# Supplementary Information for

## Identification of Key Genes and Potential Therapeutic Targets in Sepsis-Associated Acute Kidney Injury Using Transformer and Machine Learning Approaches

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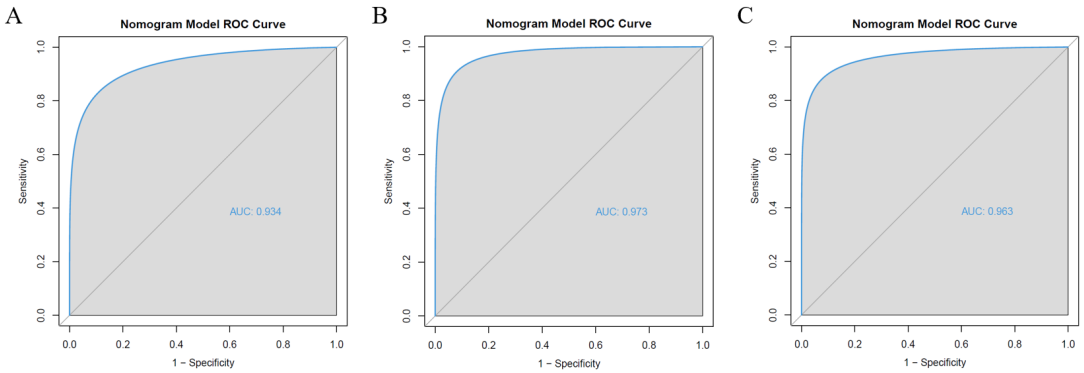
**Supplementary Figure S1. Validation of the Nomogram Model for the Diagnosis of Sepsis and AKI Using Different Gene Configurations on GSE69063. (A) 10 Genes. (B) 12 Genes. (C) 15 Genes.**



**Supplementary Table S1. Dropout loss values of 21 genes in four machine learning models.**

| Gene | LASSO | NNET | RF | SVM |
|---|---|---|---|---|
| ACTA2 | 0.0581 | 0.0515 | 0.1022 | 0.0423 |
| ACY1 | 0.0950 | 0.0505 | 0.1021 | 0.0425 |
| HLA_DRB1 | 0.0901 | 0.1433 | 0.1258 | 0.0362 |
| HSPA1B | 0.1015 | 0.1554 | 0.0984 | 0.04506 |
| IFITM2 | 0.0692 | 0.1536 | 0.1083 | 0.0312 |
| MYL12B | 0.0826 | 0.0518 | 0.1510 | 0.0266 |
| NNMT | 0.1020 | 0.0527 | 0.1625 | 0.0476 |
| PPIA | 0.0775 | 0.0786 | 0.1202 | 0.0305 |
| PSMA2 | 0.0622 | 0.0513 | 0.1086 | 0.0234 |
| PSME2 | 0.1108 | 0.1650* | 0.1709 | 0.0551 |
| PTBP1 | 0.0765 | 0.0601 | 0.1346 | 0.0283 |
| RGL3 | 0.1128 | 0.1670* | 0.1726 | 0.0573 |
| RPL10 | 0.0842 | 0.1452 | 0.1341 | 0.0277 |
| RPL17 | 0.0977 | 0.0543 | 0.1573 | 0.0238 |
| RPL28 | 0.1145 | 0.1693 | 0.1741 | 0.0599 |
| RPL3 | 0.1163 | 0.1712 | 0.1762 | 0.0617 |
| TMEM14C | 0.1049 | 0.1598 | 0.1648 | 0.0240 |
| TOMM6 | 0.0588 | 0.1574 | 0.1627 | 0.0493 |
| TOMM7 | 0.0712 | 0.0646 | 0.1065 | 0.0277 |
| TPT1 | 0.0759 | 0.1520 | 0.1190 | 0.0266 |
| VMP1 | 0.0599 | 0.0513 | 0.1557 | 0.0293 |

**Supplementary Table S2. Descriptions and Functions of the 5 Feature Genes Used for Diagnosis.**

| Gene | Expression level | Description | Function |
|---|---|---|---|
| RPL10 | High | Ribosomal protein L10, a component of the 60S ribosomal subunit. | Plays an important role in ribosome biogenesis and function, particularly in ribosomal subunit maturation, ribosomal subunit binding, and subunit rotation during translation elongation. |
| MYL12B | High | Encodes myosin light chain 12B, which forms an actin-myosin complex by binding with actin heavy chains. | MYL12B regulates the dynamic changes of the cytoskeleton, affecting cell morphology and movement. It plays a role in cytokinesis during cell division and may be involved in cell signaling processes. |
| PTBP1 | Low | A gene encoding the polypyrimidine tract-binding protein. | 1. Binds with lncRNA MIAT, induces the degradation of BECN1 mRNA, and inhibits autophagy activation. 2. Suppresses the protective effects of autophagy, exacerbating kidney damage. 3. Indirectly affects the intensity of the inflammatory response by regulating the stability of BECN1 mRNA and influencing the release of pro-inflammatory cytokines. |
| TOMM7 | High | A component of the mitochondrial outer membrane translocase. | TOMM7 aids in the transport of precursor proteins and is essential for mitochondrial function, including respiration and energy metabolism. Mutations in TOMM7 disrupt mitochondrial protein expression and oxygen consumption. |
| PPIA | Low | Encodes peptidylprolyl isomerase A. | PPIA is involved in protein folding, translation regulation, and cell signaling. It helps maintain protein homeostasis and regulates protein translation efficiency. Secreted PPIA activates inflammation pathways (e.g., ERK1/2, p38 MAPK), promoting inflammation and tissue damage. |

**Supplementary Table S3. Target and Indication of some drugs for the potential treatment of SA-AKI disease.**

| Drug Name | Target | Indication |
|---|---|---|
| PROLINE | Proline dehydrogenase 1 mitochondrial | Hepatic encephalopathy |
| SCY-635 | Cyclophilin A | Hepatitis C virus (HCV) infection |
| Voclasporan | Cyclophilin A | Hepatitis C virus (HCV) infection |
| Immunosuppressant | Multiple immune system targets | Organ transplantation |
| Alisporvir | HCV NS5A inhibitor | Hepatitis C |
| Cyclosporine | Calcineurin | Organ transplantation |
| Cycloheximide | Ribosome | Bacterial infection research |
| MT-3724 | CD20 | Leukemia and lymphoma |
| Dorlimomab Aritox | CD19 | Leukemia and lymphoma |
| Exaluren | Collagen IV | Alport syndrome caused by nonsense mutations |
| Recombinant Transforming Growth Factor | TGF-β receptor | Diabetic foot ulcers, burns, pressure sores, and other tissue injuries |
| Ataluren | DAG1 | Duchenne muscular dystrophy (DMD) |