Supplementary Figures

Figure S1.

MA plot showing log_2 fold changes as a function of mean normalized gene expression following DESeq2 analysis.

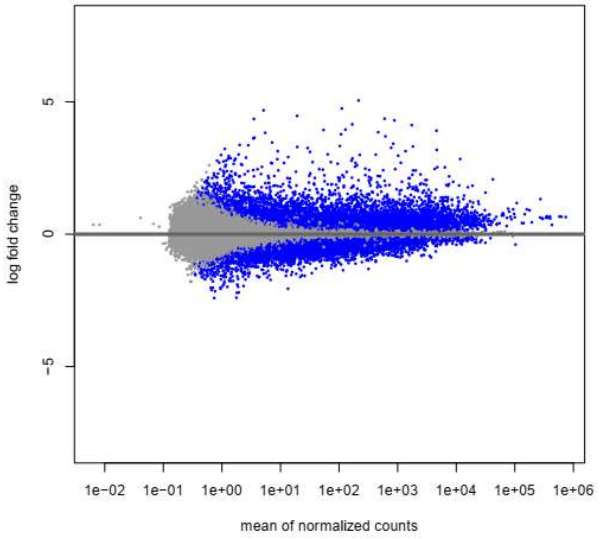


Figure S2.

DESeq2 dispersion plot showing gene-wise, fitted, and final dispersion estimates used for differential expression analysis.

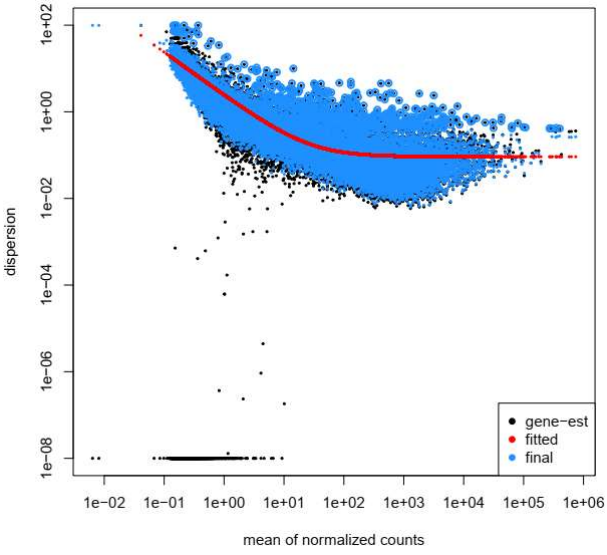


Figure S3.

Module eigengene clustering reveals higher-order relationships among PTB-derived co-expression modules.

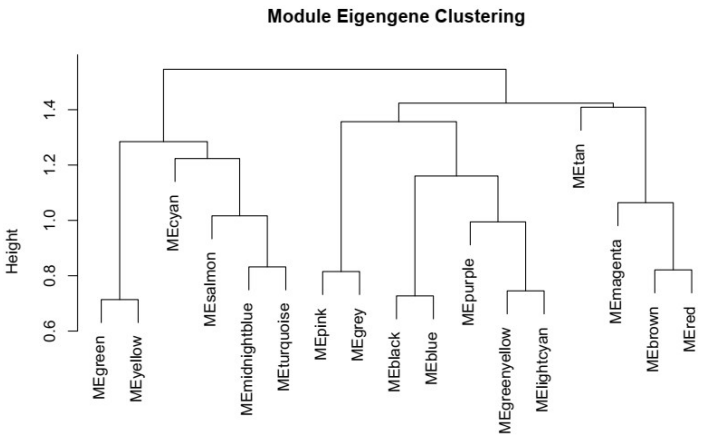


Figure S4.
Eigengene network illustrating connectivity among PTB-derived co-expression modules.

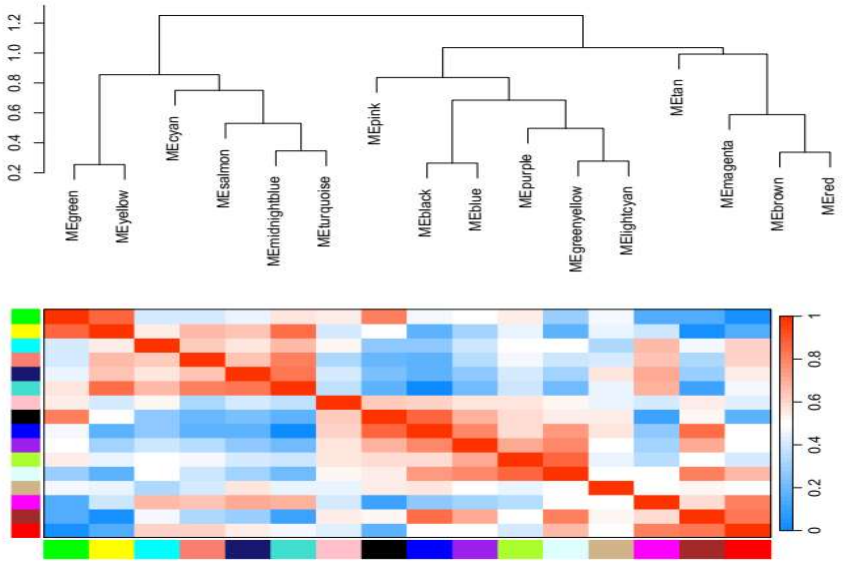


Figure S5. Precision–recall curve for external validation cohort GSE107991.

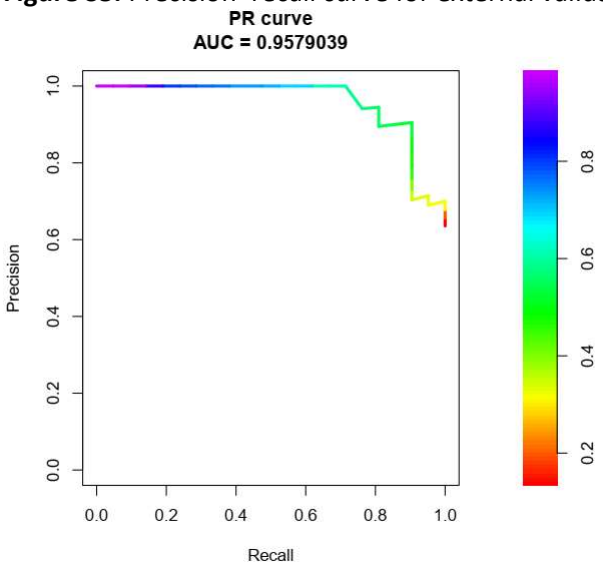


Figure S6. Precision–recall curve for external validation cohort GSE279063.

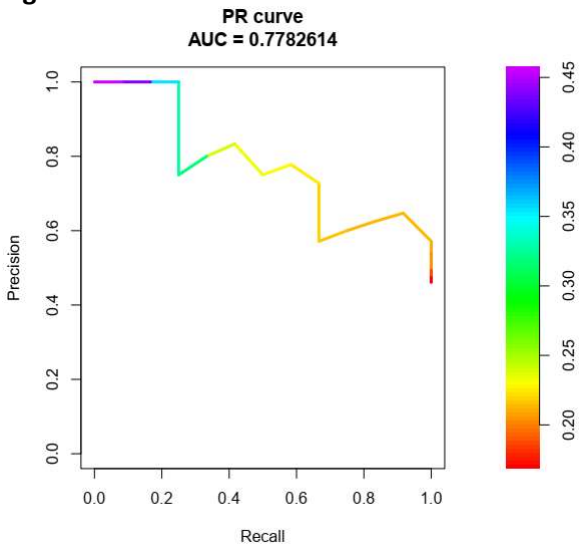


Figure S7.

Regional specificity of consensus PTB-derived neuroimmune modules across the Allen Human Brain Atlas. Modules are ranked according to the standard deviation of consensus regional Z-scores, with larger values indicating greater anatomical specificity.

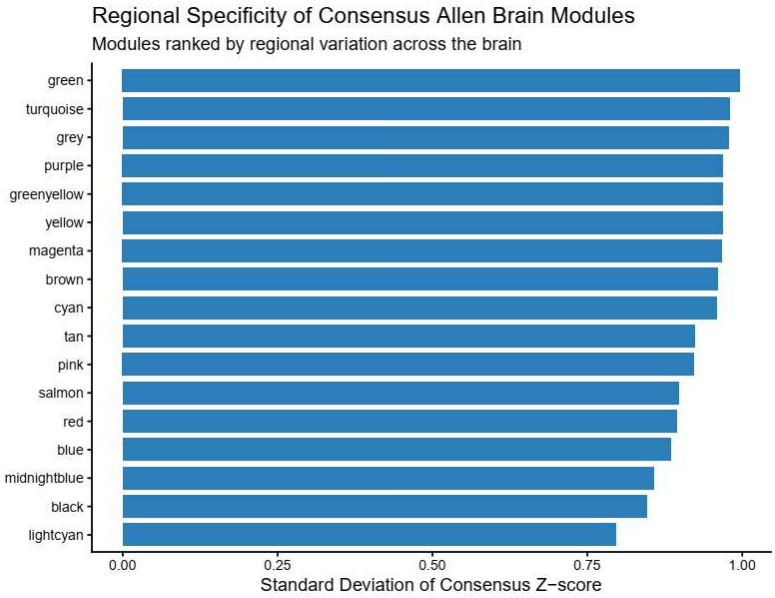


Figure S8.
Diagnosis-associated effects across validated PTB-derived neuroimmune modules. Modules are ranked according to diagnosis-associated F statistics.

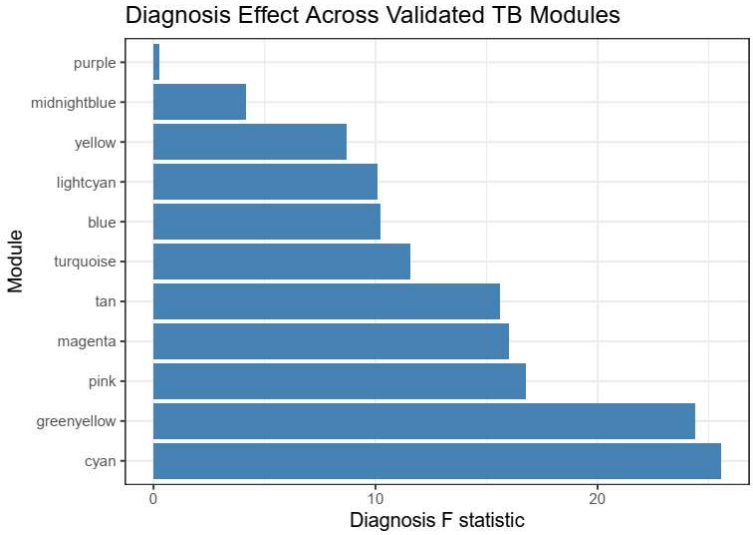


Figure S9.
Regional specificity of validated PTB-derived neuroimmune modules. Modules are ranked according to consensus regional specificity scores.

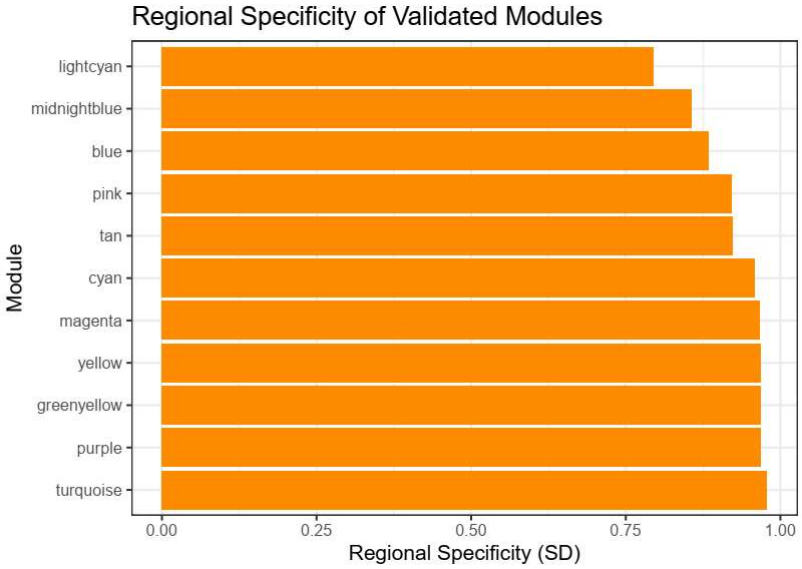
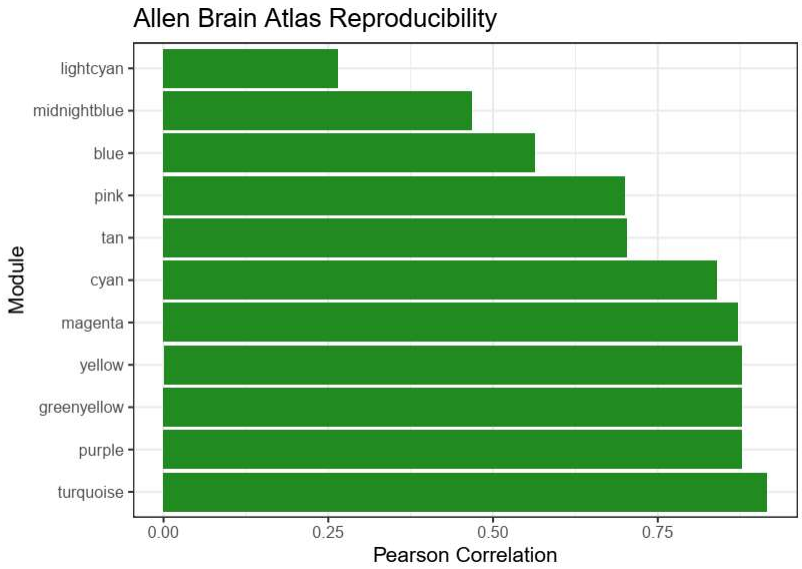


Figure S10
Inter-donor reproducibility of validated PTB-derived neuroimmune modules. Modules are ranked according to Pearson correlations of regional expression between independent Allen Brain Atlas donors.



Supplementary Tables
Table S1.
Complete differential expression results for active PTB versus healthy controls.
Available as a separate supplementary spreadsheet file:

PTB_vs_Control_DESeq2_results.csv
Table S2.
Significantly differentially expressed genes identified in active PTB.
Available as a separate supplementary spreadsheet file:
PTB_vs_Control_Significant.csv

Table S3.
Upregulated genes in active PTB relative to healthy controls.
Available as a separate supplementary spreadsheet file
PTB_vs_Control_UP.csv

Table S4.
Downregulated genes in active PTB relative to healthy controls.
Available as a separate supplementary spreadsheet file:
PTB_vs_Control_DOWN.csv

Table S5.
Sizes of PTB-derived weighted gene co-expression network modules.

Var1	Freq
black	884
blue	2612
brown	2117
cyan	144
green	1077
greenyellow	210
grey	2031
lightcyan	55
magenta	246
midnightblue	141
pink	258
purple	228
red	1071
salmon	150
tan	193
turquoise	4782
yellow	1240

Table S6.
Pearson correlations between module eigengenes and clinical traits.

	Control	PTB	PTB_PreDiagnosis	TB_Prog	TB_Prog_Contact	days_from_att	age
MEgreen	0.12	-0.13	-0.11	0.01	0.12	0.07	-0.08
MEyellow	0.41	-0.42	-0.15	0.05	0.17	0.01	-0.12
MEcyan	0.22	-0.16	-0.09	-0.09	0.04	-0.08	0.09
MEsalmon	0.46	-0.34	-0.05	-0.03	-0.08	0.01	0.09
MEmidnightblue	0.5	-0.48	-0.07	0.02	0.07	-0.12	-0.15
MEturquoise	0.56	-0.59	-0.1	0.08	0.16	-0.09	-0.12
MEpink	-0.22	0.11	0.04	0.06	0.11	-0.05	-0.02
MEblack	-0.31	0.33	-0.02	-0.03	-0.02	0.12	0
MEblue	-0.57	0.57	0.12	-0.07	-0.13	0.1	0.09
MEpurple	-0.36	0.56	-0.1	-0.07	-0.23	0.08	0.23
MEgreenyellow	-0.07	0.26	-0.02	-0.15	-0.22	0.11	0.08
MElightcyan	-0.36	0.49	0.08	-0.12	-0.27	0.11	0.13
MEtan	-0.16	0.09	0.08	0.04	0	-0.01	-0.24
MEmagenta	0.25	-0.29	0.03	0.11	0.01	-0.1	-0.06
MEbrown	-0.45	0.44	0.17	-0.06	-0.16	0.02	0.16
MEred	-0.09	0.04	0.15	0	-0.06	-0.09	0.08
MEgrey	0.15	-0.17	0	-0.01	0.05	-0.07	0.03

Table S7.
Statistical significance of module–trait associations.

	Control	PTB	PTB_PreDiagnosis	TB_Prog	TB_Prog_Contact	days_from_att	age
MEgreen	0.1935	0.1654	0.2384	0.8824	0.1892	0.444	0.3741
MEyellow	0	0	0.1169	0.596	0.073	0.9571	0.1947
MEcyan	0.0178	0.0966	0.3191	0.3328	0.658	0.4061	0.3381
MEsalmon	0	0.0002	0.5938	0.7685	0.3813	0.8775	0.3639
MEmidnightblue	0	0	0.4353	0.7978	0.4388	0.2157	0.1148
MEturquoise	0	0	0.271	0.3912	0.0938	0.3617	0.1873
MEpink	0.0169	0.2513	0.6879	0.5236	0.2641	0.5982	0.7941
MEblack	0.0008	0.0004	0.8585	0.7469	0.8296	0.1914	0.9609
MEblue	0	0	0.1912	0.4418	0.168	0.2941	0.368
MEpurple	0.0001	0	0.2978	0.4441	0.0155	0.3743	0.0157
MEgreenyellow	0.4489	0.006	0.8366	0.118	0.018	0.2382	0.4088
MElightcyan	0.0001	0	0.3942	0.1985	0.0045	0.2407	0.1666
MEtan	0.087	0.3204	0.3825	0.7115	0.9904	0.9056	0.011
MEmagenta	0.008	0.0018	0.7198	0.2349	0.9374	0.2765	0.5192
MEbrown	0	0	0.069	0.5007	0.0899	0.8741	0.0881
MEred	0.3173	0.667	0.1154	0.9742	0.5117	0.3556	0.4055
MEgrey	0.1084	0.0723	0.9711	0.9081	0.6078	0.4573	0.7624

Table S8.
Network construction parameters used for weighted gene co-expression network analysis.

Samples	Genes	SoftPower	MinModuleSize	MergeCutHeight	MaxBlockSize
113	17439	20	50	0.25	17439

Table S9.
Complete correlations between PTB-derived co-expression modules and inferred immune-cell populations.
Available as a separate supplementary spreadsheet file:
Module_Immune_Correlations.csv

Table S10.
Significant PTB module–immune-cell associations following false discovery rate correction.

Module	Immune_Cell	Spearman_Rho	Pvalue	FDR
MEblack	Neutrophils	0.860264105642257	1.19841300342362e-15	2.37285774677876e-13
MEmidnightblue	B cells naive	0.851510353060825	4.64480518216768e-15	4.598357130346e-13
MEsalmon	NK cells resting	0.817527010804322	4.35161189807833e-13	2.8720638527317e-11
MEsalmon	T cells CD8	0.783137251077826	1.80622863060398e-11	8.94083172148971e-10
MEblack	T cells CD8	-0.744415171	5.76690484740946e-10	2.28369431957415e-08
MEmagenta	Neutrophils	-0.726098439	2.41225647378063e-09	7.96044636347608e-08
MEblue	T cells CD8	-0.693970774	2.29539257574548e-08	6.49268185710864e-07
MEblue	Neutrophils	0.654549819927971	2.52205484572665e-07	6.24208574317347e-06
MEturquoise	T cells CD8	0.641796855232727	5.09074941279895e-07	1.11996487081577e-05

MEturquoise	NK cells resting	0.628427370948379	1.02764657728322e-06	2.03474022302078e-05
MEblue	NK cells resting	-0.615366146	1.97830396275144e-06	3.56094713295259e-05
MEblack	T cells regulatory (Tregs)	-0.604705882	3.30453078205727e-06	5.45247579039449e-05
MEsalmon	Neutrophils	-0.58002401	1.01198532766715e-05	0.000154133149906228
MEturquoise	Neutrophils	-0.562160864	2.15280492980022e-05	0.000304468125786031
MEmagenta	T cells regulatory (Tregs)	0.551596638655462	3.29710541407787e-05	0.000435217914658279
MEmagenta	B cells naive	0.533784759701713	6.55340235368848e-05	0.00081098354126895
MEmagenta	T cells CD8	0.526399292071636	8.61639309232319e-05	0.00100355637192941
MEbrown	NK cells resting	-0.501080432	0.000210193998077775	0.00231213397885553
MEblack	B cells naive	-0.486049083	0.000345640191341891	0.00360193462556286
MEmidnightblue	Macrophages M0	-0.466288683	0.00064253733375502	0.0063611196041747
MEblack	NK cells resting	-0.459783914	0.00078173271558702	0.00737062274696333
MEturquoise	Macrophages M0	-0.455500657	0.000887615360461633	0.0079885382441547
MEblue	T cells regulatory (Tregs)	-0.448931573	0.00107511511696846	0.00925533883303282
MEblack	Mast cells resting	-0.447050501	0.00113497245972706	0.00936352279274823
MEblue	Macrophages M0	0.442420873485355	0.00129518320174333	0.0102578509578072
MEmidnightblue	B cells memory	-0.438800311	0.0014342438656829	0.0109223186694313
MEpurple	Neutrophils	0.413301320528211	0.00285257505275369	0.0199628872323094
MEblue	B cells naive	-0.413052876	0.00287101299458832	0.0199628872323094
MEbrown	Macrophages M0	0.412348551320462	0.0029238572208938	0.0199628872323094
MEyellow	NK cells resting	0.406002400960384	0.00344011633869306	0.0220796900152416
MEmidnightblue	Neutrophils	-0.405810324	0.00345692116400247	0.0220796900152416
MEsalmon	Monocytes	-0.404177671	0.00360270749991115	0.0222917526557002
MEpurple	T cells CD8	-0.394379099	0.00459682885178407	0.0275809731107044
MEmidnightblue	T cells CD8	0.391688731245784	0.00490876187243491	0.0285863191394739
MEbrown	Monocytes	0.387370948379352	0.00544818390787368	0.0308211546788282
MEbrown	NK cells activated	0.376296492186893	0.00707487077962763	0.0375879438760978
MEturquoise	B cells naive	0.37588243942288	0.00714311130457291	0.0375879438760978
MElightcyan	Macrophages M0	0.37545685498435	0.00721384781460462	0.0375879438760978

MEturquoise	T cells regulatory (Tregs)	0.373541416566627	0.00753979999459502	0.038278984587944
MEblue	Dendritic cells activated	0.366810889468881	0.00878863798862716	0.0435037580437044

Table S11.
Final locked PTB biomarker signature identified by nested machine learning.

Gene	Coefficient
NUMB	-0.720871421
ACSL1	-1.404699705
PPP1R3B	-0.521084674
PSMB8-AS1	5.05314033393618
LAMTOR2	1.07194105373849
SNCA	-0.071396219
SHARPIN	0.883101490634273
RILP	1.47823814188206
RPS23	-2.981226998
MIR600HG	-1.775578556
HOPX	-0.563550515
OTUD4	0.465856605476768

Table S12.
Performance metrics of the nested cross-validation classifier in the discovery cohort.

Fold	mtry	ROC	Sensitivity	Specificity	SelectedGenes
1	5	0.985833333333333	0.935	0.916	13
2	2	0.985083333333333	0.94	0.936	15
3	2	0.987333333333333	0.906666666666667	0.942	11
4	2	0.989833333333333	0.923333333333333	0.956	7
5	6	0.99475	0.95	0.944	14
6	3	0.987083333333333	0.918333333333333	0.936	17
7	2	0.996666666666667	0.945	0.956	11
8	2	0.990083333333333	0.933333333333333	0.941	12
9	3	0.987166666666667	0.931666666666667	0.93	13
10	2	0.991416666666667	0.915	0.941	11

Table S13.
Calibration statistics for the locked Random Forest classifier in the discovery cohort.

Metric	Value
Brier Score	0.269489538461538
Calibration Intercept	0.992282721978571
Calibration Slope	3.90610590607215

Table S14.
Variable importance ranking of the final locked Random Forest classifier.

Gene	Control	PTB
PSMB8-AS1	100	100
RILP	82.3677475379126	82.3677475379126
MIR600HG	73.9715040059149	73.9715040059149
LAMTOR2	64.8176574848653	64.8176574848653
SHARPIN	54.5832122329669	54.5832122329669
RPS23	47.0990864118116	47.0990864118116
HOPX	27.8067726058006	27.8067726058006
ACSL1	13.261452012551	13.261452012551
PPP1R3B	8.07983140577624	8.07983140577624
NUMB	7.01060715908767	7.01060715908767
SNCA	4.44450959075312	4.44450959075312
OTUD4	0	0

Table S15.
Permutation test results for the nested Random Forest classifier.

Observed_AUC	Mean_Permuted_AUC	SD_Permuted_AUC	Max_Permuted_AUC	Empirical_P	Successful_Permutations
0.978157894736842	0.498561315789474	0.063884984057849 8	0.703947368421053	0.000999000999000 9	1000

Table S16.
Prediction results, confusion matrix, and calibration statistics for external validation in GSE107991.

Sample	Truth	Prediction	Probability
GSM2886035	PTB	PTB	0.784
GSM2886036	PTB	PTB	0.612
GSM2886039	Control	PTB	0.554
GSM2886040	Control	PTB	0.588
GSM2886041	PTB	PTB	0.534
GSM2886043	PTB	PTB	0.982
GSM2886044	PTB	PTB	0.876
GSM2886049	PTB	PTB	0.588
GSM2886051	PTB	PTB	0.732
GSM2886053	Control	Control	0.4
GSM2886054	PTB	PTB	0.764
GSM2886056	Control	Control	0.324
GSM2886057	PTB	PTB	0.732
GSM2886058	Control	Control	0.2
GSM2886059	PTB	Control	0.32
GSM2886060	Control	Control	0.138
GSM2886061	PTB	PTB	0.688

GSM2886064	PTB	PTB	0.95
GSM2886068	PTB	PTB	0.72
GSM2886070	PTB	PTB	0.806
GSM2886071	PTB	PTB	0.77
GSM2886074	Control	Control	0.354
GSM2886075	PTB	PTB	0.62
GSM2886076	Control	Control	0.476
GSM2886077	PTB	PTB	0.55
GSM2886078	PTB	Control	0.336
GSM2886079	PTB	PTB	0.98
GSM2886080	PTB	PTB	0.568
GSM2886081	PTB	PTB	0.696
GSM2886083	Control	Control	0.314
GSM2886084	Control	Control	0.458
GSM2886086	Control	Control	0.5
GSM2886087	Control	PTB	0.528

Summary: The locked Random Forest model achieved an accuracy of **84.85%** (95% CI: 68.10–94.89%), sensitivity of **90.48%**, specificity of **75.00%**, balanced accuracy of **82.74%**, and Cohen's kappa of **0.67** in the GSE107991 external validation cohort. Calibration analysis yielded a Brier score of **0.1443**, calibration intercept of **0.2448**, and calibration slope of **2.5564**.

Table S17.
Prediction results, confusion matrix, and calibration statistics for external validation in GSE279063.

Sample	Truth	Prediction	Probability
GSM8560295	PTB	Control	0.456
GSM8560298	PTB	Control	0.23
GSM8560301	PTB	Control	0.438
GSM8560304	PTB	Control	0.214
GSM8560307	PTB	Control	0.224
GSM8560310	PTB	Control	0.216
GSM8560313	PTB	Control	0.318
GSM8560316	PTB	Control	0.214
GSM8560319	PTB	Control	0.24
GSM8560322	PTB	Control	0.234
GSM8560325	PTB	Control	0.212
GSM8560328	PTB	Control	0.354
GSM8560346	Control	Control	0.212
GSM8560347	Control	Control	0.212
GSM8560348	Control	Control	0.204
GSM8560349	Control	Control	0.206
GSM8560350	Control	Control	0.224
GSM8560351	Control	Control	0.188
GSM8560352	Control	Control	0.218
GSM8560353	Control	Control	0.21
GSM8560354	Control	Control	0.17

GSM8560355	Control	Control	0.218
GSM8560356	Control	Control	0.234
GSM8560357	Control	Control	0.22
GSM8560358	Control	Control	0.326
GSM8560359	Control	Control	0.212

Summary: The locked Random Forest model achieved an accuracy of **53.85%** (95% CI: **33.37–73.41%**), sensitivity of **0.00%**, specificity of **100.00%**, balanced accuracy of **50.00%**, and Cohen's kappa of **0.00** in the GSE107991 external validation cohort. Calibration analysis yielded a Brier score of **0.2695**, calibration intercept of **0.9923**, and calibration slope of **3.9061**. Notably, the model classified all validation samples as **Control**, resulting in complete failure to identify PTB cases despite perfect specificity.

Table S18.
Two-way ANOVA results for PTB-derived co-expression modules in the Alzheimer's disease validation cohort.

Effect	DFn	DFd	F	p	p<.05	ges	Module	FDR
Diagnosis	1	198	0.799	0.373		0.004	black	0.398
Infection	1	198	3.353	0.069		0.017	black	0.272
Diagnosis:Infection	1	198	0.251	0.617		0.001	black	0.912
Diagnosis	1	198	10.195	0.002	*	0.049	blue	0.004
Infection	1	198	4.471	0.036	*	0.022	blue	0.192
Diagnosis:Infection	1	198	1.108	0.294		0.006	blue	0.658
Diagnosis	1	198	3.235	0.074		0.016	brown	0.091
Infection	1	198	1.891	0.171		0.009	brown	0.342
Diagnosis:Infection	1	198	2.245	0.136		0.011	brown	0.544
Diagnosis	1	198	25.55	9.78e-07	*	0.114	cyan	1.328e-05
Infection	1	198	0.03	0.862		0.000154	cyan	0.882
Diagnosis:Infection	1	198	1.31	0.254		0.007	cyan	0.658
Diagnosis	1	198	3.45	0.065		0.017	green	0.088
Infection	1	198	0.941	0.333		0.005	green	0.5328
Diagnosis:Infection	1	198	0.058	0.809		0.000295	green	0.925
Diagnosis	1	198	24.401	1.66e-06	*	0.11	greenyellow	1.328e-05
Infection	1	198	2.006	0.158		0.01	greenyellow	0.342
Diagnosis:Infection	1	198	1.172	0.28		0.006	greenyellow	0.658
Diagnosis	1	198	10.088	0.002	*	0.048	lightcyan	0.004
Infection	1	198	1.119	0.291		0.006	lightcyan	0.517
Diagnosis:Infection	1	198	3.643	0.058		0.018	lightcyan	0.309
Diagnosis	1	198	16.005	8.92e-05	*	0.075	magenta	0.000352
Infection	1	198	0.283	0.595		0.001	magenta	0.72
Diagnosis:Infection	1	198	0.009	0.923		4.74e-05	magenta	0.957
Diagnosis	1	198	4.151	0.043	*	0.021	midnightblue	0.0688
Infection	1	198	5.795	0.017	*	0.028	midnightblue	0.192
Diagnosis:Infection	1	198	4.386	0.038	*	0.022	midnightblue	0.304
Diagnosis	1	198	16.752	6.2e-05	*	0.078	pink	3.307e-04
Infection	1	198	0.233	0.63		0.001	pink	0.72
Diagnosis:Infection	1	198	0.236	0.627		0.001	pink	0.912
Diagnosis	1	198	0.265	0.607		0.001	purple	0.607
Infection	1	198	4.593	0.033	*	0.023	purple	0.192

Diagnosis:Infection	1	198	5.785	0.017	*	0.028	purple	0.272
Diagnosis	1	198	3.411	0.066		0.017	red	0.088
Infection	1	198	0.022	0.882		0.000112	red	0.882
Diagnosis:Infection	1	198	0.959	0.329		0.005	red	0.658
Diagnosis	1	198	1.535	0.217		0.008	salmon	0.248
Infection	1	198	0.785	0.377		0.004	salmon	0.548
Diagnosis:Infection	1	198	0.003	0.957		1.44e-05	salmon	0.957
Diagnosis	1	198	15.568	0.00011	*	0.073	tan	0.000352
Infection	1	198	2.297	0.131		0.011	tan	0.342
Diagnosis:Infection	1	198	0.405	0.525		0.002	tan	0.912
Diagnosis	1	198	11.563	0.000814	*	0.055	turquoise	2.17e-03
Infection	1	198	2.993	0.085		0.015	turquoise	0.272
Diagnosis:Infection	1	198	0.077	0.782		0.000387	turquoise	0.925
Diagnosis	1	198	8.702	0.004	*	0.042	yellow	7.11e-3
Infection	1	198	0.396	0.53		0.002	yellow	0.707
Diagnosis:Infection	1	198	0.062	0.803		0.000315	yellow	0.925

Table S19.
One-way ANOVA and FDR-adjusted significance of PTB-derived module eigengenes across Alzheimer's disease clinical groups.
A.

Module	**F**	**p**	**ges**	**FDR**
cyan	8.987	1.31e-05	0.12	0.0001296
greenyellow	8.82	1.62e-05	0.118	0.0001296
blue	5.746	0.000867	0.08	0.00266666666666667
magenta	5.345	0.001	0.075	0.00266666666666667
pink	5.665	0.000963	0.079	0.00266666666666667
tan	5.756	0.000855	0.08	0.00266666666666667
turquoise	5.308	0.002	0.074	0.00457142857142857
lightcyan	4.766	0.003	0.067	0.006
midnightblue	4.488	0.005	0.064	0.00888888888888889
purple	3.491	0.017	0.05	0.0272
yellow	2.961	0.033	0.043	0.048
brown	2.312	0.077	0.034	0.102666666666667
black	1.374	0.252	0.02	0.2688
green	1.379	0.25	0.02	0.2688
red	1.457	0.228	0.022	0.2688
salmon	0.853	0.466	0.013	0.466

B.

Module	**F**	**p**	**ges**	**FDR**
cyan	8.987	1.31e-05	0.12	0.0001296
greenyellow	8.82	1.62e-05	0.118	0.0001296
blue	5.746	0.000867	0.08	0.00266666666666667
magenta	5.345	0.001	0.075	0.00266666666666667
pink	5.665	0.000963	0.079	0.00266666666666667

tan	5.756	0.000855	0.08	0.00266666666666667
turquoise	5.308	0.002	0.074	0.00457142857142857
lightcyan	4.766	0.003	0.067	0.006
midnightblue	4.488	0.005	0.064	0.00888888888888889
purple	3.491	0.017	0.05	0.0272
yellow	2.961	0.033	0.043	0.048

Table S20.
Pairwise comparisons of PTB-derived module eigengene activity among Alzheimer's disease clinical groups.
Available as a separate supplementary spreadsheet file:
TB_Module_PairwiseComparisons.csv

Table S21.
Group mean module eigengene scores across Alzheimer's disease clinical groups.

Module	Group4	Mean	SD	N
blue	CTR_NoInf	-0.055630778	0.180585075779847	52
blue	CTR_Inf	-0.033488869	0.16351020442598	37
blue	AD_NoInf	-0.001286182	0.15502426145597	55
blue	AD_Inf	0.0724591145719491	0.182618685189047	58
cyan	CTR_NoInf	-0.035156735	0.117078883178897	52
cyan	CTR_Inf	-0.058668773	0.0990975892522732	37
cyan	AD_NoInf	0.0286546082309792	0.123971262516989	55
cyan	AD_Inf	0.041773988769181	0.102570610058307	58
greenyellow	CTR_NoInf	0.0775604560363662	0.225473375689168	52
greenyellow	CTR_Inf	0.0828484979341796	0.225832362088836	37
greenyellow	AD_NoInf	-0.098646578	0.195039066687971	55
greenyellow	AD_Inf	-0.02884442	0.193068732681834	58
lightcyan	CTR_NoInf	0.0770304135074279	0.301158945300952	52
lightcyan	CTR_Inf	0.037614265995702	0.21152658630147	37
lightcyan	AD_NoInf	-0.096890222	0.214905893400515	55
lightcyan	AD_Inf	-0.001178399	0.244888569750223	58
magenta	CTR_NoInf	0.108671104996389	0.440511645587811	52
magenta	CTR_Inf	0.144434037090578	0.325928592033293	37
magenta	AD_NoInf	-0.110075735	0.444211015941841	55
magenta	AD_Inf	-0.085186059	0.328807741018103	58
midnightblue	CTR_NoInf	-0.01996589	0.139398700868669	52
midnightblue	CTR_Inf	-0.020243405	0.135856169761053	37
midnightblue	AD_NoInf	0.0588943903258062	0.141089125793057	55
midnightblue	AD_Inf	-0.025033779	0.14123924936675	58
pink	CTR_NoInf	-0.086624695	0.305435685189931	52
pink	CTR_Inf	-0.08388276	0.281328667369107	37
pink	AD_NoInf	0.0848353786143677	0.228150866205336	55
pink	AD_Inf	0.0507275936018272	0.248189891316165	58

purple	CTR_NoInf	0.0113481368460797	0.19083779026396	52
purple	CTR_Inf	-0.004847909	0.119926018470819	37
purple	AD_NoInf	-0.061947625	0.187629035688891	55
purple	AD_Inf	0.0516618773701025	0.220991702133422	58
tan	CTR_NoInf	0.0683375823919509	0.274413953389751	52
tan	CTR_Inf	0.0981207285899355	0.276328892107451	37
tan	AD_NoInf	-0.103764733	0.229407213644278	55
tan	AD_Inf	-0.025464844	0.285905807052313	58
turquoise	CTR_NoInf	0.0343567194268099	0.101254709478212	52
turquoise	CTR_Inf	0.0156374231643666	0.0765402571954851	37
turquoise	AD_NoInf	-0.007525108	0.096055622423651	55
turquoise	AD_Inf	-0.033642295	0.0935361792918046	58
yellow	CTR_NoInf	0.0579685372197695	0.272011666481332	52
yellow	CTR_Inf	0.0714206916444767	0.275885809058799	37
yellow	AD_NoInf	-0.067078804	0.287333771691323	55
yellow	AD_Inf	-0.033924057	0.269291347950426	58

Table S22.
Summary statistics for validated PTB-derived neuroimmune biomarkers.
A.

Gene	Mean	SD	Min	Max
PSMB8-AS1	5.78306216258984	0.445438518280128	4.12593750988064	6.78365987169355
RPS23	10.7570954212021	0.478715675181622	9.47869425139256	12.308328213805
MIR600HG	9.78120799114686	0.507559611269063	8.46778833566424	10.905544244541
RILP	7.29428580151933	0.311995528931934	5.99813257013936	7.98532062931832
ACSL1	9.35918638854848	0.587043843359009	8.25588124911886	11.3210106696614
SHARPIN	8.90921625552932	0.213495851375418	8.28386131613741	9.60658967320319
LAMTOR2	7.10812133376052	0.335031984867734	5.90640932374473	7.75629070792614
NUMB	9.63199106702239	0.28111081773136	8.75352018761714	10.9640124162631
PPP1R3B	6.95803257581255	0.580817075844984	5.80332917438921	8.7540977525904
HOPX	9.6114463660635	0.634542763760537	7.27302104036364	10.9182749816905
KLRK1	4.88810904138273	0.498627717020047	4.12593750988064	6.2204304321313
SNCA	10.0406110934964	0.806975291570082	8.2789302740979	11.7982029357523

B.

Gene	p.value	FDR
HOPX	1.6075312911694e-11	1.92903754940328e-10
SNCA	1.45549998240952e-06	8.7329998944571e-06
SHARPIN	3.03821652555933e-05	0.000121528661022373
PSMB8-AS1	0.000188328699914872	0.000564986099744617
LAMTOR2	0.00100040034229026	0.00240096082149663
PPP1R3B	0.0438279000464049	0.0876558000928098

MIR600HG	0.127234158490307	0.218115700269098
KLRK1	0.223044786869938	0.297393049159917
RPS23	0.199044303810389	0.297393049159917
ACSL1	0.286896944521435	0.344276333425722
NUMB	0.388618591893437	0.423947554792841
RILP	0.78492273011411	0.78492273011411

C.

Gene	p.value	FDR
HOPX	1.6075312911694e-11	1.92903754940328e-10
SNCA	1.45549998240952e-06	8.7329998944571e-06
SHARPIN	3.03821652555933e-05	0.000121528661022373
PSMB8-AS1	0.000188328699914872	0.000564986099744617
LAMTOR2	0.00100040034229026	0.00240096082149663

Table S23.
Pairwise comparisons for validated PTB-derived neuroimmune biomarkers.

.y.	group1	group2	n1	n2	p	p.signif	p.adj	p.adj.signif
TB_Score	CTR_NoInf	CTR_Inf	52	37	0.709	ns	0.731	ns
TB_Score	CTR_NoInf	AD_NoInf	52	55	0.0261	*	0.0784	ns
TB_Score	CTR_Inf	AD_NoInf	37	55	0.0166	*	0.0784	ns
TB_Score	CTR_NoInf	AD_Inf	52	58	0.731	ns	0.731	ns
TB_Score	CTR_Inf	AD_Inf	37	58	0.488	ns	0.731	ns
TB_Score	AD_NoInf	AD_Inf	55	58	0.0522	ns	0.104	ns

Table S24.
Expression matrix of validated PTB-derived neuroimmune biomarkers in the Alzheimer's disease validation cohort.
Available as a separate supplementary spreadsheet file:
TB12Gene_ExpressionMatrix.csv

Table S25

Module	DiscoverySize	OverlapSize	Retention
magenta	246	221	0.898
green	1077	954	0.886
red	1071	919	0.858
yellow	1240	1062	0.856
lightcyan	55	46	0.836
brown	2117	1730	0.817
turquoise	4782	3815	0.798
black	884	704	0.796
blue	2612	1968	0.753
purple	228	169	0.741
greenyellow	210	150	0.714

cyan	144	101	0.701
salmon	150	100	0.667
grey	2031	1213	0.597
midnightblue	141	81	0.574
pink	258	51	0.198
tan	193	29	0.15

Table S26
Module_Preservation_Zsummary.csv

Module	moduleSize	Zsummary.pres
green	954	8.96399649162584
magenta	221	8.94772746146493
yellow	1000	8.7651636510182
gold	1000	4.84041109287157
black	704	4.40194083535085
blue	1000	3.5005879469599
red	919	2.94261374233265
brown	1000	2.86611850806786
turquoise	1000	2.20815009662553
greenyellow	150	1.94832559927724
purple	169	1.47159915877519
pink	51	1.1280175734092
midnightblue	81	0.71687292351402
tan	29	0.681606929211731
cyan	101	0.220323576852619
salmon	100	0.136803462113169
lightcyan	46	-0.014068177
grey	1000	-0.162882417

Table S27.
Kruskal–Wallis statistics for regional differences in module expression across major brain regions.
Donor_1

Module	Statistic	Pvalue	FDR
Pink	78.29640975	3.52001663478123e-13	5.98402827912809e-12
Purple	75.2062614484374	1.43882831439315e-12	1.22300406723418e-11
Grey	74.2693816367437	2.20254338733351e-12	1.24810791948899e-11
Blue	72.078109855867	5.95008681265436e-12	2.52860130875384e-11
Salmon	71.585338593349	7.43706267280542e-12	2.52860130875384e-11
greenyellow	66.4697698600455	7.46338328910087e-11	2.11462526524525e-10
Turquoise	65.5888021566115	1.10814175143018e-10	2.69120139633043e-10
Yellow	60.8064545985559	9.37122751633265e-10	1.99138584722069e-09
midnightblue	56.440000883369	6.46759662004055e-09	1.22165713934099e-08
Magenta	50.0509550062457	1.0537315284177e-07	1.79134359831009e-07

Black	48.2834861983521	2.26063596497838e-07	3.49371012769385e-07
Cyan	45.6450171165149	7.00809990726019e-07	9.92814153528527e-07
Brown	43.6164098569091	1.66070047147771e-06	2.1716852319324e-06
Tan	35.8860091721493	4.15361197562191e-05	5.04367168468375e-05
Green	22.2554579052344	0.0081036711710199	0.00918416066048922
Lightcyan	19.09454976	0.024400854178404	0.0259259075645543
Red	11.4802310828764	0.244221200849653	0.244221200849653

Donor_2

Module	Statistic	Pvalue	FDR
tan	71.3460335137923	8.28751053346692e-12	1.40887679068938e-10
pink	67.4626935815196	4.77707271987397e-11	4.06051181189287e-10
salmon	58.3807913636263	2.74674531287095e-09	1.55648901062687e-08
greenyellow	57.2397337670521	4.5465373129606e-09	1.93227835800825e-08
blue	54.9617752944216	1.23855319723381e-08	3.50923405882913e-08
magenta	55.1333351543414	1.14872852165263e-08	3.50923405882913e-08
grey	51.3829083740422	5.91237472842002e-08	1.43586243404486e-07
purple	50.7702564532489	7.71467287137166e-08	1.63936798516648e-07
midnightblue	50.4806971427026	8.74707095189654e-08	1.65222451313601e-07
turquoise	47.9810869220873	2.57492959766526e-07	4.37738031603095e-07
yellow	40.3784337291477	6.48793824345288e-06	1.00268136489726e-05
cyan	38.1362477464288	1.64770631565957e-05	2.33425061385106e-05
brown	32.8082556953946	0.00014421507652479	0.000188588946224726
lightcyan	25.455576338999	0.00250646855334148	0.00304356895762894
black	25.1597971717953	0.00279940675436687	0.00317266098828245
green	23.4504359168378	0.00526016814099971	0.00558892864981219
red	17.5970419083046	0.0401470437793478	0.0401470437793478

Table S28.
Consensus peak brain-region assignments for PTB-derived neuroimmune modules.

Module	Peak_BrainRegion	Peak_Zscore
black	Ins	1.01279493555146
blue	TL	0.956073566305828
brown	PL	0.986739398330986
cyan	GP	2.23403313927937
green	GP	2.81141905890539
greenyellow	FL	0.721502213728193
grey	Str	1.96107011299718
lightcyan	PL	1.06177920492685
magenta	GP	2.33089143386895
midnightblue	Str	1.31285285591282
pink	OL	2.08358636058483

purple	FL	0.93875742603928
red	CbCx	1.04467073061708
salmon	TL	0.812808065042337
tan	GP	1.61648797293712
turquoise	CbCx	2.02503676901758
yellow	CbCx	2.06341666372894

Table S29.
Consensus regional Z-score matrix for PTB-derived neuroimmune modules across the Allen Human Brain Atlas.
Available as a separate supplementary spreadsheet file:
Consensus_BrainRegion_Zscore.csv

Table S30.
Inter-donor reproducibility of PTB-derived neuroimmune modules across major brain regions.

Module	Pearson	Spearman	RMSE	MAD
green	0.985840920103911	0.757575757575757	0.159644429320164	0.110093308696001
turquoise	0.916297177225167	0.672727272727273	0.388156000848498	0.302489992416098
grey	0.910765487238819	0.854545454545454	0.400776899247108	0.34506017351378
purple	0.878394876221457	0.915151515151515	0.467855985108001	0.378576949164897
greenyellow	0.878363793914622	0.551515151515151	0.467915773354223	0.350709484547713
yellow	0.877040965808087	0.757575757575757	0.470453251179588	0.391563199675919
magenta	0.871747419330933	0.709090909090909	0.480473355353157	0.349167304454835
brown	0.84266722134113	0.733333333333333	0.532164449757747	0.404608983716032
cyan	0.839159587053501	0.503030303030303	0.538063884035806	0.380685345206405
tan	0.702938286738614	0.648484848484848	0.731239416245114	0.596450322098928
pink	0.700885157762031	0.866666666666667	0.733762029562954	0.505990641843603
salmon	0.609521709487542	0.418181818181818	0.838368011628798	0.591665138905698
red	0.598395927836069	0.83030303030303	0.850227810586713	0.646903869771124
blue	0.563631477482204	0.454545454545455	0.886263696950311	0.646172240698673
midnightblue	0.467563881009016	0.551515151515151	0.978971406213568	0.85411414784975
black	0.431295250877534	0.587878787878788	1.0117650658233	0.862159554026374
lightcyan	0.265019352285516	0.321212121212121	1.15020222825644	0.920503144436295

Table S31.
Summary statistics of regional reproducibility across independent Allen Brain Atlas donors.

Mean_Pearson	Median_Pearson	Min_Pearson	Max_Pearson	Mean_RMSE	Mean_MAD
0.725854617159774	0.839159587053501	0.265019352285516	0.985840920103911	0.652135511380676	0.508053753001302

Table S32.
Consensus ranking of regional enrichment across PTB-derived neuroimmune modules.

BrainRegion	Mean_Zscore	SD_Zscore

FL	0.232953483784389	0.529244418350124
PL	0.20745966318129	0.5518306358255
TL	0.170187793000474	0.540060795809002
Ins	0.122161707461814	0.645359598952963
CgG	0.0571805523990079	0.590674133218392
OL	-0.033659139	0.757600402985158
GP	-0.087712311	1.56205402982469
PHG	-0.155073787	0.505748442349951
Str	-0.23776831	1.11415495071518
CbCx	-0.275729653	1.33030590691758

Table S33.
Consensus ranking of validated PTB-derived neuroimmune modules.

Module	Mean_Zscore	SD_Zscore
pink	2.63677968348475e-16	0.922194436591881
brown	2.58126853225349e-16	0.959861245530085
midnightblue	2.4980018054066e-16	0.856610728688654
green	2.44249065417534e-16	0.996453942765021
turquoise	6.38378239159465e-17	0.978850646734518
lightcyan	-2.78E-17	0.795304769344908
greenyellow	-5.00E-17	0.969113975215151
magenta	-1.07E-16	0.967405659310233
tan	-1.50E-16	0.922750856607193
cyan	-1.94E-16	0.958947231878141
purple	-2.03E-16	0.969121993409874
salmon	-2.83E-16	0.897084641906086
yellow	-4.08E-16	0.968772668330421
black	-6.25E-16	0.845959588537636
grey	-6.49E-16	0.97743682333919
blue	-1.04E-15	0.884203448727216
red	-1.30E-15	0.893978726770405

Table S34.
Absolute ranking of regional enrichment across PTB-derived neuroimmune modules.

BrainRegion	MeanAbs_Zscore	MedianAbs_Zscore	MaxAbs_Zscore	SD_Abs_Zscore
GP	1.36832898445099	1.34347606035765	2.81141905890539	0.677379221242098
CbCx	1.15858037636277	1.04467073061708	2.24882919212974	0.651375127197942
Str	0.972880072215374	1.07866125259216	1.96107011299718	0.543835243362619

Ins	0.607107636715579	0.581782732675436	1.01279493555146	0.201815013528641
OL	0.548017569006523	0.418650989046057	2.08358636058483	0.506032269138488
CgG	0.521263215203758	0.466894163175405	1.218660309	0.252333806602288
PL	0.513214665621358	0.435297190344115	1.06177920492685	0.265321329997103
FL	0.472943218126773	0.399648391887826	0.983510406386167	0.316391679358251
TL	0.470427556815505	0.5153178678112	0.956073566305828	0.295476436052023
PHG	0.369481208688633	0.318613548571444	1.3946306622909	0.36916625301069

Table S35.
Consensus ranking of anatomical substructures showing preferential module enrichment.

Main_Region	Substructure	Mean_Zscore	SD_Zscore
FL	SFG-l	0.249574423867897	0.505055297620158
FL	MFG	0.222154117903002	0.527394167275456
PL	SMG-i	0.172478484715094	0.569601377861722
FL	orIFG	0.161258621612957	0.675566402084095
PL	PoG-cs	0.139591985930678	0.63412345612976
PL	PoG-l	0.125422206352038	0.455191295356877
TL	STG	0.113648120279151	0.456120386945825
FL	PrG	0.111817397401156	0.428974452054881
FL	SFG-m	0.108775561319206	0.48438991966038
FL	PCLa-i	0.107424506408176	0.643530568763006
TL	ITG	0.080917435019709	0.530335066847494
FL	OrbGyri	0.0771141291586843	0.677491941988278
FL	PCLa-s	0.0704778472606243	0.72698675766195
OL	pest_V2	0.056064625543159	0.882228044159467
FL	GRe	0.0555187271408815	0.644507883841292
PL	AnG-s	0.0493355137554271	0.390284793626623
PL	SPL	0.0394414123563641	0.431368849106801
TL	MTG	0.0350343911603902	0.522605967912818
PL	Pcu	0.0325565932986151	1.15505248890703
Ins	Insula	0.0259002555847972	0.656879566422442
PL	AnG-i	0.0250285527922759	0.465957576973095
TL	FuG-its	0.0107693999719871	0.517692194075338
CgG	CgG	-0.021321864	0.563871244129884
GP	GP	-0.195560851	2.42414988619808
Str	Caudate	-0.295435211	1.48912230003476
PHG	PHG	-0.305283256	0.721560608416198
OL	str_V1	-0.368541538	0.992323411268667
CbCx	CbCx	-0.385503092	1.80781684059854
Str	Putamen	-0.498658495	1.65100047592623

Table S36.
Top regionally specific PTB-derived neuroimmune modules identified from consensus Allen Brain Atlas analysis.

Module	SD_Zscore	Variance	Range	Max_Zscore	Min_Zscore
green	0.9965	0.9929	3.3207	2.8114	-0.5092
turquoise	0.9789	0.9581	3.6140	2.0250	-1.5890
grey	0.9774	0.9554	3.5299	1.9611	-1.5688
purple	0.9691	0.9392	2.5749	0.9388	-1.6362
greenyellow	0.9691	0.9392	2.5764	0.7215	-1.8549

Table S37.
Integrated validation metrics for PTB-derived neuroimmune modules, including diagnosis-associated effects, peak brain region, regional specificity, and inter-donor reproducibility.
Available as a separate supplementary spreadsheet file:
Table_Validated_Neuroanatomical_Modules.csv

Table S38.
Integrated systems-level summary of validated PTB-derived neuroimmune modules combining disease association, neuroanatomical localization, regional specificity, and reproducibility metrics.
Available as a separate supplementary spreadsheet file:
Integrated_TB_Module_Neuroanatomical_Summary.csv