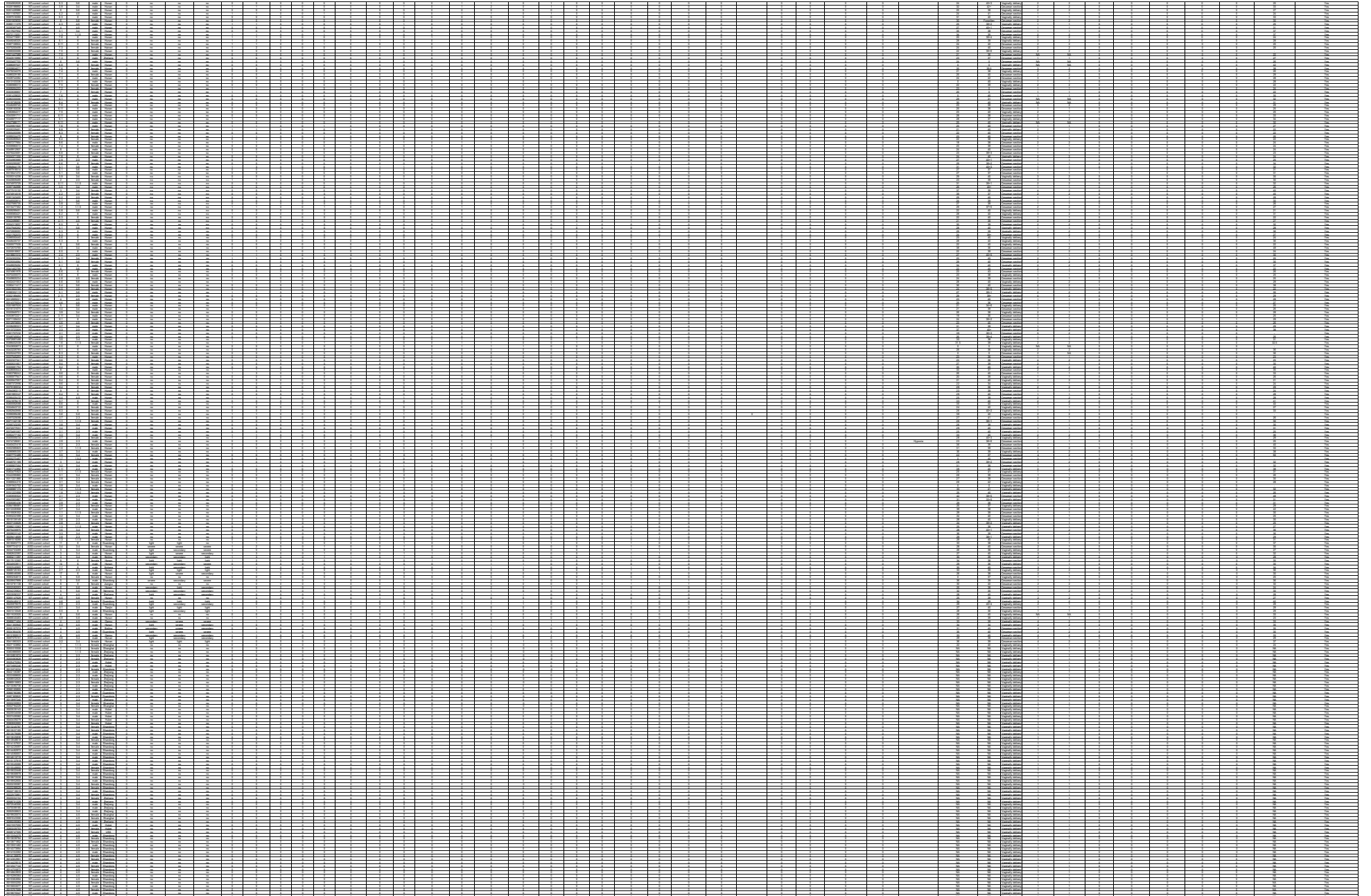
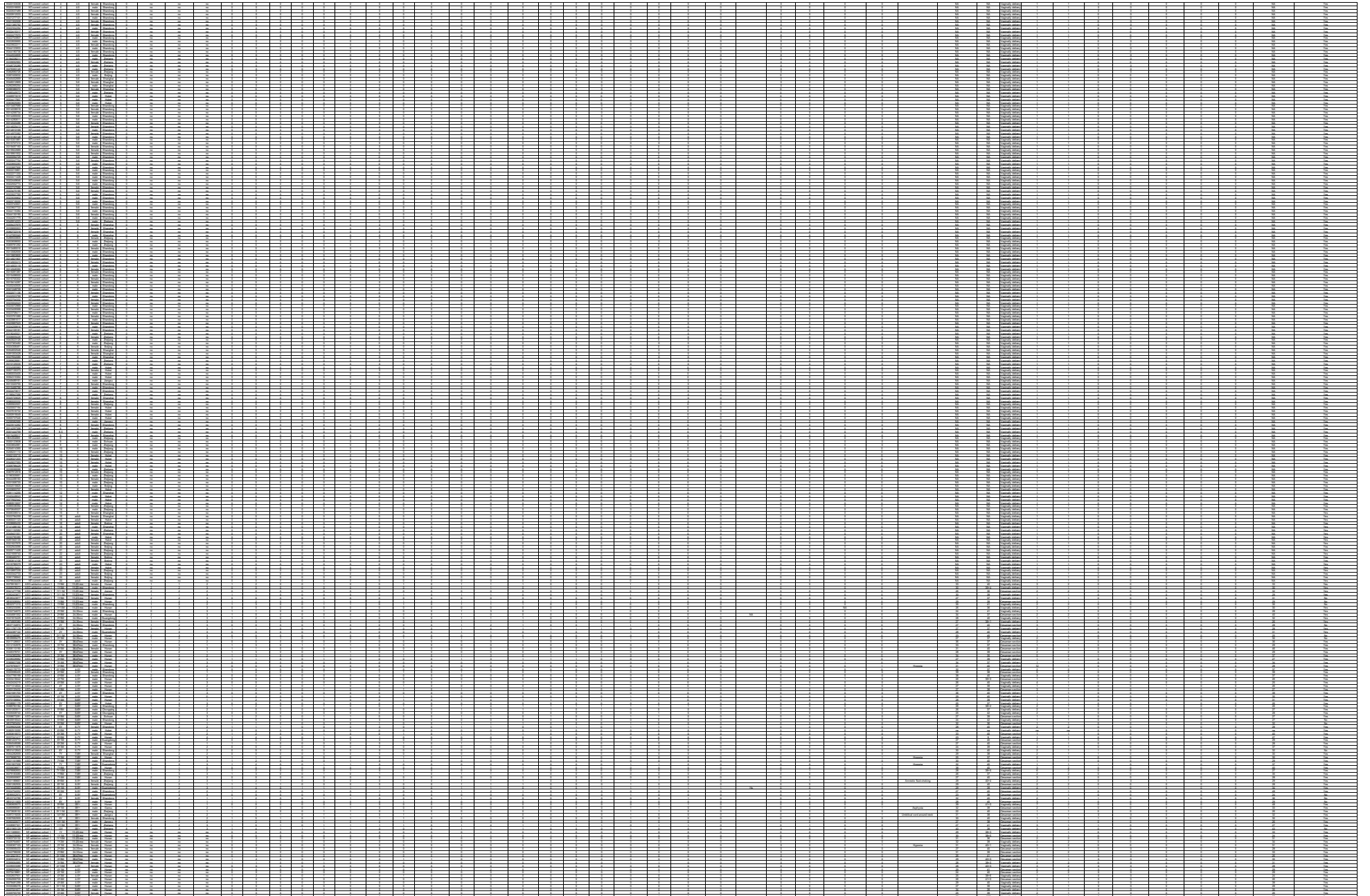


Accession	Gene	Chromosome	Start	End	Strand	Gene ID	Gene structure										Transcript structure										Other features																																																																																																																																																																																																																																																																																
							Exon 1	Exon 2	Exon 3	Exon 4	Exon 5	Exon 6	Exon 7	Exon 8	Exon 9	Exon 10	Exon 11	Exon 12	Exon 13	Exon 14	Exon 15	Exon 16	Exon 17	Exon 18	Exon 19	Exon 20	Exon 21	Exon 22	Exon 23	Exon 24	Exon 25	Exon 26	Exon 27	Exon 28	Exon 29	Exon 30	Exon 31	Exon 32	Exon 33	Exon 34	Exon 35	Exon 36	Exon 37	Exon 38	Exon 39	Exon 40	Exon 41	Exon 42	Exon 43	Exon 44	Exon 45	Exon 46	Exon 47	Exon 48	Exon 49	Exon 50	Exon 51	Exon 52	Exon 53	Exon 54	Exon 55	Exon 56	Exon 57	Exon 58	Exon 59	Exon 60	Exon 61	Exon 62	Exon 63	Exon 64	Exon 65	Exon 66	Exon 67	Exon 68	Exon 69	Exon 70	Exon 71	Exon 72	Exon 73	Exon 74	Exon 75	Exon 76	Exon 77	Exon 78	Exon 79	Exon 80	Exon 81	Exon 82	Exon 83	Exon 84	Exon 85	Exon 86	Exon 87	Exon 88	Exon 89	Exon 90	Exon 91	Exon 92	Exon 93	Exon 94	Exon 95	Exon 96	Exon 97	Exon 98	Exon 99	Exon 100	Exon 101	Exon 102	Exon 103	Exon 104	Exon 105	Exon 106	Exon 107	Exon 108	Exon 109	Exon 110	Exon 111	Exon 112	Exon 113	Exon 114	Exon 115	Exon 116	Exon 117	Exon 118	Exon 119	Exon 120	Exon 121	Exon 122	Exon 123	Exon 124	Exon 125	Exon 126	Exon 127	Exon 128	Exon 129	Exon 130	Exon 131	Exon 132	Exon 133	Exon 134	Exon 135	Exon 136	Exon 137	Exon 138	Exon 139	Exon 140	Exon 141	Exon 142	Exon 143	Exon 144	Exon 145	Exon 146	Exon 147	Exon 148	Exon 149	Exon 150	Exon 151	Exon 152	Exon 153	Exon 154	Exon 155	Exon 156	Exon 157	Exon 158	Exon 159	Exon 160	Exon 161	Exon 162	Exon 163	Exon 164	Exon 165	Exon 166	Exon 167	Exon 168	Exon 169	Exon 170	Exon 171	Exon 172	Exon 173	Exon 174	Exon 175	Exon 176	Exon 177	Exon 178	Exon 179	Exon 180	Exon 181	Exon 182	Exon 183	Exon 184	Exon 185	Exon 186	Exon 187	Exon 188	Exon 189	Exon 190	Exon 191	Exon 192	Exon 193	Exon 194	Exon 195	Exon 196	Exon 197	Exon 198	Exon 199	Exon 200	Exon 201	Exon 202	Exon 203	Exon 204	Exon 205	Exon 206	Exon 207	Exon 208	Exon 209	Exon 210	Exon 211	Exon 212	Exon 213	Exon 214	Exon 215	Exon 216	Exon 217	Exon 218	Exon 219	Exon 220	Exon 221	Exon 222	Exon 223	Exon 224	Exon 225	Exon 226	Exon 227	Exon 228	Exon 229	Exon 230	Exon 231	Exon 232	Exon 233	Exon 234	Exon 235	Exon 236	Exon 237	Exon 238	Exon 239	Exon 240	Exon 241	Exon 242	Exon 243	Exon 244	Exon 245	Exon 246	Exon 247	Exon 248	Exon 249	Exon 250	Exon 251	Exon 252	Exon 253	Exon 254	Exon 255	Exon 256	Exon 257	Exon 258	Exon 259	Exon 260	Exon 261	Exon 262	Exon 263	Exon 264	Exon 265	Exon 266	Exon 267	Exon 268	Exon 269	Exon 270	Exon 271	Exon 272	Exon 273	Exon 274	Exon 275	Exon 276	Exon 277	Exon 278	Exon 279	Exon 280	Exon 281	Exon 282	Exon 283	Exon 284	Exon 285	Exon 286	Exon 287	Exon 288	Exon 289	Exon 290	Exon 291	Exon 292	Exon 293





The image shows a large, empty grid table with many columns and rows. The grid is composed of small, uniform squares, suggesting a data table or a complex table with many columns and rows. The grid is mostly empty, with some faint, illegible text visible in the lower right quadrant, possibly representing a table header or footer that is too small to read. The overall appearance is that of a placeholder or a very large, empty table.

Table 2 Summary of subject's distributions according to age categories			
Current cohort	age brackets (y)	ASD	NT
	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	age brackets	ASD	NT
	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 subject's distributions according to district categories			
Current cohort	Region	ASD	NT
	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	
Validation cohort 1	Region	ASD	NT
	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 demographic and clinical characteristics 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				ASD	NT	
		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%)

Table 8 Predicted microbiota age and Physiological age.

Group	Physiological age	Predicted microbiota age
ASD	1.1	1.063991283
ASD	1.1	1.781075827
ASD	1.11	3.15698653
ASD	1.4	0.565391134
ASD	1.4	0.70140548
ASD	1.4	2.292544432
ASD	1.4	4.436245802
ASD	1.4	0.377813951
ASD	1.5	1.282486519
ASD	1.6	0.36967383
ASD	1.6	0.529338239
ASD	1.6	2.217356637
ASD	1.6	2.241657771
ASD	1.6	3.203106806
ASD	1.7	0.840901886
ASD	1.7	1.937369565
ASD	1.8	0.318060694
ASD	1.8	0.803481103
ASD	1.8	0.882089074
ASD	1.8	1.754950471
ASD	1.8	1.960165915
ASD	1.8	2.237232407
ASD	1.8	3.204896043
ASD	1.9	2.18280643
ASD	1.9	3.550967351
ASD	2	0.467091715
ASD	2	1.176347592
ASD	2	1.259873981
ASD	2	1.741770705
ASD	2	1.770958338
ASD	2	1.91951554
ASD	2	1.926712148
ASD	2	1.93072657
ASD	2	1.943004082
ASD	2	1.945972593
ASD	2	2.108131684
ASD	2	2.187255621
ASD	2	2.29659678
ASD	2	2.520844315
ASD	2	2.935516641
ASD	2	3.050283375
ASD	2	3.161383723
ASD	2	3.516339334
ASD	2	3.709160877
ASD	2	4.515946781
ASD	2	5.023961999
ASD	2	29.64666025
ASD	2	44.64305183
ASD	2	54.19206455
ASD	2.1	1.245212627
ASD	2.1	1.2649716
ASD	2.1	1.559959012
ASD	2.1	1.766049805
ASD	2.1	1.77713922
ASD	2.1	1.96702221
ASD	2.1	2.124653667
ASD	2.1	2.251197644
ASD	2.1	2.252430715
ASD	2.1	2.527564928
ASD	2.1	2.900313087
ASD	2.1	3.562744701
ASD	2.1	3.674741159
ASD	2.1	3.822704226
ASD	2.1	3.318712701
ASD	2.11	1.760552255
ASD	2.11	1.932818675
ASD	2.11	2.595862962
ASD	2.11	3.365695231

Mean value of Physiological age - Predicted microbiota age of each subject				
mean \pm SEM, p value were calculated by one-way ANOVA respectively.				
	NT		ASD	
	mean	SEM	mean	SEM
0-16mo	-7.388849941	6.164149533	-0.867568166	0.615385255
16-18mo	-0.698748974	0.742024791	-0.385390627	0.539326174
18-20mo	-0.547379962	0.228995236	-0.080775177	0.362014509
20-22mo	-0.980615501	0.265384868	-0.109104888	0.538079514
22-24mo	-2.569078497	0.184055844	-5.626443526	2.997902786
24-26mo	-2.180152462	0.793446388	-1.061452151	0.2511445
26-28mo	-1.294482887	0.658205823	-1.170565375	0.483696901
28-30mo	-0.634614481	0.416162351	0.017160573	0.142037715
30-32mo	-0.661850718	0.369507484	-0.904633062	0.286685052
32-34mo	-0.515342378	0.713771612	-0.802546909	0.31722984
34-36mo	-2.395941997	0.411907781	-3.125436405	1.530681936
3-4y	-2.89390495	1.938138562	-1.476573692	0.885561967
4-5y	-5.079561805	1.481656833	-2.768736079	1.069005948
5-6y	-8.958558559	2.389885103	-2.195826422	1.160442858
6-7y	-10.03102089	2.415255895	-1.895388965	1.378608687
7-8y	-8.594485612	3.648938311	-7.303945452	3.21544231
8-9y	-11.1081029	3.833408235	0.063331717	1.765338513
9-16y	-3.629092634	2.295032983	-8.023251275	3.075474676
adults	-2.663537246	3.010763383	-18.17773156	14.77089379

Microbiota-for-age Z score (MAZ) of each subject.		
The value of MAZ of each subject was calculated as: (microbiota age - median microbiota age of healthy children of same physiological age) / (standard deviation of microbiota age of healthy children of the same physiological age).		
	ASD	
	Physiological age	MAZ
	1.1	-0.039034064
	1.1	-0.00024896
	1.11	0.074170215
	1.4	-0.066001956
	1.4	-0.05864532
	1.4	0.027414951
	1.4	0.143361783
	1.4	-0.076147483
	1.5	-0.720506371
	1.6	-1.46481042
	1.6	-1.334620658
	1.6	0.041783222
	1.6	0.061598276
	1.6	0.845560218
	1.7	-3.011405719
	1.7	-0.18657188
	1.8	-1.506895578
	1.8	-1.111085594
	1.8	-1.046988949
	1.8	-0.335261034
	1.8	-0.167929129
	1.8	0.05798985
	1.8	0.847019155
	1.9	-0.468395672
	1.9	1.935357817
	2	-3.48277444
	2	-2.236666425
	2	-2.089916985
	2	-1.243261513
	2	-4.796785208
	2	-4.430704934
	2	-4.412970781
	2	-4.40307829
	2	-4.372823582
	2	-4.365508465
	2	-3.965909901
	2	-3.770929706
	2	-3.501487087
	2	-2.948887834
	2	-1.927036615
	2	-1.64422409
	2	-1.370446412
	2	-0.495751377
	2	-0.020593243
	2	1.96751908
	2	3.219389384
	2	excluded
	2	excluded
	2	excluded
	2.1	-1.044695913
	2.1	-1.03346807
	2.1	-0.865844365
	2.1	-0.748735291
	2.1	-0.74243384
	2.1	-0.634534692
	2.1	-0.544962161
	2.1	-0.473054787
	2.1	-0.472354107
	2.1	-0.316011787
	2.1	-0.104201299
	2.1	0.272218973
	2.1	0.335859863
	2.1	0.419938425
	2.1	0.133550181

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
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ASD	2.3	1.934150894
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ASD	2.3	1.975056921
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ASD	2.4	1.769037947
ASD	2.4	1.770056576
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ASD	2.4	1.799120598
ASD	2.4	2.436815482
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ASD	2.4	3.041442528
ASD	2.4	1.589790419
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	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
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	2.2	-2.508143147
	2.2	-1.71084678
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	2.2	0.280232072
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	2.3	-1.848566219
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	2.3	-1.667653992
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	2.5	-1.503341403
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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

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																	1.56%	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	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
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				715.2168	4315.926	0.012537												
7	MGB009 Histamine synthesis				6216.852	5725.541	0.171932																					
8	MGB031 17- β -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																					
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																											
16	MGB023 Dopamine degradation																											
17	MGB021 GABA synthesis II																											
18	MGB020 GABA synthesis I																											
19	MGB016 p-Cresol degradation																											
20	MGB048 Propionate synthesis I																											
21	MGB010 Histamine degradation																											
22	MGB026 Nitric oxide synthesis II (nitrite reductase)																											
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)																											
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 S5 Summary of the statistical results of the 286 significant changed METACYC across age

Table with 18 columns: No, Row name, Higher level functional annotation, mean NT, mean ASO, p-value, and columns 2 through 18. The table lists 286 metabolic pathways and their associated statistical data across different age groups.

Table with 27 columns and 275 rows listing gene identifiers, descriptions, and associated numerical data. The table is densely packed with text and numbers, organized into columns.

Table 16 Summary of the statistical results of correlations between bacterial taxa and clinical phenotypes according to Spearman's rank correlations analysis

Table with columns for taxonomic group (e.g., g. Veillonella, f. Faecalibacterium), clinical phenotype (e.g., age, BMI score, positive faecal SCFA production), and Spearman's rank correlation coefficients (rho) for various conditions. The table is organized into brackets (1-23 mo, 24-36 mo, etc.) and includes a detailed header for the correlation analysis.

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

Age bracket	Gene	Group	ASD score	Repetitive	Social	Language	any GI prob	GI problem	sephageal	peptic ulcer	Dyspepsia	abdominal	abdominal	constipation	abnormal	within 1 mo	any sleep	deep	difficult	fat	sleep	fragm	short	Shallow	any neonate	food allergy	skin allergy	respiratory	Antibiotic	within 3 months		
age bracket 1 (11-23 mo)	MOR25 Nitric oxide synthase I (NO synthase)	p-value																														
	RHO	0.039539																														
age bracket 2 (24-35 mo)	MOR50 Glutamate degradation I	p-value																														
	RHO	0.251453																														
age bracket 3 (36-47 mo)	MOR34 Isovaleric acid synthase II (KADH pathway)	p-value																														
	RHO	0.157589																														
age bracket 4 (48-59 mo)	MOR16 p-Cresol degradation	p-value																														
	RHO	0.004352																														
age bracket 5 (6-8 y)	MOR38 Inositol degradation	p-value																														
	RHO	0.249315																														
age bracket 6 (9-10 y)	MOR20 GABA synthesis I	p-value																														
	RHO	0.0165376																														
age bracket 7 (11-12 y)	MOR20 GABA synthesis I	p-value																														
	RHO	0.0165376																														
age bracket 8 (13-14 y)	MOR20 GABA synthesis I	p-value																														
	RHO	0.0165376																														

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, direction, p-value, rank, and Spearman's correlation coefficient. It lists various metabolic pathways such as PWW-7527 L-methionine salvage cycle II and PWW-1298 Nucleoside degradation, along with their associated p-values and correlation coefficients.

Gene	Gene ID	Enzyme	EC	Pathway	KEGG ID	KEGG Pathway	KEGG Link	log2(FC)		log2(FC)		log2(FC)		log2(FC)		log2(FC)		log2(FC)		log2(FC)		
								Protein	Gene	Protein	Gene	Protein	Gene	Protein	Gene	Protein	Gene	Protein	Gene	Protein	Gene	Protein
age bracket 4 (4-5 y)	GLYCOL-GLYOXIDE-PWY superpathway of glycol metabolism and degradation	PFKP	1.14931771	PFKP	0.000261	0.000261	0.000261	0.000261														
		PFKL	0.000261	0.000261	0.000261	0.000261																
		PFFB	0.000261	0.000261	0.000261	0.000261																
		PFDL	0.000261	0.000261	0.000261	0.000261																
		PFB	0.000261	0.000261	0.000261	0.000261																
		PFKL	0.000261	0.000261	0.000261	0.000261																
		PFKL	0.000261	0.000261	0.000261	0.000261																
		PFKL	0.000261	0.000261	0.000261	0.000261																
		PFKL	0.000261	0.000261	0.000261	0.000261																
		PFKL	0.000261	0.000261	0.000261	0.000261																
age bracket 5 (6-9 y)	GLYCOL-GLYOXIDE-PWY superpathway of glycol metabolism and degradation	PFKP	0.000261	0.000261	0.000261	0.000261																
		PFKL	0.000261	0.000261	0.000261	0.000261																
		PFFB	0.000261	0.000261	0.000261	0.000261																
		PFDL	0.000261	0.000261	0.000261	0.000261																
		PFB	0.000261	0.000261	0.000261	0.000261																
		PFKL	0.000261	0.000261	0.000261	0.000261																
		PFKL	0.000261	0.000261	0.000261	0.000261																
		PFKL	0.000261	0.000261	0.000261	0.000261																
		PFKL	0.000261	0.000261	0.000261	0.000261																
		PFKL	0.000261	0.000261	0.000261	0.000261																

Table containing metabolic pathway descriptions (e.g., PWW-733, PWW-728) and their corresponding numerical values across multiple columns. Includes sub-sections like 'age bracket 9 (9-)', '< 3y', and '> 3y'.

											0.06114281					0.0282771	0.06728292				0.03811595					
	FADN-ELONG-FWY fatty acid elongation - saturated	-2.0297	0.00501193	0.00698381	0.01613801	0.00113180	0.01007651																			
		SDC ²	0.11242031	0.1086721	0.32242921	0.32092922	0.36742494					0.02142482										0.05819274				
		-2.0297	0.11242031	0.1086721	0.32242921	0.32092922	0.36742494			0.02098882							0.0282771	0.06728292				0.03811595				
	DENOVOPURINE2-FWY superpathway of purine nucleotides de novo biosynthesis II	-2.0297	0.11242031	0.1086721	0.32242921	0.32092922	0.36742494			0.02098882							0.0282771	0.06728292				0.03811595				
		SDC ²	0.11242031	0.1086721	0.32242921	0.32092922	0.36742494			0.02098882							0.0282771	0.06728292				0.03811595				
		-2.0297	0.11242031	0.1086721	0.32242921	0.32092922	0.36742494			0.02098882							0.0282771	0.06728292				0.03811595				
	CDDN-FWY reductive amination of lysine pathway	-2.0297	0.11242031	0.1086721	0.32242921	0.32092922	0.36742494			0.02098882							0.0282771	0.06728292				0.03811595				
		SDC ²	0.11242031	0.1086721	0.32242921	0.32092922	0.36742494			0.02098882							0.0282771	0.06728292				0.03811595				
		-2.0297	0.11242031	0.1086721	0.32242921	0.32092922	0.36742494			0.02098882							0.0282771	0.06728292				0.03811595				
	ARGONA-FWY L-arginine biosynthesis Lys L- ornithine	-2.0297	0.11242031	0.1086721	0.32242921	0.32092922	0.36742494			0.02098882							0.0282771	0.06728292				0.03811595				
		SDC ²	0.11242031	0.1086721	0.32242921	0.32092922	0.36742494			0.02098882							0.0282771	0.06728292				0.03811595				
		-2.0297	0.11242031	0.1086721	0.32242921	0.32092922	0.36742494			0.02098882							0.0282771	0.06728292				0.03811595				
		SDC ²	0.11242031	0.1086721	0.32242921	0.32092922	0.36742494			0.02098882							0.0282771	0.06728292				0.03811595				
		-2.0297	0.11242031	0.1086721	0.32242921	0.32092922	0.36742494			0.02098882							0.0282771	0.06728292				0.03811595				
		SDC ²	0.11242031	0.1086721	0.32242921	0.32092922	0.36742494			0.02098882							0.0282771	0.06728292				0.03811595				