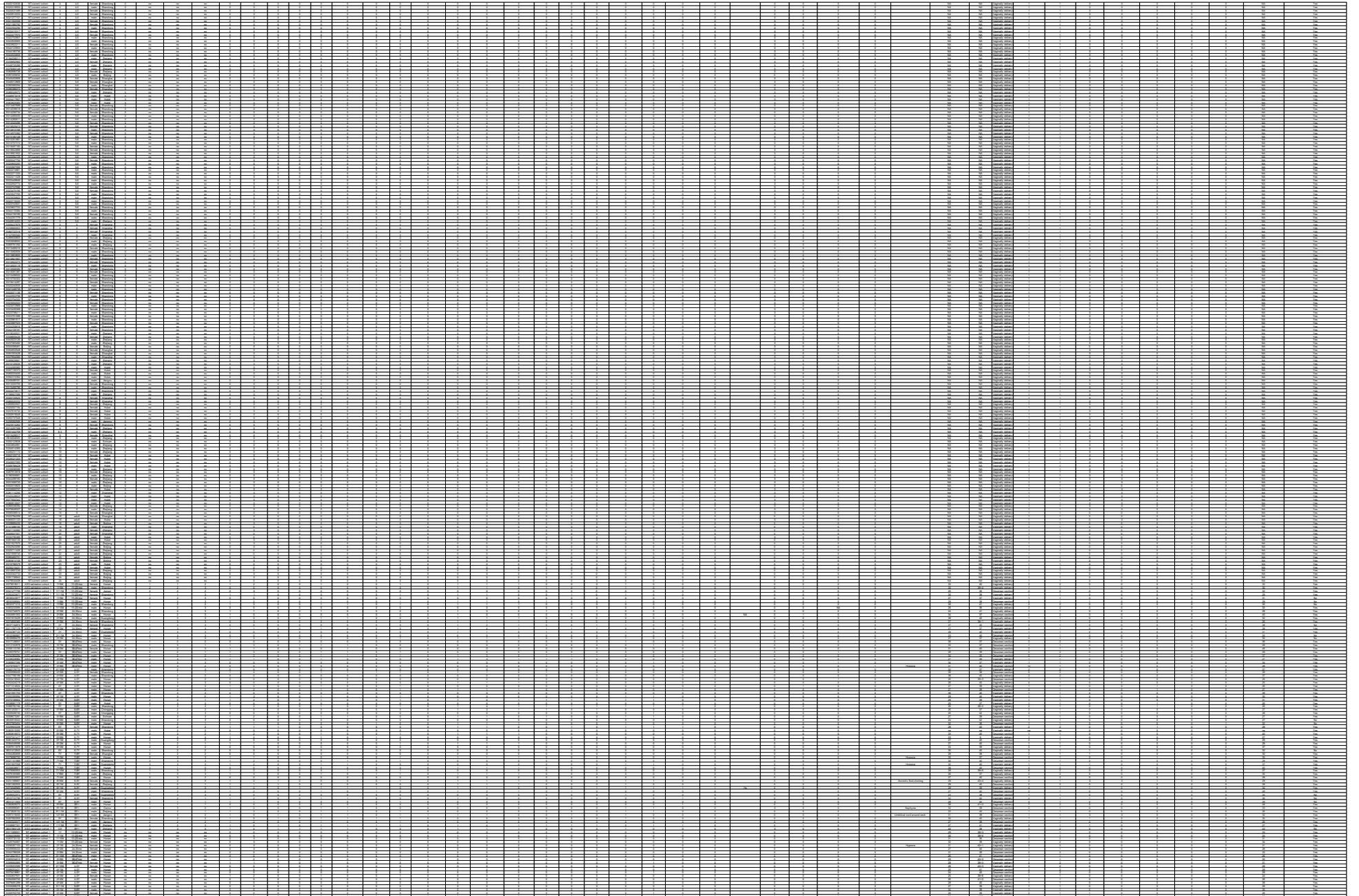


Figure S1  
Taxonomic composition of the gut microbiome in the study population. The table displays the relative abundance of bacterial taxa at various taxonomic levels across the study population. The columns represent different taxonomic levels, and the rows represent individual bacterial taxa. The table is organized into several hierarchical groups, including Kingdom, Phylum, Class, Order, Family, Genus, and Species. The taxa are listed in ascending order of relative abundance within each group. The table contains a large number of rows, each representing a different bacterial taxon, and columns representing the relative abundance of that taxon across the study population. The data is presented in a grid format, with the first column listing the taxonomic level and the subsequent columns listing the relative abundance for each taxon. The table is a comprehensive overview of the bacterial composition of the gut microbiome in the study population.



The image displays a large, dense grid of data, likely a heatmap or a table of values. The grid is composed of many small cells, with a vertical column of text on the right side. The text in this column appears to be a list of identifiers or labels, possibly corresponding to the rows of the grid. The overall appearance is that of a complex data visualization or a detailed table of results.







<b>Table 2 Summary of subject's distributions according to age categories</b>			
Current cohort	<b>age brackets (y)</b>	<b>ASD</b>	<b>NT</b>
	1-1.5	11	16
	1.5-2	14	3
	2-3	128	40
	3-4	179	70
	4-5	134	63
	5-6	152	75
	6-7Y	34	65
	7-8Y	40	33
	8-9Y	29	29
	9-12Y	39	28
	12-15Y	9	8
	adult	3	20
	total	772	450
Validation cohort 1	<b>age brackets</b>	<b>ASD</b>	<b>NT</b>
	11-23 mo	8	4
	24-35mo	9	3
	36-47mo	8	3
	4-5Y	9	6
	5-6Y	8	5
	6-7Y	8	4
	7-8Y	8	3
	8-9Y	7	4
	9Y~	8	none
	total	73	32

**Table 3 Identification of severity levels for autism spectrum disorder based on DSM-IV and DSM-V**

	Social communication	Restricted, repetitive behaviors	Language development delay
Mild	Requiring support. Without supports in place, deficits in social communication cause noticeable impairments. Difficulty initiating social interactions, and clear examples of atypical or unsuccessful response to social overtures of others. May appear to have decreased interest in social interactions.	Requiring support. Inflexibility of behavior causes significant interference with functioning in one or more contexts. Difficulty switching between activities. Problems of organization and planning hamper independence.	Difficulty in putting words together into a sentence or leaving words out of a sentence.
Moderate	Requiring substantial support. Marked deficits in verbal and nonverbal social communication skills; social impairments apparent even with supports in place; limited initiation of social interactions; and reduced or abnormal responses to social overtures from others.	Requiring substantial support. Inflexibility of behavior, difficulty coping with change, or other restricted/repetitive behaviors appear frequently enough to be obvious to the casual observer and interfere with functioning in a variety of contexts. Distress and/or difficulty changing focus or action.	Imitation, just babbling or inability to speak in short sentences.
Severe	Requiring very substantial support. Severe deficits in verbal and nonverbal social communication skills cause severe impairments in functioning, very limited initiation of social interactions, and minimal response to social overtures from others.	Requiring very substantial support. Inflexibility of behavior, extreme difficulty coping with change, or other restricted/repetitive behaviors markedly interfere with functioning in all spheres. Great distress/difficulty changing focus or action.	Language only for needs or not talking.

Table 4 Summary of <b>subject's distributions</b> according to district categories			
<b>Current cohort</b>	<b>Region</b>	<b>ASD</b>	<b>NT</b>
	Hunan	285	198
	Guandong	104	2
	Shandong	65	120
	Beijing	56	10
	Sichuan	36	1
	Hubei	28	33
	Shanghai	25	25
	Zhejiang	24	57
	Jiangsu	20	3
	Jiangxi	18	0
	Shanxi	15	0
	Hebei	13	0
	Chongqing	11	0
	Tianjin	11	0
	Xinjiang	11	0
	Anhui	9	0
	Henan	9	0
	Gansu	6	0
	Guanxi	5	0
	Fujian	4	0
	Hainan	4	1
	Liaoning	4	0
Neimeng	4	0	
Guizhou	3	1	
Jilin	2	0	
<b>Validation cohort 1</b>	<b>Region</b>	<b>ASD</b>	<b>NT</b>
	Hunan	31	32
	Shandong	20	0
	Guandong	6	0
	Zhejiang	6	0
	Chongqing	2	0
	Hubei	2	0
	Jiangsu	2	0
	Gansu	1	0
	Jiangxi	1	0
	Shanghai	1	0
	Sichuan	1	0

Table5 Alpha diversity under different under different parameters						
shannon	20 adults	5.73 ± 0.756	p value	Adults vs. NT	Adults vs. ASD	NT vs. ASD
	NT	5.4206 ± 1.14		0.4691	0.0007	<0.0001
	ASD	4.77 ± 1.16				
simpson	20 adults	0.94 ± 0.04	p value	Adults vs. NT	Adults vs. ASD	NT vs. ASD
	NT	0.91 ± 0.09		0.3992	0.0141	<0.0001
	ASD	0.87 ± 0.12				
chao1	20 adults	2355.07 ± 1274.39	p value	Adults vs. NT	Adults vs. ASD	NT vs. ASD
	NT	2977.13 ± 1583.84		0.1283	0.9587	<0.0001
	ASD	2267.15 ± 1294.37				
ace	20 adults	2394.17 ± 1329.29	p value	Adults vs. NT	Adults vs. ASD	NT vs. ASD
	NT	3052.70 ± 1630.33		0.1118	0.9717	<0.0001
	ASD	2319.87 ± 1319.99				
goods_coverage	20 adults	99.51% ± 0.33%	p value	NA		
	NT	99.35% ± 0.39%				
	ASD	99.55% ± 0.29%				

Shannon index				
	NT		ASD	
	mean	sd	mean	sd
0-16mo	4.759399451	1.359547967	3.836082927	0.964003457
16-18mo	3.764213312	1.025357825	2.849265085	1.619845272
18-20mo	4.196894667	0.606140885	3.616706239	1.347681161
20-22mo	4.926090339	0.752870905	3.775844587	1.573532974
22-24mo	5.542285549	1.01700189	3.841787444	1.387423655
24-26mo	5.463804669	1.194155942	4.701179309	0.926512271
26-28mo	5.022808685	1.136191124	4.458895719	0.733147925
28-30mo	4.353316031	0.753168643	4.586324527	1.110997305
30-32mo	4.745291597	0.912644623	4.570967246	1.179000381
32-34mo	4.642527458	0.76418573	5.26308442	0.960932
34-36mo	5.21101315	0.84406933	4.647607285	1.099560467
3-4y	4.543924885	1.135308193	4.568936906	1.000936654
4-5y	5.59501416	0.995748552	4.928618373	1.122853308
5-6y	5.47851421	1.041302464	4.858354881	1.109141125
6-7y	5.743279675	1.157214041	4.97313772	1.213777533
7-8y	5.60510922	1.060199335	4.984953987	1.299020924
8-9y	6.011443948	1.199575446	5.329017922	1.058225814
9-16y	5.781164334	1.030728251	5.299373648	1.081186082
adults	5.7284785	0.757131446	5.230236748	0.22090182

**Table 6 Host multifactorial effects on composition of gut microbiota calculated by EnvFit**

Factors	EnvFit			
	≤3y		>3y	
	r-square	p value	r-square	p value
ASD diagnosis	0.0170	0.038	0.0173	0.001
District	0.0544	0.981	0.0295	0.196
Age	0.0384	0.001	0.0283	0.001
Gender	0.0059	0.292	0.0010	0.379
Any GI problem	0.0033	0.49	0.0050	0.01
Esophageal reflux	0.0033	0.505	0.0019	0.165
Peptic ulcer	0.0019	0.687	0.0030	0.041
Dyspepsia	0.0019	0.69	0.0022	0.106
Abdominal distension	0.0166	0.033	0.0003	0.753
Abdominal pain	0.0168	0.021	0.0016	0.198
Constipation	0.0064	0.266	0.0049	0.009
Abnormal stool consistency	0.0137	0.055	0.0006	0.569
Any Sleep complaints	0.0153	0.045	0.0011	0.334
Difficulty falling asleep	0.0089	0.149	0.0001	0.92
Sleep fragmentation	0.0155	0.042	0.0024	0.089
Short sleep duration	0.0021	0.638	0.0006	0.565
Shallow sleep	0.0131	0.057	0.0001	0.914
Food allergy or intolerance	0.0070	0.233	0.0103	0.001
Skin allergy	0.0015	0.724	0.0004	0.707
Respiratory hypersensitivity	0.0113	0.084	0.0027	0.072
Antibiotic usage with in 3 mo	0.0149	0.047	0.0113	0.001
Infection within 1 mo	0.0025	0.605	0.0002	0.791
Age of mother during pregnancy	0.0000	1.000	0.0000	1.000
Age of father during pregnancy	0.0000	1.000	0.0000	1.000
Assisted reproduction	0.0111	0.09	0.0028	0.069
Smoking	0.0000	1.000	0.0001	0.965
Drinking	0.0056	0.329	0.0002	0.825
Infection during pregnancy	0.0023	0.603	0.0007	0.489
Eclampsia/Pre-eclampsia	0.0052	0.37	0.0011	0.355
Gestational age	0.0000	1.000	0.0000	1.000
Mode of delivery	0.0037	0.454	0.0024	0.081
Neonatal asphyxia	0.0001	0.971	0.0028	0.062
Family history of mental disorders	0.0129	0.054	0.0030	0.049
...				

Table 7 Summary of <b>demographic and clinical characteristics</b> of healthy children (NT) and kids with ASD							
				ASD	NT (healthy adults included)		
			mean ± SEM				
Current cohort	Diagnosis	Total ASD score	mean ± SEM	4.18 ± 0.15	/		
		Repetitive behavior	mean ± SEM	1.38 ± 0.05	/		
		Social retardation	mean ± SEM	2.00 ± 0.07	/		
		Language retardation	mean ± SEM	2.04 ± 0.07	/		
	Demographic	Gender	Female (Male)		127 (645)	217 (233)	
		Any GI problems	Yes/all		494/772 (63.9%)	48/450 (10.7%)	
	Comorbidity	Mean value of total GI problem score of each subject	mean ± SEM		1.05 ± 1.33	0.18 ± 0.56	
		Esophageal reflux	Yes/all		54/772 (6.9%)	2/450 (0.4%)	
		Peptic ulcer	Yes/all		10/772 (1.3%)	1/450 (0.2%)	
		Dyspepsia	Yes/all		238/772 (30.8%)	15/450 (3.3%)	
		Abdominal distension	Yes/all		129/772 (16.7%)	1/450 (0.2%)	
		Abdominal pain	Yes/all		61/772 (7.9%)	9/450 (2%)	
		Constipation	Yes/all		346/772 (44.8%)	19/450 (4.2%)	
		Abnormal stool consistency	Yes/all		127/772 (16.4%)	7/450 (1.6%)	
		Any sleep complaints	Yes/all		354/772 (45.8%)	21/450 (4.7%)	
		Mean value of sleep complaints score	mean ± SEM		0.71 ± 1.02	0.07 ± 0.25	
		Difficulty falling asleep	Yes/all		193/772 (25.0%)	2/450 (0.4%)	
		Sleep fragmentation	Yes/all		216/772 (27.9%)	9/450 (2.1%)	
		Short sleep duration	Yes/all		84/772 (10.9%)	7/450 (1.6%)	
		Shallow sleep	Yes/all		119/772 (15.4%)	7/450 (1.6%)	
		Total Allergy score	mean ± SEM		0.67 ± 0.03	0.13 ± 0.02	
		Food allergy or intolerance	Yes/all		353/772 (45.7%)	15/450 (3.3%)	
		Skin allergy	Yes/all		157/772 (20.3%)	15/450 (3.3%)	
		Respiratory hypersensitivity	Yes/all		109/772 (14.1%)	5/450 (1.1%)	
		Clinical	Antibiotic usage within 3 mo	Yes/all		67/772 (8.7%)	3/450 (0.6%)
			Any infection within 1 mo	Yes/all		21/772 (2.7%)	2/450 (0.4%)
	Any neonatal asphyxia		Yes/all		51/772 (6.6%)	1/450 (0.02%)	
	Perinatal	Age of mother during pregnancy	mean ± SEM		29.28 ± 0.20	26.58 ± 0.34	
		Age of father during pregnancy	mean ± SEM		31.83 ± 0.21	29.88 ± 0.26	
		Premature delivery	Yes/all/NA or Forgotten		83/772 (10.7%) /0	18/197 (9.1%) /253	
		Mode of delivery	Cesarean section/Vaginally delivery		446/327	106/343	
		Assisted reproduction	Yes/all		97/772 (12.5%)	7/450 (1.6%)	
		Eclampsia/Pre-eclampsia	Yes/all		9/772 (1.2%)	2/450 (0.4%)	
		Infection during pregnancy	Yes/all		55/772 (7.1%)	1/450 (0.2%)	
	Family history	Family history of mental disorders	Yes/all		42/772 (5.4%)	0/450 (0%)	
	Validation cohort 1	Diagnosis	Total ASD score	mean ± SEM	6.21 ± 0.18	/	
			Repetitive behavior	mean ± SEM	1.62 ± 0.08	/	
			Social retardation	mean ± SEM	2.34 ± 0.07	/	
			Language retardation	mean ± SEM	2.27 ± 0.09	/	
		Demographic	Gender	Female (Male)		15 (73)	14 (32)
Any GI problems			Yes/all		45/73 (61.6%)	5/32 (15.6%)	
Comorbidity		Mean value of total GI problem score of each subject	mean ± SEM		1.33 ± 0.17	0.31 ± 0.15	
		Esophageal reflux	Yes/all		8/73 (10.9%)	0/32 (0%)	
		Peptic ulcer	Yes/all		3/73 (4.1%)	0/32 (0%)	
		Dyspepsia	Yes/all		32/73 (43.8%)	3/32 (9.4%)	
		Abdominal distension	Yes/all		19/73 (26.0%)	0/32 (0%)	
		Abdominal pain	Yes/all		8/73 (10.9%)	1/32 (3.1%)	
		Constipation	Yes/all		23/73 (31.5%)	4/32 (12.5%)	
		Abnormal stool consistency	Yes/all		1/73 (1.44%)	2/32 (6.3%)	
		Any sleep complaints	Yes/all		37/73 (50.7%)	2/32 (6.3%)	
		Mean value of sleep complaints score	mean ± SEM		0.78 ± 0.13	0.09 ± 0.07	
		Difficulty falling asleep	Yes/all		24/73 (32.9%)	0/32 (0%)	

	Clinical	Sleep fragmentation	Yes/all	13/73 (17.8%)	2/32 (6.3%)
		Short sleep duration	Yes/all	11/73 (15.1%)	0/32 (0%)
		Shallow sleep	Yes/all	9/73 (12.3%)	1/32 (3.1%)
		Total Allergy score	mean ± SEM	0.64 ± 0.10	0.28 ± 0.09
		Food allergy or intolerance	Yes/all	26/73 (35.6%)	3/32 (9.4%)
		Skin allergy	Yes/all	14/73 (19.2%)	5/32 (15.6%)
		Respiratory hypersensitivity	Yes/all	7/73 (9.6%)	1/32 (3.1%)
		Antibiotic usage within 3 mo	Yes/all	7/73 (9.6%)	2/32 (6.3%)
		Any infection within 1 mo	Yes/all	2/73 (2.7%)	0/32 (0%)
		Any neonatal asphyxia	Yes/all	6/73 (8.2%)	1/32 (3.1%)
	Perinatal	Age of mother during pregnancy	mean ± SEM	28.83 ± 0.41	28.67 ± 0.27
		Age of father during pregnancy	mean ± SEM	30.00 ± 0.43	28.33 ± 0.80
		Premature delivery	Yes/all/NA or Forgotten	4/72 (5.5%) /1	1/32 (3.1%) /0
		Mode of delivery	Cesarean section/Vaginally delivery	31/42	12/20
		Assisted reproduction	Yes/all	11/73 (15.1%)	1/32 (3.1%)
		Eclampsia/Pre-eclampsia	Yes/all	1/73 (1.44%)	0/32 (0%)
		Infection during pregnancy	Yes/all	8/73 (10.9%)	0/32 (0%)
		Family history	Family history of mental disorders	Yes/all	3/72 (4.2%)



ASD	2.11	3.590261744
ASD	2.11	4.105028244
ASD	2.11	4.652653031
ASD	2.11	7.336691931
ASD	2.11	8.579041071
ASD	2.2	0.383731536
ASD	2.2	1.133225705
ASD	2.2	1.909490027
ASD	2.2	3.842345749
ASD	2.2	3.848045799
ASD	2.2	3.92455407
ASD	2.2	4.01154422
ASD	2.3	1.753805439
ASD	2.3	1.76626794
ASD	2.3	1.768342674
ASD	2.3	1.775403517
ASD	2.3	1.934150894
ASD	2.3	1.951543423
ASD	2.3	1.969422452
ASD	2.3	1.975056921
ASD	2.3	2.32311893
ASD	2.3	2.840479095
ASD	2.3	2.916988897
ASD	2.3	3.070233725
ASD	2.3	3.506979659
ASD	2.4	1.182039351
ASD	2.4	1.433945643
ASD	2.4	1.769037947
ASD	2.4	1.770056576
ASD	2.4	1.777827079
ASD	2.4	1.799120598
ASD	2.4	2.436815482
ASD	2.4	2.49150978
ASD	2.4	3.041442528
ASD	2.4	1.589790419
ASD	2.5	0.888687275
ASD	2.5	1.696395082
ASD	2.5	1.924532332
ASD	2.5	1.933812387
ASD	2.5	1.934680137
ASD	2.5	2.234722289
ASD	2.5	2.462285846
ASD	2.5	2.565051084
ASD	2.5	2.826727351
ASD	2.5	3.132576088
ASD	2.5	3.706315006
ASD	2.6	1.542560885
ASD	2.6	1.595070732
ASD	2.6	1.753531106
ASD	2.6	1.780306071
ASD	2.6	1.805664947
ASD	2.6	1.894824741
ASD	2.6	1.909931041
ASD	2.6	1.955851225
ASD	2.6	3.133341616
ASD	2.6	3.173000092
ASD	2.6	3.229318281
ASD	2.6	3.257407069
ASD	2.6	3.455729425
ASD	2.6	3.796997905
ASD	2.6	3.883443524
ASD	2.6	3.891048426
ASD	2.7	1.730023456
ASD	2.7	1.7549687
ASD	2.7	1.768088582
ASD	2.7	1.907207444
ASD	2.7	2.988800014
ASD	2.7	4.382687517
ASD	2.8	1.944459197
ASD	2.8	2.286573842
ASD	2.8	2.662176127
ASD	2.8	2.818519699
ASD	2.8	3.087934721

	2.11	-0.75185922
	2.11	-0.653970516
	2.11	-0.277202098
	2.11	0.160247543
	2.11	0.287855263
	2.11	0.580366281
	2.11	0.891548699
	2.11	3.863399312
	2.11	5.139408564
	2.2	-3.277944053
	2.2	-2.508143147
	2.2	-1.71084678
	2.2	0.274377586
	2.2	0.280232072
	2.2	0.358813252
	2.2	0.448160307
	2.3	-1.870749474
	2.3	-1.857949314
	2.3	-1.855818368
	2.3	-1.848566219
	2.3	-1.685517752
	2.3	-1.667653992
	2.3	-1.64929055
	2.3	-1.643503421
	2.3	-1.286011047
	2.3	-0.754633566
	2.3	-0.676050813
	2.3	-0.518653982
	2.3	-0.070074887
	2.4	-2.458006948
	2.4	-2.317962595
	2.4	-1.771870471
	2.4	-1.770210436
	2.4	-1.757547028
	2.4	-1.722845476
	2.4	-0.683608975
	2.4	-0.59447495
	2.4	0.301737642
	2.4	-2.063985994
	2.5	-3.206557459
	2.5	-1.890254857
	2.5	-1.518464894
	2.5	-1.503341403
	2.5	-1.501927253
	2.5	-1.012955545
	2.5	-0.642100515
	2.5	-0.474626401
	2.5	-0.048178683
	2.5	0.450255882
	2.5	1.385264835
	2.6	-2.140954864
	2.6	-2.05538079
	2.6	-1.797141609
	2.6	-1.753507072
	2.6	-1.712180303
	2.6	-1.566878663
	2.6	-1.542260277
	2.6	-1.338984049
	2.6	0.28453038
	2.6	0.339211174
	2.6	0.416862246
	2.6	0.455590845
	2.6	0.729036139
	2.6	1.199574417
	2.6	1.318764953
	2.6	1.329250532
	2.7	-1.650353588
	2.7	-1.615959283
	2.7	-1.597869694
	2.7	-1.406053708
	2.7	0.085237564
	2.7	2.007118617
	2.8	-0.10017412

ASD	2.8	3.439633355
ASD	2.8	3.463212465
ASD	2.8	4.314469988
ASD	2.8	1.941287967
ASD	2.9	0.877654367
ASD	2.9	2.942514612
ASD	2.9	2.982310828
ASD	2.9	3.120210965
ASD	2.9	3.316236645
ASD	2.9	3.393061275
ASD	2.9	3.492670981
ASD	2.9	3.881833807
ASD	3	0.279977415
ASD	3	1.69775407
ASD	3	1.812554288
ASD	3	1.889455816
ASD	3	1.913101432
ASD	3	1.920273411
ASD	3	1.926564964
ASD	3	1.933868368
ASD	3	1.950875952
ASD	3	1.997979799
ASD	3	2.223934968
ASD	3	2.229050172
ASD	3	2.270732445
ASD	3	2.286069299
ASD	3	2.299678108
ASD	3	2.309151491
ASD	3	2.31924965
ASD	3	2.33338209
ASD	3	2.341143345
ASD	3	2.371425274
ASD	3	2.394555312
ASD	3	2.467509714
ASD	3	2.467827638
ASD	3	2.527927329
ASD	3	2.56099319
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NT	2.9	2.120537216
NT	2.9	3.465408541
NT	2.9	3.774797305
NT	2.9	3.95020403
NT	2.9	6.450540684
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NT	3	1.824284114
NT	3	1.961698974
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NT	3	2.492011984
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NT	3	2.769971304
NT	3	3.098932323
NT	3	3.15361811
NT	3	3.167651931
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NT	3	3.261732787
NT	3	3.301943511
NT	3	3.640047714
NT	3	3.691994583
NT	3	3.769852338
NT	3	3.877041072
NT	3	3.96430516
NT	3	4.263707514
NT	3	4.280934647
NT	3	4.319455935
NT	3	4.352751109
NT	3	4.395606078
NT	3	4.515759575
NT	3	4.904170632
NT	3	5.252478488
NT	3	5.546847984
NT	3	5.776309565
NT	3	6.566344306
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NT	3	6.949182436
NT	3	8.423214816
NT	3	11.76847551
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NT	3	3.587889103
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NT	3.1	1.933497847

NT	3.1	2.331238031
NT	3.1	3.349932934
NT	3.1	4.492395793
NT	3.11	4.002659778
NT	3.11	62.6083836
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NT	3.2	6.327465698
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NT	3.6	22.85844216
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NT	3.7	3.21963121
NT	3.7	4.121153521
NT	3.8	2.180745684
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NT	3.9	3.13980416
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NT	4	2.369955901
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NT	4	7.642111227
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NT	4.4	3.081995469
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NT	5	3.779157468
NT	5	3.835106653
NT	5	3.838940274
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NT	5	6.537914693
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NT	5.1	3.653374915

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NT	5.7	5.913600937
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NT	6	6.499116704
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NT	6	6.682326384
NT	6	7.058818936
NT	6	7.162552673
NT	6	7.244620018
NT	6	7.360554837
NT	6	7.42443613
NT	6	7.544490479
NT	6	7.607961401
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NT	6	38.92448997
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NT	6.1	4.023228779
NT	6.1	7.412595868
NT	6.1	8.784032546
NT	6.1	47.95186661
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NT	6.11	4.046571968
NT	6.11	5.103651352
NT	6.11	6.584584005
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NT	6.3	6.148170888

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NT	6.3	82.16958302
NT	6.4	6.503220096
NT	6.4	7.180370361
NT	6.5	23.52753642
NT	6.5	52.54075468
NT	6.6	3.145264802
NT	6.6	3.540997232
NT	6.6	5.519839016
NT	6.6	6.781930033
NT	6.6	8.404903509
NT	6.6	52.70533599
NT	6.7	63.07433881
NT	6.8	4.78792916
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NT	7	3.82147599
NT	7	3.962634784
NT	7	4.003436729
NT	7	4.437029396
NT	7	4.578022629
NT	7	4.624758559
NT	7	4.790863365
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NT	7	5.569822319
NT	7	5.887372568
NT	7	6.263387211
NT	7	6.413942993
NT	7	6.676628213
NT	7	7.677997641
NT	7	7.678637169
NT	7.1	3.763747563
NT	7.2	53.84473443
NT	7.3	3.132457415
NT	7.3	3.422572571
NT	7.3	31.56373563
NT	7.4	43.13162628
NT	7.4	57.62435235
NT	7.5	3.112055426
NT	7.5	6.822186589
NT	7.5	7.409681
NT	7.5	7.695746616
NT	7.5	62.74466619
NT	7.6	3.15945105
NT	7.6	6.194381803
NT	7.6	7.247949436
NT	7.6	35.97218405
NT	7.8	47.3497697
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NT	8	3.991396
NT	8	4.17714576
NT	8	4.558316827
NT	8	4.669973622
NT	8	5.401487619
NT	8	5.94328694
NT	8	6.221544012
NT	8	8.270407736
NT	8	8.567906357
NT	8	38.62195185
NT	8	38.76929824
NT	8	62.63769113
NT	8.11	7.771798279
NT	8.2	47.74887018
NT	8.3	3.822458744
NT	8.3	9.630596191
NT	8.3	35.42342876
NT	8.4	6.724911198
NT	8.4	27.3035804
NT	8.4	35.62927192
NT	8.5	5.718995713
NT	8.5	47.47516915
NT	8.6	2.297761204
NT	8.6	7.415941283

NT	8.6	8.429633021
NT	8.6	35.42397942
NT	8.8	6.422391549
NT	9	4.032637601
NT	9	4.44376656
NT	9	6.264302731
NT	9	7.374531351
NT	9	8.313376736
NT	9	8.451855559
NT	9	8.501022313
NT	9.1	31.8006908
NT	9.4	4.817738314
NT	9.6	3.354520847
NT	9.6	57.06053339
NT	9.7	3.856545771
NT	10	4.343403948
NT	10	4.470079993
NT	10	6.462623708
NT	10	6.6969634
NT	10	7.324179351
NT	10	7.640650049
NT	10	7.810621612
NT	10	8.456500515
NT	10	8.524332032
NT	10	8.622698203
NT	10	8.641267918
NT	10	8.857038129
NT	10	8.986138605
NT	10	14.05543176
NT	10.1	3.207058276
NT	11	8.880952284
NT	12	5.513352126
NT	12	8.393864058
NT	12	15.91727522
NT	12	35.7308249
NT	12	38.67477627
NT	12	23.84917989
NT	14	13.31918075
NT	15	6.639530703
NT-adult	16	6.62644159
NT-adult	16	10.3384876
NT-adult	16	14.81856329
NT-adult	18	35.22878225
NT-adult	18	35.27905016
NT-adult	20	5.115192011
NT-adult	20	7.595294051
NT-adult	20	15.23135571
NT-adult	20	17.47241873
NT-adult	20	35.20237386
NT-adult	21	23.26303528
NT-adult	22	30.60271771
NT-adult	23	3.833688798
NT-adult	23	6.113175362
NT-adult	23	8.396139041
NT-adult	23	24.05636355
NT-adult	23	25.58359872
NT-adult	23	25.69227237
NT-adult	24	22.92748238
NT-adult	24	35.18252164







**Table 12 Enlarging microbial relationship alternation with increasing ASD score**

index	Taxon1	Taxon2	Group 1	Group 2	Group 3	Group 4	R-square	coefficient	Taxon1 detect	Taxon2 detection rate
1	d	Bacteri	0	0.03042191	0.177473584	0.414827419	0.98194699	0.192212614	0.449593496	0.258536585
2	d	Bacteri	0.023748621	0	0.110463288	0.395503352	0.913334129	0.185900866	0.639837398	0.258536585
3	d	Bacteri	0.023635102	0	0.108514535	0.383252946	0.914739418	0.179107079	0.473170732	0.309756098
4	d	Bacteri	0	0.052013578	0.347375405	0.405893343	0.874802924	0.178472282	0.334146341	0.25303252
5	d	Bacteri	0.099926855	0	0.101828421	0.456326731	0.754001498	0.178199338	0.494308943	0.258536585
6	d	Bacteri	0.086644323	0.121380717	0	0.431995102	0.824598097	0.17267539	0.565835859	0.318699187
7	d	Bacteri	0	0.01102791	0.014173968	0.232526338	0.751431186	0.150149259	0.369918699	0.28699187
8	d	Bacteri	0.012065936	0.18235507	0	0.327553328	0.997896068	0.157743896	0.369918699	0.258536585
9	d	Bacteri	0.020062529	0.02715604	0.327051117	0	0.767314024	0.153492914	0.42601626	0.31300813
10	d	Bacteri	0	0.065714028	0.113487186	0.364164551	0.866499156	0.149225162	0.531707317	0.257723577
11	d	Bacteri	0	0.001069837	0.06821461	0.282069571	0.916705326	0.140498967	0.742276423	0.309756098
12	d	Bacteri	0.057002013	0.06881672	0.329716111	0	0.782428395	0.136357049	0.403252033	0.369918699
13	d	Bacteri	0	0.060738219	0.178146912	0.329131261	0.91947012	0.134196521	0.363414634	0.29382937
14	d	Bacteri	0.00084512	0	0.056072492	0.25995212	0.901132794	0.1295335	0.449593496	0.423577236
15	d	Bacteri	0.012213275	0.117099432	0	0.270772682	0.988271454	0.129279704	0.663414634	0.25203252
16	d	Bacteri	0.051784664	0.168763272	0.306393477	0	0.997811796	0.117300406	0.574796748	0.468293283
17	d	Bacteri	0	0.008278091	0.150726293	0.256752623	0.992860592	0.124237266	0.28699187	0.271544715
18	d	Bacteri	0.115123806	0.119556459	0.407929303	0.432233013	0.835636456	0.123970046	0.369918699	0.31300813
19	d	Bacteri	0.092291017	0.114711334	0	0.339014151	0.817271958	0.123311567	0.501626016	0.331707317
20	d	Bacteri	0.011881272	0.076745968	0.253252791	0.351257541	0.97164616	0.119463563	0.4	0.369918699
21	d	Bacteri	0.004325414	0.06394526	0.235094524	0	0.927766146	0.115384555	0.411382114	0.332520325
22	d	Bacteri	0.0053728	0	0.065154918	0.233226345	0.929861524	0.113826772	0.404878049	0.371544715
23	d	Bacteri	0	0.05196818	0.087604647	0.278473112	0.864631674	0.113252466	0.318699187	0.258536585
24	d	Bacteri	0.027066119	0.104629283	0	0.245828533	0.972567831	0.109381207	0.899186992	0.25203252
25	d	Bacteri	0	0.116599337	0.268246561	0.330462256	0.944921176	0.106931446	0.359349593	0.309756098
26	d	Bacteri	0.002354059	0	0.073293788	0.21509536	0.864335264	0.106370888	0.336353866	0.309756098
27	d	Bacteri	0.003205371	0.046971201	0	0.240278073	0.801946854	0.103888351	0.722764228	0.565835859
28	d	Bacteri	0.117008024	0	0.147996596	0.319150603	0.861876097	0.101072289	0.359349593	0.334146341
29	d	Bacteri	0.015447881	0.130807556	0	0.215945452	0	0.100190785	0.576422764	0.251219512
30	d	Bacteri	0.003376937	0.079387598	0	0.202788849	0.981521756	0.099705956	0.276422764	0.257723577
31	d	Bacteri	0.081460367	0.12470783	0.279834188	0	0.904139076	0.099186991	0.814634146	0.25284528
32	d	Bacteri	0.041914965	0	0.099050416	0.239401589	0.944121829	0.098743312	0.825203252	0.269105691
33	d	Bacteri	0	0.058389053	0.08340845	0.253551838	0.844369203	0.097581392	0.358536585	0.25203252
34	d	Bacteri	0.117008024	0	0.111752145	0.295358974	0.306649989	0.097448922	0.336353866	0.251219512
35	d	Bacteri	0.029409561	0	0.087115548	0.23218857	0.948379144	0.096904498	0.722764228	0.258536585
36	d	Bacteri	0	0.048883358	0.17326723	0.239705352	0.970179351	0.095410997	0.359349593	0.25284528
37	d	Bacteri	0.022268124	0.094254489	0.211206385	0	0.981053202	0.094762572	0.42601626	0.25284528
38	d	Bacteri	0	0.14254242	0.205135171	0.330065365	0.964473646	0.093761472	0.460162602	0.369918699
39	d	Bacteri	0	0.038125728	0.06607506	0.214382938	0.865477583	0.088128605	0.288617886	0.278661789
40	d	Bacteri	0.076582864	0	0.158717037	0.251335956	0.998001539	0.087376546	0.62195122	0.258536585
41	d	Bacteri	0.074137919	0	0.105454162	0.248811134	0.979395819	0.087336008	0.62195122	0.309756098
42	d	Bacteri	0.056668778	0	0.109921633	0.230653646	0.952252858	0.086992434	0.641463415	0.297560976
43	d	Bacteri	0.039755924	0.14422583	0.206873837	0.307395873	0.991491458	0.086556785	0.473170732	0.269105691
44	d	Bacteri	0.032874903	0.041753922	0	0.20110612	0.78949793	0.084115609	0.528943089	0.4
45	d	Bacteri	0.125021265	0.186589755	0.266986772	0.371486405	0.985599159	0.08170164	0.370731707	0.369918699
46	d	Bacteri	0.044619261	0	0.066441916	0.207194647	0.848620797	0.081287693	0.38699187	0.25284528
47	d	Bacteri	0.042536155	0	0.185733871	0.204514319	0.835657744	0.080989882	0.460162602	0.332520325
48	d	Bacteri	0.032411456	0.074644446	0.107523267	0.273201022	0.855344802	0.075556552	0.9	0.30282937
49	d	Bacteri	0.015889585	0.03472553	0.038108974	0.245495837	0.679573089	0.069215518	0.473170732	0.334146341
50	d	Bacteri	0.093511349	0.184044756	0	0.224981329	0.954709739	0.06573499	0.403252033	0.25203252
51	d	Bacteri	0.106764786	0.122792022	0	0.228229293	0.846031977	0.061382254	0.517073171	0.297560976
52	d	Bacteri	0.135826107	0	0.220416102	0.24961324	0.926788298	0.058835666	0.52601626	0.371544715
53	d	Bacteri	0.184601111	0	0.256590113	0.291608441	0.961733295	0.053503665	0.54796748	0.334146341
54	d	Bacteri	0.145877766	0.171130851	0.179044719	0.311546317	0.766421797	0.050521952	0.369918699	0.334146341

Taxon1: relationship node  
 Taxon2: relationship node  
 Group 1: PM score of ASD cohort with ASD score 1 to 3 compared to NT  
 Group 2: PM score of ASD cohort with ASD score 4 to 5 compared to NT  
 Group 3: PM score of ASD cohort with ASD score 7 compared to NT  
 Group 4: PM score of ASD cohort with ASD score 7 to 9 compared to NT  
 R-square: the linear regression R-square  
 coefficient: the linear regression coefficient  
 Taxon1 detection rate: detection rate of taxon1  
 Taxon2 detection rate: detection rate of taxon2

**Table13 Summary of the statistical results of the 20 significant changed microbial taxa across age**

Row.names	1			2			3			4			5			6			7			8			9				
	mean NT	mean ASD	p-value	mean NT	mean ASD	p-value	mean NT	mean ASD	p-value	mean NT	mean ASD	p-value	mean NT	mean ASD	p-value	mean NT	mean ASD	p-value	mean NT	mean ASD	p-value	mean NT	mean ASD	p-value	mean NT	mean ASD	p-value		
g_Lachnospiraceae_UCG-004							0.44%	0.77%	0.025199	0.45%	0.95%	0.020612																	
g_Escherichia-Shigella															5.40%	7.38%	0.001517				6.77%	2.27%	0.025688						
g_Butyricoccus																													
g_Faecalibacterium	11.98%	4.12%	0.03829					17.55%	13.00%	0.013482															0.46%	0.24%	0.01217		
g_Parabacteroides																													
f_Enterobacteriaceae												2.75%	6.82%	0.014322				4.99%	5.13%	0.004266	7.21%	3.53%	1.13724E-05	1.75%	2.48%	0.011476	1.69%	1.70%	0.019414
g_Lachnospiraceae_NK4A136_group																													
g_Bifidobacterium												2.70%	5.00%	0.007976															
g_Haemophilus							0.29%	0.83%	0.047153																				
g_Veillonella	10.25%	19.99%	0.032053	1.69%	10.47%	5.7118E-05	3.60%	8.03%	0.003709	0.80%	5.48%	8.03E-05	0.76%	6.52%	0.001105	0.66%	3.87%	0.030332								0.25%	0.50%	0.039359	
f_Ruminococcaceae	0.03%	0.14%	0.030366					0.16%	0.09%	0.015762																	0.47%	2.76%	0.047391
g_Anaerostipes											0.23%	0.43%	0.00098																
g_Lachnospira								1.87%	3.58%	0.014366						1.56%	3.01%	0.024705	1.65%	2.58%	0.028512499								
g_Blautia														1.43%	0.71%	0.002988													
g_Granulicatella														0.08%	0.08%	0.01799				0.01%	0.06%	0.003949691	0.01%	0.05%	0.020742				
g_Romboutsia							0.15%	0.17%	0.014176				0.11%	0.33%	0.032767														
g_Actinomyces													0.05%	0.32%	0.007576												0.04%	0.12%	0.011881
g_Roseburia																3.08%	3.30%	0.022073											
g_Incertae Sedis													0.22%	0.21%	0.025056														
g_Hungatella				0.13%	0.80%	0.000636712																				0.07%	0.35%	0.017442	

**Total proportion of the 20 microbial taxa in different age brackets**

age bracket	1	2	3	4	5	6	7	8	9
NT	65.91%	40.10%	50.53%	40.04%	37.16%	38.59%	40.97%	33.41%	35.09%
ASD	62.42%	55.85%	50.09%	45.66%	46.73%	46.45%	39.02%	37.09%	35.70%

Table 14 Summary of the statistical results of the 39 significant changed GBM across age

No.	Row name	1			2			3			4			5			6			7			8			9			
		mean NT	mean ASD	p-value	mean NT	mean ASD	p-value	mean NT	mean ASD	p-value																			
1	MGB004 Kynurenine synthesis	1092.797	297.3598	0.021074																									
2	MGB025 Nitric oxide synthesis I (NO synthase)	48.63158	3.12	0.00303																									
3	MGB045 Acetate synthesis III				78271.83	94693.84	0.039124																						
4	MGB047 Acetate degradation				34185.86	33968.58	0.035049																						
5	MGB050 Glutamate degradation I				5282.641	14521.4	5.68E-05						4234.183	11689.16	0.028959														
6	MGB028 Nitric oxide degradation II (NO reductase)				1300.1	6200.144	0.142984	1576.387	4628.157	0.023838																			
7	MGB009 Histamine synthesis				6216.852	5725.541	0.171932																						
8	MGB031 17-beta-Estradiol degradation							56799.02	52701.34	0.044281																			
9	MGB055 Propionate synthesis III							35100.37	47227.69	0.015738																34050.77	53703.55	0.000129	
10	MGB044 Acetate synthesis II							69193.54	44421.63	0.033508																			
11	MGB034 Isovaleric acid synthesis I (KADH pathway)							21377.53	29567.96	0.001956																	19892.22	33138.89	0.01256
12	MGB024 DOPAC synthesis							19395.03	16628.75	0.001334																			
13	MGB051 Glutamate degradation II							6278.562	3765.424	0.021857	5264.89	4397.712	0.008437																
14	MGB015 p-Cresol synthesis																												
15	MGB056 Propionate degradation I										2259.034	247.979	5.97E-06	1231.779	2904.984	0.042978	1478.688	88.24674	5.86E-06	1161.897	870.508	0.001545							
16	MGB023 Dopamine degradation																												
17	MGB021 GABA synthesis II																												
18	MGB020 GABA synthesis I																												
19	MGB016 p-Cresol degradation										1687.501	1012.833	0.033167	398.9685	2864.111	0.041861													
20	MGB048 Propionate synthesis I																												
21	MGB010 Histamine degradation																												
22	MGB026 Nitric oxide synthesis II (nitrite reductase)										696.2562	653.8108	0.043096																
23	MGB052 Butyrate synthesis I																												
24	MGB007 Glutamate synthesis II																												
25	MGB038 Inositol degradation																												
26	MGB006 Glutamate synthesis I																												
27	MGB033 Quinolinic acid degradation																												
28	MGB035 Isovaleric acid synthesis II (KADC pathway)																												
29	MGB036 S-Adenosylmethionine (SAM) synthesis																												
30	MGB049 Tryptophan degradation																												
31	MGB037 Inositol synthesis																												
32	MGB027 Nitric oxide degradation I (NO dioxygenase)										33992.74	39414.31	0.014555																
33	MGB019 GABA degradation																												
34	MGB005 Tryptophan synthesis																												
35	MGB040 Menquinone synthesis (vitamin K2) I																												
36	MGB029 ClpB (ATP-dependent chaperone protein)																												
37	MGB032 Quinolinic acid synthesis																												
38	MGB039 g-Hydroxybutyric acid (GHB) degradation																												
39	MGB043 Acetate synthesis I																												







**Table S6 Summary of the statistical results of correlations between bacterial taxa and clinical symptoms according to Spearman's rank correlations analysis.**

Symptom	Bacterial Taxa	Spearman's rank correlation	p-value	Spearman's rank correlation		p-value		FDR																				
				Gender	Age	ABO type	Genetic																					Latitude
Age bracket 1 (0-29 mo)	g_Vellota	0.01701581	0.8749047	0.01701581	0.8749047	0.01701581	0.8749047	NA																				
	g_Faecalibacterium	0.16283214	0.0478191	0.16283214	0.0478191	0.16283214	0.0478191	NA																				
	l_Ruminococcaceae	0.00023812	0.9997619	0.00023812	0.9997619	0.00023812	0.9997619	NA																				
Age bracket 2 (24-35 mo)	g_Vellota	0.01701581	0.8749047	0.01701581	0.8749047	0.01701581	0.8749047	NA																				
	g_Faecalibacterium	0.16283214	0.0478191	0.16283214	0.0478191	0.16283214	0.0478191	NA																				
	l_Ruminococcaceae	0.00023812	0.9997619	0.00023812	0.9997619	0.00023812	0.9997619	NA																				
Age bracket 3 (24-47 mo)	g_Vellota	0.01701581	0.8749047	0.01701581	0.8749047	0.01701581	0.8749047	NA																				
	g_Faecalibacterium	0.16283214	0.0478191	0.16283214	0.0478191	0.16283214	0.0478191	NA																				
	l_Ruminococcaceae	0.00023812	0.9997619	0.00023812	0.9997619	0.00023812	0.9997619	NA																				
Age bracket 4 (5-9 y)	g_Vellota	0.01701581	0.8749047	0.01701581	0.8749047	0.01701581	0.8749047	NA																				
	g_Faecalibacterium	0.16283214	0.0478191	0.16283214	0.0478191	0.16283214	0.0478191	NA																				
	l_Ruminococcaceae	0.00023812	0.9997619	0.00023812	0.9997619	0.00023812	0.9997619	NA																				
Age bracket 5 (9-11 y)	g_Vellota	0.01701581	0.8749047	0.01701581	0.8749047	0.01701581	0.8749047	NA																				
	g_Faecalibacterium	0.16283214	0.0478191	0.16283214	0.0478191	0.16283214	0.0478191	NA																				
	l_Ruminococcaceae	0.00023812	0.9997619	0.00023812	0.9997619	0.00023812	0.9997619	NA																				

Table 17 Summary of the statistical results of correlations between GIMs and clinical phenotypes according to spearman's rank correlations analysis

Age bracket	GIM	Group	Age	ASD score	Repetitive	Social return	Language	ADOS	any GI prob G	sephageal	gastric ulcer	dyspepsia	abdominal	abdominal	constipation	abnormal c	within 1 mo	any sleep c	deep coma	difficulty fall sleep	fragm sleep	short sleep	Shallow sleep	any neonate	food allergy	skin allergy	respiratory	Antibiotic	within 3 months		
																														p-value	Rho
age bracket 1 (11-23 mo)	MG025 Nitric oxide synthesis (NO synthase)																														
age bracket 2 (24-35 mo)	MG050 Glutamate degradation I																														
age bracket 3 (36-47 mo)	MG034 Isovaleic acid synthesis II (KADH pathway)																														
age bracket 4 (48-59 mo)	MG037 Inositol synthesis																														
age bracket 5 (6-8 y)	MG038 Inositol degradation																														
age bracket 6 (9-13 y)	MG043 Acetate synthesis II																														
age bracket 7 (14-19 y)	MG039 Dopamine degradation																														
age bracket 8 (20-29 y)	MG023 p-Hydroxybutyric acid (PHB) degradation																														



Table S3 Summary of the statistical results of correlations between METACYC and clinical phenotypes according to spearman's rank correlations analysis

Table with columns for pathway name, gene, tissue, sex, ANS score, p-value, and Spearman's rank correlation coefficient (rho).









