

Supplementary file 2. Correlation between metadata and features restored or not-restored by treatment.

We sought to determine whether features restored by the different treatments at 142 dpi or that failed to be restored presented differential association with the disease severity metadata. Specifically, we observed that a greater proportion of not-restored metabolite features were correlated with metadata at 142 days post-infection in the ventricles, compared to restored metabolite features. There was no clear differentiation between treatment groups. ("/" means that there were no metabolite features correlated with disease severity metadata in that section).

Table A. Proportion of features in each outcome group and position that were correlated to metadata, at 142 dpi.

Section	Restored by any treatment	Restored by BNZ+Tc24 combination	Restored by BNZ-only treatment	Restored by both treatments	Not restored by any treatment
LA	58%	100%	67%	50%	74%
RA	23%	/	67%	22%	/
LVT	16%	7%	75%	29%	100%
LVB	4%	7%	50%	75%	72%
RVT	35%	25%	/	50%	63%
RVB	10%	36%	/	/	91%

We then sought to determine whether these same features (restored or not by treatment at 142 dpi) had pre-existing correlations between their peak area at 75 dpi and the disease severity indicators at 72 dpi. Only a few of these restored or not-restored features were correlated with metadata at 75 dpi. Nevertheless, we observed that a greater proportion of not-restored metabolite features were correlated with metadata at 142 days post-infection in the left ventricle bottom, compared to restored metabolite features. The opposite pattern was observed in the right ventricle bottom. There was no clear differentiation between treatment groups. ("/" means that there is no metabolite correlated with disease severity metadata)

Table B. Proportion of features in each outcome group and position that were correlated to metadata, at 72 dpi.

Section	Restored by any treatment	Restored by BNZ+Tc24 combination	Restored by BNZ-only treatment	Restored by both treatments	Not restored by any treatment
LA	/	/	/	/	/
RA	/	/	/	/	/
LVT	/	/	/	/	/
LVB	16%	7%	83%	/	48%
RVT	/	/	/	/	/
RVB	10%	/	38%	14%	6%

Likewise, there was no clear association between treatments, restored or not-restored metabolite features, and being correlated with more than one disease severity metadata parameter.

Table C. Proportion of features in each outcome group and position that were correlated to multiple metadata parameters, at 142 dpi.

Sections	Restored	Not restored	Fisher’s exact test
LA	43%	36%	Non-significant
RA	No features correlated to multiple metadata parameters	All features were restored by treatment	Not applicable
LVT	25%	50%	Non-significant
LVB	0%	36%	Non-significant
RVT	55%	10%	p=0.012
RVB	0%	28%	Non-significant

Table D. Correlation between disease metadata and metabolite peak area at 75DPI in LVB heart section.

Note that correlations are performed separately for each treatment effects, so the list of features that met our FDR-corrected p-value cutoff of <0.05 may not fully overlap between “Metabolites restored by any treatment” and metabolites restored by individual treatments.

Effect of treatment	Disease severity metadata	Metabolites	Annotation	Correlation	FDR_pval
Metabolites restored by any treatment	Liver_weight/Body_weight	X291.146_2.39	Didanosine_C10H12N4O3_(M+H+C4H6)	-0.7461	0.000387
	Liver_weight/Body_weight	X620.356_2.913	No annotation	-0.65606	0.003621
	Liver_weight/Body_weight	X604.362_2.948	PC 22:3;O_C30H54NO9P	-0.67297	0.003621
	Ejection_Fraction	X291.146_2.39	Didanosine_C10H12N4O3_(M+H+C4H6)	-0.65835	0.003621
	Ejection_Fraction	X494.325_2.865	LPC 16:1_C24H48NO7P or LPC O-16:2;O_C24H48NO7P	0.568551	0.036584
Restored only by BNZ + Tc24 vaccine treatment	Liver_weight/Body_weight	X604.362_2.948	PC 22:3;O_C30H54NO9P	-0.67297	0.004838
Restored only by BNZ treatment	Liver_weight/Body_weight	X291.146_2.39	Didanosine_C10H12N4O3_(M+H+C4H6)	-0.7461	9.29E-05
	Liver_weight/Body_weight	X620.356_2.913	No annotation	-0.65606	0.001159
	Ejection_Fraction	X291.146_2.39	Didanosine_C10H12N4O3_(M+H+C4H6)	-0.65835	0.001159
	Ejection_Fraction	X494.325_2.865	LPC 16:1_C24H48NO7P or LPC O-16:2;O_C24H48NO7P	0.568551	0.010975
	Ejection_Fraction	X386.717_2.856	No annotation	-0.52709	0.023222
	Liver_weight/Body_weight	X386.717_2.856	No annotation	-0.51117	0.023347
	P Amplitude (V)	X251.037_0.323	No annotation	0.515071	0.023347
	Liver_weight/Body_weight	X494.325_2.865	LPC 16:1_C24H48NO7P or LPC O-16:2;O_C24H48NO7P	0.488085	0.032622
Not restored by any treatments	Liver_weight/Body_weight	X136.062_0.301	No annotation	-0.72444	0.000609
	Ejection_Fraction	X682.363_3.329	No annotation	-0.73773	0.000609
	Liver_weight/Body_weight	X301.115_0.413	No annotation	-0.70525	0.000913
	Liver_weight/Body_weight	X476.24_2.164	No annotation	-0.69392	0.001072
	Ejection_Fraction	X137.046_0.35	Hypoxanthine_C5H4N4O	-0.68276	0.00131
	Liver_weight/Body_weight	X682.364_3.313	No annotation	0.670758	0.001687
	Liver_weight/Body_weight	X475.989_2.164	No annotation	-0.65863	0.001926

	Ejection_Fraction	X682.364_3.313	No annotation	0.658869	0.001926
	Liver_weight/Body_weight	X682.363_3.329	No annotation	-0.65201	0.002137
	Liver_weight/Body_weight	X301.115_0.328	No annotation	-0.63974	0.002861
	Liver_weight/Body_weight	X137.046_0.42	No annotation	-0.63026	0.003495
	Ejection_Fraction	X580.362_2.984	PC 20:1;O_C28H54NO9P	0.621978	0.004114
	Liver_weight/Body_weight	X380.993_2.164	No annotation	-0.59561	0.007476
	Ejection_Fraction	X203.007_0.309	No annotation	-0.59756	0.007476
	Ejection_Fraction	X137.046_0.42	No annotation	-0.58932	0.007753
	P Amplitude (V)	X301.115_0.413	No annotation	0.590605	0.007753
	P Amplitude (V)	X136.062_0.301	No annotation	0.583222	0.008557
	Ejection_Fraction	X301.115_0.328	No annotation	-0.58111	0.008557
	Liver_weight/Body_weight	X136.097_0.551	No annotation	0.56922	0.010012
	Liver_weight/Body_weight	X203.007_0.309	No annotation	-0.57157	0.010012
	Ejection_Fraction	X136.062_0.301	No annotation	-0.56892	0.010012
	Ejection_Fraction	X301.115_0.413	No annotation	-0.56515	0.010496
	Ejection_Fraction	X475.989_2.164	No annotation	-0.55009	0.014019
	P Amplitude (V)	X137.046_0.35	Hypoxanthine_C5H4N4O	0.549561	0.014019
	P Amplitude (V)	X203.007_0.309	No annotation	0.543322	0.015567
	Liver_weight/Body_weight	X324.327_3.455	Erucylamide	0.53661	0.017452
	Ejection_Fraction	X476.24_2.164	No annotation	-0.53401	0.017822
	Liver_weight/Body_weight	X137.046_0.35	Hypoxanthine_C5H4N4O	-0.52436	0.021277
	P Amplitude (V)	X137.046_0.42	No annotation	0.488597	0.043062

Table E. Correlation between disease metadata and metabolite peak area at 75DPI in RVB heart section.

Note that correlations are performed separately for each treatment effects, so the list of features that met our FDR-corrected p-value cutoff of <0.05 may not fully overlap between “Metabolites restored by any treatment” and metabolites restored by individual treatments.

Effect of treatment	Disease severity metadata	Metabolites	Annotation	Correlation	FDR_pval
Metabolites restored by any treatment	Liver_weight/Body_weight	X568.341_2.887	LPC 22:6_C30H50NO7P or PC O-22:6_C30H50NO7P	0.599555	0.034157
	Liver_weight/Body_weight	X590.322_2.887	No annotation	0.593764	0.034157
	Liver_weight/Body_weight	X132.102_0.307	No annotation	0.615128	0.034157
	P Amplitude (V)	X568.341_2.887	LPC 22:6_C30H50NO7P or PC O-22:6_C30H50NO7P	-0.57604	0.040867
Restored only by BNZ treatment	Liver_weight/Body_weight	X568.341_2.887	LPC 22:6_C30H50NO7P or PC O-22:6_C30H50NO7P	0.599555	0.015181
	Liver_weight/Body_weight	X590.322_2.887	No annotation	0.593764	0.015181
	P Amplitude (V)	X568.341_2.887	LPC 22:6_C30H50NO7P or PC O-22:6_C30H50NO7P	-0.57604	0.016145
	P Amplitude (V)	X522.357_2.957	LPC 18:1_C26H52NO7P or PC O-18:1_C26H52NO7P or LPC O-18:2;O_C26H52NO7P	-0.52909	0.037031
Restored by both treatment	Liver_weight/Body_weight	X132.102_0.307	No annotation	0.615128	0.012496
Not restored by any treatments	Liver_weight/Body_weight	X150.059_0.3	Methionine_C5H11NO2S	0.650568	0.024341
	Liver_weight/Body_weight	X303.648_2.884	No annotation	0.628398	0.024553

Table F. Correlation between disease metadata and metabolite peak area at 142DPI in LA heart section.

Note that correlations are performed separately for each treatment effects, so the list of features that met our FDR-corrected p-value cutoff of <0.05 may not fully overlap between “Metabolites restored by any treatment” and metabolites restored by individual treatments.

Effect of treatment	Disease severity metadata	Metabolites	Annotation	Correlation	FDR_pval
Metabolites restored by any treatment	QTc (s)	X679.068_2.179	No annotation	0.622574	0.020068
	Liver_weight/Body_weight	X385.165_2.771	No annotation	0.598082	0.020239
	Liver_weight/Body_weight	X679.068_2.179	No annotation	0.57173	0.020615
	PR Interval (s)	X679.068_2.179	No annotation	0.571054	0.020615
	Liver_weight/Body_weight	X387.192_2.843	No annotation	-0.54941	0.027941
	Liver_weight/Body_weight	X616.308_2.766	No annotation	0.539232	0.028487
	CD3.CD8.IFN γ .	X114.092_1.761	3-Aminocaproic acid_C6H13NO2	0.533942	0.028487
	PR Interval (s)	X114.092_1.761	3-Aminocaproic acid_C6H13NO2	-0.5247	0.030588
	CD3.CD8.IFN γ .	X608.393_3.098	PC 22:1;O_C30H58NO9P	0.516079	0.032743
	Liver_weight/Body_weight	X377.146_2.225	Riboflavin_C17H20N4O6	-0.49759	0.043217
	Liver_weight/Body_weight	X608.393_3.098	PC 22:1;O_C30H58NO9P	-0.48604	0.049388
Restored only by BNZ + Tc24 vaccine treatment	Liver_weight/Body_weight	X377.146_2.225	Riboflavin_C17H20N4O6	-0.49759	0.036014
Restored only by BNZ treatment	Liver_weight/Body_weight	X616.308_2.766	No annotation	0.539232	0.036836
	CD3.CD8.IFN γ .	X608.393_3.098	PC 22:1;O_C30H58NO9P	0.516079	0.036836
	Liver_weight/Body_weight	X608.393_3.098	PC 22:1;O_C30H58NO9P	-0.48604	0.045273
Restored by both treatments	QTc (s)	X679.068_2.179	No annotation	0.622574	0.013379
	Liver_weight/Body_weight	X385.165_2.771	No annotation	0.598082	0.013493
	Liver_weight/Body_weight	X679.068_2.179	No annotation	0.57173	0.013743
	PR Interval (s)	X679.068_2.179	No annotation	0.571054	0.013743
	Liver_weight/Body_weight	X387.192_2.843	No annotation	-0.54941	0.018628
	CD3.CD8.IFN γ .	X114.092_1.761	3-Aminocaproic acid_C6H13NO2	0.533942	0.022157
	PR Interval (s)	X114.092_1.761	3-Aminocaproic acid_C6H13NO2	-0.5247	0.023305
Not restored by any treatment	Liver_weight/Body_weight	X137.046_0.35	Hypoxanthine_C5H4N4O	-0.6022	0.021252
	Liver_weight/Body_weight	X648.468_2.995	No annotation	0.606568	0.021252
	PR Interval (s)	X137.046_0.35	Hypoxanthine_C5H4N4O	-0.58783	0.021252
	P Amplitude (V)	X532.385_3.004	No annotation	-0.58763	0.021252
	Liver_weight/Body_weight	X650.403_3.014	PC 24:2;O2_C32H60NO10P	0.571511	0.025812
	Liver_weight/Body_weight	X532.385_3.004	No annotation	0.563337	0.026369

	Liver_weight/Body_weight	X516.39_3.018	No annotation	0.543746	0.029755
	Liver_weight/Body_weight	X604.442_3.001	No annotation	0.550523	0.029755
	P Amplitude (V)	X620.437_2.993	No annotation	-0.54119	0.029755
	Liver_weight/Body_weight	X560.416_3.006	No annotation	0.521915	0.031665
	Liver_weight/Body_weight	X620.437_2.993	No annotation	0.52907	0.031665
	P Amplitude (V)	X444.332_3.016	No annotation	-0.52447	0.031665
	P Amplitude (V)	X664.463_2.992	No annotation	-0.5233	0.031665
	Liver_weight/Body_weight	X576.411_2.999	No annotation	0.514435	0.033494
	Liver_weight/Body_weight	X664.463_2.992	No annotation	0.509506	0.033494
	P Amplitude (V)	X576.411_2.999	No annotation	-0.5111	0.033494
	QTc (s)	X137.046_0.35	Hypoxanthine_C5H4N4O	-0.50211	0.036721
	Liver_weight/Body_weight	X472.363_3.023	No annotation	0.496124	0.037089
	P Amplitude (V)	X708.489_2.982	No annotation	-0.49861	0.037089
	P Amplitude (V)	X666.433_3.092	PC 25:1;O2_C33H64NO10P	0.481719	0.046755

Table G. Correlation between disease metadata and metabolite peak area at 142DPI in RA heart section.

Note that correlations are performed separately for each treatment effects, so the list of features that met our FDR-corrected p-value cutoff of <0.05 may not fully overlap between “Metabolites restored by any treatment” and metabolites restored by individual treatments.

Effect of treatment	Disease severity metadata	Metabolites	Annotation	Correlation	FDR_pval
Metabolites restored by any treatment	Liver_weight/Body_weight	X263.091_2.771	No annotation	0.635334	0.016996
	Liver_weight/Body_weight	X296.258_2.976	No annotation	-0.647	0.016996
	Liver_weight/Body_weight	X295.227_3.017	No annotation	-0.60308	0.022098
	Liver_weight/Body_weight	X538.315_2.977	No annotation	-0.60296	0.022098
	Liver_weight/Body_weight	X137.046_0.35	Hypoxanthine_C5H4N4O	-0.56771	0.037362
	Liver_weight/Body_weight	X696.443_3.1	No annotation	0.573466	0.037362
	Liver_weight/Body_weight	X305.248_3.26	cis-5,8,11,14-Eicosatetraenoic acid_C20H32O2	0.554974	0.04372
Restored only by BNZ treatment	Liver_weight/Body_weight	X137.046_0.35	Hypoxanthine_C5H4N4O	-0.56771	0.022417
	Ejection_Fraction	X137.046_0.35	Hypoxanthine_C5H4N4O	-0.51591	0.024648
	P Amplitude (V)	X696.445_3.083	No annotation	0.520571	0.024648
Restored by both treatments	Liver_weight/Body_weight	X263.091_2.771	No annotation	0.635334	0.015296
	Liver_weight/Body_weight	X296.258_2.976	No annotation	-0.647	0.015296
	Liver_weight/Body_weight	X295.227_3.017	No annotation	-0.60308	0.019888
	Liver_weight/Body_weight	X538.315_2.977	No annotation	-0.60296	0.019888
	Liver_weight/Body_weight	X696.443_3.1	No annotation	0.573466	0.034909
	Liver_weight/Body_weight	X305.248_3.26	cis-5,8,11,14-Eicosatetraenoic acid_C20H32O2	0.554974	0.045906

Table H. Correlation between disease metadata and metabolite peak area at 142DPI in LVT heart section.

Note that correlations are performed separately for each treatment effects, so the list of features that met our FDR-corrected p-value cutoff of <0.05 may not fully overlap between “Metabolites restored by any treatment” and metabolites restored by individual treatments.

Effect of treatment	Disease severity metadata	Metabolites	Annotation	Correlation	FDR_pval
Metabolites restored by any treatment	Ejection_Fraction	X440.337_2.765	CAR 18:2;O_C25H45NO5	0.672242	0.004138
	P Amplitude (V)	X272.222_2.957	N-Lauroylsarcosine_C15H29NO3	0.679644	0.004138
	Liver_weight/Body_weight	X440.337_2.765	CAR 18:2;O_C25H45NO5	0.64704	0.006504
	Liver_weight/Body_weight	X366.373_3.699	Oleamide_C18H35NO_(M+H+C6H12)	0.572637	0.041262
	Liver_weight/Body_weight	X296.258_2.976	No annotation	-0.55854	0.046812
Restored only by BNZ + Tc24 vaccine treatment	P Amplitude (V)	X272.222_2.957	N-Lauroylsarcosine_C15H29NO3	0.679644	0.003546
Restored only by BNZ treatment	Ejection_Fraction	X440.337_2.765	CAR 18:2;O_C25H45NO5	0.672242	0.001324
	Liver_weight/Body_weight	X440.337_2.765	CAR 18:2;O_C25H45NO5	0.64704	0.001561
	Liver_weight/Body_weight	X203.007_0.309	No annotation	-0.52487	0.027088
	P Amplitude (V)	X293.211_2.933	trans-EKODE-(E)-Ib_C18H30O4	0.485651	0.045613
Restored by both treatments	Liver_weight/Body_weight	X296.258_2.976	No annotation	-0.55854	0.032768
	Liver_weight/Body_weight	X366.373_3.699	Oleamide_C18H35NO_(M+H+C6H12)	0.572637	0.032768
Not restored by any treatment	Liver_weight/Body_weight	X442.353_2.823	CAR 18:1;O_C25H47NO5	0.672949	0.000646
	Ejection_Fraction	X442.353_2.823	CAR 18:1;O_C25H47NO5	0.588102	0.004419
	Liver_weight/Body_weight	X240.116_2.324	No annotation	0.562088	0.005724

Table I. Correlation between disease metadata and metabolite peak area at 142DPI in LVB heart section.

Note that correlations are performed separately for each treatment effects, so the list of features that met our FDR-corrected p-value cutoff of <0.05 may not fully overlap between “Metabolites restored by any treatment” and metabolites restored by individual treatments.

Effect of treatment	Disease severity metadata	Metabolites	Annotation	Correlation	FDR_pval
Metabolites restored by any treatment	Liver_weight/Body_weight	X249.112_2.768	No annotation	0.625096	0.038764
Restored only by BNZ + Tc24 vaccine treatment	Liver_weight/Body_weight	X249.112_2.768	No annotation	0.625096	0.023259
Restored only by BNZ treatment	P Amplitude (V)	X291.146_2.39	Didanosine_C10H12N4O3_(M+H+C4H6)	0.574694	0.037595
	Liver_weight/Body_weight	X119.049_2.765	No annotation	0.523439	0.041921
	Liver_weight/Body_weight	X494.325_2.865	LPC 16:1_C24H48NO7P or LPC O-16:2;O_C24H48NO7P	0.527634	0.041921
Restored by both treatments	Liver_weight/Body_weight	X792.329_2.764	No annotation	0.584014	0.019692
	Liver_weight/Body_weight	X387.193_2.842	No annotation	-0.55604	0.019886
	Liver_weight/Body_weight	X811.309_2.773	No annotation	0.519417	0.030487
	Ejection_Fraction	X811.309_2.773	No annotation	0.469188	0.049883
	P Amplitude (V)	X792.329_2.764	No annotation	-0.47378	0.049883
Not restored by any treatment	Liver_weight/Body_weight	X682.363_3.329	No annotation	-0.71238	0.002042
	Liver_weight/Body_weight	X256.264_3.225	Palmitamide_C16H33NO	-0.67113	0.003469
	Ejection_Fraction	X416.337_2.79	CAR 16:0;O_C23H45NO5	0.669968	0.003469
	Liver_weight/Body_weight	X128.018_0.344	No annotation	0.645294	0.004533
	Liver_weight/Body_weight	X476.24_2.164	No annotation	-0.64133	0.004533
	Liver_weight/Body_weight	X682.364_3.313	No annotation	0.642567	0.004533
	Liver_weight/Body_weight	X475.989_2.164	No annotation	-0.62451	0.006537
	Liver_weight/Body_weight	X296.258_2.976	No annotation	-0.60151	0.007792
	Liver_weight/Body_weight	X380.993_2.164	No annotation	-0.60843	0.007792
	Liver_weight/Body_weight	X440.337_2.765	CAR 18:2;O_C25H45NO5	0.600116	0.007792
	Liver_weight/Body_weight	X442.353_2.823	CAR 18:1;O_C25H47NO5	0.602918	0.007792
	Liver_weight/Body_weight	X466.25_2.226	No annotation	-0.59972	0.007792
	P Amplitude (V)	X351.217_2.741	No annotation	0.57269	0.014708
	Liver_weight/Body_weight	X137.046_0.35	Hypoxanthine_C5H4N4O	-0.55591	0.018702
	Liver_weight/Body_weight	X416.337_2.79	CAR 16:0;O_C23H45NO5	0.547621	0.018702
	Ejection_Fraction	X440.337_2.765	CAR 18:2;O_C25H45NO5	0.547234	0.018702
	Ejection_Fraction	X442.353_2.823	CAR 18:1;O_C25H47NO5	0.556979	0.018702

	PR Interval (s)	X440.337_2.765	CAR 18:2;O_C25H45NO5	0.548586	0.018702
	CD3.CD8.IFN γ .	X256.264_3.225	Palmitamide_C16H33NO	0.552468	0.018702
	Liver_weight/Body_weight	X458.23_2.165	No annotation	-0.54307	0.01957
	Liver_weight/Body_weight	X136.062_0.301	No annotation	-0.53316	0.023352
	Liver_weight/Body_weight	X580.362_2.984	PC 20:1;O_C28H54NO9P	0.52401	0.027288
	CD3.CD8.IFN γ .	X136.097_0.551	No annotation	-0.52034	0.028264
	Ejection_Fraction	X256.264_3.225	Palmitamide_C16H33NO	-0.50894	0.034487
	Liver_weight/Body_weight	X136.097_0.551	No annotation	0.506943	0.03451
	P Amplitude (V)	X580.362_2.984	PC 20:1;O_C28H54NO9P	-0.50096	0.037518
	Liver_weight/Body_weight	X203.007_0.309	No annotation	-0.4885	0.043147
	P Amplitude (V)	X420.899_2.103	No annotation	0.489322	0.043147
	CD3.CD8.IFN γ .	X476.24_2.164	No annotation	0.489205	0.043147
	Liver_weight/Body_weight	X351.217_2.741	No annotation	-0.48664	0.043252
	Liver_weight/Body_weight	X137.046_0.42	No annotation	-0.48403	0.044031

Table J. Correlation between disease metadata and metabolite peak area at 142DPI in RVT heart section.

Note that correlations are performed separately for each treatment effects, so the list of features that met our FDR-corrected p-value cutoff of <0.05 may not fully overlap between “Metabolites restored by any treatment” and metabolites restored by individual treatments.

Effect of treatment	Disease severity metadata	Metabolites	Annotation	Correlation	FDR_pval
Metabolites restored by any treatment	Liver_weight/Body_weight	X249.112_2.768	No annotation	0.709902	0.002419
	Liver_weight/Body_weight	X489.228_2.768	No annotation	0.646489	0.004105
	Liver_weight/Body_weight	X599.241_2.765	No annotation	0.652943	0.004105
	Ejection_Fraction	X249.112_2.768	No annotation	0.668012	0.004105
	Ejection_Fraction	X489.228_2.768	No annotation	0.647608	0.004105
	Ejection_Fraction	X792.329_2.764	No annotation	0.650838	0.004105
	Liver_weight/Body_weight	X200.165_3.207	No annotation	-0.63854	0.004538
	Ejection_Fraction	X369.17_2.767	No annotation	0.628921	0.005351
	Liver_weight/Body_weight	X111.044_2.768	No annotation	0.623457	0.00561
	Liver_weight/Body_weight	X792.329_2.764	No annotation	0.612692	0.006423
	Ejection_Fraction	X599.241_2.765	No annotation	0.612013	0.006423
	Ejection_Fraction	X111.044_2.768	No annotation	0.591684	0.010371
	Liver_weight/Body_weight	X130.087_0.452	Daunosamine_C6H13NO3	-0.5844	0.011621
	Liver_weight/Body_weight	X175.148_2.71	alpha-Bisabolol_C15H26O	-0.5726	0.014631
	QTc (s)	X198.15_2.471	No annotation	-0.56396	0.016947
	Liver_weight/Body_weight	X198.15_2.471	No annotation	-0.5479	0.023371
	Liver_weight/Body_weight	X333.063_2.524	No annotation	-0.53477	0.029741
Restored only by BNZ + Tc24 vaccine treatment	Liver_weight/Body_weight	X130.087_0.452	Daunosamine_C6H13NO3	-0.5844	0.02643
	Liver_weight/Body_weight	X175.148_2.71	alpha-Bisabolol_C15H26O	-0.5726	0.02643
Restored by both treatments	Liver_weight/Body_weight	X249.112_2.768	No annotation	0.709902	0.001717
	Liver_weight/Body_weight	X489.228_2.768	No annotation	0.646489	0.002913
	Liver_weight/Body_weight	X599.241_2.765	No annotation	0.652943	0.002913
	Ejection_Fraction	X249.112_2.768	No annotation	0.668012	0.002913
	Ejection_Fraction	X489.228_2.768	No annotation	0.647608	0.002913
	Ejection_Fraction	X792.329_2.764	No annotation	0.650838	0.002913
	Liver_weight/Body_weight	X200.165_3.207	No annotation	-0.63854	0.00322
	Ejection_Fraction	X369.17_2.767	No annotation	0.628921	0.003797
	Liver_weight/Body_weight	X111.044_2.768	No annotation	0.623457	0.003981
	Liver_weight/Body_weight	X792.329_2.764	No annotation	0.612692	0.004558

	Ejection_Fraction	X599.241_2.765	No annotation	0.612013	0.004558
	Ejection_Fraction	X111.044_2.768	No annotation	0.591684	0.00736
	QTc (s)	X198.15_2.471	No annotation	-0.56396	0.013877
	Liver_weight/Body_weight	X198.15_2.471	No annotation	-0.5479	0.018955
	Liver_weight/Body_weight	X333.063_2.524	No annotation	-0.53477	0.023921
	Liver_weight/Body_weight	X216.16_2.471	No annotation	-0.50313	0.044246
	Liver_weight/Body_weight	X604.362_2.948	PC 22:3;O_C30H54NO9P	-0.49922	0.045094
Not restored by any treatment	Liver_weight/Body_weight	X137.046_0.35	Hypoxanthine_C5H4N4O	-0.73039	0.000617
	Liver_weight/Body_weight	X278.248_3.1	No annotation	-0.72638	0.000617
	Liver_weight/Body_weight	X280.264_3.159	No annotation	-0.69456	0.001539
	Liver_weight/Body_weight	X268.105_0.35	Adenosine_C10H13N5O4	-0.6551	0.004786
	Liver_weight/Body_weight	X228.196_2.71	No annotation	-0.6298	0.008604
	Liver_weight/Body_weight	X256.227_2.847	No annotation	-0.6229	0.008833
	Liver_weight/Body_weight	X242.212_2.78	No annotation	-0.59375	0.013134
	Liver_weight/Body_weight	X296.259_2.971	No annotation	-0.6002	0.013134
	Liver_weight/Body_weight	X306.279_2.989	No annotation	-0.58729	0.013134
	Ejection_Fraction	X269.088_0.35	Inosine_C10H12N4O5	-0.58843	0.013134
	P Amplitude (V)	X272.222_2.957	N-Lauroylsarcosine_C15H29NO3	0.593771	0.013134
	Liver_weight/Body_weight	X306.279_3.212	No annotation	-0.57016	0.018742
	Liver_weight/Body_weight	X308.295_3.045	No annotation	-0.56059	0.021925
	Liver_weight/Body_weight	X258.207_2.775	No annotation	-0.54813	0.027175
	Liver_weight/Body_weight	X282.28_3.246	Oleamide_C18H35NO	-0.54278	0.027175
	Liver_weight/Body_weight	X308.295_3.285	No annotation	-0.54323	0.027175
	Liver_weight/Body_weight	X399.395_3.152	No annotation	0.539657	0.027463
	Liver_weight/Body_weight	X811.31_2.767	No annotation	0.537175	0.027463
	Ejection_Fraction	X399.395_3.152	No annotation	0.533812	0.028069
	Liver_weight/Body_weight	X399.394_3.159	No annotation	-0.52046	0.035771
	P Amplitude (V)	X811.309_2.773	No annotation	0.513207	0.039769
	Ejection_Fraction	X137.046_0.35	Hypoxanthine_C5H4N4O	-0.50078	0.049107

Table K. Correlation between disease metadata and metabolite peak area at 142DPI in RVB heart section.

Note that correlations are performed separately for each treatment effects, so the list of features that met our FDR-corrected p-value cutoff of <0.05 may not fully overlap between “Metabolites restored by any treatment” and metabolites restored by individual treatments.

Effect of treatment	Disease severity metadata	Metabolites	Annotation	Correlation	FDR_pval
Metabolites restored by any treatment	Ejection_Fraction	X142.035_0.315	No annotation	-0.59822	0.044391
	Ejection_Fraction	X214.181_2.634	No annotation	-0.58665	0.044391
	Ejection_Fraction	X300.199_2.264	No annotation	-0.58855	0.044391
Restored only by BNZ + Tc24 vaccine treatment	Ejection_Fraction	X142.035_0.315	No annotation	-0.59822	0.02143
	Ejection_Fraction	X214.181_2.634	No annotation	-0.58665	0.02143
	Ejection_Fraction	X300.199_2.264	No annotation	-0.58855	0.02143
	Liver_weight/Body_weight	X795.335_2.768	No annotation	0.553911	0.036624
	Liver_weight/Body_weight	X300.199_2.264	No annotation	-0.54172	0.038991
	Liver_weight/Body_weight	X308.295_3.045	No annotation	-0.52454	0.047753
Not restored by any treatment	Liver_weight/Body_weight	X528.311_2.928	No annotation	-0.72462	0.001459
	Liver_weight/Body_weight	X790.38_2.768	No annotation	0.678091	0.004692
	Liver_weight/Body_weight	X111.044_2.768	No annotation	0.655559	0.005823
	Liver_weight/Body_weight	X137.046_0.35	Hypoxanthine_C5H4N4O	-0.64404	0.005823
	Liver_weight/Body_weight	X249.112_2.768	No annotation	0.640246	0.005823
	Liver_weight/Body_weight	X489.228_2.768	No annotation	0.639368	0.005823
	Liver_weight/Body_weight	X105.07_2.767	No annotation	0.609102	0.006842
	Liver_weight/Body_weight	X267.123_2.767	No annotation	0.614221	0.006842
	Liver_weight/Body_weight	X268.105_0.35	Adenosine_C10H13N5O4	-0.62056	0.006842
	Liver_weight/Body_weight	X285.133_2.768	No annotation	0.613108	0.006842
	Liver_weight/Body_weight	X369.17_2.767	No annotation	0.613775	0.006842
	Liver_weight/Body_weight	X404.207_2.768	No annotation	0.628686	0.006842
	Liver_weight/Body_weight	X406.154_2.765	No annotation	0.608212	0.006842
	Liver_weight/Body_weight	X387.181_2.767	No annotation	0.604429	0.00707
	Liver_weight/Body_weight	X486.098_2.765	No annotation	0.595812	0.008376
	Liver_weight/Body_weight	X511.21_3.171	No annotation	-0.59039	0.008558
	Liver_weight/Body_weight	X599.241_2.765	No annotation	0.591364	0.008558
	Liver_weight/Body_weight	X269.088_0.35	Inosine_C10H12N4O5	-0.58818	0.008573
	Liver_weight/Body_weight	X306.279_3.212	No annotation	-0.58418	0.00903
	Liver_weight/Body_weight	X303.648_2.884	No annotation	-0.57563	0.010706

	Liver_weight/Body_weight	X608.227_2.768	No annotation	0.568927	0.012081
	Liver_weight/Body_weight	X430.223_2.768	No annotation	0.566704	0.012189
	Liver_weight/Body_weight	X475.989_2.164	No annotation	-0.56371	0.012555
	Liver_weight/Body_weight	X415.14_2.768	No annotation	0.561478	0.01271
	Liver_weight/Body_weight	X446.218_2.884	No annotation	0.553466	0.013709
	Liver_weight/Body_weight	X637.306_3.32	No annotation	-0.55525	0.013709
	Liver_weight/Body_weight	X792.329_2.764	No annotation	0.553678	0.013709
	Liver_weight/Body_weight	X278.248_3.1	No annotation	-0.54946	0.014536
	Ejection_Fraction	X278.248_3.1	No annotation	-0.54216	0.016637
	Ejection_Fraction	X269.088_0.35	Inosine_C10H12N4O5	-0.5208	0.025788
	Ejection_Fraction	X280.264_3.159	No annotation	-0.51947	0.025788
	Liver_weight/Body_weight	X280.264_3.159	No annotation	-0.51541	0.027244
	Liver_weight/Body_weight	X476.24_2.164	No annotation	-0.50751	0.030266
	Liver_weight/Body_weight	X570.357_2.934	LPC 22:5_C30H52NO7P or LPC 22:5_C30H52NO7P or LPC O-22:6;O_C30H52NO7P or PC O- 22:5_C30H52NO7P	-0.50868	0.030266
	Ejection_Fraction	X654.332_3.32	No annotation	-0.50389	0.03168
	Ejection_Fraction	X637.306_3.32	No annotation	-0.49588	0.035253
	QTc (s)	X303.648_2.884	No annotation	-0.49604	0.035253
	P Amplitude (V)	X476.24_2.164	No annotation	0.491619	0.037369
	Liver_weight/Body_weight	X654.332_3.32	No annotation	-0.48804	0.039071
	Ejection_Fraction	X511.21_3.171	No annotation	-0.48183	0.042973
	QTc (s)	X111.044_2.768	No annotation	0.473831	0.04881