

**Fig. S1. Factors associated with seropositivity of neutralizing antibodies at D57 and D180, respectively.** (A) Multivariable logistic regression analysis was used to investigate factors associated with the generation of NABs at D57 after adjusting sex, BMI and diastolic blood pressure. (B) Multivariable logistic regression analysis was used to investigate factors associated with the persistence of NABs at D180 after adjusting leukocytes, monocytes, RBC, lymphocytes, hemoglobin, LDL, HDL, TG, ALT, and AST.

**Fig. S2. Quality controls of the proteomics data.** (A) Study design of our TMT-labeling-based quantitative proteomics analysis of PBMCs and sera samples. Together, PBMCs and serum generated 528 peptide samples, including 33 pooled controls, distributed into 33 batches and analyzed using TMTpro 16-plex labeling based proteomics. (B) The proteomics data's coefficients of variation were calculated using the abundance of the quantified proteins in the 33 pooled controls of the 33 batches. Also, they were computed after removing the outliers. (C) Quality control of the technical replicates based on the Pearson correlation coefficients. (D-E) PCA analyses were performed on all the proteomics data derived from the PBMC (D) and serum samples (E), for three immune response groups on D57 (Group 0, Group 1, and Group 2) and two immune response groups on D180 (Group 3 and Group 4). Group 1: the late seropositive group; Group 2: the early seropositive group.

**Fig. S3. Machine learning-based prediction of Group 1 (being negative at D28 and then converting) and Group 0 (being negative at D28 and never converting) before vaccination.** (A) Our machine learning-based predictor was based on PBMC, serum, and both types of proteins. We used the samples from a discovery cohort (Cohort 1, N = 137) to optimize the model's parameters. The model was then tested using a test cohort (Cohort 2, N = 26): the first based on PBMC biomarkers and the second on serum biomarkers. We next developed a third model that was an ensemble of the two previous ones. This third model led to an AUC of 0.853, which was higher than using PBMC or serum proteins individually. (B) The SHAP values of the five PBMC proteins were prioritized using the machine learning model. (C) The SHAP values of the five serum proteins were prioritized using the machine learning model. Identification of NAb status-associated proteins in PBMC (D) and serum (E) using volcano plot analysis on D0, D28, and D57 (two-sided unpaired Welch's t-test). The  $\log_{10}$  (B-H adjusted p-value) is plotted as a function of the  $\log_2$ (fold change) between Group 1 and Group 0 samples (B-H adjusted p-value < 0.05,  $|\log_2(\text{fold change})| > 0.25$ ).

**Fig. S4. Immune response and pathway analyses using the PBMC data.** (A) Heatmap of 985 proteins selected using the ANOVA test. Each protein is compared among the three immune response groups (Group 0, 1, and 2) on D0, D28, and D57 (p-value < 0.05). Group 0: the seronegative group; Group 1: the late seropositive group; Group 2: the early seropositive group. (B-D) Pathways' enrichment based on the proteins selected using the ANOVA test to compare the three immune response groups on D0 (B), D28 (C), and D57 (D) using Metascape ( $\log_{10}$  p-value). (E)

Barplots visualizing the estimated proportions of 20 immune cell types in each PBMC sample. Each column represents a sample; the colors indicate the inferred immune cell components. **(F)** Average proportions of 20 immune cell types, in Group 0, Group 1, and Group 2, at three time points. The asterisks indicate the statistical significance based on the Kruskal-Wallis test. P-value: \*, < 0.05; \*\*, < 0.01; \*\*\*, < 0.001. **(G)** Barplots visualizing the estimated proportions of 20 immune cell types, in Group 0, Group 1, and Group 2, at three time points. Different colors indicate the predicted composition of immune cell types.

**Fig. S5. Immune response and pathway analysis using the serum data. (A)** Heatmap of 129 proteins selected using the ANOVA test. Each protein is compared between the three immune response groups (Group 0, 1, and 2) on D0, D28, and D57 (P-value < 0.05). Group 0: the seronegative group; Group 1: the late seropositive group; Group 2: the early seropositive group. **(B)** Pathways' enrichment based on the proteins selected in **(A)** using Metascape. **(C-D)** Comparison among three immune response groups (Group 0, 1, and 2) of the canonical pathways of proteins in **(A)** by IPA (Kramer et al., 2014).

**Fig. S6. Immune response and pathway analysis using the PBMC and the serum data. (A-B)** Pathways' enrichment analysis of selected PBMC proteins. Specifically, 6331 PBMC proteins and 961 serum proteins were grouped into 12 discrete clusters using mFuzz, respectively. This analysis included all the proteins from the PBMC dataset that steadily increased **(A)** or decreased **(B)** over time. And the serum dataset that steadily increased **(C)** or decreased **(D)** over time. The 20 most significantly enriched pathways involving these DEPs were analyzed using Metascape.

**Fig. S7. Immune response and network analysis of the seropositive groups: comparison between PBMC and serum data.** The most significantly dysregulated proteins identified using mFuzz from the following groups are here compared: **(A)** upregulated in both PBMC and serum, **(B)** downregulated in both PBMC and serum, **(C)** upregulated in PBMC and downregulated in serum, and **(D)** downregulated in PBMC and upregulated in serum. The Venn diagrams show the overlaps between the PBMC (blue) and the serum proteins (red). Pathways and heatmaps were generated from the overlapping proteins from each pair. **(E)** The most significantly enriched networks generated using the DEPs from **(A-D)**. The proteins involved in the complement system, including platelet degranulation, neutrophil degranulation, and protein-lipid complex remodeling.

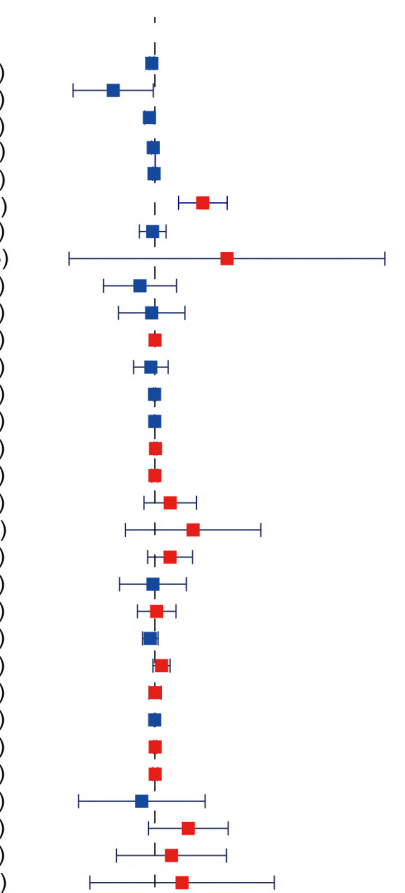
Figure S1

A

**Seropositive of NAb titers at D57**

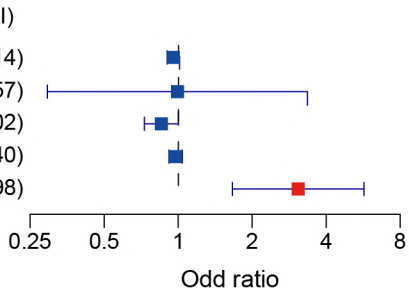
**Univariable analysis**

	pvalue	Odd ratio (95%CI)
Age	0.005	0.930(0.884-0.979)
Sex (vs male)	0.042	0.364(0.137-0.963)
BMI	0.027	0.878(0.782-0.985)
Diastolic Blood Pressure	0.030	0.951(0.909-0.995)
Systolic Blood Pressure	0.093	0.970(0.937-1.005)
NAb titers at day 28	<0.001	3.173(1.755-5.737)
Leukocytes	0.757	0.950(0.686-1.315)
Monocytes	0.370	5.804(0.124-271.388)
RBC	0.428	0.698(0.287-1.698)
Lymphocytes	0.854	0.927(0.413-2.081)
Platelets	0.377	1.004(0.996-1.012)
Neutrophils	0.652	0.908(0.596-1.383)
Hemoglobin	0.693	0.995(0.969-1.021)
UA	0.444	0.998(0.993-1.003)
GGT	0.340	1.017(0.983-1.052)
TBIL	0.986	1.001(0.930-1.077)
LDL	0.248	1.457(0.769-2.760)
HDL	0.267	2.542(0.489-13.217)
TC	0.180	1.453(0.841-2.509)
TG	0.914	0.956(0.424-2.157)
Glucose	0.847	1.047(0.655-1.674)
IR	0.262	0.896(0.741-1.085)
Alb	0.119	1.179(0.958-1.449)
CRP	0.922	1.007(0.868-1.169)
Cr	0.865	0.999(0.983-1.014)
ALT	0.538	1.011(0.977-1.046)
AST	0.713	1.011(0.952-1.074)
Drug(vs without drug)	0.688	0.729(0.156-3.400)
MAFLD(vs non-MAFLD)	0.099	2.261(0.857-5.968)
Hypertension(vs non-hypertension)	0.553	1.500(0.393-5.718)
T2DM (vs non-T2DM)	0.562	1.944(0.206-18.367)



**Multivariable analysis**

	pvalue	Odd ratio (95%CI)
Age	0.136	0.956(0.902-1.014)
Sex (vs male)	0.992	0.994(0.294-3.357)
BMI	0.053	0.855(0.729-1.002)
Diastolic Blood Pressure	0.467	0.977(0.918-1.040)
NAb titers at day 28	<0.001	3.079(1.663-5.698)

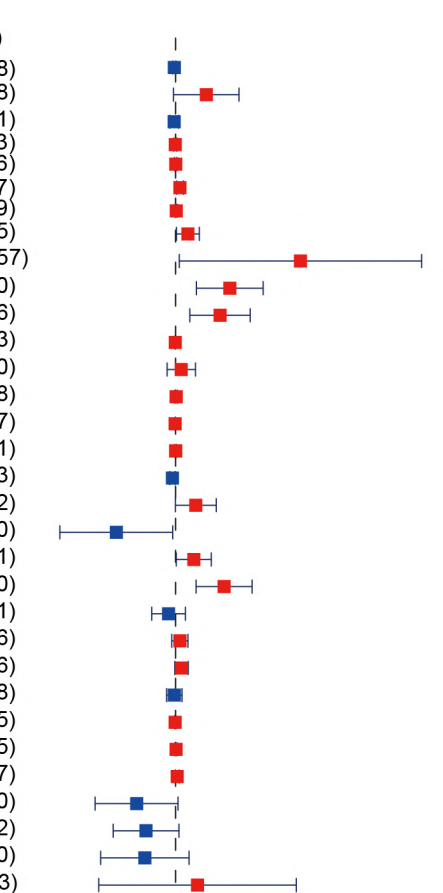


B

**Seropositive of NAb titers at D180**

**Univariable analysis**

	pvalue	Odd ratio (95%CI)
Age	0.340	0.984(0.950-1.018)
Sex (vs male)	0.061	2.017(0.967-4.208)
BMI	0.699	0.981(0.890-1.081)
Diastolic Blood Pressure	0.634	1.008(0.975-1.043)
Systolic Blood Pressure	0.209	1.018(0.990-1.046)
NAb titers at day 28	0.003	1.121(1.041-1.207)
NAb titers at day 57	0.002	1.030(1.011-1.049)
Leukocytes	0.028	1.334(1.032-1.725)
Monocytes	0.043	16.744(1.100-254.957)
RBC	0.001	3.425(1.618-7.250)
Lymphocytes	0.003	2.748(1.394-5.416)
Platelets	0.060	1.006(1.000-1.013)
Neutrophils	0.390	1.150(0.836-1.580)
Hemoglobin	0.029	1.025(1.002-1.048)
UA	0.087	1.003(1.000-1.007)
GGT	0.089	1.014(0.998-1.031)
TBIL	0.062	0.943(0.888-1.003)
LDL	0.047	1.593(1.007-2.522)
HDL	0.041	0.267(0.075-0.950)
TC	0.036	1.525(1.028-2.261)
TG	0.001	3.010(1.603-5.650)
Glucose	0.449	0.864(0.592-1.261)
IR	0.240	1.115(0.930-1.336)
Alb	0.061	1.156(0.993-1.346)
CRP	0.846	0.983(0.828-1.168)
Cr	0.610	1.003(0.991-1.015)
ALT	0.025	1.024(1.003-1.045)
AST	0.021	1.051(1.007-1.097)
Drug(vs without drug)	0.069	0.422(0.166-1.070)
MAFLD(vs non-MAFLD)	0.084	0.521(0.249-1.092)
Hypertension(vs non-hypertension)	0.181	0.508(0.188-1.370)
T2DM (vs non-T2DM)	0.656	1.657(0.180-15.273)



**Multivariable analysis**

	pvalue	Odd ratio (95%CI)
NAb titers at day 28	0.043	1.096(1.003-1.198)
NAb titers at day 57	0.043	1.021(1.001-1.041)
Leukocytes	0.422	0.836(0.540-1.295)
Monocytes	0.241	3.551(0.426-29.587)
RBC	0.123	3.260(0.727-14.613)
Lymphocytes	0.085	2.427(0.885-6.657)
Hemoglobin	0.642	0.990(0.949-1.032)
LDL	0.364	0.000(0.000-1.276E+37)
HDL	0.364	0.000(0.000-1.571E+37)
TC	0.362	1.566E+32(0.000-2.488E+101)
TG	0.372	0.000(0.000-1.370E+17)
ALT	0.706	0.990(0.938-1.044)
AST	0.659	1.024(0.921-1.140)

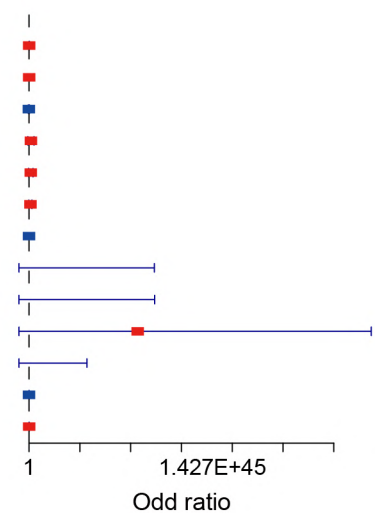
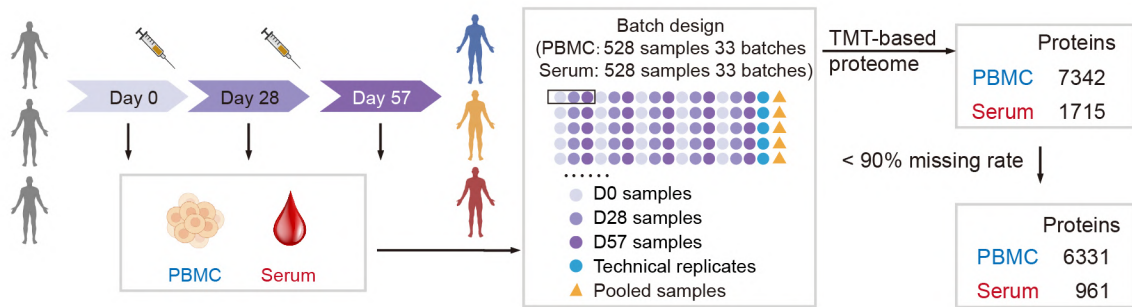
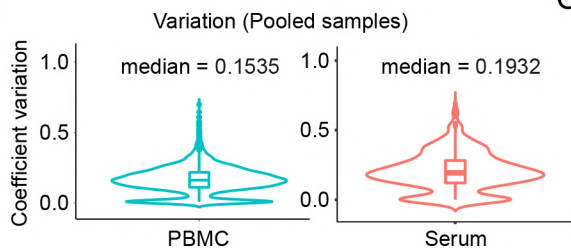


Figure S2

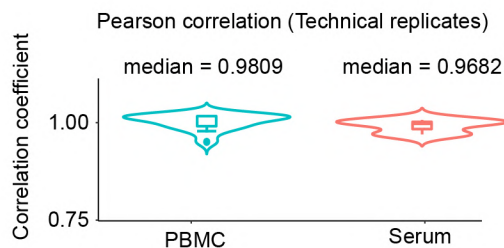
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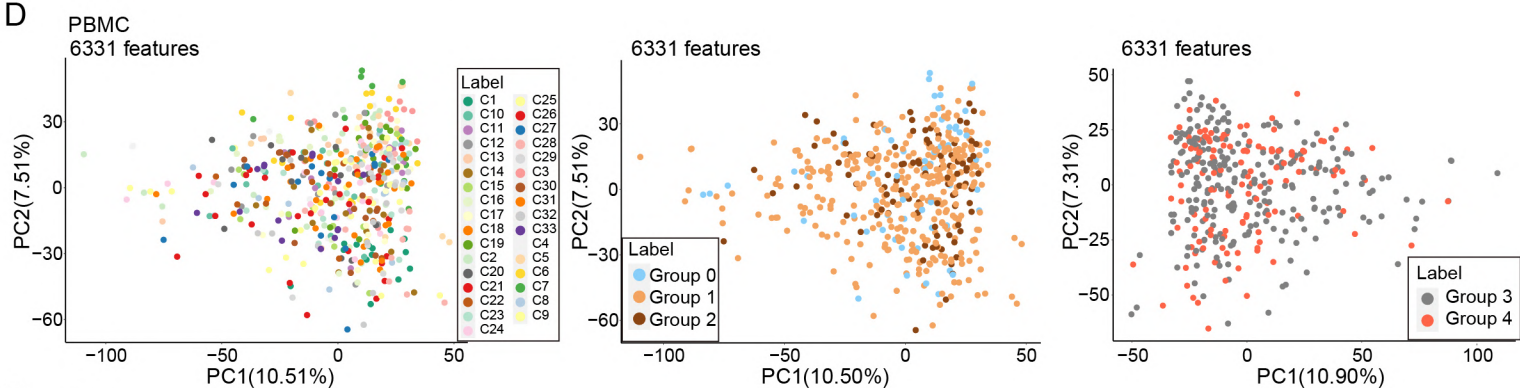
B



C



D



E

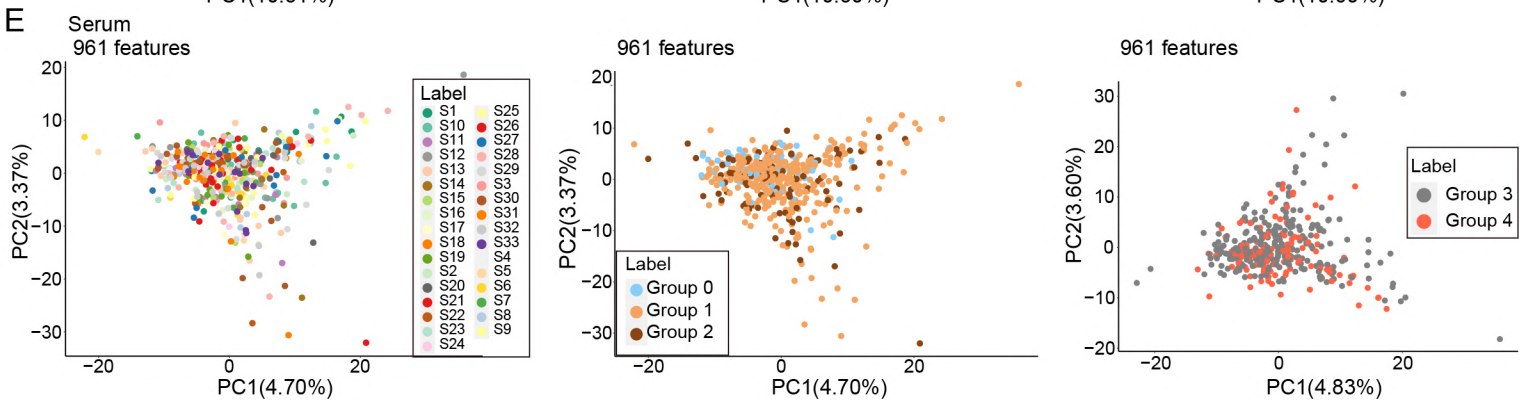


Figure S3

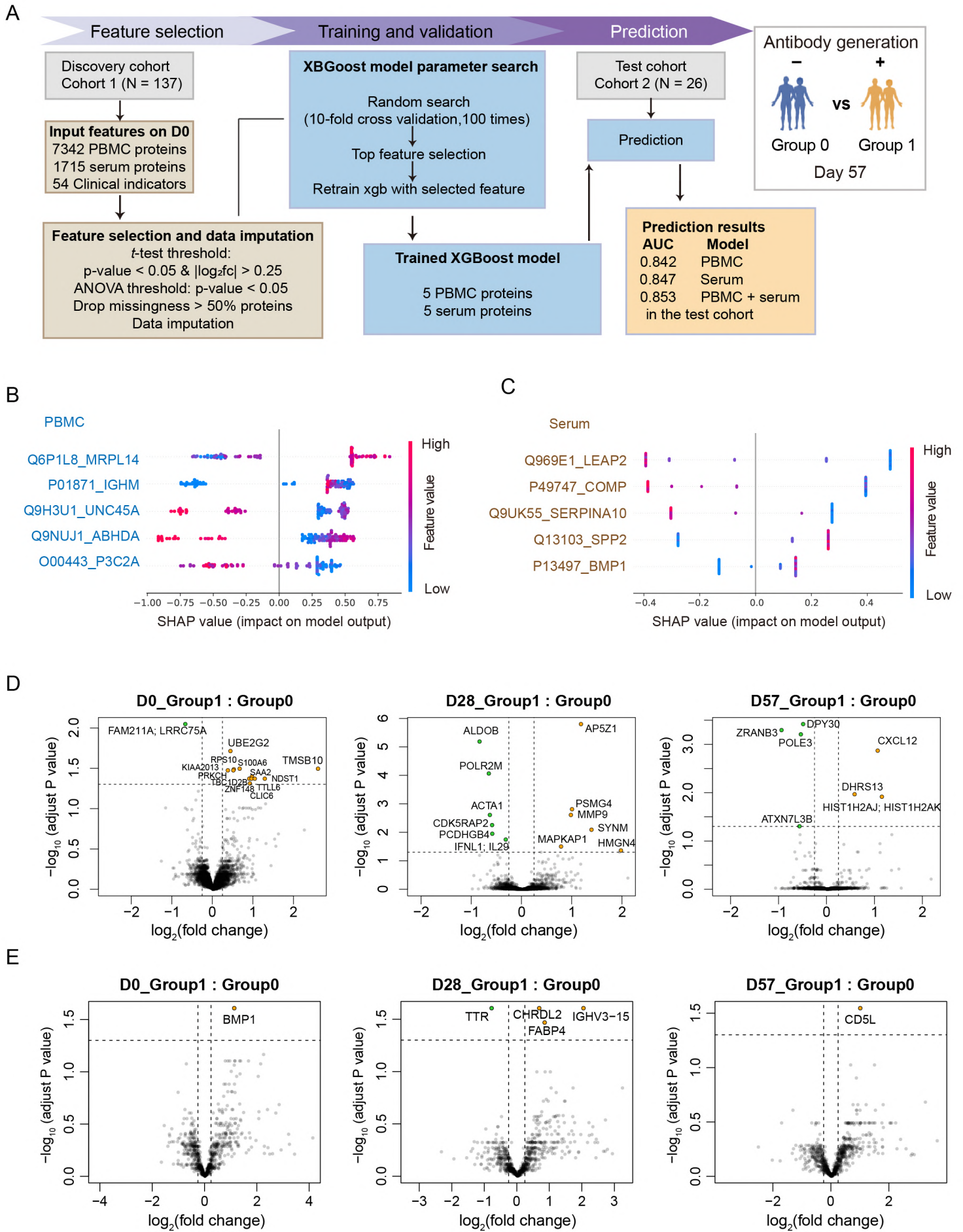
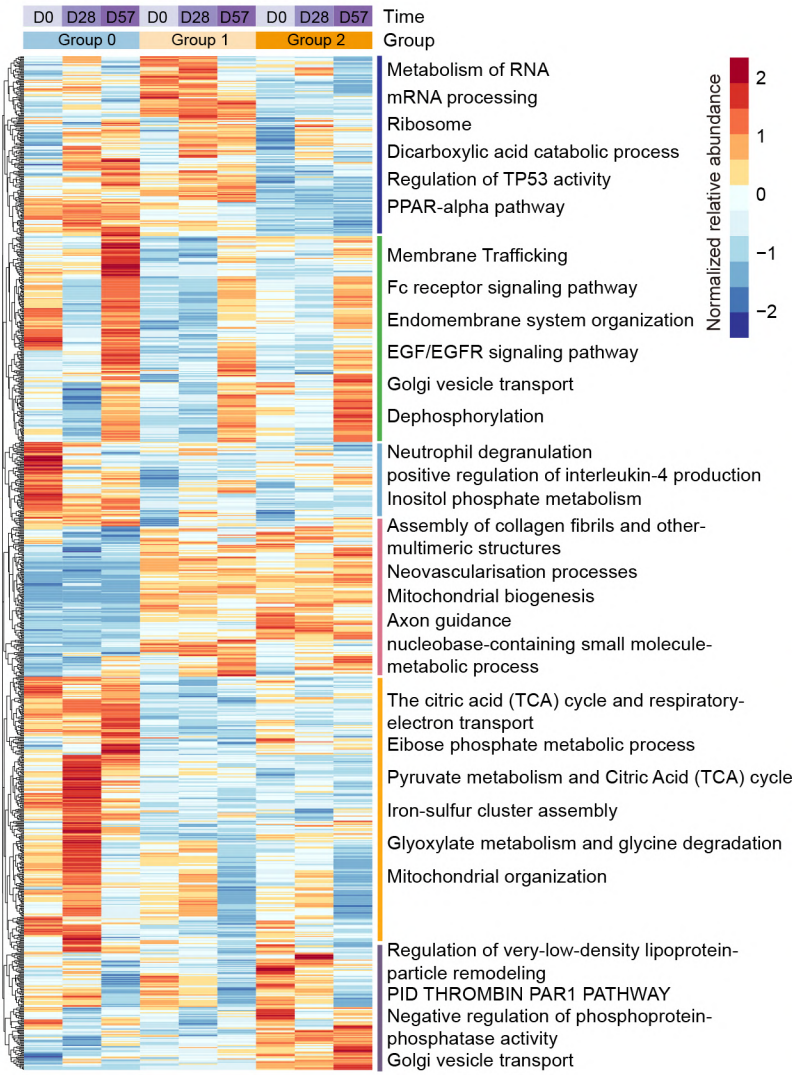
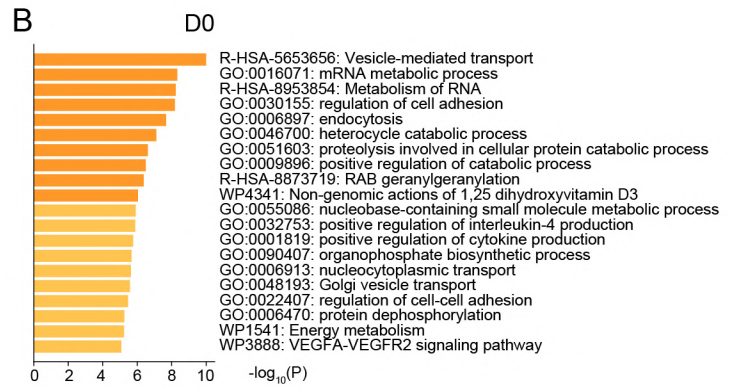


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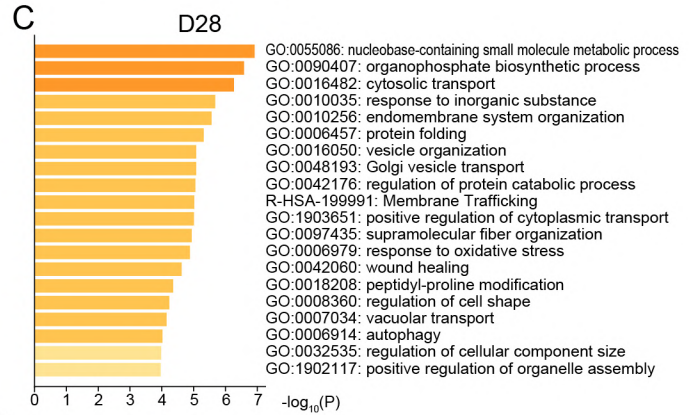
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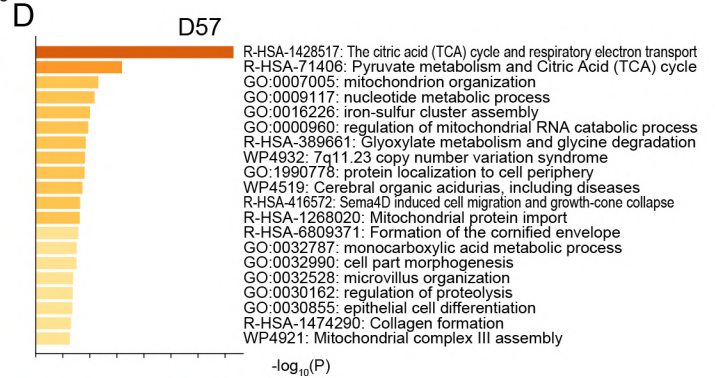
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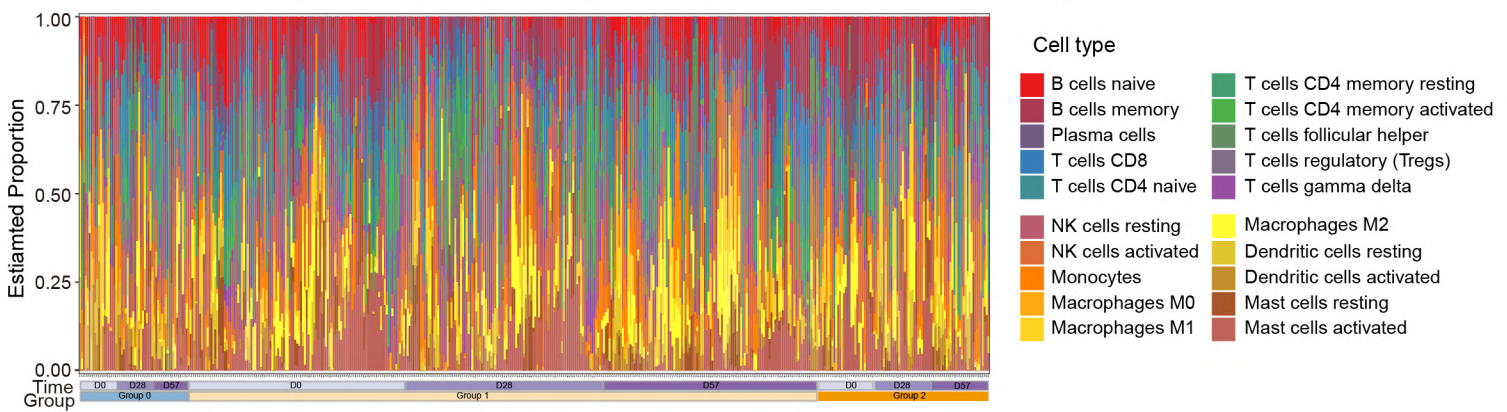
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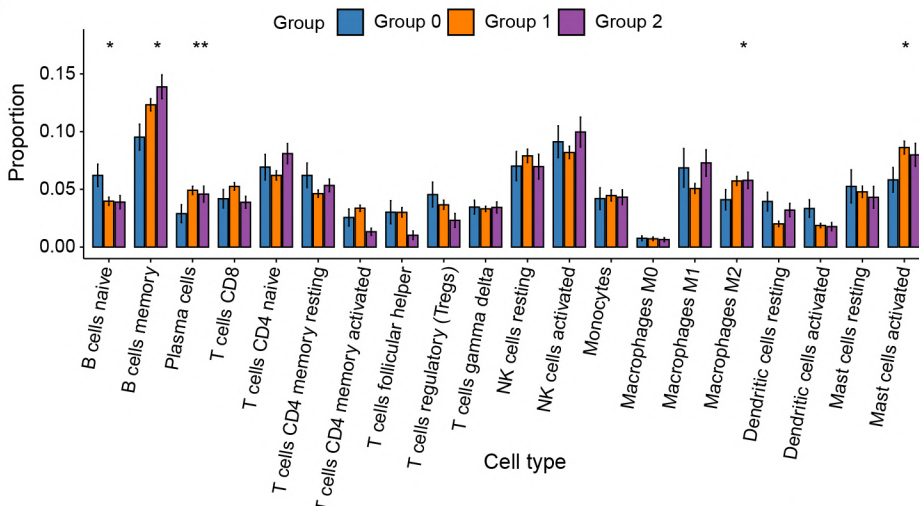
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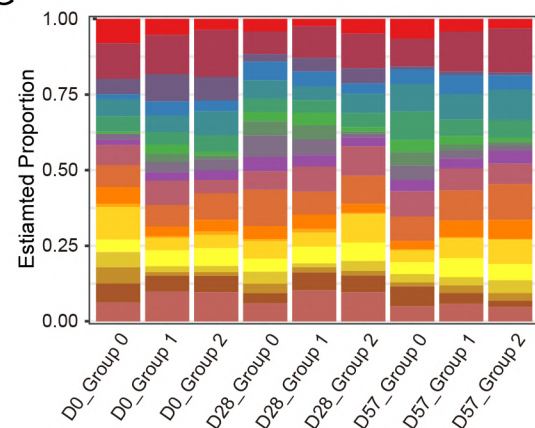


Figure S5

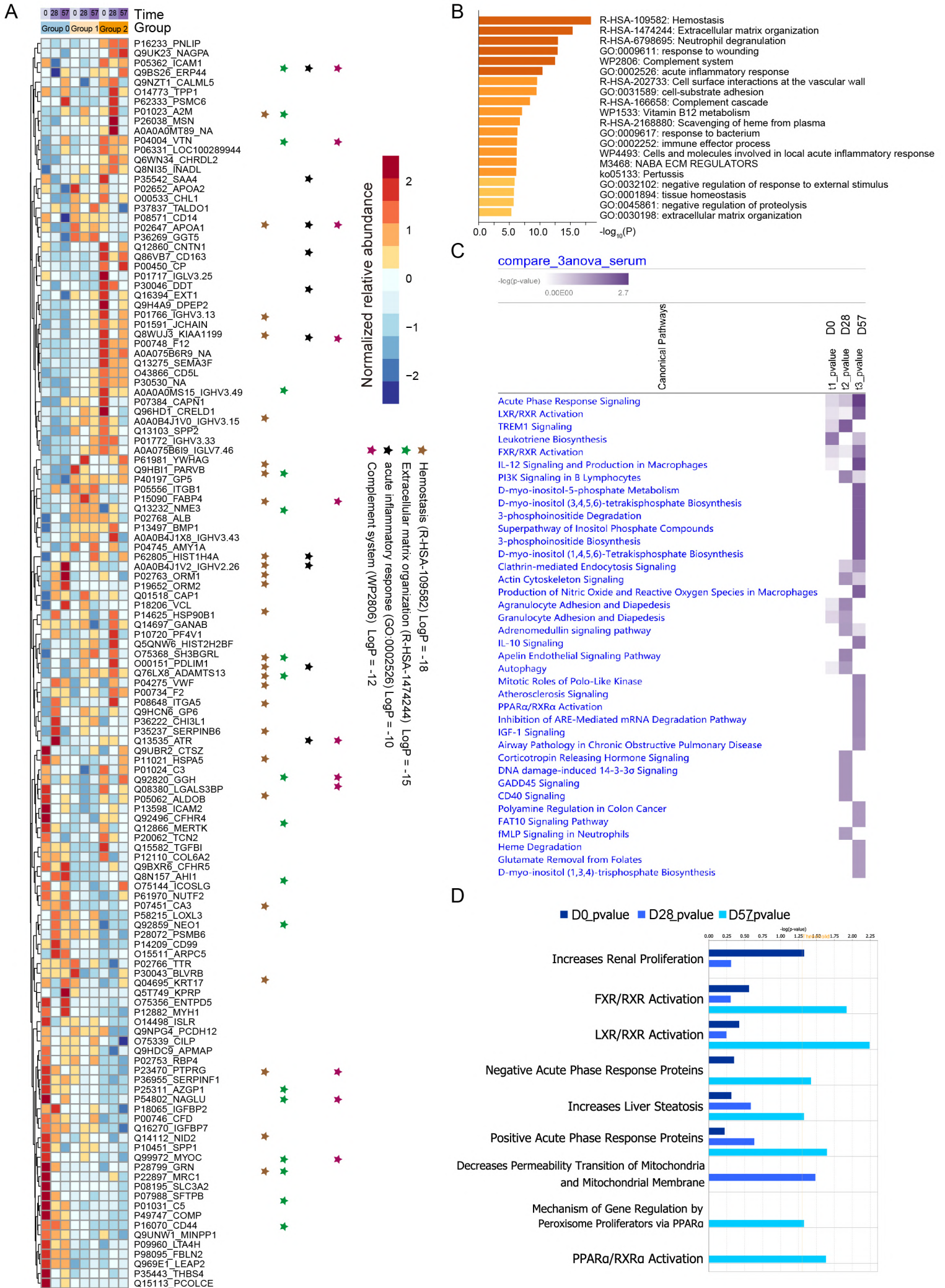


Figure S6

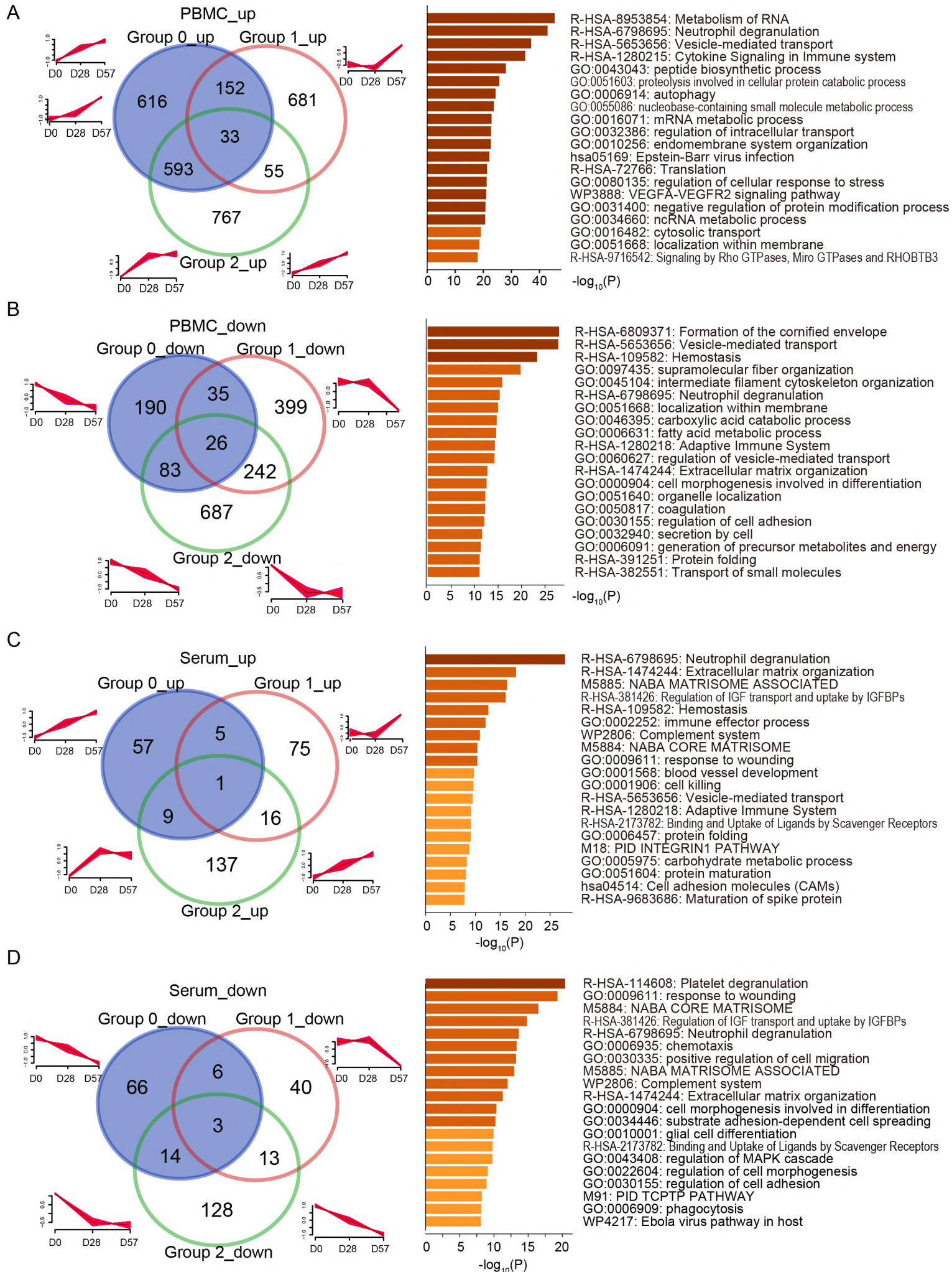
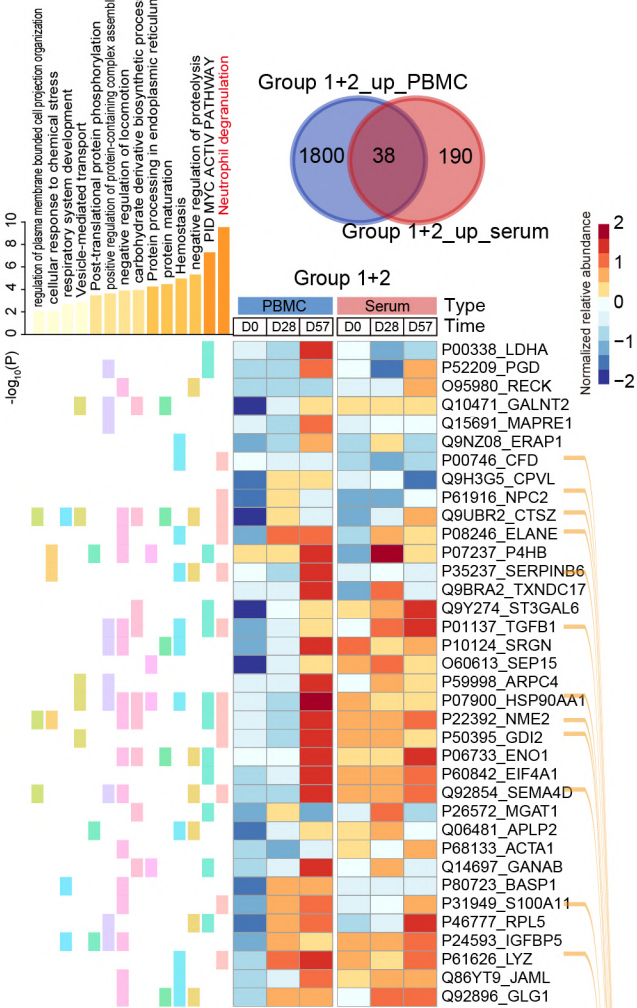
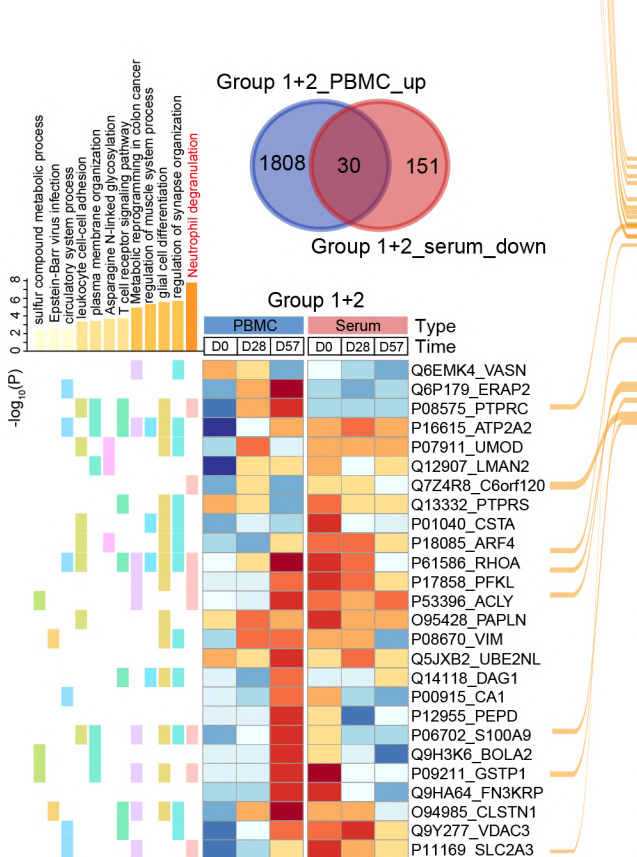


Figure S7

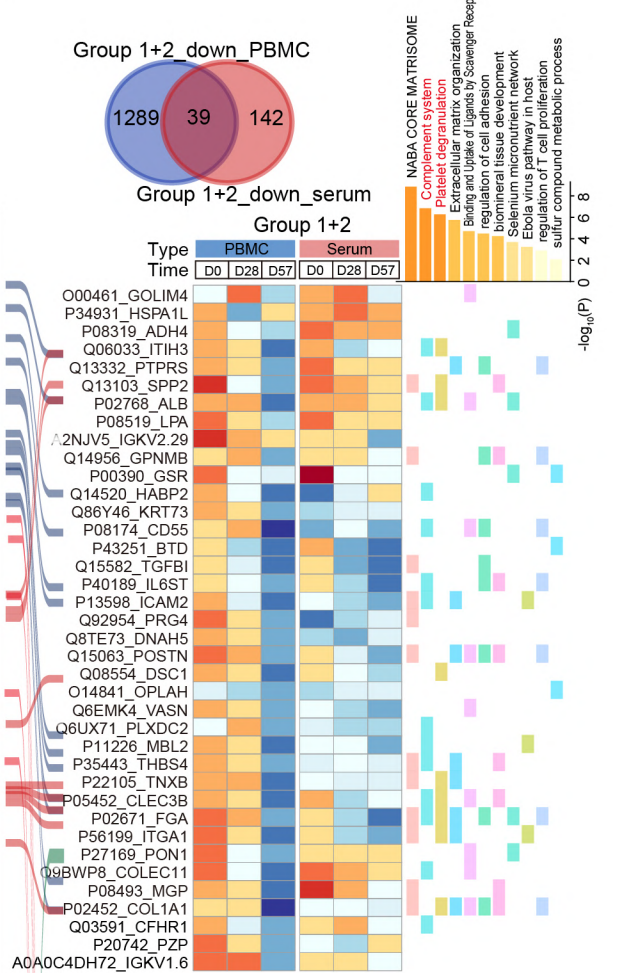
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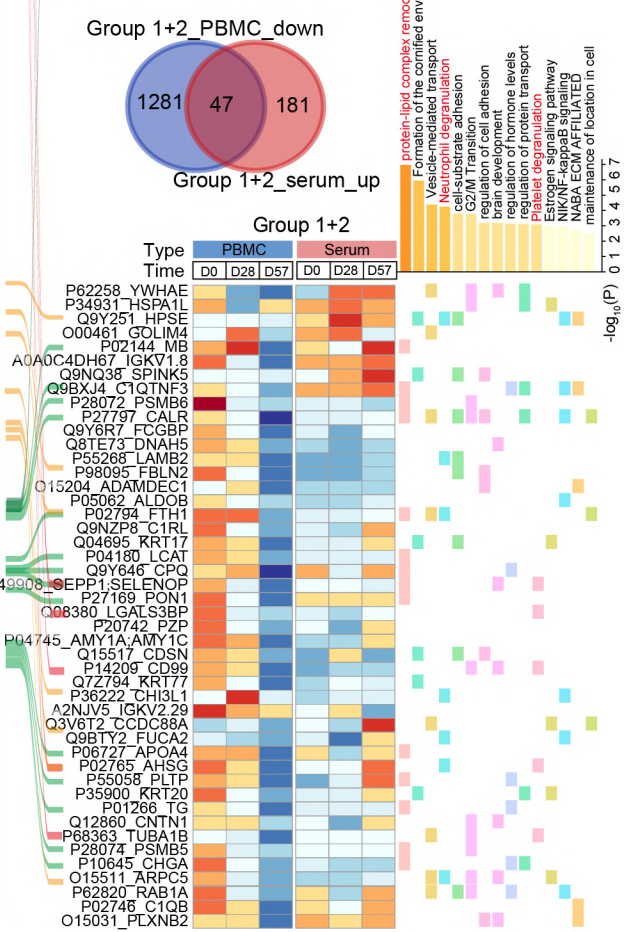
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