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**Fig.S1. Clinical trajectory was different in patients with brain injury. (Related to Fig.2)**

**A-B)** K-M curves show the survival trajectories of no brain injury (NBI, n=62) (**A**) and traumatic brain injury (TBI, n=87) (**B**) trauma patients, grouped by treatment arms. p-value was calculated by log-rank test.

**C-F)** K-M curves show the survival trajectories of trauma patients divided by endotype (E1: low systemic response, E2: high systemic response) and absence (NBI: No brain injury) or presence of TBI (C: E1-NBI, n=37, D: E1-TBI, n=43, E: E2-NBI, n=25, F: E2-TBI, n=44), grouped by TP treatment arms. p-value was calculated by log-rank test.

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**Fig.S2. Both coagulation dependent and independent pathways were enriched in mediated proteins. (Related to Fig.2)**

Dot plot shows the top 10 pathways enriched from 64 proteins with mediation proportion over 30% for 3d-mortality from the linear regression + mediation analysis.

Abbreviations: Insulin-like growth factor (IGF), Insulin-like growth factor binding protein (IGFBP).

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**Fig.S3. Plasma lipids mediate the protective effect for reducing early mortality only in E2-TBI subgroup. (Related to Fig.2)**

Forest plot shows the total effect, average causal mediation effects and proportion of mediation effects with 95% confidence interval for top 10 lipids from in E2-NBI (n=25) and E2-TBI patients (n=44). Outcome was set as 3d mortality. OR: Odds Ratio. Prop: Proportion.

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**Fig.S4. Plasma metabolites weakly associated with the protective effect for reducing early mortality only in E2-TBI subgroup. (Related to Fig.2)**

Forest plot shows the total effect, average causal mediation effects and proportion of mediation effects with 95% confidence interval for top 10 metabolites from in E2-NBI (n=25) and E2-TBI patients (n=44). Outcome was set as 3d mortality. OR: Odds Ratio. Prop: Proportion.

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**Fig.S5. Comparison of levels for Coagulation and Fibrinolysis related proteins in each sub-group and treatment group (TP: thawed plasma). (Related to Fig.4)**

Z scores for 20 proteins of coagulation pathway and 9 proteins of the fibrinolysis pathway measured in the SomaLogic platform were normalized across all patient groups and relative levels shown. Low ISS is a group of low injury trauma patients that serve as control (n=29). Proteins(rows) were clustered by hierarchical clustering.

# Indicates increased percentage>20% between the two treatment arms for each patient sub-group.