

Supplementary Tables

Table S1. R² values for contributions of all metadata factors to beta diversity measures.

	Jaccard distance				Bray-Curtis distance				Aitchison distance			
	Cecal		Fecal		Cecal		Fecal		Cecal		Fecal	
	R ²	p	R ²	p	R ²	p	R ²	p	R ²	p	R ²	p
Genotype	0.265	< 0.001	0.254	< 0.001	0.228	< 0.001	0.251	< 0.001	0.263	< 0.001	0.263	< 0.001
Age	0.091	< 0.001	0.089	< 0.001	0.155	< 0.001	0.160	< 0.001	0.094	< 0.001	0.088	< 0.001
Sex	0.007	0.883	0.007	0.906	0.006	0.971	0.005	0.982	0.007	0.998	0.007	0.889

Significant results (p < 0.01) are bolded.

Table S2: P-values for results of Beta dispersion tests comparing Genotype groups at each timepoint in both fecal and cecal samples.

	Jaccard distance		Bray-Curtis distance		Aitchison distance	
	Cecal	Fecal	Cecal	Fecal	Cecal	Fecal
P17	0.301	0.461	0.003	0.481	0.72	0.174
P24	0.478	0.047	0.715	0.025	0.001	0.002
P28	0.106	0.244	0.005	0.531	0.455	0.002
P84	0.231	0.148	0.122	0.002	0.001	0.001

Significant results (p < 0.01) are bolded.

Table S3: Similarity matrix used to build the circos plot.

		Butyrate	Valine	Isoleucine	Alanine	Acetate	Aspartate	Xylose	Maltose	Hypoxanthine	Formate	Inosine	Valerate	Acetoin	Ornithine	Malonate	Glycero-phosphocholine	Glucose-6-phosphate	5-AV
Family (ASV)		-	-	-	-	0.092	-	0.116	0.215	-	-	0.023	-	-	-	-	0.280	0.221	0.116
Lachnospiraceae	sp19	0.111	0.110	0.155	0.098	-	0.033	-	-	0.163	0.057	-	0.227	0.137	0.076	0.073	-	-	-
Rikenellaceae	sp8	0.523	0.336	0.455	0.132	0.061	0.103	0.202	0.287	0.106	0.134	0.240	0.685	0.432	0.312	0.229	0.181	0.569	0.554
Lachnospiraceae	sp85	0.299	0.058	0.057	0.168	0.240	0.250	0.138	0.372	0.427	0.375	0.236	0.108	0.089	0.144	0.049	0.736	0.023	0.323
Lachnospiraceae	sp240	0.235	0.009	-	0.199	0.265	0.250	0.178	0.440	0.470	0.377	0.213	0.006	0.026	0.103	0.016	0.810	0.115	0.255
Muribaculaceae	sp26	0.510	0.322	0.434	0.117	0.047	0.109	0.185	0.256	0.082	0.144	0.238	0.655	0.414	0.303	0.220	0.138	0.539	0.540
Rikenellaceae	sp60	0.533	0.335	0.453	0.121	0.047	0.115	0.192	0.264	0.083	0.152	0.249	0.683	0.432	0.316	0.229	0.140	0.561	0.565
Lachnospiraceae	sp181	0.098	0.097	0.137	0.087	0.082	0.030	0.103	0.191	0.145	0.051	0.019	0.201	0.121	0.067	0.064	0.249	0.196	0.102
Lachnospiraceae	sp152	0.223	0.175	0.242	0.114	0.091	0.002	0.146	0.250	0.161	0.014	0.079	0.360	0.222	0.141	0.117	0.277	0.326	0.235
Muribaculaceae	sp61	0.524	0.347	0.471	0.150	0.081	0.089	0.221	0.327	0.142	0.113	0.233	0.707	0.444	0.315	0.236	0.242	0.596	0.555
Muribaculaceae	sp39	0.620	0.387	0.523	0.136	0.049	0.138	0.218	0.296	0.086	0.183	0.293	0.789	0.499	0.367	0.265	0.145	0.646	0.657
Muribaculaceae	sp46	0.524	0.325	0.438	0.111	0.038	0.119	0.181	0.243	0.066	0.159	0.248	0.662	0.419	0.310	0.223	0.111	0.540	0.555
Lachnospiraceae	sp151	0.328	0.126	0.157	0.071	0.136	0.186	0.033	0.159	0.242	0.272	0.213	0.250	0.171	0.174	0.092	0.417	0.136	0.351

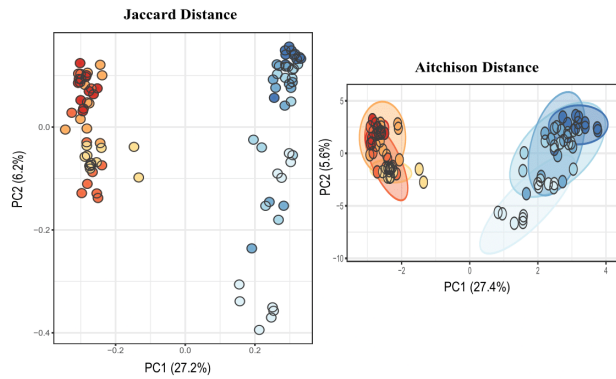
Lachnospiraceae	sp332	0.226	0.001	-	0.022	0.205	0.270	-	0.251	0.185	0.454	-	-	-	0.017	0.097	0.010	0.826	0.130	-	0.246
Ruminococcaceae	sp288	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Muribaculaceae	sp105	0.006	0.048	0.072	0.081	0.091	0.062	0.086	0.180	0.162	0.096	0.030	0.102	0.057	0.015	0.030	0.278	0.121	0.005	-	-
Lachnospiraceae	sp328	0.556	0.354	0.478	0.134	0.057	0.114	0.208	0.291	0.100	0.150	0.258	0.721	0.455	0.331	0.242	0.170	0.595	0.589	-	-
Muribaculaceae	sp81	0.201	-	0.016	0.044	0.212	0.274	0.247	0.196	0.469	0.487	0.374	0.200	0.043	0.004	0.083	0.001	0.838	0.158	0.220	-
Lachnospiraceae	sp122	-	-	-	-	-	0.039	0.108	0.173	0.234	0.069	0.144	0.230	0.622	0.393	0.289	0.209	0.116	0.509	0.518	-
Muribaculaceae	sp121	0.488	0.305	0.412	0.108	-	-	-	-	-	-	-	-	0.563	0.357	0.263	0.189	0.101	0.461	0.470	-
Lachnospiraceae	sp121	0.444	0.277	0.373	0.096	0.034	0.099	0.155	0.210	0.060	0.132	0.210	-	-	-	-	-	-	-	-	-
Muribaculaceae	sp123	0.487	0.318	0.431	0.131	0.066	0.089	0.197	0.287	0.117	0.114	0.220	0.648	0.408	0.292	0.217	0.199	0.542	0.516	-	-
Muribaculaceae	sp112	0.498	0.309	0.417	0.106	-	-	-	-	0.062	0.151	0.236	0.629	0.398	0.294	0.212	0.105	0.513	0.528	-	-
Muribaculaceae	sp112	-	-	-	-	0.036	0.113	0.172	0.230	-	-	-	-	-	-	-	-	-	-	-	-
Muribaculaceae	sp96	0.607	0.369	0.496	0.115	0.027	0.150	0.194	0.249	0.047	0.203	0.294	0.751	0.477	0.357	0.253	0.078	0.606	0.644	-	-
Muribaculaceae	sp168	-	-	-	-	-	-	-	-	-	-	-	-	0.666	0.423	0.317	0.225	0.068	0.537	0.572	-
Muribaculaceae	sp237	0.539	0.328	0.440	0.101	0.024	0.133	0.172	0.220	0.041	0.180	0.261	0.630	0.399	0.292	0.212	0.125	0.517	0.522	-	-
Muribaculaceae	sp172	0.493	0.310	0.418	0.111	0.042	0.107	0.177	0.242	0.074	0.142	0.231	0.640	0.399	0.292	0.212	0.125	0.517	0.522	-	-
Muribaculaceae	sp137	0.488	0.314	0.425	0.124	0.057	0.095	0.189	0.270	0.101	0.124	0.224	0.605	0.404	0.291	0.214	0.171	0.532	0.517	-	-
Muribaculaceae	sp137	0.514	0.298	0.398	0.071	0.007	0.148	0.137	0.152	0.014	0.204	0.260	0.694	0.387	0.299	0.206	0.026	0.475	0.546	-	-
Muribaculaceae	sp270	-	-	-	-	0.037	0.127	0.188	0.251	0.065	0.170	0.262	0.694	0.440	0.326	0.234	0.109	0.566	0.584	-	-
Ruminococcaceae	sp418	0.488	0.316	0.429	0.128	-	-	-	-	0.110	0.119	0.222	0.645	0.406	0.292	0.216	0.186	0.538	0.517	-	-
Lachnospiraceae	sp365	0.217	0.026	0.017	0.151	0.208	0.205	0.131	0.335	0.370	0.308	0.184	0.044	0.046	0.100	0.026	0.637	0.059	0.236	-	-
Lachnospiraceae	sp261	-	-	-	-	-	-	-	-	-	-	-	-	0.330	0.204	0.132	0.108	0.236	0.296	0.221	-
Muribaculaceae	sp629	0.210	0.161	0.222	0.100	0.078	0.004	0.130	0.220	0.138	0.004	0.077	0.704	0.445	0.326	0.237	0.142	0.578	0.583	-	-
Lachnospiraceae	sp234	0.550	0.346	0.467	0.125	0.048	0.119	0.198	0.271	0.084	0.158	0.258	0.624	0.396	0.295	0.210	0.077	0.505	0.531	-	-
Muribaculaceae	sp266	0.215	0.008	0.034	0.211	0.275	0.251	0.193	0.467	0.489	0.380	0.207	0.680	0.429	0.312	0.228	0.163	0.562	0.555	-	-
Peptococcaceae	sp342	0.501	0.306	0.412	0.098	0.027	0.120	0.164	0.214	0.046	0.162	0.241	0.692	0.436	0.312	0.231	0.212	0.579	0.551	-	-
Peptococcaceae	sp327	0.524	0.334	0.451	0.127	0.055	0.107	0.197	0.276	0.096	0.141	0.242	0.690	0.433	0.307	0.230	0.240	0.581	0.540	-	-
Peptococcaceae	sp304	-	-	-	-	0.071	0.095	0.210	0.306	0.125	0.122	0.235	0.662	0.420	0.311	0.223	0.097	0.538	0.559	-	-
Ruminococcaceae	sp889	0.520	0.339	0.460	0.140	0.071	0.095	0.210	0.306	0.125	0.122	0.235	0.692	0.436	0.312	0.231	0.212	0.579	0.551	-	-
Lachnospiraceae	sp758	0.510	0.338	0.459	0.147	0.080	0.086	0.216	0.321	0.141	0.108	0.226	0.690	0.433	0.307	0.230	0.240	0.581	0.540	-	-
Lachnospiraceae	sp308	0.528	0.325	0.438	0.108	0.033	0.123	0.178	0.235	0.058	0.165	0.252	0.662	0.420	0.311	0.223	0.097	0.538	0.559	-	-
Ruminococcaceae	sp889	-	-	-	-	0.105	-	0.110	0.220	-	-	-	-	-	-	-	0.321	0.177	0.047	-	-
Lachnospiraceae	sp758	0.046	0.078	0.114	0.100	0.061	0.110	0.220	0.249	0.187	0.096	0.015	0.164	0.095	0.040	0.050	0.321	0.177	0.047	-	-
Lachnospiraceae	sp308	0.215	0.008	0.034	0.211	0.275	0.251	0.193	0.467	0.489	0.380	0.207	0.028	0.006	0.091	0.005	0.842	0.147	0.235	-	-
Ruminococcaceae	sp805	-	-	-	-	0.038	0.123	0.186	0.249	0.067	0.165	0.256	0.682	0.432	0.319	0.230	0.112	0.556	0.572	-	-
Muribaculaceae	sp546	0.023	0.025	0.040	0.066	0.079	0.062	0.066	0.146	0.140	0.095	0.040	0.053	0.027	0.004	0.014	0.241	0.078	0.027	-	-
Defluvitaleaceae	sp1196	-	-	-	-	0.095	0.018	0.135	0.240	-	-	-	0.052	-	-	-	0.288	0.282	0.180	-	-
Lachnospiraceae	sp518	0.172	0.147	0.204	0.109	0.095	0.018	0.135	0.240	0.168	0.037	0.052	0.302	0.185	0.112	0.098	0.288	0.282	0.180	-	-
Ruminococcaceae	sp935	0.049	0.080	0.116	0.100	0.105	0.060	0.110	0.221	0.187	0.096	0.014	0.167	0.097	0.042	0.051	0.321	0.179	0.049	-	-
Clostridiales_vadinBB60_group	sp8105	0.398	0.160	0.201	0.073	0.150	0.215	0.027	0.163	0.266	0.314	0.253	0.319	0.216	0.213	0.116	0.460	0.184	0.426	-	-
Lachnospiraceae	sp8105	-	-	-	-	0.103	0.042	0.124	0.235	0.182	0.071	0.016	0.233	0.140	0.075	0.074	0.313	0.230	0.111	-	-
Lachnospiraceae	sp813	0.106	0.112	0.159	0.107	0.105	0.061	0.110	0.220	0.187	0.096	0.015	0.164	0.095	0.040	0.050	0.321	0.177	0.047	-	-
Lachnospiraceae	sp877	0.046	0.078	0.114	0.100	0.105	0.061	0.110	0.220	0.187	0.096	0.015	0.164	0.095	0.040	0.050	0.321	0.177	0.047	-	-
Lachnospiraceae	sp892	0.230	0.033	0.026	0.151	0.209	0.210	0.128	0.334	0.372	0.315	0.191	0.058	0.055	0.108	0.030	0.641	0.049	0.249	-	-
Lachnospiraceae	sp1102	0.215	0.008	0.034	0.211	0.275	0.251	0.193	0.467	0.489	0.380	0.207	0.028	0.006	0.091	0.005	0.842	0.147	0.235	-	-
Lachnospiraceae	sp693	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lachnospiraceae	sp834	0.046	0.078	0.114	0.100	0.105	0.061	0.110	0.220	0.187	0.096	0.015	0.164	0.095	0.040	0.050	0.321	0.177	0.047	-	-
Clostridiales_vadinBB60_group	sp842	0.215	0.008	0.034	0.211	0.275	0.251	0.193	0.467	0.489	0.380	0.207	0.028	0.006	0.091	0.005	0.842	0.147	0.235	-	-
Ruminococcaceae	sp927	0.220	0.029	0.021	0.150	0.206	0.205	0.128	0.331	0.367	0.308	0.185	0.050	0.049	0.102	0.027	0.632	0.054	0.239	-	-
Erysipelotrichaceae	sp969	0.169	0.045	0.051	0.073	0.111	0.125	0.055	0.162	0.198	0.185	0.125	0.087	0.065	0.085	0.035	0.341	0.018	0.182	-	-
Lachnospiraceae	sp1393	0.215	0.008	0.034	0.211	0.275	0.251	0.193	0.467	0.489	0.380	0.207	0.028	0.006	0.091	0.005	0.842	0.147	0.235	-	-
Lachnospiraceae	sp1566	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lachnospiraceae	sp1284	0.046	0.078	0.114	0.100	0.105	0.061	0.110	0.220	0.187	0.096	0.015	0.164	0.095	0.040	0.050	0.321	0.177	0.047	-	-
Ruminococcaceae	sp1612	-	-	-	-	0.097	0.063	0.095	0.196	-	-	-	-	-	-	-	0.297	0.141	0.018	-	-
Lachnospiraceae	sp1612	0.019	0.058	0.087	0.089	0.097	0.063	0.095	0.196	0.173	0.099	0.026	0.123	0.070	0.023	0.037	0.321	0.177	0.047	-	-
Lachnospiraceae	sp1612	-	-	-	-	0.105	0.061	0.110	0.220	0.187	0.096	0.015	0.164	0.095	0.040	0.050	0.321	0.177	0.047	-	-

Lachnospiraceae	sp12 16	0.215	-	-	-	0.275	-	0.193	0.467	-	-	-	-	0.006	0.091	0.005	0.842	0.147	-	0.235
Lachnospiraceae	sp12 75	0.215	0.008	0.034	0.211	0.275	0.251	0.193	0.467	0.489	0.380	0.207	0.028	0.006	0.091	0.005	0.842	0.147	-	0.235
Clostridiales_vadinBB60_group	sp98 0	0.222	0.016	0.001	0.175	0.235	0.226	0.155	0.387	0.418	0.340	0.196	0.022	0.034	0.100	0.019	0.721	0.090	-	0.241
Ruminococcaceae	sp88 2	0.123	-	-	-	0.193	-	0.143	0.337	-	-	-	-	-	0.048	-	0.591	0.129	-	0.136
Eubacteriaceae	sp10 95	-	0.022	0.046	-	0.152	0.169	-	-	0.343	0.257	0.132	0.052	0.017	-	0.008	-	0.265	0.247	0.152
Clostridiales_vadinBB60_group	sp94 7	0.145	0.127	0.178	0.099	0.087	0.021	0.121	0.217	0.155	0.039	0.041	0.262	0.160	0.095	0.085	-	-	-	-
Lachnospiraceae	sp18 52	0.252	0.107	0.136	0.036	0.083	0.128	0.006	0.081	0.148	0.187	0.156	0.214	0.144	0.136	0.077	0.257	-	-	0.270
Lachnospiraceae	sp18 53	-	-	-	-	0.105	0.061	0.110	0.220	-	-	-	-	-	-	-	0.321	0.177	-	0.047
Ruminococcaceae	sp10 37	0.046	0.078	0.114	0.100	0.105	-	0.110	0.220	0.187	0.096	0.015	0.164	0.095	0.040	0.050	-	-	-	-
Ruminococcaceae	sp11 11	0.046	0.078	0.114	0.100	0.105	0.061	0.110	0.220	0.187	0.096	0.015	0.164	0.095	0.040	0.050	0.321	0.177	-	0.047
Lachnospiraceae	sp17 52	0.201	0.062	0.073	0.071	0.115	0.136	0.049	0.159	0.204	0.201	0.142	0.121	0.087	0.103	0.047	0.352	-	-	0.217
Lachnospiraceae	sp13 08	0.241	0.049	0.049	0.131	0.189	0.198	0.107	0.291	0.336	0.297	0.189	0.092	0.074	0.116	0.041	0.579	0.013	-	0.260
Rikenellaceae	sp13 03	0.011	-	-	-	0.077	0.057	0.068	0.147	-	-	-	-	-	-	-	0.237	0.088	-	0.014
Ruminococcaceae	sp17 11	0.215	0.031	0.048	0.067	0.275	0.251	0.193	0.467	0.138	0.088	0.034	0.067	0.036	0.003	0.019	0.842	0.147	-	0.235
Muribaculaceae	sp19 05	0.197	0.029	0.023	0.128	0.178	0.179	0.109	0.284	0.317	0.269	0.163	0.051	0.048	0.092	0.026	0.546	0.040	-	0.214
Lachnospiraceae	sp19 06	0.239	0.016	0.001	0.190	0.255	0.244	0.168	0.420	0.453	0.367	0.211	0.022	0.035	0.107	0.020	0.780	0.098	-	0.259
Ruminococcaceae	sp20 64	0.215	-	-	-	0.275	-	0.193	0.467	-	-	-	-	0.006	0.091	0.005	0.842	0.147	-	0.235
Lachnospiraceae	sp20 65	0.215	0.008	0.034	0.211	0.275	0.251	0.193	0.467	0.489	0.380	0.207	0.028	0.006	0.091	0.005	0.842	0.147	-	0.235
Lachnospiraceae	sp20 66	0.215	-	-	-	0.275	-	0.193	0.467	-	-	-	-	0.006	0.091	0.005	0.842	0.147	-	0.235
Lachnospiraceae	sp20 67	0.215	0.008	0.034	0.211	0.275	0.251	0.193	0.467	0.489	0.380	0.207	0.028	0.006	0.091	0.005	0.842	0.147	-	0.235
Lachnospiraceae	sp20 68	0.215	-	-	-	0.275	-	0.193	0.467	-	-	-	-	0.006	0.091	0.005	0.842	0.147	-	0.235
Lachnospiraceae	sp20 69	0.215	0.008	0.034	0.211	0.275	0.251	0.193	0.467	0.489	0.380	0.207	0.028	0.006	0.091	0.005	0.842	0.147	-	0.235
Lachnospiraceae	sp20 70	0.215	-	-	-	0.275	-	0.193	0.467	-	-	-	-	0.006	0.091	0.005	0.842	0.147	-	0.235

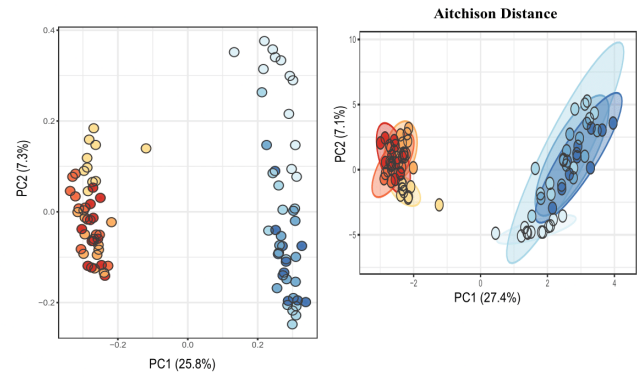
The similarity matrix is calculated as the correlation between the variables' loadings, and is an approximation of Pearson correlation. Positive (> 0.6) and negative (< -0.6) correlations are indicated by red and black squares, respectively.

Supplementary Figures

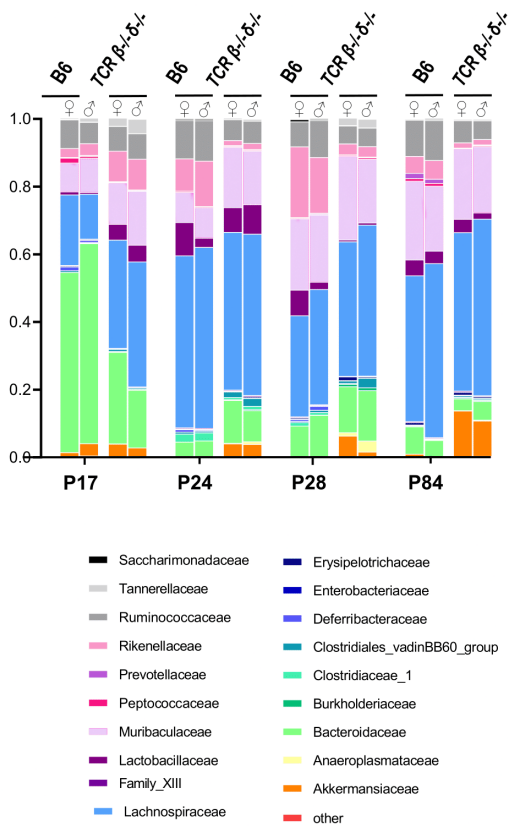
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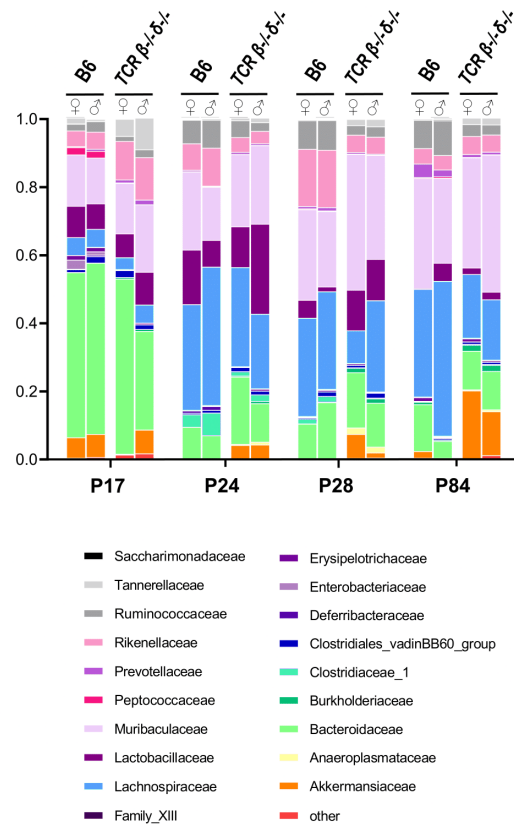
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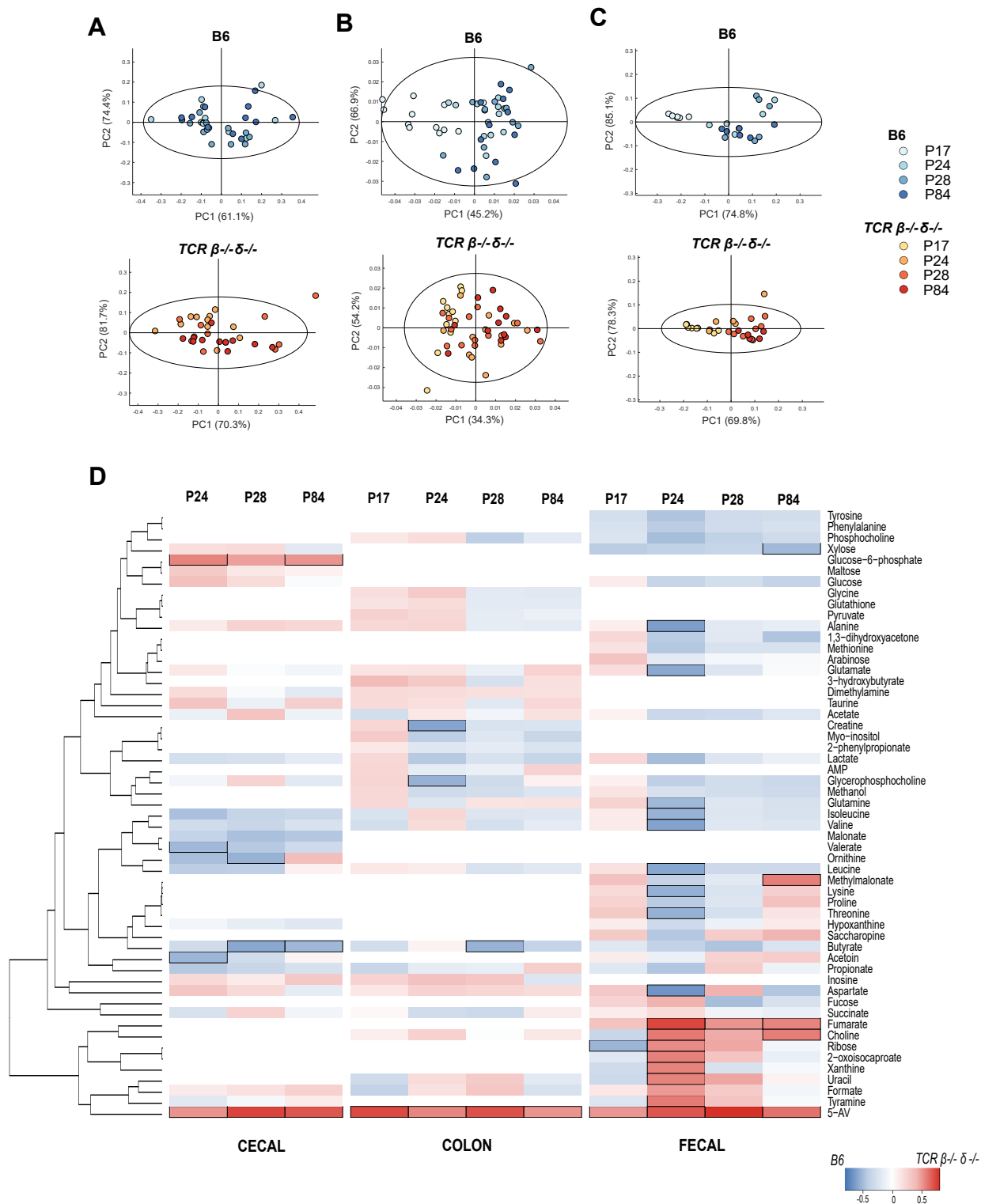
C



D



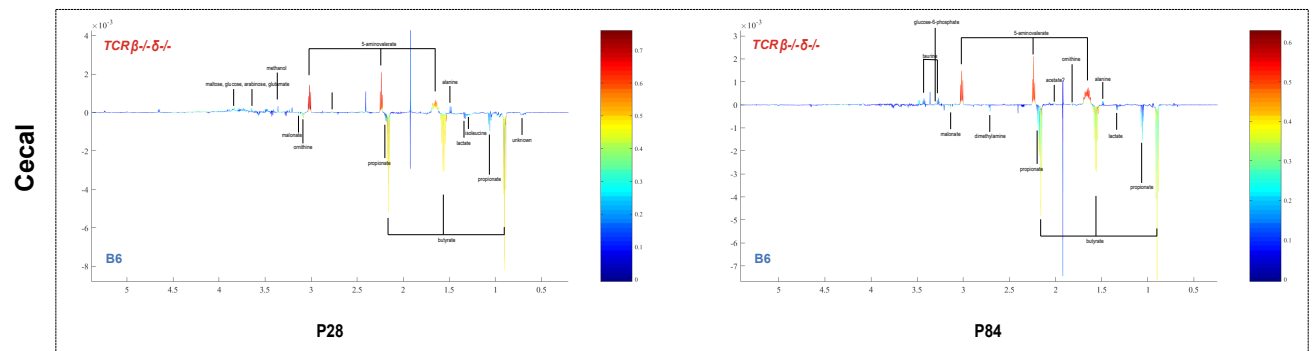
Supplemental Figure S1. *TCR $\beta^{-/-}\delta^{-/-}$* mice exhibit compositional changes in the microbiome. Upper row shows the first two principal components of Jaccard and Aitchison distance matrices for (A) cecal and (B) fecal samples. Bottom row shows the family-level distribution barplots for cecal (C) and (D) fecal samples, averaged across each group at each postnatal timepoint. Only the top 20 families are displayed.



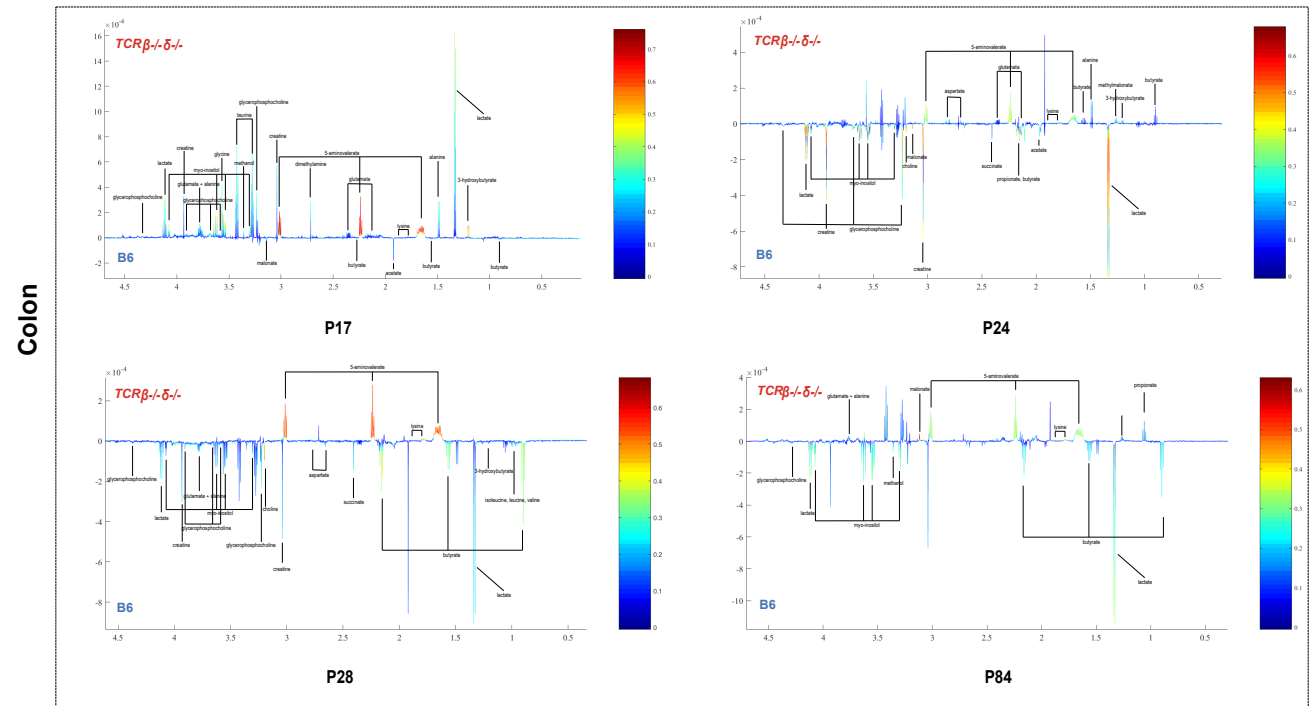
Supplemental Figure S2. Metabolic variation of cecal, colon and fecal samples associated with age. PCA scores of (A) cecal, (B) colon and (C) fecal samples from B6 (left) and *TCR β-/-δ-/-* (right) mice colored by age. In cecal samples from both B6 and *TCR β-/-δ-/-* mice, the effect of age was very weak. In colon and fecal samples obtained from B6 mice, a clear separation can be observed between B6 mice at P17 and B6 mice at later ages (P24-84), while this metabolic difference is no longer evident in mice depleted of T-cells. (D) OPLS-DA models constructed separately on the metabolic profiles of the B6 and *TCR β-/-δ-/-* mice using age as the outcome variable allowed the differences in the age-related metabolic changes to be studied in the presence and absence of T-cells. The heatmap illustrates the

correlation coefficient (r) obtained from OPLS models constructed against age for each genotype. In red are metabolites that are positively associated with age, in blue those negatively associated with age. Black squares indicate correlations with $r > |0.5|$. Increasing age was associated with an elevation in cecal ornithine and colonic myo-inositol in B6, but not *TCR β -/- δ -/-* mice. However, in *TCR β -/- δ -/-* mice xylose was observed to decreased in the cecum with age while cecal choline increased. Such changes were not observed in B6 mice. *TCR β -/- δ -/-* mice also exhibited a decrease in fecal tyramine, phenylalanine, hypoxanthine, formate and an increase in lactate with age, which was not observed in B6 mice.

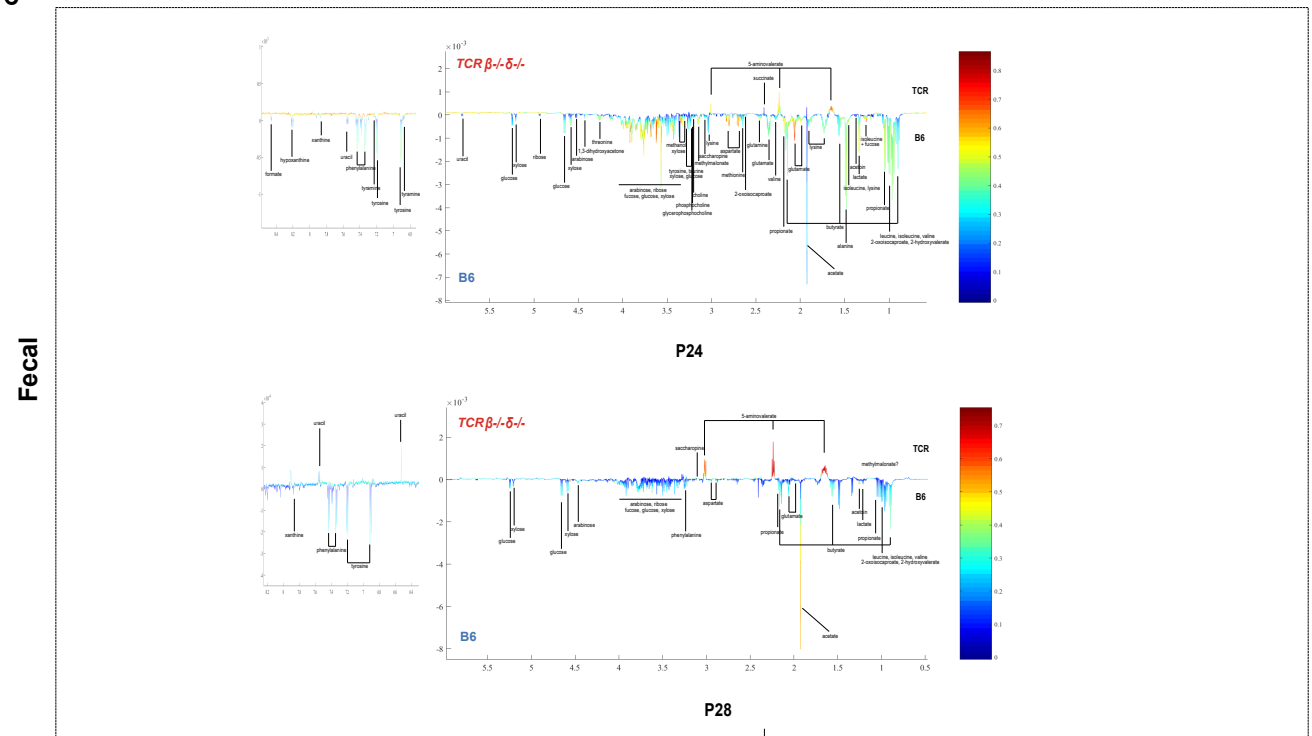
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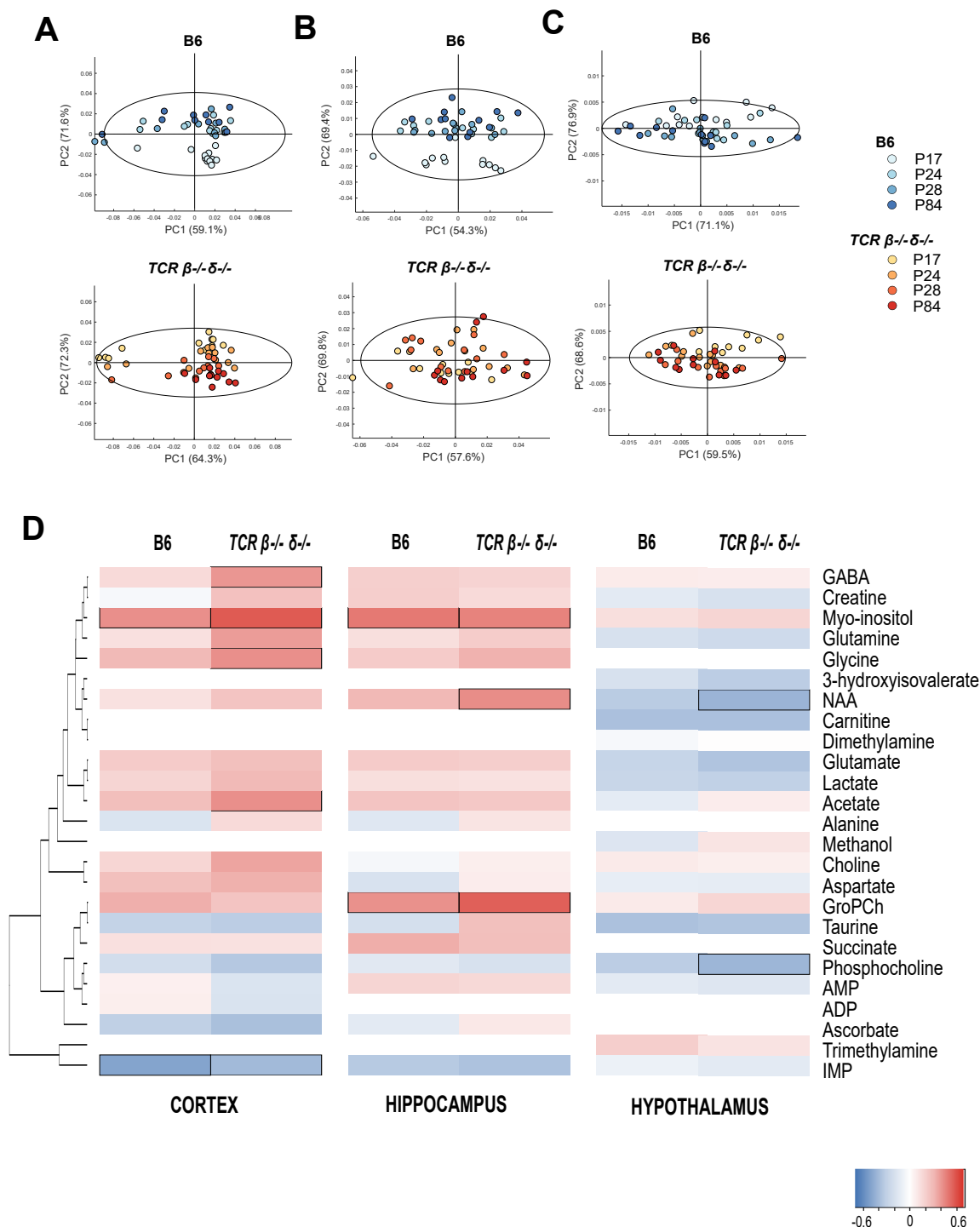
B



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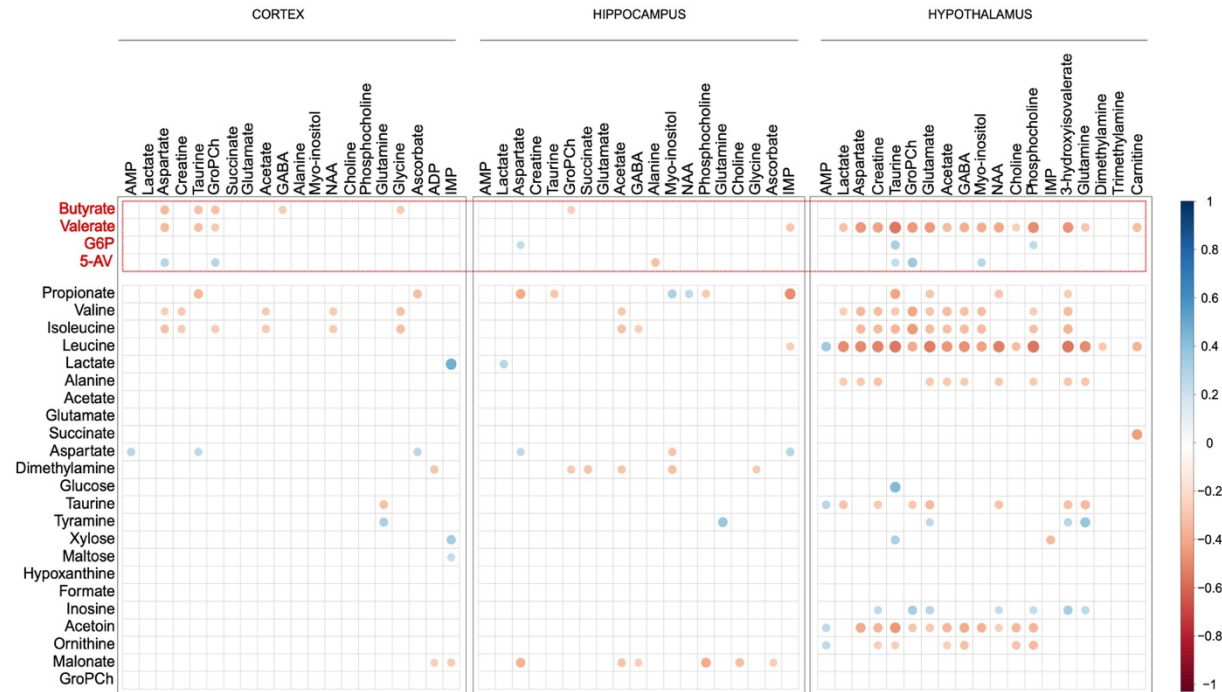


Supplemental Figure S3. OPLS-DA correlation plots showing the metabolic variation between B6 and *TCR β -/- δ -/-* mice. OPLS models were constructed on the (A) cecal, (B) colon and (C) fecal ^1H nuclear magnetic resonance spectroscopic profiles of age-matched B6 and *TCR β -/- δ -/-* mice, with genotype as the response variable. The plots show the contribution of each metabolite to the sample classification (*i.e.* loadings). Peaks pointing up represent those metabolites that are more abundant in *TCR β -/- δ -/-* mice, while peaks pointing down are metabolites that are more abundant in B6 mice. The Y represents arbitrary units (a.u.). The color of the peaks indicates the magnitude of the correlation between that metabolite and class membership, with red indicating a strong correlation and blue indicating a weak correlation. Only significant models are shown.

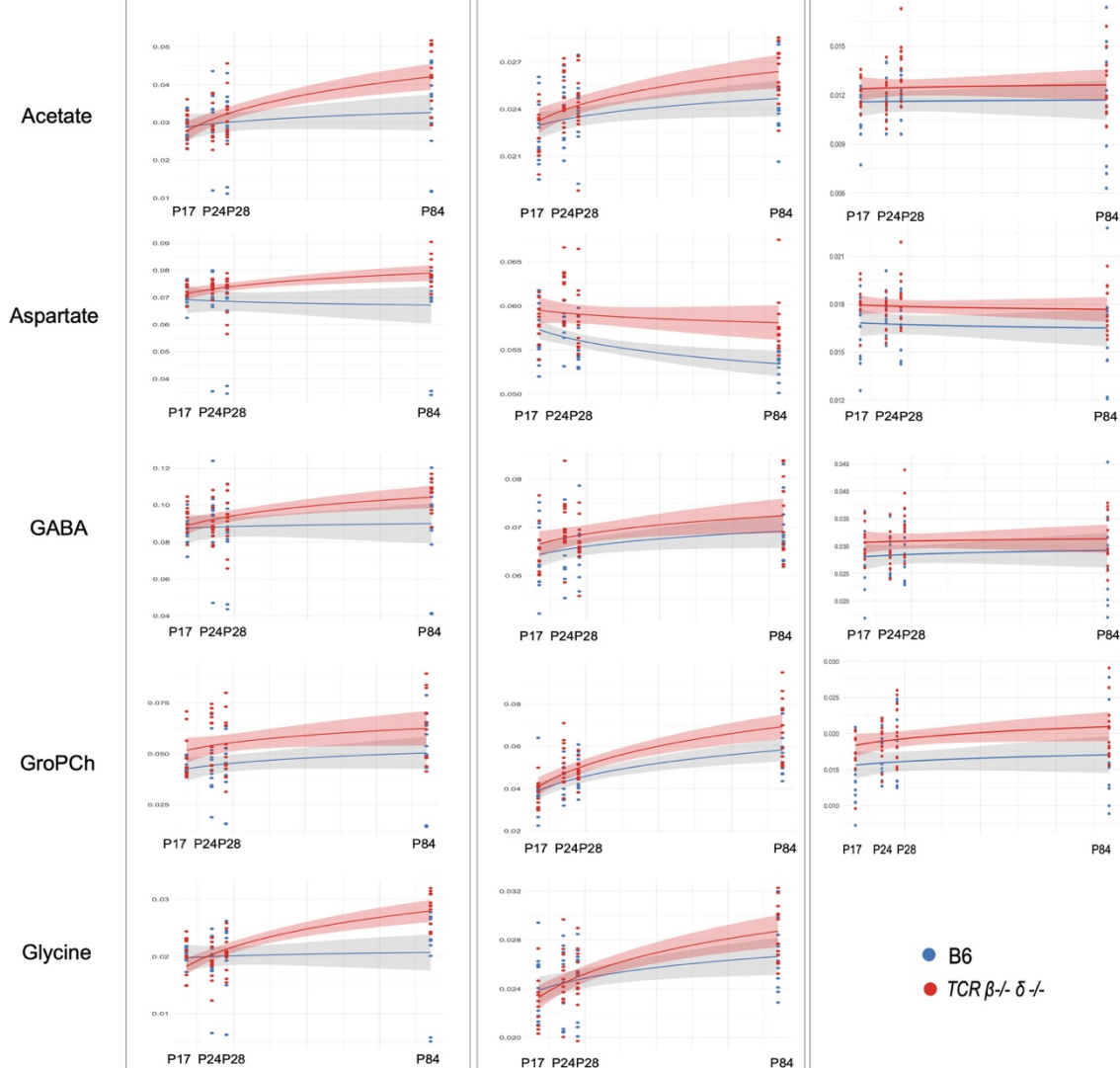


Supplemental Figure S5. Metabolic variation of cortical, hippocampal and hypothalamic samples associated with age. PCA scores of (A) cortical, (B) hippocampal and (C) hypothalamic samples from B6 (left) and $TCR \beta^{-/-}\delta^{-/-}$ (right) mice colored by age. (D) The age-related metabolic changes for each genotype and sample type were assessed by constructing OPLS-DA models (for B6 and $TCR \beta^{-/-}\delta^{-/-}$ mice separately). The heatmap illustrates the correlation coefficient (r) obtained from OPLS models constructed against age for each genotype. In red are metabolites that are positively associated with age, in blue those negatively associated with age. Black squares indicate correlations with $r > |0.4|$. An age-related increase in GABA, glycine and acetate was observed in the cortex of $TCR \beta^{-/-}\delta^{-/-}$ mice, but not in B6 mice. *N*-Acetyl-aspartate (NAA) increased with age in the hippocampus, while it decreased with age in the hypothalamus of $TCR \beta^{-/-}\delta^{-/-}$ mice only. Similarly, only $TCR \beta^{-/-}\delta^{-/-}$ mice showed an age-associated decrease in hypothalamic phosphocholine.

A



B



Supplemental Figure S6. Genotype differences in developmental trajectories of neuroactive metabolites in brain tissue. (A) Correlogram depicting the Pearson correlation coefficients between the abundance of cecal and brain (cortical, hippocampal and hypothalamic) metabolites. In the cortex, aspartate, taurine, glycerophosphocholine, GABA and glycine were negatively correlated with the expression of butyrate in the cecum. Cortical aspartate, taurine and glycerophosphocholine were negatively associated with cecal valerate, while cortical aspartate and glycerophosphocholine were positively associated with cecal 5-aminovalerate. In the hippocampus, a positive correlation emerged between aspartate and cecal glucose-6-phosphate, and a negative association between alanine and cecal 5-aminovalerate and between IMP and cecal valerate. The hypothalamus showed the highest number of significant associations, with 15/20 metabolites exhibiting a negative correlation with cecal valerate. These included aspartate, taurine, glycerophosphocholine, glutamate, acetate, GABA, myo-inositol and phosphocholine. In the hypothalamus, taurine and phosphocholine were also positively associated with cecal glucose-6-phosphate, while taurine, myo-inositol and glycerophosphocholine were positively associated with cecal 5-aminovalerate. (B) Line plots showing the developmental trajectories of cortical, hippocampal and hypothalamic metabolites across the four developmental timepoints (P17, P24, P28, P84) for B6 (blue) and *TCR β ^{-/-} δ ^{-/-}* mice (red). Across brain samples, the inhibitory neurotransmitter GABA and amino acid glycine, as well as the short-chain fatty acid acetate and the membrane component glycerophosphocholine exhibited a steep increase with age in *TCR β ^{-/-} δ ^{-/-}* mice, while they were relatively stable in B6 mice. At P84, these metabolites were elevated in *TCR β ^{-/-} δ ^{-/-}* compared to B6 mice. While the excitatory amino acid aspartate was also elevated in *TCR β ^{-/-} δ ^{-/-}* mice relative to B6, its trajectory was different in the cortex compared to hippocampus and hypothalamus. In the cortex, aspartate increased slightly with age in *TCR β ^{-/-} δ ^{-/-}* mice, while it remained stable in B6 mice. In the hippocampus and hypothalamus, its concentrations decreased in both genotypes, but was elevated in *TCR β ^{-/-} δ ^{-/-}* mice compared to B6 at all timepoints. Plots were created by fitting a linear model with formula $y \sim \log(x)$, where x = age and y = metabolite abundance. Shaded areas represent the 95% confidence interval.