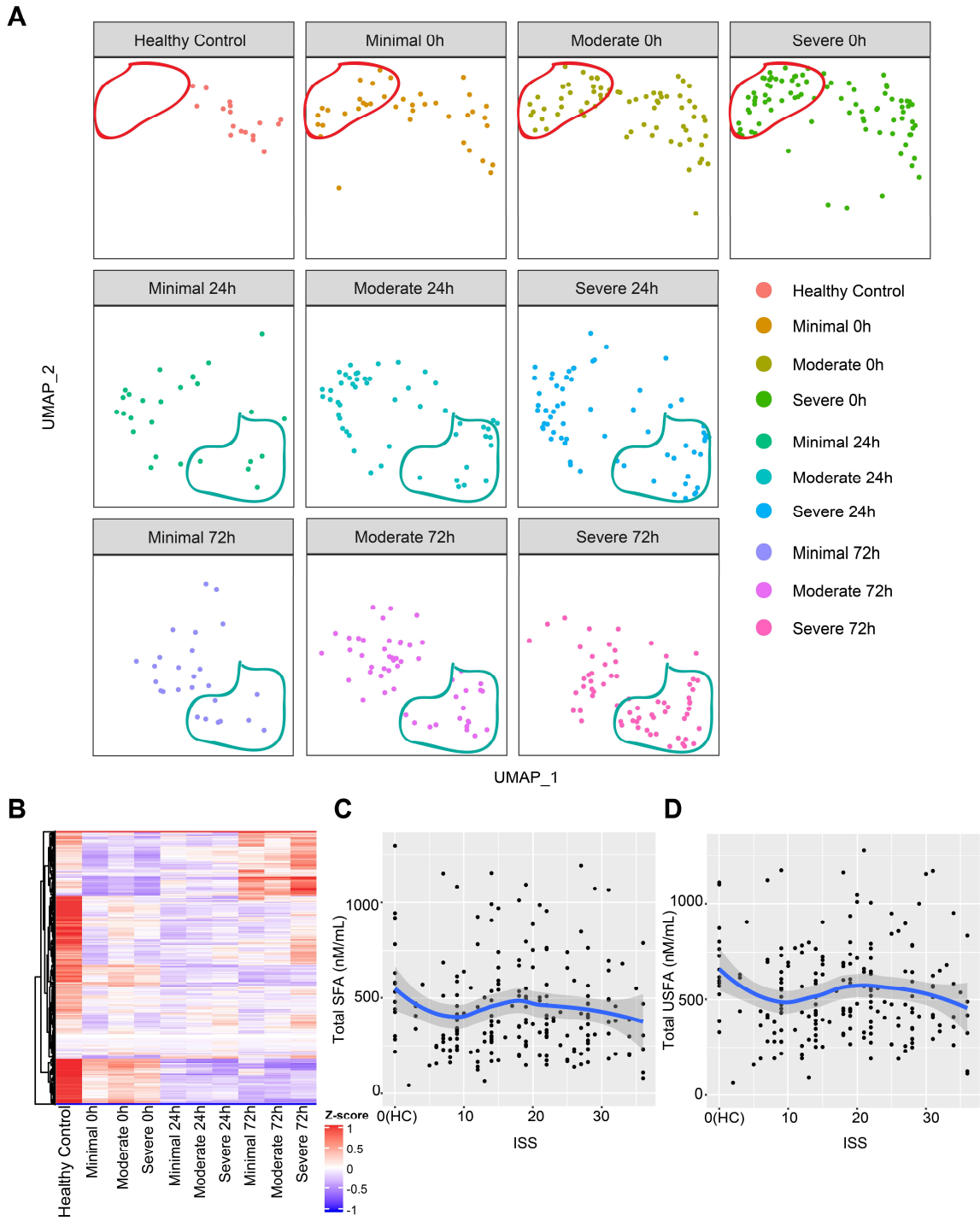


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847 **Figure S1. Consort diagram.** Screening, randomization and sampling for lipidomic analysis.  
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**Figure S2. Relationship of the circulating lipidome to injury severity.**

852 **(A)** Uniform Manifold Approximation and Projection (UMAP) plot shows the distribution of healthy  
853 subjects (n=17) and patients with trauma (n=193), grouped by injury severity and sampling timepoints.  
854 (Minimal: ISS<10, Moderate: 10<=ISS<25, Severe: ISS>=25)

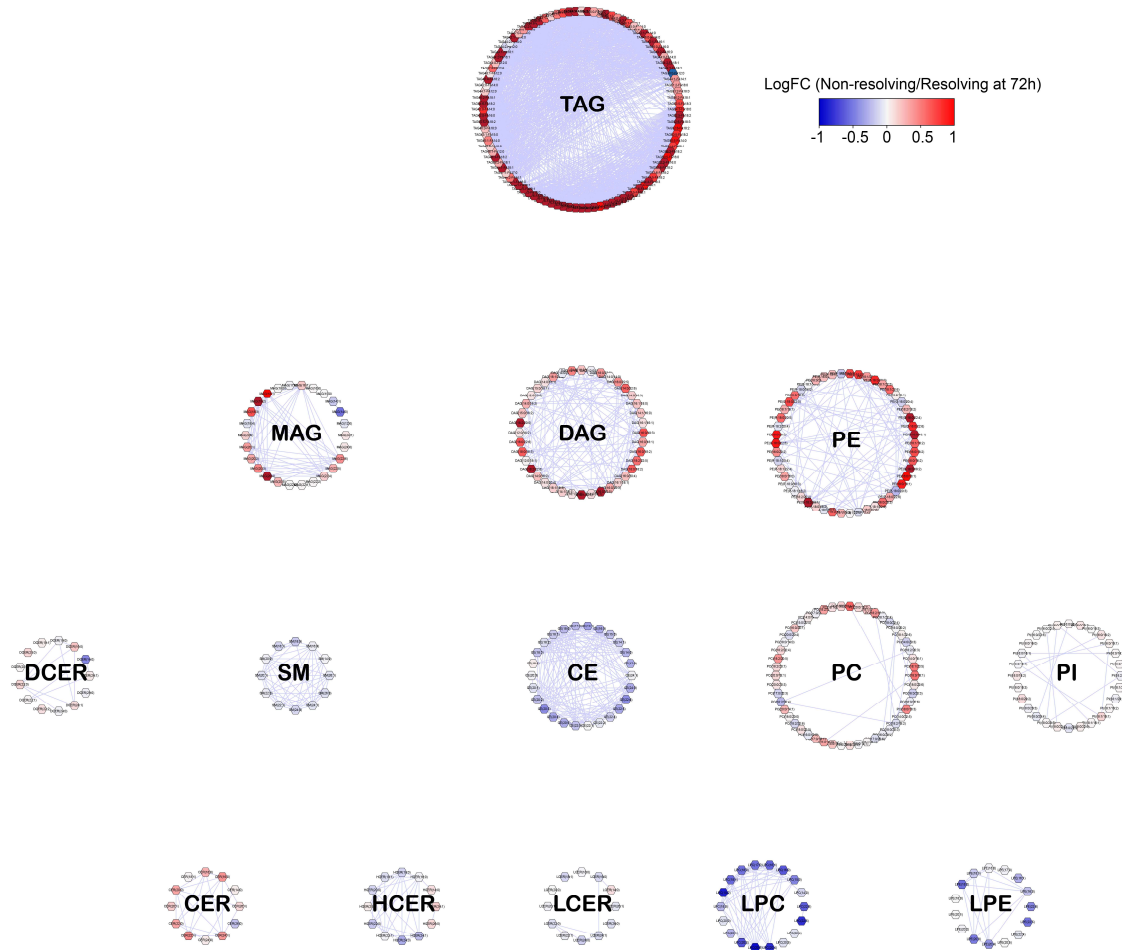
855 **(B)** Heatmap showing relative levels of 996 lipid species for healthy subjects and trauma patients, grouped  
856 by injury severity and sampling timepoints. Exp, z-score normalized concentration. Rows are clustered by  
857 hierarchical clustering.

858 **(C-D)** Relationship of ISS to absolute concentration of total saturated fatty acid (C) and unsaturated fatty  
859 acid (D) at 0h revealed by scatterplot.

860 ISS, injury severity score; SFA: saturated fatty acid; USFA: unsaturated fatty acid.

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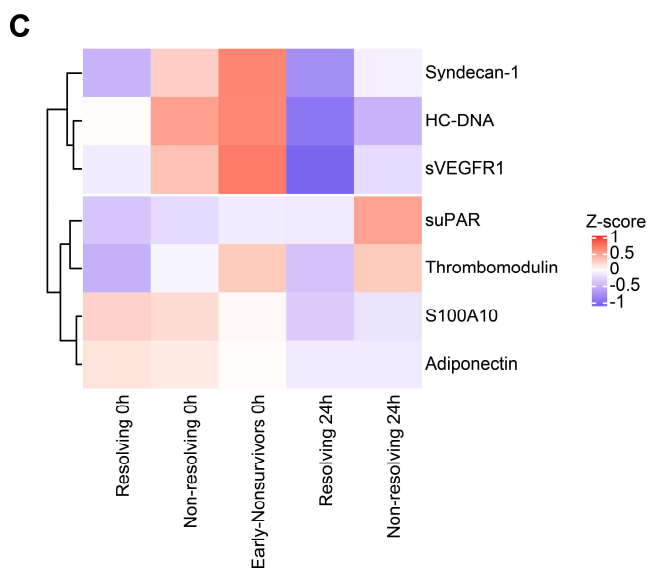
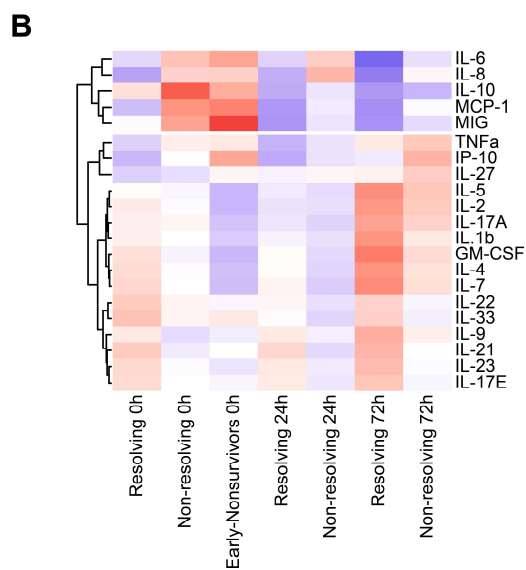
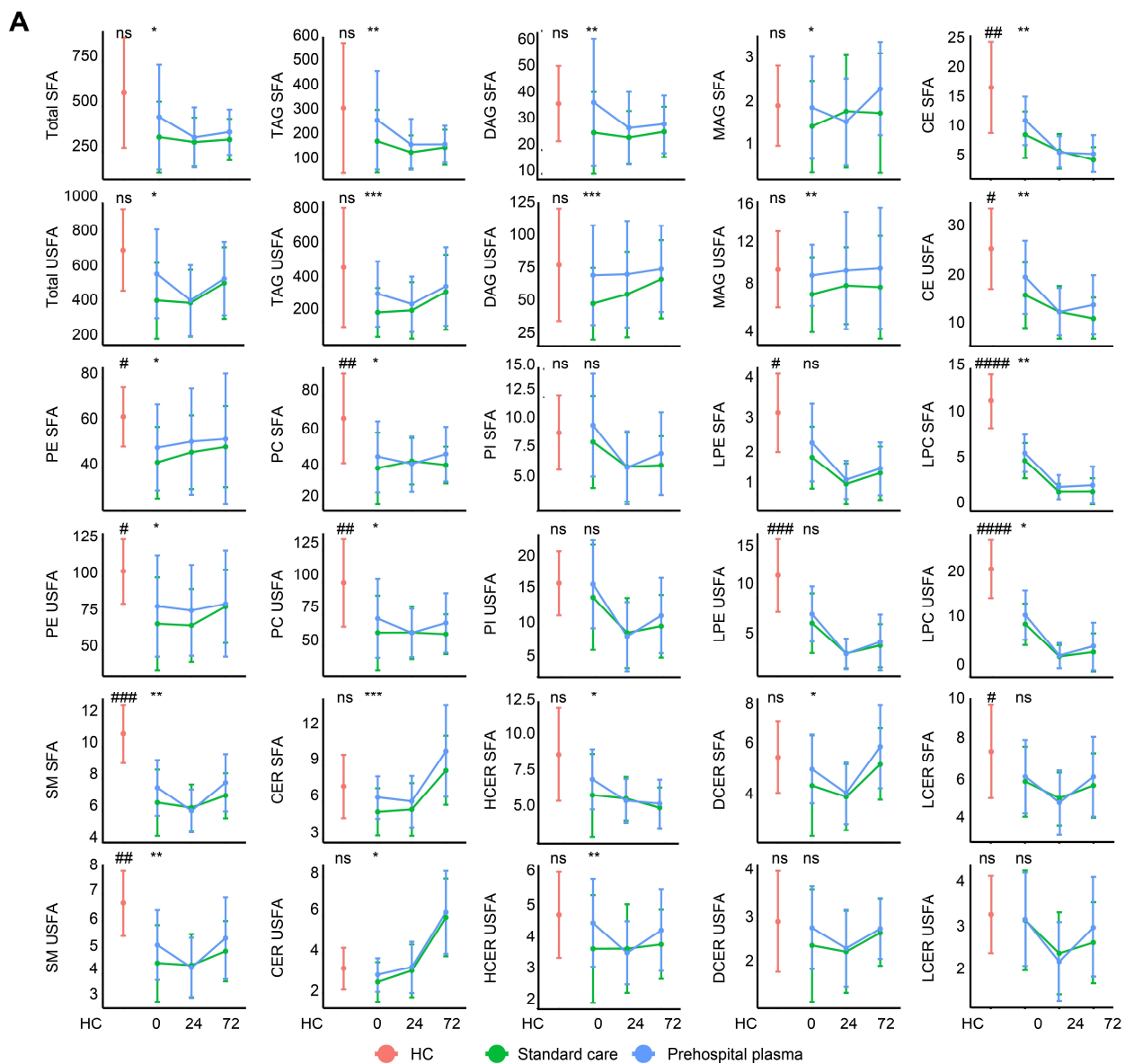


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**Figure S3. Lipid intra-class network in non-resolving trauma patients at 72h**

864 Correlation network for 412 lipids from 14 classes from the lipidomic dataset. Each dot indicates a lipid and  
865 is organized by circle if it belongs to one class. Edge between 2 dots designates high correlation (Pearson  
866 coefficient  $> 0.7$ ). Only intra-class correlations are shown. Coloring indicates levels between non-resolving  
867 and resolving trauma patients.  
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873 **Figure S4. Prehospital fresh frozen plasma (FFP) can enhance levels of major lipid class**

874 **(A)** Comparison of circulating total lipid concentration between standard care and prehospital FFP. Lipids  
875 are grouped by classes and fatty acid (saturated or unsaturated) contained in the lipids. Patients are grouped  
876 by treatment and sampling timepoints. Center dots and error bars represent median value and median  
877 absolute deviation, respectively. SFA: saturated fatty acid; USFA: unsaturated fatty acid. Asterisks indicate  
878 statistical significance between baseline and prehospital FFP arm. Number sign indicates statistical  
879 significance between treatment arms in 0h. Kruskal-wallis test was used among baseline and treatment arms  
880 at 0h with post-hoc analysis of Dunn test. p value was adjusted by Benjamini-Hochberg method: \*, < 0.05;  
881 \*\*, < 0.01, \*\*\*, < 0.001; #, < 0.05; ##, < 0.01; ###, < 0.001, ##### < 0.0001.

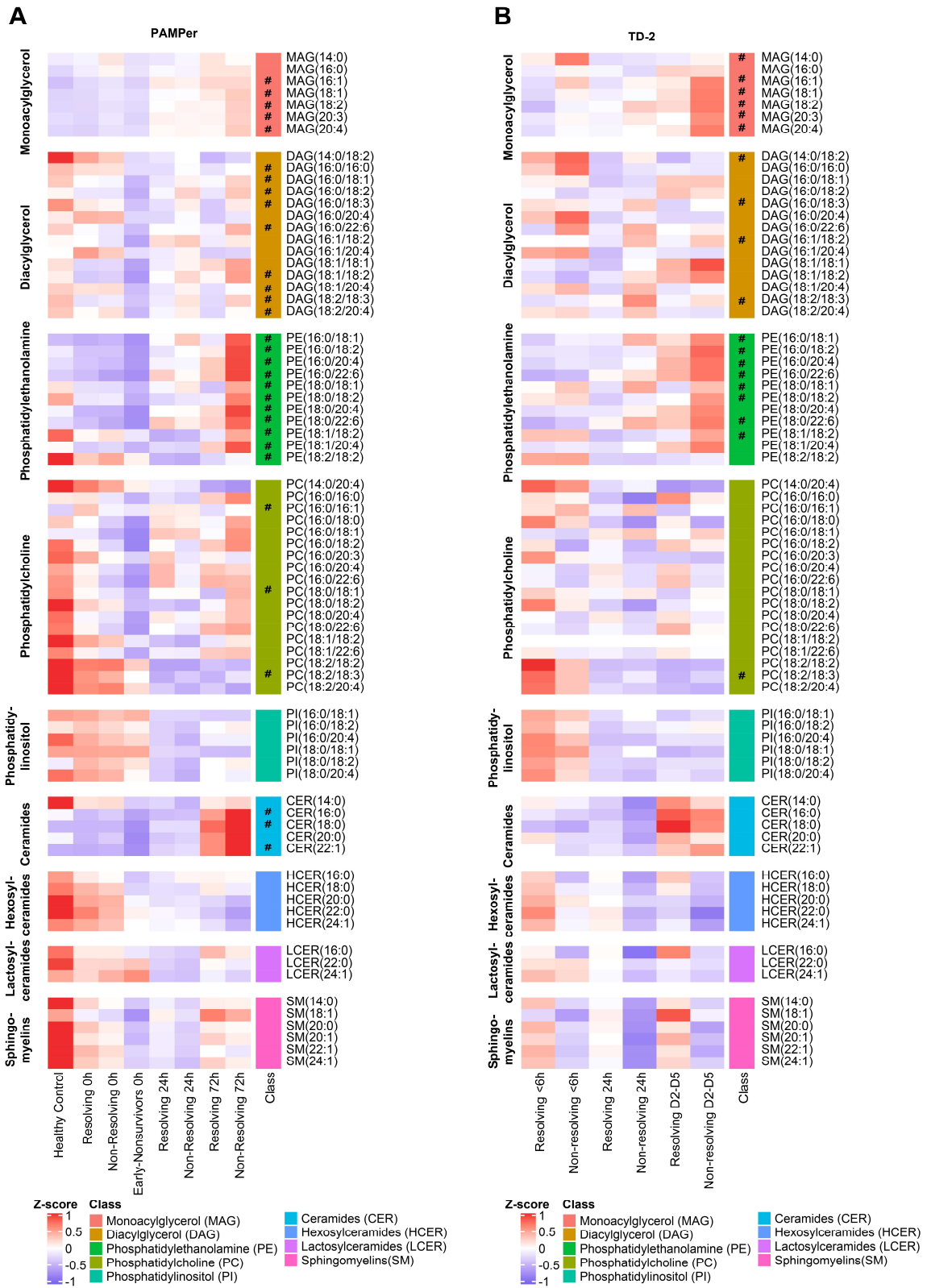
882 **(B)** Heatmap shows temporal pattern of circulating cytokines in trauma patients at 0h,24h and 72h after  
883 admission.

884 **(C)** Heatmap shows temporal pattern of circulating biomarkers in trauma patients at 0h and 24h after  
885 admission.

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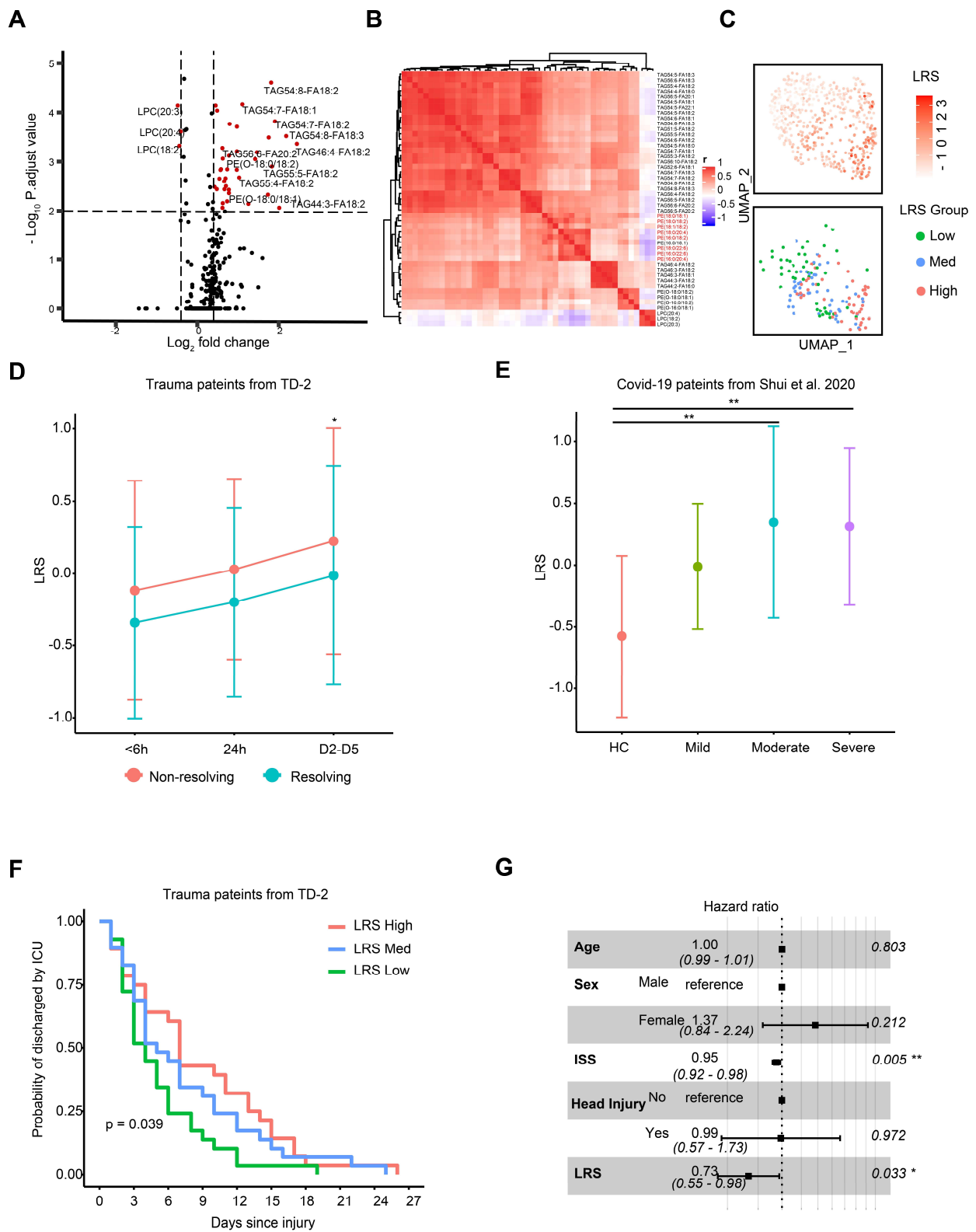
890

**Figure S5. Temporal pattern of common lipids of trauma patients from PAMPer and TD-2.**



891 **(A-B)** Heatmap shows relative levels of 99 common lipid species from 9 major classes across patients.  
892 Patients are group by outcome and sampling timepoint. Data comes from PAMPer lipidomics dataset **(A)** or  
893 TD-2 untargeted metabolomics dataset **(B)**.  
894 Number sign (#) indicate lipids with log<sub>2</sub> fold change >0.4 between non-resolving and resolving trauma  
895 patients at 72h (A); non-resolving and resolving trauma patients at D2-D5 (B).

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**Figure S6. Evaluation and external validation of lipid reprogramming score (LRS).**

899 **(A)** Volcano plot shows the differential lipids in non-resolving patients compared to resolving patients at 72h  
900 after admission.

901 **(B)** Correlation heatmap of 8 common lipids and 37 selected differential lipids.

902 **(C)** UMAP plot of LRS and LRS group among trauma patients.

903 **(D)** Comparison of LRS from patients with trauma in TD-2 dataset. Patients are grouped according to  
904 outcome and sampling timepoint. Center dots and error bars represent median value and median absolute  
905 deviation respectively.

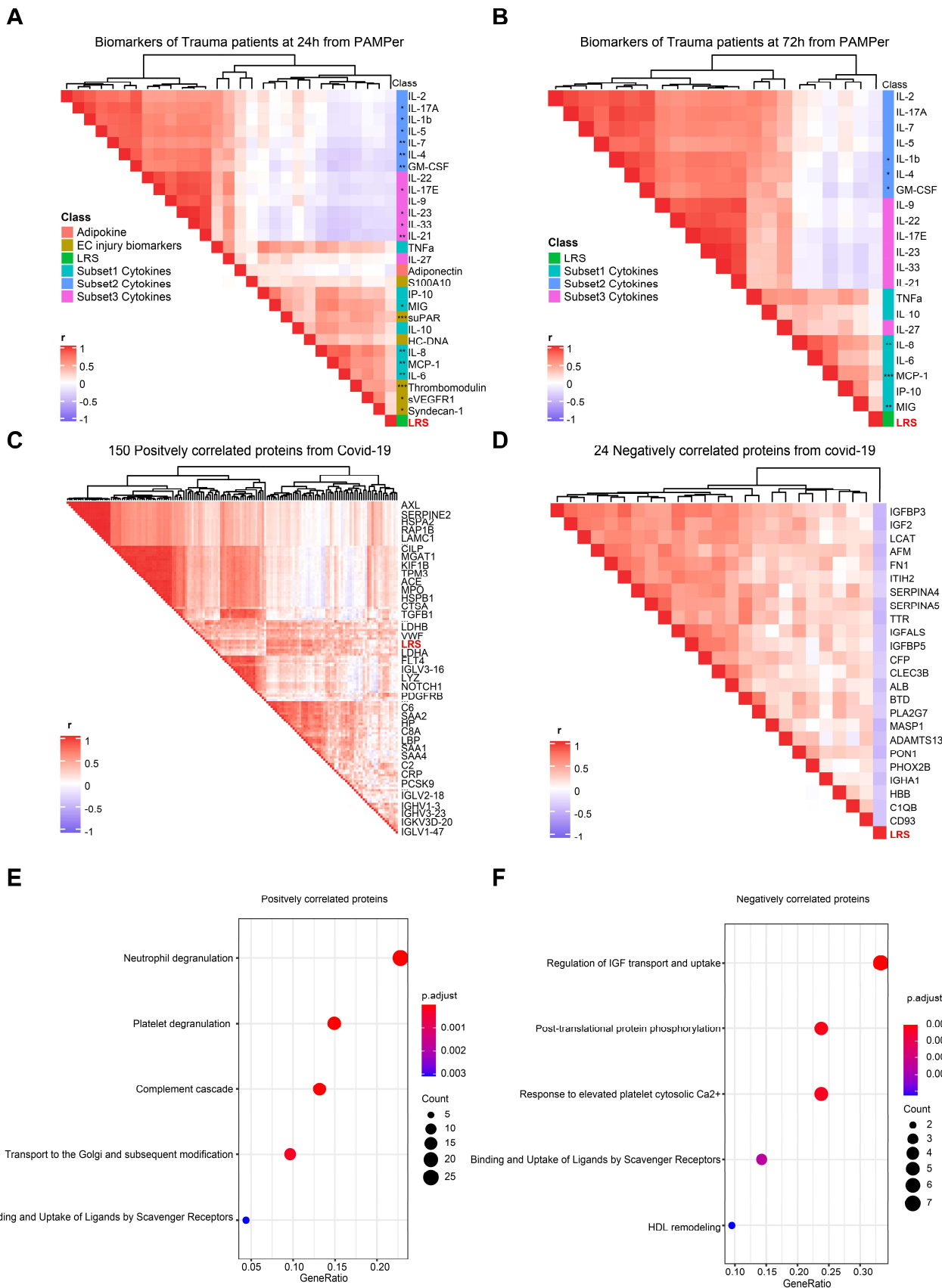
906 **(E)** Comparison of LRS from patients with COVID-19. Patients are grouped with outcome. Center dots and  
907 error bars represent median value, median absolute deviation respectively.

908 **(F)** Recovery probability (defined as discharged by intensive care unit) of different LRS groups across days  
909 since injury revealed by K-M curve in TD-2 dataset.

910 **(G)** Forest plot shows the Hazard ratios of clinical factors and LRS score for recovery using cox regression  
911 in the TD-2 dataset. ISS, injury severity score.

912 Asterisks in (D) indicate statistical significance in based on 2-way AVOVA test of time-series analysis of  
913 resolving and non-resolving groups. Pairwise Comparisons was conducted by Estimated Marginal Means  
914 test. p value was adjusted by Benjamini-Hochberg method: \* < 0.05. Asterisks in (E) indicate statistical  
915 significance based on Kruskal-wallis test among 4 group with post-hoc analysis of Dunn test. p value was  
916 adjusted by Benjamini-Hochberg method: \*\*, < 0.01.

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**Figure S7. Association between LRS and circulating biomarkers or pathways**

922 **(A-B)** Heatmap shows the correlation between LRS and circulating biomarkers at 24h and 72h after  
923 admission in trauma patients, measured by spearman correlation coefficients.

924 **(C-D)** Heatmap shows 150 positive (C) and 24 negative (D) correlating proteins with LRS in COVID-19  
925 patients, measured by spearman correlation coefficients.

926 **(E-F)** Enriched pathways among 150 positive correlated proteins (E) and 24 negative correlated proteins (F).  
927 P value was adjusted by Benjamini-Hochberg method.

928 Asterisks in (A&B) indicate statistical significance for correlation coefficient. P-values are approximated by  
929 using the t distributions: \*, < 0.05; \*\*, < 0.01; \*\*\*, <0.001.

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