Intensive Care Unit Acquired Weakness genes exist between non-survivors and survivors in patients with sepsis

Supplementary Information

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Supplementary Table 1. The study characteristics of the original study, GSE54514. APACHE II: Acute Physiology and Chronic Health Evaluation II.

Characteristics		**Survivors (n=26)**	**Non-survivors (n=9)**
Site of infection			
Primary bacteremia		Survivors (n=3)	Non-survivors (n=3)
	Age, years (IQR)	68.0 (43.0-74.5)	72.0 (62.5-76.0)
	APACHE II	24.0 (17.5-28.0)	28.0 (24.0-31.5)
	Female, n (%)	3 (100)	0 (0)
Respiratory		Survivors (n=10)	Non-survivors (n=5)
	Age, years (IQR)	59.5(52.0-63.0)	66.0 (64.0-80.0)
	APACHE II	16.5 (15.3-22.3)	23.0 (19.0-24.0)
	Female, n (%)	6 (60)	4 (80)
Urinary tract		Survivors (n=4)	Non-survivors (n=1)
	Age, years (IQR)	79.0 (74.5-83.75)	77.0
	APACHE II	18.5 (16.0-19.5)	26.0
	Female, n (%)	2 (50)	1 (100)
Others		Survivors (n=9)	Non-survivors (n=0)
	Age, years (IQR)	47.0 (32.0-58.0)	-
	APACHE II	20.0 (13.0-20.0)	-
	Female, n (%)	5 (55.6)	-

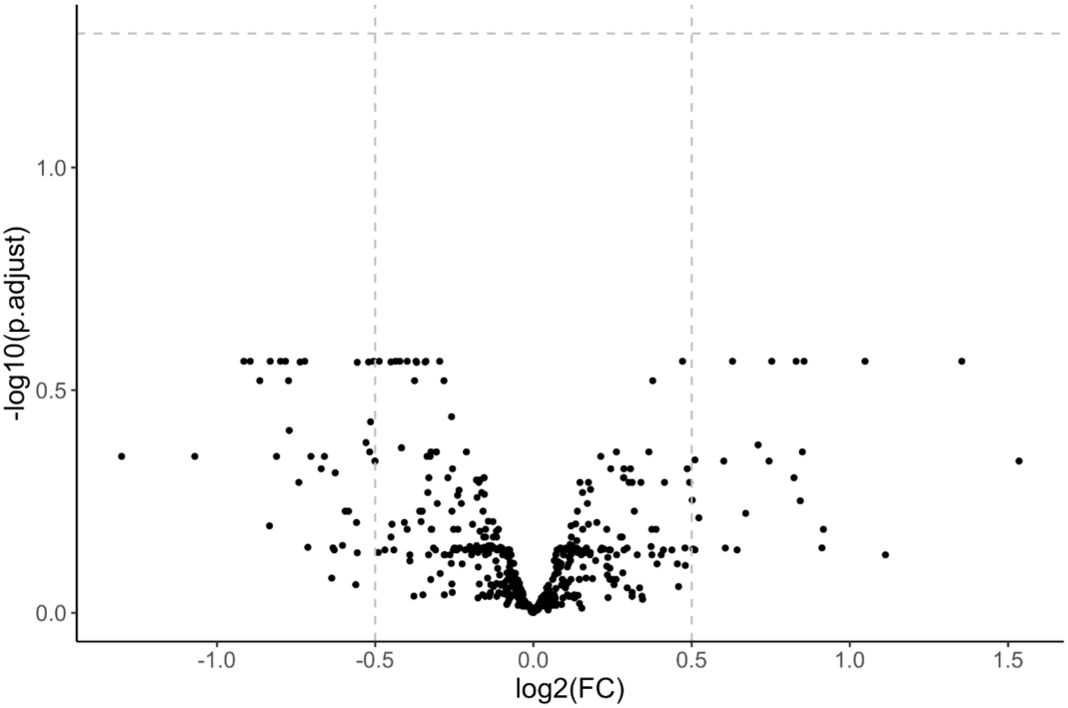
Supplementary Table 2. Gene Ontology terms enriched in patients with respiratory-triggered sepsis. Gene Ontology (GO) terms include the biological process (BP), cell component (CC), and molecular function (MF).

ID	Description	Adjusted p value	Gene count	Direction	Ontology
GO:0006007	glucose catabolic process	1.06e-03	3	down	BP
GO:0006096	glycolytic process	1.21e-02	3	down	BP
GO:0006757	ATP generation from ADP	1.21e-02	3	down	BP
GO:0046031	ADP metabolic process	1.36e-02	3	down	BP
GO:0046034	ATP metabolic process	1.43e-02	4	down	BP
GO:0006165	nucleoside diphosphate phosphorylation	1.43e-02	3	down	BP
GO:0046939	nucleotide phosphorylation	1.43e-02	3	down	BP
GO:0009135	purine nucleoside diphosphate metabolic process	1.43e-02	3	down	BP
GO:0009179	purine ribonucleoside diphosphate metabolic process	1.43e-02	3	down	BP
GO:0009185	ribonucleoside diphosphate metabolic process	1.46e-02	3	down	BP
GO:0002335	mature B cell differentiation	1.49e-02	2	down	BP
GO:0006734	NADH metabolic process	1.56e-03	3	down	BP
GO:0009132	nucleoside diphosphate metabolic process	1.93e-02	3	down	BP
GO:0016241	regulation of macroautophagy	2.00e-02	3	down	BP

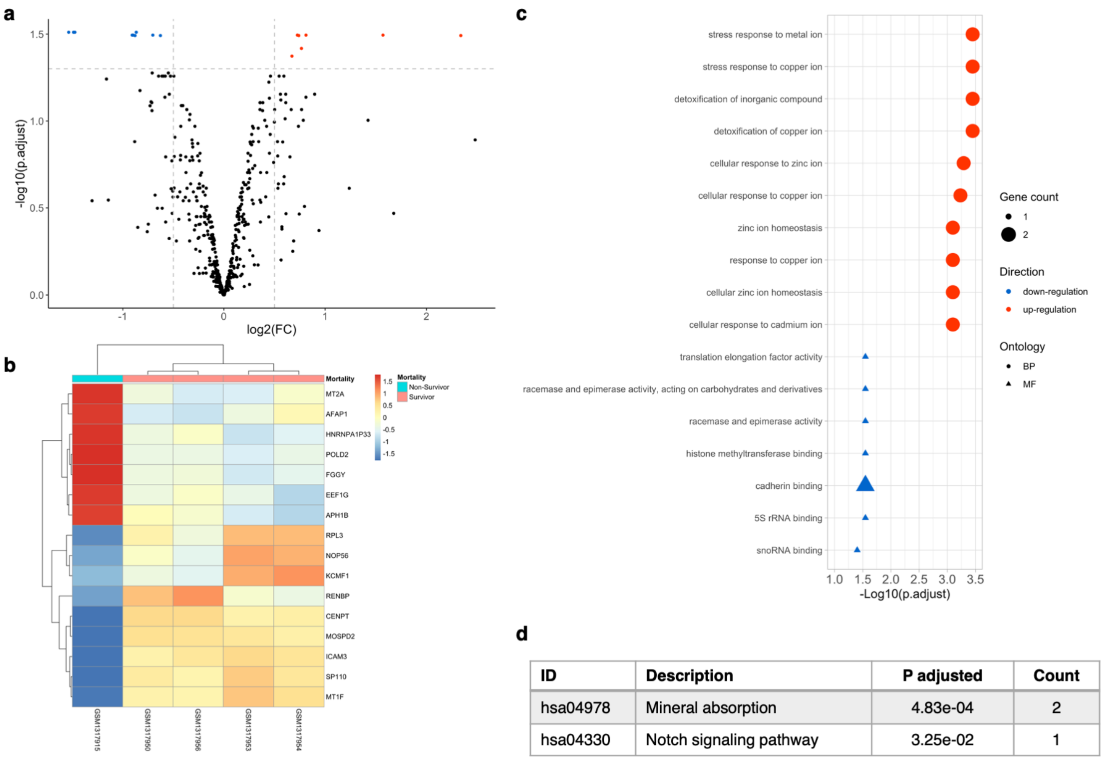
GO:0006090	pyruvate metabolic process	2.03e-03	4	down	BP
GO:0019674	NAD metabolic process	2.03e-03	3	down	BP
GO:0034237	protein kinase A regulatory subunit binding	2.08e-02	2	up	MF
GO:0015078	proton transmembrane transporter activity	2.08e-02	3	up	MF
GO:0019320	hexose catabolic process	2.42e-03	3	down	BP
GO:0015175	neutral amino acid transmembrane transporter activity	2.44e-02	2	up	MF
GO:0046365	monosaccharide catabolic process	2.99e-03	3	down	BP
GO:0045333	cellular respiration	3.02e-02	3	down	BP
GO:0016504	peptidase activator activity	3.11e-02	2	up	MF
GO:0044282	small molecule catabolic process	3.35e-02	4	down	BP
GO:0031430	M band	3.52e-02	2	down	CC
GO:0031672	A band	3.52e-02	2	down	CC
GO:0070820	tertiary granule	3.52e-02	3	down	CC
GO:0051018	protein kinase A binding	3.64e-02	2	up	MF
GO:0101002	ficolin-1-rich granule	3.74e-02	3	down	CC
GO:0016051	carbohydrate biosynthetic process	3.79e-02	3	down	BP
GO:0006006	glucose metabolic process	3.79e-02	3	down	BP

GO:0006754	ATP biosynthetic process	3.79e-02	2	down	BP
GO:0005765	lysosomal membrane	4.05e-02	4	up	CC
GO:0098852	lytic vacuole membrane	4.05e-02	4	up	CC
GO:0016469	proton-transporting two-sector ATPase complex	4.05e-02	2	up	CC
GO:0005774	vacuolar membrane	4.05e-02	4	up	CC
GO:0015179	L-amino acid transmembrane transporter activity	4.16e-02	2	up	MF
GO:0016052	carbohydrate catabolic process	4.20e-03	4	down	BP
GO:1904724	tertiary granule lumen	4.40e-02	2	down	CC
GO:0043312	neutrophil degranulation	4.49e-02	4	down	BP
GO:0002283	neutrophil activation involved in immune response	4.49e-02	4	down	BP
GO:0002446	neutrophil mediated immunity	4.63e-02	4	down	BP
GO:0042119	neutrophil activation	4.63e-02	4	down	BP
GO:0009206	purine ribonucleoside triphosphate biosynthetic process	4.67e-02	2	down	BP
GO:0009145	purine nucleoside triphosphate	4.68e-02	2	down	BP

	biosynthetic process				
GO:0019318	hexose metabolic process	4.95e-02	3	down	BP
GO:0045296	cadherin binding	5.20e-03	5	down	MF
GO:0006735	NADH regeneration	6.53e-04	3	down	BP
GO:0061621	canonical glycolysis	6.53e-04	3	down	BP
GO:0061718	glucose catabolic process to pyruvate	6.53e-04	3	down	BP
GO:0061620	glycolytic process through glucose-6-phosphate	6.53e-04	3	down	BP
GO:0061615	glycolytic process through fructose-6-phosphate	6.53e-04	3	down	BP
GO:0006094	gluconeogenesis	7.20e-03	3	down	BP
GO:0019319	hexose biosynthetic process	7.38e-03	3	down	BP
GO:0015173	aromatic amino acid transmembrane transporter activity	7.98e-03	2	up	MF
GO:0046364	monosaccharide biosynthetic process	8.32e-03	3	down	BP



Supplementary Figure 1. Volcano plot of differentially expressed ICUAW-associated genes between non-survivors and survivors in patients with primary bacteremia-triggered sepsis The vertical dot line indicates a statistically significant threshold of adjusted p value <0.05, and horizontal dot line indicates a biological significant threshold of an absolute value of log2(fold change) >0.5. There were no significantly expressed genes between non-survivors and survivors in patients with primary bacteremia-triggered sepsis.



ID	Description	P adjusted	Count
hsa04978	Mineral absorption	4.83e-04	2
hsa04330	Notch signaling pathway	3.25e-02	1

Supplementary Figure 2. Differential gene expression analysis in patients with urinary tract-triggered sepsis. (a) Volcano plot of differentially expressed ICUAW-associated genes (ICUAW DEGs) between non-survivors and survivors in patients with urinary tract-triggered sepsis. Of the 16 ICUAW DEGs, 7 genes were up-regulated (red dots) and 9 genes were down-regulated (blue dots). **(b)** Heat map of 50 ICUAW DEGs with mortality as an annotation. **(c)** Functional enrichment using Gene Ontology (GO) analysis. GO terms include the biological process (BP), cell component (CC), and molecular function (MF). Up-regulated ICUAW DEGs in patients with urinary tract-triggered sepsis enriched mineral absorption, response, and detoxification. Down-regulated ICUAW DEGs enriched cadherin, RNA, and histone binding. **(d)** Enriched Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis identified mineral absorption and notch signaling pathways with up-regulated ICUAW DEGs.