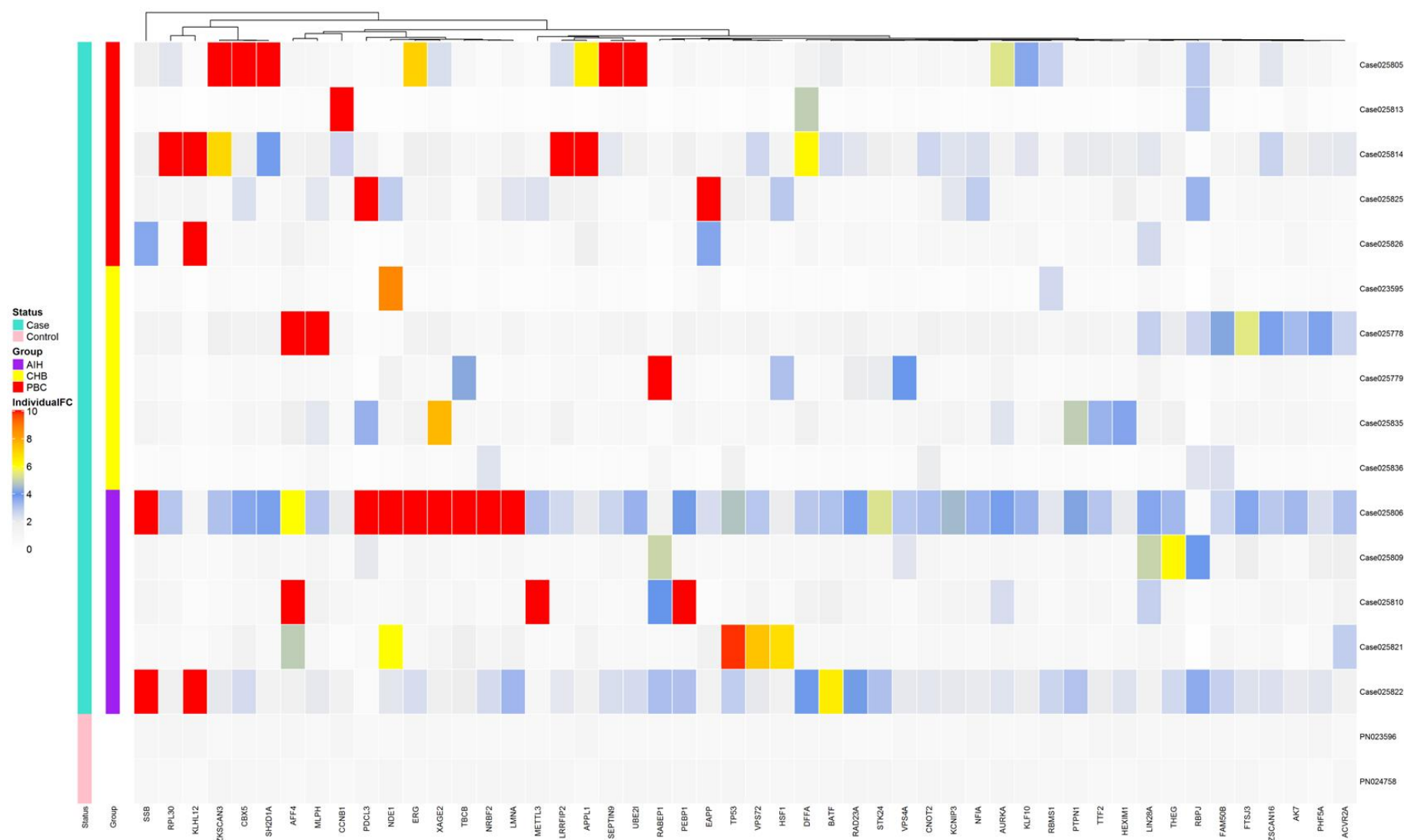




Supplementary Figure 1 The top 50 antigens with high autoantibody titers in primary biliary cholangitis, autoimmune hepatitis, and chronic hepatitis B. PBC: Primary biliary cholangitis; AIH: Autoimmune hepatitis; CHB: Chronic hepatitis B.

Supplementary Table 1 Top 50 autoantigens identified in primary biliary cholangitisby the IMMUNOME™ protein array

Primary biliary cirrhosis with penetrance frequency ≥ 20%												
Protein		Penetrance	Penetrance	Mean	Penetrance	Penetrance	Penetrance	Mean	Penetrance	Frequency	Frequency	Penetrance
		Frequency	Frequency	Penetrance	Fold	Frequency	Frequency	Penetrance	Fold			
		(PBC)	(PBC)	(PBC)	Change	(PN)	(PN)	(PN)	Change	Difference	Difference	Change
					(PBC)				(PN)			Difference
				%								
PSIP1	3	60	2122.147	4.600791	0	0	0	0	3	60	4.600791	461.257
RBPJ	3	60	3455.998	3.157255	0	0	0	0	3	60	3.157255	1094.621
RPL30	2	40	3694.15	38.3014	0	0	0	0	2	40	38.3014	96.44

			8	7							7	95
KLHL1				30.6108							30.6108	269.6
2	2	40	8253.64	2	0	0	0	0	2	40	2	315
CCNB												117.3
1	2		3060.81	26.0813	0	0	0	0	2	40	26.0813	565
ZKSC				25.9316							25.9316	93.50
AN3	2	40	2424.68	5	0	0	0	0	2	40	5	3
SH2D1				25.0129							25.0129	58.49
A	2	40	1463.18	8	0	0	0	0	2	40	8	7
CBX5				24.2336							24.2336	89.62
	2	40	2171.92	4	0	0	0	0	2	40		45
ZBTB2				10.2254							10.2254	338.9
5	2	40	3465.57	7	0	0	0	0	2	40	7	165
SEPTI				9.84928							9.84928	127.2
N9	2	40	1253.05	4	0	0	0	0	2	40	4	23
LRRFI				9.07139							9.07139	142.2
P2	2	40	1290.22	5	0	0	0	0	2	40	5	305

APPL1	2	40	1315.39	8.80972	0	0	0	0	2	40	8.80972	149.3
			4	7							7	115
EAPP	2	40	1065.57	7.58330	0	0	0	0	2	40	7.58330	140.5
			6	4							4	16
PPID	2	40	695.906	7.04059	0	0	0	0	2	40	7.04059	98.84
			5	5							5	2
DFFA	2	40	603.271	5.55790	0	0	0	0	2	40	5.55790	108.5
			5	3							3	43
RPS6K B2	2	40	655.645	4.99998	0	0	0	0	2	40	4.99998	131.1
			5	5							5	295
KLF10	2	40	199.342	2.97432	0	0	0	0	2	40	2.97432	67.02
			5	9							9	1
NFIA	2	40	235.106	2.64978	0	0	0	0	2	40	2.64978	88.72
			5	9							9	65
RUNX 1T1	2	40	479.550	2.62881	0	0	0	0	2	40	2.62881	182.4
			5	2							2	21
TPM1	2	40	1778.42	2.61202	0	0	0	0	2	40	2.61202	680.8

			4	1							1	61
ZSCA				2.49738							2.49738	96.59
N16	2	40	241.24	6	0	0	0	0	2	40	6	7
LIN28				2.38559							2.38559	64.38
A	2	40	153.6	3	0	0	0	0	2	40	3	65
KCNIP												77.92
3	2	40	176.822	2.269	0	0	0	0	2	40	2.269	95
BATF				2.26543							2.26543	100.1
	2	40	226.829	6	0	0	0	0	2	40	6	26
LDB1				2.25287							2.25287	89.94
	2	40	202.625	5	0	0	0	0	2	40	1	1
BAG4				29.0376							29.0376	177.0
	1	20	5141.70	4	0	0	0	0	1	20	9	7
PDCL3				24.7484							24.7484	323.1
	1	20	7996.51	5	0	0	0	0	1	20	3	12
BANK				15.3059							15.3059	156.9
1	1	20	2402.29	7	0	0	0	0	1	20	3	52

UBE2I	1	20	984.827	14.8132 2	0	0	0	0	1	20	14.8132 2	66.48 3
BCKD K	1	20	1121.31 1	10.8143 3	0	0	0	0	1	20	10.8143 3	103.6 875
MLH1	1	20	5843.09 1	10.1792 6	0	0	0	0	1	20	10.1792 6	574.0 19
STAT4	1	20	1341.27 4	9.87356 2	0	0	0	0	1	20	9.87356 2	135.8 45
NME7	1	20	1357.12 7	9.76245	0	0	0	0	1	20	9.76245	139.0 15
TPM4	1	20	1216.00 4	8.47129 8	0	0	0	0	1	20	8.47129 8	143.5 44
ERG	1	20	987.77	7.16273 6	0	0	0	0	1	20	7.16273 6	137.9 04
ZC4H2	1	20	1631.62 9	7.16247 2	0	0	0	0	1	20	7.16247 2	227.8 025
PSME3	1	20	1470.77	6.81831	0	0	0	0	1	20	6.81831	215.7

			6	8							8	095
ZKSC				6.04583							6.04583	61.26
AN4	1	20	370.38	6	0	0	0	0	1	20	6	2
CDC25				5.45665							5.45665	82.34
C	1	20	449.304	9	0	0	0	0	1	20	9	05
AURK												172.3
A	1	20	928.895	5.38846	0	0	0	0	1	20	5.38846	86
PAGE5				4.82583							4.82583	88.97
	1	20	429.376	2	0	0	0	0	1	20	2	45
TOLLI				4.70509							4.70509	123.8
P	1	20	582.867	4	0	0	0	0	1	20	4	8
MSH2				4.61180							4.61180	111.6
	1	20	514.892	6	0	0	0	0	1	20	6	465
TACC1				4.57299							4.57299	867.0
	1	20	3965.05	3	0	0	0	0	1	20	4	585
				4								123.4
CFL1				4.55149							4.55149	745
	1	20	561.993		0	0	0	0	1	20		

PCBD1	1	20	1162.559	4.234671	0	0	0	0	1	20	4.234671	274.5335
NPM1	1	20	554.946	4.16209	0	0	0	0	1	20	4.16209	133.3335
HSPE1	1	20	665.468	4.156123	0	0	0	0	1	20	4.156123	160.1175
ZMYM2	1	20	470.109	4.121124	0	0	0	0	1	20	4.121124	114.073
PIK3C3	1	20	406.241	3.983263	0	0	0	0	1	20	3.983263	101.987

PBC: Primary biliary cholangitis; PN: Pooled normal; OD: Optical density; IQR: Interquartile range.

Supplementary Table 2 Disease associations of biomarkers identified in primary biliary cholangitis samples

Disease	No. of associated targets	All targets
Primary Biliary Cirrhosis	7	STAT4, BANK1, RPL30, KLHL12, PSIP1, PIK3C3, BATF

Data obtained from the Open Targets platform. STAT4: Signal transducer and activator of transcription 4; BANK1: B cell scaffold protein with ankyrin repeats 1; RPL30: Ribosomal protein L30; KLHL12: Kelch-like protein 12; PSIP1: PC4 and SFRS1 interacting protein 1; PIK3C3: Phosphatidylinositol 3-kinase catalytic subunit type 3; BATF: Basic leucine zipper ATF-like transcription factor; PBC: Primary biliary cholangitis.

Supplementary Table 4 The clinical data comparison of anti-RPL30 positive and anti-RPL30 negative of primary biliary cholangitis patients

Variable	Anti-RPL30 (+)	Anti-RPL30 (-)	<i>P</i> value	Statistic	Method
Number	55	7			
Gender, <i>n</i> (%)			1		Fisher test
Female	48 (77.4)	7 (11.3)			
Male	7 (11.3)	0 (0)			
Age (yr), mean ± SD	59.073 ± 9.3191	57.857 ± 9.9905	0.748	0.323	T test
RPL30 OD value, median (IQR)	0.098 (0.086, 0.122)	0.068 (0.065, 0.069)	< 0.001		Wilcoxon
IgG4 (g/L), median (IQR)	0.68 (0.37, 0.82)	0.34 (0.195, 0.635)	0.204		Wilcoxon

IgA (g/L), median (IQR)	2.87 (2.600, 3.715)	2.55 (2.35, 2.685)	0.128		Wilcoxon
IgM (g/L), median (IQR)	2.36 (1.495, 3.855)	3.46 (1.745, 5.41)	0.339		Wilcoxon
IgG (g/L), median (IQR)	15.7 (13.85, 18.9)	15.7 (14.2, 17.65)	0.578		Wilcoxon
ANA titer, <i>n</i> (%)			0.717	2.100	Yates' correction
0	4 (6.5)	1 (1.6)			
1:100	3 (4.8)	0 (0)			
1:320	9 (14.5)	0 (0)			
1:1000	32 (51.6)	5 (8.1)			
1:3200	7 (11.3)	1 (1.6)			
AMA, <i>n</i> (%)			0.279	1.171	Yates' correction
Negative	24 (38.7)	1 (1.6)			
Positive	31 (50)	6 (9.7)			
AMA-M2, <i>n</i> (%)			0.928	0.008	Yates' correction
Negative	29 (46.8)	3 (4.8)			

Positive	26 (41.9)	4 (6.5)			
Anti-gp210, <i>n</i> (%)			0.45	0.571	Yates' correction
Negative	43 (69.4)	4 (6.5)			
Positive	12 (19.4)	3 (4.8)			
Anti-Sp100, <i>n</i> (%)			0.786	0.073	Yates' correction
Negative	46 (74.2)	5 (8.1)			
Positive	9 (14.5)	2 (3.2)			
TBIL (μmol/L), median (IQR)	17.3 (12.2, 37)	19.1 (18, 27.65)	0.632		Wilcoxon
DBIL (μmol/L), median (IQR)	5.6 (2.6, 16.45)	11.2 (5.25, 12.35)	0.555		Wilcoxon
IBIL (μmol/L), median (IQR)	12.7 (8.65, 19.8)	13.4 (11.05, 15.95)	0.973		Wilcoxon
TBA (μmol/L), median (IQR)	20.3 (7.05, 65.4)	82.5 (48.1, 94.2)	0.102		Wilcoxon
GGT (U/L), median (IQR)	150 (75, 297.5)	396 (335.5, 522.5)	0.004		Wilcoxon

ALP (U/L), median (IQR)	180 (131, 323)	439 (416.5, 590.5)	< 0.001		Wilcoxon
ALT (U/L), median (IQR)	41 (30.5, 73.5)	83 (72, 100.5)	0.010		Wilcoxon
AST (U/L), median (IQR)	63 (43.5, 83)	86 (67.5, 111.5)	0.100		Wilcoxon
ALB (g/l), mean $\pm$ SD	36.455 $\pm$ 6.5456	37.143 $\pm$ 5.2099	0.790	-0.267	T test
CHE (U/L), mean $\pm$ SD	5908.3 $\pm$ 3056	6718 $\pm$ 1941.8	0.499	-0.681	T test
SCr (μ mol/l), median (IQR)	58 (50.5, 66)	53 (49.5, 56)	0.196		Wilcoxon
BUN (mmol/l), median (IQR)	4.6 (3.85, 5.3)	4.9 (3.9, 5.4)	0.911		Wilcoxon
WBC ($\times 10^9$ /L), mean $\pm$ SD	5.0795 $\pm$ 1.5717	4.1829 $\pm$ 1.3009	0.154	1.444	T test
HGB (g/l), mean $\pm$ sd	111.76 $\pm$ 25.226	110.43 $\pm$ 16.672	0.892	0.136	T test
RBC ($\times 10^{12}$ /L), mean	3.7653 $\pm$ 0.87194	3.8629 $\pm$ 0.61905	0.776	-0.286	T test

± SD					
LY (×10 ⁹ /L), median (IQR)	1.49 (0.925, 2.015)	1.25 (1.035, 2.19)	0.689		Wilcoxon
ANC (×10 ⁹ /L), mean ± SD	3.0216 ± 1.1695	2.18 ± 0.99438	0.074	1.819	T test
PLT (×10 ⁹ /L), median (IQR)	166 (110, 235)	209 (167, 213)	0.328		Wilcoxon
PT (sec), median (IQR)	12.4 (11.75, 13.7)	11.4 (10.9, 11.55)	0.004		Wilcoxon
PTA (%), median (IQR)	103 (93.5, 120)	137.8 (118, 151)	0.016		Wilcoxon
INR, median (IQR)	0.99 (0.9, 1.04)	0.85 (0.805, 1)	0.077		Wilcoxon
APTT (sec), mean ± SD	36.176 ± 7.1028	37.586 ± 2.7943	0.607	-0.517	T test
Fib (g/l), mean ± SD	3.0062 ± 0.79427	3.2843 ± 0.42485	0.369	-0.905	T test
Cirrhosis stage, <i>n</i> (%)			0.072	10.099	Yates' correction
stage 0	27 (43.5)	4 (6.5)			

stage 1	4 (6.5)	3 (4.8)			
stage 2	4 (6.5)	0 (0)			
stage 3	9 (14.5)	0 (0)			
stage 4	5 (8.1)	0 (0)			
stage 5	6 (9.7)	0 (0)			
Ascites, <i>n</i> (%)	17 (27.4)	1 (1.6)	0.638	0.221	Yates' correction
EGVB, <i>n</i> (%)	4 (6.5)	0 (0)	1.000	< 0.001	Yates' correction
HE, <i>n</i> (%)	2 (3.2)	0 (0)	1.000	< 0.001	Yates' correction
Infection, <i>n</i> (%)	6 (9.7)	0 (0)	1.000		Fisher test
Thrombosis, <i>n</i> (%)	1 (1.6)	0 (0)	1.000		Fisher test
EGV, <i>n</i> (%)	12 (19.4)	0 (0)	0.385	0.754	Yates' correction

P values were calculated using Fisher's exact test, *t* test, Wilcoxon test, and Yates' correction. Cirrhosis stages are defined as follows: stage 0, non-cirrhosis; stage 1, no esophagogastric varices or ascites; stage 2, with varices but without ascites; stage 3, with ascites ± varices; stage 4, with bleeding ± ascites; stage 5, with sepsis or hepatic encephalopathy. RPL30: Ribosomal protein L30; PBC: Primary biliary cholangitis; OD: Optical density; IQR: Interquartile range; SD: Standard deviation; CI: confidence interval; TBIL: Total bilirubin; DBIL: Direct bilirubin; IBIL: Indirect bilirubin; TBA: Total bile acid; GGT: Gamma-glutamyl transferase; ALP: Alkaline phosphatase; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; ALB: Albumin; CHE: Cholinesterase; SCr:

Serum creatinine; BUN: Blood urea nitrogen; WBC: White blood cell count; HGB: Hemoglobin; RBC: Red blood cell count; LY: Lymphocyte count; ANC: Absolute neutrophil count; PLT: Platelet count; PT: Prothrombin time; PTA: Prothrombin activity; INR: International normalized ratio; APTT: Activated partial thromboplastin time; FIB: Fibrinogen; EGVB: Esophagogastric variceal bleeding; HE: Hepatic encephalopathy; EGV: Esophagogastric varices.