

Biomarkers	Genes	Other gene names	Level	Stages	Sources	pathway	Other biomarkers	Sepsis related	Articles
1.PCT	CALCA	Calcitonin Related Polypeptide Alpha CGRP-Alpha Calcitonin CALC1 CGRP Calcitonin Gene-Related Peptide 1 Calcitonin Gene-Related Peptide I Alpha Type CGRP Calcitonin 1 CGRP4 Calcitonin/Calcitonin-Related Polypeptide, Alpha Kalsitoxin CGRP1 PCT CT KC	Protein level	Diagnostic/Prognostic	Gram - bacterial infection	Neuroendocrine Pathways		GeneCards/NO MetaCards/NO KEGG/NO UniProt/NO	<p>1.The CALCA gene is not commonly used directly for sepsis diagnosis, as its product, PCT, is already well-established as a protein biomarker.</p> <p>2.Procalcitonin (PCT) is a reliable diagnostic and prognostic biomarker for sepsis and localized infections in burn ICU patients, outperforming traditional markers and aiding in monitoring treatment efficacy and outcomes.</p> <p>3.PCT is a valuable biomarker for sepsis management, aiding in:</p> <p>Early diagnosis. Differentiating bacterial infections from other inflammatory states. Guiding antibiotic therapy to reduce overuse and resistance. Monitoring treatment effectiveness through PCT kinetics.</p> <p>4.Diagnostic Value: PCT levels are significantly elevated in sepsis patients and are especially high in cases of G- bacterial infections. PCT can help distinguish between G- and G+ bacterial bloodstream infections. Prognostic Role: PCT levels correlate with disease severity and mortality, making it a valuable biomarker for sepsis prognosis. 5.PCT is a moderate predictor of 30-day mortality in septic ED patients, with a high specificity but limited sensitivity. A threshold of 32.5 µg/L identifies patients at high risk of death but has limited utility in predicting ICU admission.</p> <p>6. Diagnostic Utility: PCT is a reliable early marker for differentiating sepsis from severe sepsis and septic shock, with high sensitivity and specificity for severe sepsis. PCT is superior to CRP, WBC, and APACHE in diagnosing sepsis severity. Prognostic Role: Higher PCT levels are associated with increased mortality and disease severity, making it a useful prognostic marker. Limitations: PCT's diagnostic utility for septic shock is limited compared to severe sepsis.</p> <p>7. PCT as a Diagnostic Marker: PCT is one of the most reliable biomarkers for bacterial sepsis, with high diagnostic accuracy and rapid response kinetics. PCT in Prognosis: PCT levels predict disease severity and treatment response, aiding in patient risk stratification. Limitations: Elevated PCT can occur in non-infectious inflammatory states (e.g., trauma, surgery). Not a standalone marker; must be used in conjunction with clinical findings and other diagnostic tools.</p> <p>8. PCT as a Biomarker: PCT is a reliable marker for diagnosing bacterial sepsis and predicting outcomes in critically ill patients. It is superior to CRP and WBC but should be used alongside clinical judgment and other diagnostic tools.</p> <p>9. While PCT (protein) is a well-established marker for bacterial infections and sepsis, CALCA gene expression (mRNA) appears to lack sufficient sensitivity and specificity for clinical use in this study.</p> <p>10. PCT remains a robust biomarker for bacterial sepsis, and this assay enhances its clinical utility in rapid, bedside diagnostics. However, CALCA gene expression was not discussed as a diagnostic target in this study; the focus is on PCT protein levels.</p> <p>11. CALCA encodes Calcitonin Gene-Related Peptide 1, which was upregulated in AKI patients. However, its specific role as a diagnostic marker for sepsis alone (excluding AKI) remains unclear.</p>
2.CRP	C-reactive protein	C-Reactive Protein PTX1 C-Reactive Protein, Pentraxin-Related Pentaxin 1	Protein level	Diagnosis/Prognosis		Acute Phase Response Pathway	WBC	GeneCards/Athritis Sepsis MetaCards/1 Sepsis Arthritis 2.Bacterial Sepsis- 3.Sepsis in Premature Infants UniProt/disease/YES	<p>1. Protein Level: The study validated CRP as a diagnostic marker at the protein level using a turbidimetric assay, a standard wet-lab method. Gene Level: The study did not evaluate CALCA gene expression (mRNA level). It focused exclusively on the protein concentrations in plasma.</p> <p>2. CRP is an acute-phase protein produced by the liver in response to inflammatory cytokines, particularly IL-6, TNF-α, and IL-1β. CRP is validated at the protein level through wet-lab methods like immunoturbidimetry and nephelometry, making it a robust diagnostic and prognostic tool for sepsis. While PCT rises earlier in response to bacterial infections, CRP is more cost-effective and widely available. Both markers complement each other in certain clinical scenarios.</p> <p>3.The study validates CRP as a protein-level marker for identifying individuals at risk of sepsis. It does not involve gene-level validation but emphasizes the CRP's role in the inflammatory cascade, reinforcing its relevance in sepsis monitoring.</p> <p>4.CRP is a reliable indicator of sepsis resolution in ICU patients. A significant decrease in daily CRP levels provides clinicians with a valuable tool to evaluate the effectiveness of sepsis treatment and predict recovery, particularly in less severe cases.</p> <p>5.The review emphasizes that biomarkers like CRP are invaluable for early detection and monitoring at the protein level but should be used as part of a multi-modal diagnostic approach.</p> <p>6.CRP remains a key biomarker for sepsis due to its availability and diagnostic utility, but its lack of specificity necessitates combination with other markers like PCT or cytokines for improved accuracy.</p>
3.sTREM-1	TREM-1	Triggering Receptor Expressed On Myeloid Cells 1 TREM-1 CD144 Triggering Receptor Expressed On Monocytes 1 CD144 Antigen	protein biomarker	diagnostic/prognostic	infectious sepsis from non-infectious inflammatory	Inflammatory and Immune Pathways	TLR4	GeneCards/Sepsis, septic shock MetaCards/Bacterial Sepsis KEGG/NO UniProt/septic shock	<p>1. A cell-surface receptor expressed on neutrophils and monocytes/macrophages. Amplifies inflammation by promoting the release of pro-inflammatory cytokines like TNF-α, IL-6, and IL-1β. Activated during bacterial and fungal infections. TREM-1 is activated by both pathogen-associated molecular patterns (PAMPs) and damage-associated molecular patterns (DAMPs). Works synergistically with Toll-like receptors (TLRs), particularly TLR4, amplifying the inflammatory response. TREM-1, particularly its soluble form sTREM-1, is a promising biomarker and therapeutic target in sepsis. It offers potential for early diagnosis, prognosis, and personalized treatment strategies. Current research focuses on developing inhibitors and decoy receptors to modulate the TREM-1 pathway, aiming to balance immune response and reduce sepsis-related mortality.</p> <p>2. Expression of TREM-1 is significantly upregulated in septic conditions, particularly in neutrophils and monocytes infiltrating infected tissues. Activation of TREM-1 requires its interaction with the DAP12 adaptor protein. This signaling cascade enhances inflammatory cytokine secretion, chemokine production, and immune cell recruitment. The study highlights the potential of sTREM-1 as a diagnostic protein biomarker and TREM-1 inhibition as a therapeutic strategy, particularly in mitigating the hyperinflammatory phase of septic shock.</p> <p>3. Diagnostic Potential: TREM-1 and its soluble form (sTREM-1) are valuable biomarkers for distinguishing sepsis from non-infectious inflammatory conditions. Therapeutic Targeting: Complete inhibition of TREM-1 is detrimental in bacterial infections due to impaired immune clearance. Partial modulation could balance inflammation and bacterial control, reducing mortality in sepsis.</p> <p>4. The dynamic modulation of TREM-1 expression during sepsis and its dependence on infection type and pathogen. While sTREM-1 is a valuable diagnostic tool, surface TREM-1 expression provides deeper insights into imm</p> <p>5. Elevated sTREM-1 levels have shown specificity in identifying sepsis in critically ill patients compared to other markers like CRP and PCT. It is particularly effective in distinguishing bacterial infections from non-infectious inflammatory conditions. While sTREM-1 is a reliable biomarker, variability in expression levels may occur based on pathogen type and disease severity.</p> <p>6.Diagnostic Value of TREM-1 TREM-1 expression dynamics (gene and surface levels) are valuable for prognosis rather than initial diagnosis. TREM-1's role as a biomarker lies in identifying patients at higher risk of poor outcomes based on early immunosuppression.</p> <p>7. TREM1 as a Diagnostic and Prognostic Marker: Reduced TREM1 gene expression correlates with disease severity, making it a valuable marker for identifying critically ill patients and monitoring their recovery. Measurement of TREM1 mRNA levels could complement traditional biomarkers like CRP and PCT. TREM1 mRNA levels in PBMs reflect the severity of bacterial infections and can serve as a specific biomarker for diagnosing and monitoring sepsis progression.</p> <p>8. TREM-1 Gene Expression No Significant Changes in Gene Expression: TREM-1 gene expression in monocytes did not increase with sepsis severity, unlike sTREM-1 levels in serum. Lack of correlation between serum sTREM-1 and monocyte TREM-1 gene expression. Cytokine Correlation Increased cytokines (TNF-α, IL-6, IL-8, IL-10) in serum correlated with disease severity. Cytokines showed stronger associations with mortality than sTREM-1 levels.</p>
4.suPAR	PLAUR	Plasminogen Activator, Urokinase Receptor UPAR Urokinase Plasminogen Activator Surface Receptor UPROR CD87 Urokinase-Type Plasminogen Activator (UPA) Receptor Monocyte Activation Antigen (Mo) U-PA-R U-Plasminogen Activator Receptor Form 2 CD87 Antigen MCS	Protein biomarker	diagnostic/prognostic	not specific to a particular pathogen or infection type	Coagulation Pathways Vascular and Endothelial Inflammatory and Immune	CRP - PCT	GeneCards/NO MetaCards/NO KEGG/NO UniProt/NO	<p>1.Provides reliable prognostic information. Complements traditional biomarkers like CRP and PCT. Useful for triaging critically ill patients and identifying those at higher risk. While suPAR is not superior to CRP or PCT for diagnosing sepsis, its strength lies in prognostic value and its ability to reflect disease severity. suPAR could complement other biomarkers in managing sepsis but should not be r</p> <p>2.Diagnostic Use: suPAR complements existing sepsis biomarkers like CRP and PCT. Its high specificity makes it particularly useful in ruling out non-sepsis conditions. Prognostic Applications: suPAR levels can guide clinicians in assessing disease severity and risk of mortality. May help identify high-risk patients needing intensive care.</p> <p>3. suPAR is a valuable biomarker for risk stratification in septic patients, particularly for predicting 30-day mortality. While less effective for diagnosing sepsis compared to CRP and PCT, it plays a crucial role in long-term outcome prediction and complements other biomarkers in comprehensive sepsis management.</p> <p>4. suPAR is a useful biomarker for immune system activation and sepsis severity, showing promise as a complement to other markers like CRP and PCT. suPAR reflects immune system activation rather than direct inflammatory activity. Its correlation with SOFA scores indicates that it can serve as a marker of disease severity but not mortality.</p> <p>5.suPAR is a valuable biomarker for sepsis diagnosis and prognosis, particularly when combined with other markers like PCT and clinical scoring systems. uPAR lacks specificity for sepsis alone; its elevation reflects general immune activation.</p>
5.LBP	LBP	Lipopolysaccharide Binding Protein Lipopolysaccharide-Binding Protein BPIFD BPI Fold Containing Family D, Member LPS-binding Protein	Protein biomarker	Prognostic level	Gram - bacterial infection	Toll-like Receptor (TLR) Signaling Cytokine Storm Acute Phase Response Endothelial Dysfunction	LTR4	GeneCards/ Publication part MetaCards/Bacterial sepsis KEGG/NO UniProt/NO	<p>1. LBP plays a central role in amplifying endotoxin-mediated inflammation and renal damage during sepsis. Targeting LBP either through blood purification or pharmacological inhibitors, holds promise for preventing and managing sepsis-induced AKI. LBP levels could serve as a biomarker for detecting endotoxemia and predicting AKI risk in sepsis.</p>

9 IL8	CXCL8	C-X-C Motif Chemokine Ligand 8 MOPF NAP-1 MOPF GCP-1 Monocyte-Derived Neutrophil Chemoattract Factor Monocyte-Derived Neutrophil-Activating Peptide Granulocyte Chemotactic Protein Chemokine (C-X-C Motif) Ligand 8 SCYB8 LYNAP LUCT LECT IL-8 GCP1 NAP1 NAP IL8 Beta Endothelial Cell-Derived Neutrophil Activating Peptide Lung Giant Cell Carcinoma-Derived Chemotactic Protein Lymphocyte-Derived Neutrophil Activating Peptide Alveolar Macrophage Chemotactic Factor 1 Tumor Necrosis Factor-Induced Gene 1 Neutrophil-Activating Peptide 1 T-Cell Chemotactic Factor Interleukin 8 Interleukin 8 Enkefalin ANP-1 BENAP TSS-1 3-10C KIS Small Inducible Cytokine Subfamily B, Member 8 Beta-Thromboglobulin-Like Protein Neutrophil-Activating Protein C-X-C Motif Chemokine 8 Protein 3-10C	Protein biomarker	Prognostic marker		Inflammatory and Immune Vascular and Endothelial Coagulation	associated with increased levels of IL-1 β , IL-6, IL-10, TNF- α , and CRP		1. IL-8 serves as a sensitive and specific biomarker for: Predicting infections and sepsis in burn patients with IL-8 levels above 234 pg/mL. Correlating with burn severity and MOF in patients with levels below 234 pg/mL. High IL-8 levels are indicative of severe inflammatory responses, leading to poor outcomes in burn patients. IL-8 measurement could guide early diagnosis and management of sepsis in burn patients. This biomarker provides clinicians with an early warning system to target timely therapeutic interventions.
							IL-1 β , IL-6, IL-10, IL-12p70, TNF- α CRP and PCT CD64		2. IL-8 A potent chemoattractant that activates neutrophils. Levels increase with disease severity and are predictive of mortality. CD64 A marker of neutrophil activation, specific for bacterial infections. Rapidly measurable and reliable for assessing sepsis progression. Clinical Relevance: A single measurement of CD64 and IL-8 within 24 hours of sepsis onset is sufficient to: Differentiate stages of sepsis. Assess severity and organ dysfunction. Predict 28-day mortality. 3. Increased Chemokine/Cytokine Levels: Five chemokines—CXCL8 (IL-8), CXCL10, CXCL12, CCL13, and CCL20—were significantly elevated in all three sepsis cases. Other chemokines, such as CXCL1, CXCL2, and CCL1, showed elevated levels in two of the three cases. No mRNA Changes: Despite increased protein levels of these chemokines, their corresponding mRNA expression levels were not altered, suggesting post-transcriptional regulation or accumulation of circulating proteins. 4. It emphasizes the role of miR-3663-3p as a potential biomarker for the rapid and reliable diagnosis of sepsis when combined with pro-inflammatory cytokines such as IL-6, IL-21, CXCL8, and MCP-1, along with mRNA markers TDAG8 and TLR4.
							IL-6, IL-21, MCP-1 miR-3663-3p mRNA markers TDAG8 and TLR4		5. The study highlights the significant elevation of IL-8 in sepsis, particularly in patients with shock. While IL-8 correlates with several clinical and inflammatory parameters, its prognostic value remains limited. IL-8 could serve as a biomarker for assessing shock severity and inflammatory activity in sepsis patients. 6. Procalcitonin (PCT) is a highly effective biomarker for diagnosing sepsis and differentiating it from SIRS in critically ill patients. IL-6 and IL-8 are less reliable for diagnosis but may provide additional prognostic insights. IL-8, however, correlated with mortality risk in patients with sepsis. 7. The study highlights the potential of ICAM-1, VEGFR2, and urokinase as diagnostic tools for sepsis. Sepsis patients had significantly higher levels of IL-6, IL-8, IL-10, ICAM-1, and urokinase compared to SIRS patients. These markers were also elevated compared to healthy controls. VEGFR2 levels were lower in sepsis patients compared to SIRS. 8. Whole blood IL-8 outperforms plasma IL-8 and CRP in diagnosing sepsis in postoperative ICU patients. Its high diagnostic accuracy and practical advantages make it a promising biomarker for early sepsis detection.
							PCT, IL6 ICAM-1, VEGFR2, and urokinase IL-6, IL-10		
							CRP		
miRNA150	MIR150	MicroRNA-150 Hsa-MIR-150-5p Hsa-MIR-150-3p Hsa-Mir-150 MIRN150 Hsa-Mir-150_pre MIMAT0004610 MIMAT000461 MID000479 MiRNA150 Mir-150	gene biomarker	diagnostic/prognostic	general sepsis biomarker across diverse infection types	Inflammatory and Immune Cytokine Storm Regulates MYD88, CXCL8 Vascular and Endothelial Modulates VEGFA and ANGPT2 Apoptosis and Cell Death Controls FOXO1 and MCL2 Epigenetic Regulation	downregulation of ARG1, IL-6, and anti-inflammatory cytokines (TNF- β , IL-10).	GeneCardsNO MalaCardsNO KEGGNO UniProtNO	1. MicroRNA-150 (miR-150): Central regulator downregulated in sepsis. ARG1 (Arginase-1): Key protein suppressed by miR-150, reducing MDSC-mediated immunosuppression. IL-6, IL-10, TGF- β : Cytokines influenced by miR-150 modulation.
							negatively correlated with pro-inflammatory cytokines (TNF-alpha, IL-18) and the anti-inflammatory cytokine IL-10. miR-182 and miR-342-5p		2. This study highlights miR-150 as a candidate for non-invasive sepsis diagnostics and suggests its potential role in regulating immune responses during sepsis. Its expression levels in plasma and leukocytes can distinguish sepsis patients from healthy individuals. A proposed miR-150L-18 ratio could further refine severity assessment. miR-150 was significantly downregulated in both leukocytes and plasma of sepsis patients compared to controls. miR-182 and miR-342-5p were also altered but to a lesser extent.
							miR-223: Associated with sepsis severity. miR-146a and miR-150: Correlated with survival and inflammatory regulation. miR-155 and miR-126: Implicated in endothelial function and sepsis progression.		3. The study highlights the potential of combining miR-150 levels with the SOFA score to enhance prognostic accuracy in sepsis patients. miR-150 could serve as a valuable prognostic marker, reflecting underlying immune dysregulation in sepsis. 4. The study highlights miR-150's potential as a prognostic biomarker in critically ill patients but suggests limited utility for sepsis diagnosis. Reduced miR-150 levels may indicate unfavorable outcomes and reflect immune dysregulation in critical illness. No significant difference was found in miR-150 levels between septic and non-septic critically ill patients. miR-150 levels were not correlated with common markers of inflammation or infection, such as C-reactive protein (CRP), procalcitonin (PCT), interleukin-6 (IL-6), interleukin-10 (IL-10), or tumor necrosis factor (TNF). 5. miR-150: Downregulated in most studies, associated with immune modulation, anti-inflammatory effects, and endothelial integrity. miR-146a: Also downregulated, with anti-inflammatory and immune-regulating roles.
							miR-25 demonstrated superior diagnostic accuracy Upregulated: miR-25, miR-122, miR-133a, miR-150, miR-223 Downregulated: miR-146a miRNA-223 and miRNA-146a miRNA-133a, miRNA-574-5p, and miRNA-16 miRNA-122 miRNA-4772 miRNA-181b		6. Prognostic Potential: miR-150 can serve as a biomarker to assess sepsis progression and predict outcomes. (yellow article) Levels of white blood cells (WBC), IL-6, CRP, and TNF- α were significantly elevated in sepsis rats compared to controls. Downregulated in Sepsis: miR-150 levels were significantly reduced in sepsis rats compared to both sham operation and control groups. Time-Dependent Decline: Levels of miR-150 progressively decreased over time (6 hours, 12 hours, and 24 hours post-operation). 7. Several miRNAs were highlighted as upregulated or downregulated in sepsis: Upregulated: miR-25, miR-122, miR-133a, miR-150, miR-223 Downregulated: miR-146a These miRNAs correlate with disease severity, prognosis, and stages of sepsis. Notably, miR-150 and miR-223 were linked with disease severity and patient survival. miRNA like miR-25 demonstrated superior diagnostic accuracy compared to CRP and PCT. miR-150 and miR-133a levels were strongly associated with mortality in critically ill patients. 8. miRNA-150: Low levels are associated with poor prognosis in critically ill patients. miRNA-223 and miRNA-146a: Downregulated in sepsis patients. miRNA-133a, miRNA-574-5p, and miRNA-16: Upregulated in sepsis patients. miRNA-122: Shows significant expression differences between septic and healthy patients. miRNA-4772 family (e.g., miRNA-4772-3p): Upregulated in sepsis. miRNA-181b: Downregulated in sepsis patients.
miRNA155	miRNA155	MicroRNA-155 Hsa-MIR-155-5p Hsa-Mir-155 Hsa-MIR-155-3p MIRN155 Hsa-Mir-155_pre MIMAT000646 MIMAT000468 MID000681 MiRNA155 Mir-155	gene biomarker	diagnostic/prognostic	blend of source-dependent specificity pathogen or inflammatory stimulus general immune system functions	Inflammatory and Immune Pathways/ Amplifies TNF- α , IL-6, and IL-1 β Promotes Th1/Th17 Vascular and Endothelial Pathways/ Epigenetic and Transcriptional Regulation/ Targets SOCS1, SHP1, and VEGFA		GeneCards miRNA role in immune response in sepsis MalaCards NO	1. Diagnostic Use: miR-155 helps identify sepsis early, offering a marker for timely intervention. Prognostic Use: It indicates disease severity, progression, and likely outcomes, aiding in treatment decisions and risk stratification.
									2 Diagnostic Value: miR-155 levels distinguish between healthy individuals and sepsis patients. Prognostic Value: High miR-155 levels predict disease severity and poor survival outcomes. Mechanism: miR-155 drives immunosuppression by promoting the proliferation of CD39+ Tregs, which exacerbates disease progression. The percentage of CD39+ Tregs was higher in sepsis patients, with the highest levels in septic shock cases. 3 Diagnostic Role: miR-155 is a promising marker for early diagnosis of ALI/ARDS in septic patients, with high sensitivity and specificity. Prognostic Insights: Elevated miR-155 levels indicate more severe lung injury and poorer pulmonary function.

									S100A9			8. S100A9 gene expression in blood was significantly elevated in septic arthritis mice compared to non-arthritis mice as early as day 2 post-infection. Elevated gene expression correlated positively with bone erosion severity on day 10. Plasma S100A9 protein levels were upregulated in all infected mice but did not differentiate between arthritic and non-arthritis groups. S100A9 gene expression shows promise as an early biomarker for septic arthritis, enabling timely intervention. It plays a critical role in the inflammatory response and joint damage, especially in Staphylococcus aureus-induced infections.
									S100A9, S100I2			9. S100A9/S100A9 and S100A12 are valuable biomarkers for assessing mortality risk in septic shock patients, particularly in the early phase. Highlights the diagnostic and prognostic value of S100A9/S100A9 and S100A12, demonstrating their potential to predict mortality and complement clinical scoring systems.
13.S100A9	S100A9	S100 Calcium Binding Protein A9 MRP-14 P14 Migration Inhibitory Factor-Related Protein 14 Leukocyte L1 Complex Heavy Chain Calprotectin L1H Subunit S100-A9 MAC387 808BAG LING COLB CAGB CFAG MIF NIF Protein S100-A9 Calgranulin B S100 Calcium-Binding Protein A9 (Calgranulin B) S100 Calcium-Binding Protein A9 Calgranulin-B LING	Protein marker/ gene	diagnostic/prognostic	universal role in the inflammatory response	Inflammatory and Immune Pathways/Cytokine Storm/ Neutrophil Recruitment and Activation Endothelial Dysfunction Act as DAMPs, amplifying pro-inflammatory cytokines Promote chemotaxis and NET formation Drive ROS release, contributing to tissue damage.	GeneCards/ NO MalaCards/ Bacterial Septis	1. Study primarily evaluates the therapeutic role of targeting S100A9, the significant elevation of S100A9 levels in plasma and lungs during sepsis suggests potential diagnostic value as a biomarker for inflammation severity.				
												2. This study identifies S100A9 as a critical mediator of inflammation and pyroptosis in sepsis-associated acute kidney injury. It highlights S100A9 as both a potential diagnostic biomarker and a therapeutic target for mitigating kidney injury in sepsis patients. 3. Elevated plasma S100A9 levels suggest it could serve as a biomarker for sepsis diagnosis. Deficiency of S100A9 mitigates these effects, suggesting therapeutic potential for targeting S100A9 in sepsis.
14.S100A12	S100A12	S100A12 S100 Calcium Binding Protein A12 CAAT1 GGRP CAGC PI Extracellular Newly Identified RAGE-Binding Protein Migration Inhibitory Factor-Related Protein 6 Calcium-Binding Protein In Amniotic Fluid 1 Neutrophil S100 Protein ENRAGE MRP8 Protein S100-A12 Calgranulin C EN-RAGE MRP-6 S100 Calcium-Binding Protein A12 (Calgranulin C) S100 Calcium-Binding Protein A12 Calgranulin C Calcterm.	protein marker/ gene	diagnostic marker	universal role in the inflammatory response	Inflammatory and Immune Pathways/Cytokine Storm/ Neutrophil Recruitment and Activation Endothelial Dysfunction Act as DAMPs, amplifying pro-inflammatory cytokines Promote chemotaxis and NET formation Drive ROS release, contributing to tissue damage.	GeneCards/ NO MalaCards/ NO	1. Monitoring S100A12 levels could help in diagnosing sepsis and assessing its severity. This study identifies S100A12 as a proinflammatory amplifier of innate immunity, particularly through TLR4-mediated monocyte activation. It has potential diagnostic value in sepsis and may serve as a therapeutic target to modulate excessive inflammatory responses.				
									S100A9, CHPT1, CPB84, DNAJC3, MAFG, NARF, SNX3, METTL9			2. S100A12 is a promising biomarker for systemic inflammation in severe sepsis, with significant elevation across all infection types. The high local levels during peritonitis suggest that S100A12 is released predominantly at the site of infection. S100A12 has diagnostic value for identifying systemic inflammation and sepsis, but its lack of correlation with disease severity limits its prognostic utility. 3. S100A12 demonstrated high diagnostic value for sepsis (AUC = 0.907) and moderate value for AF (AUC = 0.632). S100A12 expression was significantly elevated in sepsis and AF, correlating with immune and inflammatory pathways. S100A12 upregulation in serum and aortic tissue was associated with inflammation, reduced heart rate, and increased susceptibility to AF in septic mice. The study initially identified S100A12 at the gene level using bioinformatics and MR methods. It validated these findings at the protein level in experimental mouse models, demonstrating functional and therapeutic relevance. 4. This study is a combination of in silico (bioinformatics) and wet lab (experimental validation) approaches. The identified genes, particularly S100A12 and S100A9, demonstrate strong potential as diagnostic biomarkers for sepsis. Nine key dysregulated genes were identified: CHPT1, CPB84, DNAJC3, MAFG, NARF, SNX3, S100A9, S100A12, and METTL9. These genes were progressively upregulated in sepsis and demonstrated strong predictive potential with AUC values of 0.967 (logistic regression) and 0.987 (random forest).
15.sCD14-ST/ CD14	CD14	CD14 Molecule Myeloid Cell-Specific Leucine-Rich Glycoprotein Monocyte Differentiation Antigen CD14 CD14 Antigen MyD3 Antigen	protein marker	diagnostic/prognostic	universal pattern recognition receptor (pathogen-associated molecular patterns (PAMPs))	Inflammatory and Immune Pathways/ Toll-like Receptor (TLR)/ Signaling Cytokine Storm/ Endothelial Dysfunction Acute Phase Response/ Systemic Inflammation	GeneCards/ NO MalaCards/ Bacterial Septis Septic Arthritis	1. CD14: The decreased mCD14 and elevated sCD14 levels in sepsis patients suggest its diagnostic utility for distinguishing sepsis severity. mCD14: Reduced levels on cell surfaces may reflect immune cell dysfunction, a hallmark of immune suppression in severe sepsis or septic shock. sCD14: Elevated levels in the bloodstream indicate a systemic inflammatory response, often proportional to the disease's severity. 2. Elevated TLR2, TLR4, and CD14 protein level expression distinguishes sepsis patients from healthy individuals. Decreased expression of TLR2 and CD14 on monocytes at admission correlates with higher mortality, indicating potential as prognostic biomarkers. 3. Diagnostic Value: Elevated protein levels of sCD14-ST in plasma were specific to sepsis and distinguished it from SIRS and healthy controls. sCD14-ST is a sensitive biomarker for early and rapid diagnosis of sepsis. Prognostic Value: sCD14-ST levels correlate with sepsis severity, as indicated by SOFA scores, and track the response to treatment. This makes sCD14-ST a potential prognostic marker for monitoring sepsis progression and therapeutic efficacy. 4. Diagnostic Rule: Elevated protein levels of Presepsin in plasma make it a reliable diagnostic biomarker for distinguishing sepsis from SIRS and other conditions. Faster and more accurate than traditional markers. Prognostic Rule: Presepsin levels correlate with the severity of sepsis and predict mortality, supporting its use as a prognostic biomarker.				
									PCT, CRP			5. sCD14-ST (Presepsin) production is tightly linked to bacterial infections, making it a specific diagnostic biomarker for sepsis. Unlike general inflammatory markers, its production depends on bacterial phagocytosis, enhancing specificity for sepsis. 6. Diagnostic Value: Presepsin shows higher specificity for bacterial infections than other markers such as CRP and procalcitonin (PCT). Levels rise significantly in the early stages of sepsis, making it an early diagnostic biomarker. Prognostic Value: Levels correlate with the severity of infection and systemic inflammatory response. Elevated presepsin levels are linked to poor outcomes, including mortality.
16.CD64	FCGR1A	Fc Gamma Receptor Ia FcgamaR1a FCG1 FcgamaR1 CD64A CD64 Fc Fragment Of IgG, High Affinity Ia, Receptor For (CD64) Fc Fragment Of IgG, High Affinity Ia, Receptor (CD64) High Affinity Immunoglobulin Gamma Fc Receptor 1 Fc Fragment Of IgG Receptor Ia IgG Fc Receptor Fc-Gamma R1A Fc-Gamma R1 IGFR1 Fc-Gamma Receptor 1A1 CD64 Antigen Fc-Gamma R1 FCR1 FCR1	protein marker	diagnostic/prognostic	bacterial infections	Inflammatory and Immune/ Cytokine Storm Pathogen Recognition and Phagocytosis Oxidative Stress/ ROS production Acute Phase Response/ immune activation	GeneCards/ NO MalaCards/ Bacterial Septis Septic Arthritis	1. Diagnostic: CD64 and IL-8 distinguished sepsis severity stages effectively. Prognostic: Both markers predicted 28-day mortality with high sensitivity and specificity				
									PCT, CRP, WBC			2. The CD64 index is identified as the most reliable biomarker among those tested for the diagnosis of severe systemic bacterial infection and sepsis in critically ill patients. Its high diagnostic accuracy supports its use as a diagnostic marker rather than focusing on prognostic implications. Prognostic Value: While the primary focus was diagnostic, the CD64 index also provided insights into the severity of systemic bacterial infections and sepsis progression, potentially aiding early therapeutic decisions.
												3. Diagnostic: sCD64 protein expression is highly sensitive and specific for diagnosing sepsis at ICU admission. Adding sCD64 to CRP improves diagnostic accuracy. Prognostic: sCD64 levels correlate with treatment appropriateness and can monitor response to antibiotics. Persistently elevated levels after three days suggest inappropriate antibiotic therapy. 4. Prognostic Value: CD64 expression showed limited ability to predict mortality. The diagnostic value of CD64 protein expression on neutrophils for identifying sepsis in ICU patients.
									BCL2A1 gene			5. BCL2A1 and FCGR1A showed strong potential as diagnostic biomarkers for sepsis. BCL2A1 emerged as a novel candidate with clinical relevance, validated across multiple independent datasets. Highlights BCL2A1 as a novel gene-level biomarker with significant diagnostic and prognostic value for sepsis, validated by both bulk RNA-seq and scRNA-seq data

17	CD11b, ITGAM/ITGAM, CD11b	Integrin Subunit Alpha M MAC-1 CD11b CR3A Integrin, Alpha M (Complement Component 3 Receptor 3 Subunit) Cell Surface Glycoprotein MAC-1 Subunit Alpha Complement Component 3 Receptor 3 Subunit Macrophage 1 Antigen Alpha Subunit CD11 Antigen Like Family Member B Leukocyte Adhesion Receptor MD1 Integrin Alpha M CR3 Alpha Chain Integrin, Alpha M (Complement Component Receptor 3, Alpha) Also Known As CD11b (P170) Macrophage Antigen Alpha Polypeptide Neutrophil Adherence Receptor Alpha M Subunit Macrophage Antigen Alpha Polypeptide Neutrophil Adherence Receptor Antigen CD11b (P170) CD11b Antigen MAC1A SLEB6 CD11B MO1A	protein marker	diagnostic/prognostic	universal immune receptor	Inflammatory and Immune/ Pathogen Recognition and Phagocytosis Leukocyte Adhesion and Migration Vascular and Endothelial/ Endothelial Dysfunction Oxidative Stress/ ROS Production Acute Phase Response/ Immune Activation	CD14	GeneCards/ NO MalaCards/ Bacterial Sepsis	1. sCD14 levels can serve as a potential biomarker for detecting sepsis and stratifying disease severity. The dynamic regulation of CD11b and cytokine profiles may help in identifying stages of sepsis.
							CD64		2. The study highlights neutrophil CD64 as a superior diagnostic biomarker for severe sepsis, with excellent sensitivity and specificity. CD11b also provides additional diagnostic value but is less effective than CD64. Both markers show potential prognostic relevance for monitoring immune recovery in sepsis survivors.
							CSP CXCR2		3. Introduces the CRP/CD11b ratio as a novel and effective diagnostic parameter for identifying gram-positive sepsis 4. CD11b: Significantly increased on neutrophils of septic patients compared to healthy controls over the 5-day study period. CXCR2: Significantly reduced in septic patients compared to controls (p < 0.02). CXCR1: No significant changes or correlations were observed with disease severity or oxygenation. Focusing on protein-level markers like CD11b and CXCR2. These changes correlate with disease severity, highlighting their potential as both diagnostic and prognostic markers in septic shock.
18	CSAR1/CSaR CSAR1	Complement C3a Receptor 1 CSAR A2L C3a Anaphylatoxin Chemotactic Receptor Complement Component 3a Receptor 1 HNF4G29 Complement Component 3 Receptor 1 C3a-R CSR1 /	protein/gene marker	diagnostic/prognostic	universal / level of activation may vary based on The type of pathogen	Inflammatory and Immune/ Cytokine Storm Neutrophil Recruitment and Activation Vascular and Endothelial/ Endothelial Dysfunction Oxidative Stress/ ROS production	ITGAM, CD44, IL2RG	GeneCards/NO MalaCards/ NO	1. CD63 and CSAR1 are identified as key diagnostic markers for septic shock due to their significant differential gene expression and involvement in immune and inflammatory pathways./gene
		Complement C3a Receptor 1 CSAR 2 3 4 5 CD88 CSR1 CSA C3a Anaphylatoxin Chemotactic Receptor 1 Complement Component 3a Receptor 1 C3a-R Complement Component 5 Receptor 1 (C3a Ligand) C3a Anaphylatoxin Chemotactic Receptor CD88 Antigen C3a Ligand CSaR							2. Single-Cell RNA Sequencing./gene ITGAM and CSAR1 were predominantly expressed in macrophage clusters. CD44 and IL2RG were expressed across various immune cell types, reflecting their widespread involvement in immune modulation. Diagnostic: The core genes (ITGAM, CD44, CSAR1, IL2RG) provide potential biomarkers for distinguishing sepsis from SIRS and tracking disease progression. Prognostic: The expression levels of ITGAM and CSAR1 in macrophages correlate with inflammatory responses, suggesting their use as markers for immune dysregulation severity.
							Csa		3. Diagnostic./protein Elevated levels of C3a and C3a in plasma could indicate the degree of complement system activation and immune dysregulation in sepsis. Prognostic: The balance between C3a and C3a activity could serve as a marker of disease severity and guide therapeutic strategies.
							caspase-5		4. Identifies CSaR1 and caspase-5 as potential biomarkers for diagnosing and understanding the severity of sepsis./gene
									5. Diagnostic: Elevated protein C3a, C3a, Bb, and M-ficolin levels could serve as early biomarkers of sepsis.
									6. Diagnostic Value: Increased expression of CSaR at both the mRNA and protein levels during sepsis suggests it could serve as a biomarker for disease severity. Prognostic Value: High levels of CSaR correlate with poor outcomes. Blocking CSaR reduces cytokine levels and bacterial load, improving survival, which highlights its potential as a therapeutic target.
									7. This study demonstrates that CSaR and CSaR are upregulated during lung inflammation caused by sepsis./gene These receptors could serve as both diagnostic markers and therapeutic targets in sepsis and other inflammatory lung conditions.
									8. The C3a- CSaR axis holds both diagnostic and prognostic significance in sepsis./protein Measuring C3a and CSaR levels could help stratify patients based on disease severity and predict clinical outcomes
									9. Diagnostic and Prognostic Relevance./protein Diagnostic: Reduced CSaR expression on neutrophils reliably differentiated septic shock patients from healthy controls with high sensitivity and specificity. Prognostic: Lower CSaR expression and higher cCSaR levels were associated with worse outcomes, making them potential prognostic markers.
20	LCN2	LCN2 Lipocalin NGAL Neutrophil Gelatinase-Associated Lipocalin Oncogene 24p3 24p3 25 KDa Alpha-2-Microglobulin-Related Subunit Of MMP-9 Siderocalin P25 Migration-Stimulating Factor Inhibitor Lipocalin 2 (Oncogene 24p3) Siderocalin LCN2 Lipocalin-2 MGP1 HNL	protein/gene marker	diagnostic/prognostic	Not Pathogen-Dependent	Inflammatory and Immune/ Nutritional/Immunity/ Cytokine Storm Vascular and Endothelial/ Endothelial Dysfunction Oxidative Stress/ Iron regulation Organ-Specific Pathways/ Acute Kidney Injury (AKI)	OLF44	GeneCards/ Pathways & Interactions for LCN2 Gene MalaCards/ NO	1. Diagnostic Role./gene/protein Elevated plasma LCN-2 serves as a biomarker for SIC and correlates with myocardial injury severity. Prognostic Role: High LCN-2 levels are associated with worse cardiac function, suggesting its potential as a prognostic indicator for SIC outcomes.
									2. Diagnostic Role./gene Early expression of LCN2, OLF44, and other neutrophil-related genes could help identify patients at risk of ARDS. Prognostic Role: The association of these genes with disease severity and outcomes suggests their potential for stratifying risk and tailoring interventions.
							VEGFA MPO, MMP9, TLR2 IL10, LCN2, IL1R, CD40LG, CD28		3. Lcn2 functions as a diagnostic marker on both the protein and gene levels, with protein-level validation providing stronger support for its utility in clinical settings.Sustained Lcn2 Expression: Liver: Lcn2 mRNA levels were rapidly induced 3 hours post-CLP and remained elevated for 30 hours. This persistent expression was confirmed at the protein level. Lung: Lcn2 mRNA levels were higher at baseline compared to the liver and showed similar rapid and sustained elevation post-CLP.
									4. mRNA and mRNA changes (LCN2, VEGFA) correlate with organ dysfunction, making them potential diagnostic markers for specific SOFA components. 5. study highlights the potential of hub genes as biomarkers and therapeutic targets for sepsis and COVID-19./gene MPO, MMP9, TLR2, and LCN2 emerge as key diagnostic candidates, while CD247, CD2, and CD40LG may help in prognostic assessments.
									6.Diagnostic Role: The identified hub genes (IL10, LCN2, IL1R, CD40LG, CD28) serve as reliable diagnostic markers for sepsis. Prognostic Role: LCN2 showed significant differences between shock and non-shock patients, suggesting a role in predicting sepsis severity.
							Resistin, and IL-8		7. Diagnostic Role./protein Elevated serum Lcn-2 is an early biomarker for sepsis-induced kidney injury. Prognostic Role: MB-derived iron-bound Lcn-2 predicts renal recovery during sepsis.
									8. NGAL (Neutrophil Gelatinase-Associated Lipocalin), Resistin, and IL-8 are identified as protein biomarkers differentiate severe sepsis/shock from uncomplicated sepsis.. No Temporal Changes in mRNA: mRNA expression of target genes remained stable over time, indicating that transcriptional changes occurred early in the disease course.

21.CXCL10 IP-10	CXCL10	C-X-C Motif Chemokine Ligand 10 IP-10 GBP-10 SCYB10 IFN10 Cys-2 M3b-1 INP10 C7 Small Inducible Cytokine Subfamily B (Cys-X-Cys), Member 10 10 kDa Interferon Gamma-Induced Protein Small-Inducible Cytokine B10 C-X-C Motif Chemokine 10 Protein 10 From Interferon (Gamma)-Induced Cell Line Interferon-Inducible Cytokine IP-10 Chemokine (C-X-C Motif) Ligand 10 Gamma IP10 Gamma-IP10	protein/gene marker	diagnostic/prognostic	not pathogen-dependent	Inflammatory and Immune Pathways/ Cytokine Storm/ T-cell and NK Cell Recruitment Vascular and Endothelial/ Endothelial Dysfunction Immune Dysregulation/ Immune Exhaustion		GeneCards/ NO Malacards/ Bacterial Sepsis Septic Arthritis	1. Diagnostic and Prognostic Relevance:protein(yellow) Diagnostic Value: MMP-1, MMP-2, MMP-7, MMP-13, and soluble E-selectin are effective in differentiating SIRS from sepsis. IL-1α, IP-10, sTNF-R2, and sFas are indicative of sepsis severity. Prognostic Value: Elevated levels of MMP-3, MMP-10, IL-1α, IP-10, and sTNF-R2 correlate with higher mortality risk. 2. Diagnostic Role:protein IL-1β, IL-7, IL-12, RANTES, MMP-18, and IP-10 show strong diagnostic potential to distinguish sepsis from malaria and febrile controls. 3. CXCL10 is Elevated During Septic Shock: High concentrations of CXCL10 were observed in plasma and peritoneal lavage fluid during CLP-induced sepsis, peaking 8 hours after the procedure. CXCL10 levels correlated with hyperthermia, increased cytokine production, and poor survival. Elevated CXCL10 levels in plasma can serve as an indicator of sepsis severity. 4. Elevated synovial fluid CXCL10 levels make it a promising diagnostic marker and therapeutic target in septic arthritis:protein 5. The identified genes (TNFAIP6, GBP1, CXCL10, CXCL5, FCN1, PID1) can stratify septic patients and identify those who might benefit from IFN-γ therapy.
22.IFN-γ	IFNG	Interferon Gamma Immune Interferon IFN-Gamma IM269 IFG IFI	protein marker	therapeutic role	IFN gamma production is largely infection-dependent bacterial/virus	Inflammatory and Immune Pathways/ Cytokine Storm/ T-cell and Macrophage Activation Vascular and Endothelial Pathways/ Endothelial Dysfunction Immune Dysregulation Pathways/ Immune Exhaustion	TLR4	GeneCards/NO Malacards/ bacterial sepsis Septic Arthritis	1. study demonstrates that IFN-γ effectively restores immune function in sepsis by reducing T-cell apoptosis, modulating cytokine responses, and downregulating regulatory T cells. :protein These findings highlight IFN-γ as a promising therapeutic candidate for targeted immune enhancement in sepsis. 2. The findings suggest that therapeutic modulation of the type I IFN pathway could improve outcomes in sepsis by balancing immune activation and inflammation:protein 3. Diagnostic Value:protein Altered TLR4 expression on NK cells may help differentiate sepsis from SIRS. Impaired IFN-γ production could serve as a biomarker of immune dysfunction in sepsis. Prognostic Value: Reduced NK cell counts and function (e.g., diminished IFN-γ production) may indicate worse immune status and poorer outcomes in sepsis.
23.IFN-α	IFNA1	Interferon Alpha 1 IFN-Alpha2 IFNA1PVA IFNA13 IFNA1g IFN IFN Interferon Alpha-1/13 Interferon Alpha 1b Interferon Alpha-D IFN-Alpha-1/13 LeIF-D Interferon-Alpha1 IFN-Alpha 1b	protein marker	Therapeutic role	More virus infection	Inflammatory and Immune Pathways/ cytokine storm/ Anticiral Defense/Immune Dysregulation Vascular and Endothelial/ Endothelial Dysfunction Oxidative Stress/ ROS Production		GeneCards/ No Malacards/ No	4
24.IFN-β	IFNB1	Interferon Beta 1 IFB IFNB Interferon, Beta 1, Fibroblast Fibroblast Interferon Interferon Beta IFN-Beta Interferon-Beta	protein marker	therapeutic role	viral, bacterial, or parasitic infections	Inflammatory and Immune Pathways/cytokine storm/ Anticiral Defense/Immune Dysregulation Vascular and Endothelial/ Endothelial Dysfunction Oxidative Stress/ROS Production		GeneCards/ No Malacards/ No	4. IFN-β restored immune function, indicating potential as a prognostic marker for therapeutic response and survival improvement, study demonstrates that IFN-β effectively restores alveolar macrophage function, enhances neutrophil recruitment, and reduces lung injury. IFN-β may represent a promising therapeutic strategy for sepsis-induced ARDS. These findings suggest IFN-β as a potential therapeutic strategy for sepsis-related immune suppression and ARDS. 5. Prognostic Value: IFN-β expression levels correlate with survival outcomes in experimental sepsis models, suggesting potential as a prognostic biomarker. 6. Type I IFNs, particularly IFN-β, are central mediators of inflammation in sepsis. While they play essential roles in host defense, their overproduction during sepsis can exacerbate inflammation and tissue damage, making them a potential therapeutic target.
25.CCL19	CCL19	C-C Motif Chemokine Ligand 19 ELC CX Beta-11 Eotaxin-3 MIP-3α SCYB19 Ox11 Small Inducible Cytokine Subfamily A (Cys-Cys), Member 19 Epstein Barr Virus-Induced Molecule 1 Ligand Chemokine Macrophage Inflammatory Protein 3-Beta	protein marker	more prognostic	not pathogen-dependent	Inflammatory and Immune/ Cytokine Storm/ Immune Dysregulation Adaptive Immune/ T-cell Activation and Trafficking	CCL28, and VEGF-A	GeneCards/ NO malacards/ No	1.Elevated levels of CCL19, CCL28, and VEGF-A could serve as biomarkers for sepsis susceptibility and severity:protein
26.CCL25	CCL25	C-C Motif Chemokine Ligand 25 TECK SCYB25 Ox15 Small Inducible Cytokine Subfamily A (Cys-Cys), Member 25 Chemokine (C-C Motif) Ligand 25 Small-Inducible Cytokine A25 Thymus-Expressed Chemokine C-C Motif Chemokine 25 Chemokine TECK Cx Beta-15 TECKα Thymus-Expressed Chemokine	protein/gene marker	Therapeutic	not pathogen-dependent primarily expressed in the thymus and intestinal mucosa	Inflammatory and Immune/ Immune Dysregulation Gut Barrier and Mucosal Integrity/ Gut Barrier Integrity		GeneCards/ NO malacards/ No	Diagnostic and Prognostic Relevance: Elevated serum levels of CCL25 were associated with sepsis and could serve as a biomarker for inflammation and endothelial dysfunction in ALL. Therapeutic Potential: Neutralizing CCL25 showed promise as a therapeutic strategy to reduce inflammation, improve endothelial barrier function, and mitigate sepsis-induced ALL.
27.CX3CR1	CX3CR1	C-X3-C Motif Chemokine Receptor 1 V2B CMKBR1 CMKDR1 CX3R1 GPR13 Chemokine (C-X3-C Motif) Receptor 1 Beta Chemokine Receptor-Like 1 Chemokine (C-X3-C) Receptor 1 G-Protein Coupled Receptor 13 CX3C Chemokine Receptor 1 Fractalkine Receptor C-X3-C CRK-1 CMK-BRL-1 CMK-BRL1 Chemokine (C-C) Receptor-Like 1 GPRV2B	protein/gene marker	more prognostic than diagnostic	not pathogen-dependent	Inflammatory and Immune Pathways/ cytokine storm/ Monocyte and Macrophage Recruitment Vascular and Endothelial Pathways/ Endothelial Dysfunction Immune Dysregulation/ Immune Exhaustion Oxidative Stress/ ROS production		GeneCards/ NO malacards/ NO	1. mRNA Level: CX3CR1 mRNA expression was significantly downregulated in septic shock patients compared to healthy controls. Non-survivors showed persistently lower CX3CR1 mRNA levels than survivors. Protein Level: CX3CR1 protein expression on monocytes was similarly reduced. The downregulation was more pronounced in non-survivors. Soluble CX3CL1 Levels: Elevated sCX3CL1 levels in septic patients' serum correlated with disease severity and poor outcomes. Diagnostic Value: The significant reduction in CX3CR1 mRNA and protein levels in septic patients suggests its potential as a diagnostic marker for immune dysfunction in septic shock. Prognostic Value: CX3CR1 mRNA levels predicted patient survival with: Sensitivity: 88% Specificity: 78% (threshold: 0.00136). Persistent CX3CR1 downregulation correlated with poor outcomes and higher mortality rates. 2. The study suggests potential therapeutic manipulation of CX3CR1-mediated signals to enhance bacterial clearance and reduce mortality in sepsis:gene While the focus was on the mechanistic roles, it hints at diagnostic implications for CX3CR1 expression or function in sepsis susceptibility. 3. CX3CR1 mRNA and protein levels were downregulated in the same tissues post-CLP, highlights the regulatory relationship between fractalkine and CX3CR1 in sepsis, suggesting that targeting NF-κB could modulate these interactions and potentially improve outcomes. 4. Fractalkine could serve as a biomarker for sepsis severity and mortality. :protein(yellow) Blocking Fractalkine or its receptor CX3CR1 may represent a therapeutic strategy for reducing inflammation and improving outcomes in sepsis. 5. CX3CR1 Expression:gene:protein CX3CR1 mRNA and protein levels were significantly decreased in monocytes from septic shock patients compared to healthy controls. Non-survivors exhibited a more pronounced and persistent downregulation than survivors. sCX3CL1 Levels: Serum levels of soluble fractalkine were elevated in septic shock patients, particularly in non-survivors, suggesting increased cleavage of membrane-bound CX3CL1. The study highlights the potential of CX3CR1 as a prognostic biomarker for mortality in septic shock. Persistent downregulation of CX3CR1 on monocytes is associated with poor outcomes, underscoring its role in sepsis-induced immunosuppression. 6. Survival Analysis: Patients with CX3CR1 expression above the threshold showed significantly better survival rates at both D7 and D28 compared to those below the threshold. highlights CX3CR1 mRNA as a reliable, early biomarker of mortality in ICU patients, potentially useful for risk stratification and immunomonitoring. Its role in identifying high-risk patients for tailored interventions is emphasized.

28.P2X7	P2RX7	P2RX7 Purinergic Receptor P2X 7 P2X7 P2X Purinoceptor 7 ATP Receptor P2Z Receptor MG20008 Purinergic Receptor P2X, Ligand Gated Ion Channel, 7 Purinergic Receptor P2X, Ligand Gated Ion Channel, 7 Purinergic Receptor P2X 7 Purinergic Receptor P2X7 Receptor External Ids for P2RX7 Gene	protein/gene marker	more prognostic than diagnostic	not pathogen-dependent	Inflammatory and Immune Pathways/ Cytokine Storm/ Immune Cell Activation Vascular and Endothelial Pathways/Endothelial Dysfunction Apoptosis and Cell Death Pathways/Pyroptosis Oxidative Stress/ ROS production	NLRP3	GeneCards/ NO MalaCards/ NO	1. Diagnostic./protein P2X7 receptor expression and mitochondrial dysfunction could serve as biomarkers for immune paralysis in sepsis. Prognostic Early NLRP3 inflammasome dysfunction strongly correlated with mortality, suggesting its potential as a prognostic marker. The study identifies the P2X7 receptor as a critical regulator of mitochondrial function and immune suppression in sepsis, offering a potential target for therapeutic intervention. Restoring NLRP3 inflammasome activation could improve outcomes in septic patients.
							CD39		2.study highlights P2X7 and CD39 as potential therapeutic and diagnostic targets for managing SAE and its associated cognitive impairments in sepsis.gene/protein P2X7 receptor mRNA expression was significantly increased in the hippocampus of septic mice 24 hours after sepsis induction (CLP group) compared to the sham-operated group. This suggests an upregulation of P2X7 as part of the inflammatory response in the brain region. General Cortex No significant change in P2X7 receptor mRNA expression was observed in the cerebral cortex of septic mice. This indicates regional specificity in the brain's inflammatory response to sepsis.
							CD14		3. Elevated plasma CD14 and P2X7 expression in septic patients could serve as biomarkers of sepsis severity./protein Prognostic The ability of CD14 to modulate bacterial clearance and inflammation suggests a potential role in predicting sepsis outcomes.
							ATP, ADP		4.P2X7 Receptor: Expression in Septic Patients Similar to P2Y2, P2X7 mRNA levels did not show significant differences between septic patients and the control groups. This indicates that transcriptional changes in P2X7 are not prominent in sepsis or are potentially regulated post-transcriptionally. dysregulated ATP-signaling is a feature of early sepsis and identifies ATP, ADP, and related enzymatic activities as promising diagnostic biomarkers. Elevated A2a receptor expression in neutrophils and monocytes highlights its role in sepsis-related immune dysfunction and potential as a therapeutic target. 5. systemic blockade of P2X7R protects against sepsis-induced intestinal barrier dysfunction. /protein This protective effect is mediated through the suppression of pro-inflammatory cytokines, reduced M1 macrophage activation, and maintenance of tight junction integrity via ERK1/2-48 signaling pathways.
29.PTX3	PTX3	PTX3 Pentraxin 3 TSG-14 Tumor Necrosis Factor-Inducible Gene 14 Protein TNFAIF9 Tumor Necrosis Factor Alpha Induced Protein 5 Pentraxin-Related Protein PTX3 TNF Alpha-Induced Protein 5 Long Pentraxin 3 Pentraxin-Related Gene, Rapidly Induced By IL-1 Beta Pentraxin-Related Gene, Rapidly Induced By IL-1 Beta Tumor Necrosis Factor, Alpha-Induced Protein 5 Tumor Necrosis Factor Inducible Protein TSG-14 Pentraxin-Related Protein PTX3 Pentraxin 3, Long 2 TSG14	protein/gene marker	prognostic more than diagnostic	not pathogen-dependent	Inflammatory and Immune Pathways/ Acute Phase Response / Pathogen Recognition and Clearance/ Complement Activation and Regulation Vascular and Endothelial/ Endothelial Dysfunction Coagulation/ Coagulation and Fibrinolysis Immune Regulation/ Resolution of Inflammation		GeneCards/ NO MalaCards/ NO	1. Studies confirm PTX3 as an early and independent predictor of mortality in septic patients. Elevated PTX3 levels predict disease severity in bacterial (e.g., pneumonia), fungal (e.g., aspergillosis), and viral infections (e.g., dengue). PTX3 levels decrease with effective treatment, making it a marker for therapeutic response. PTX3 is a robust biomarker for diagnosing and monitoring sepsis. Its rapid response to infection and strong correlation with disease severity and outcomes make it a valuable tool in clinical settings. PTX3's role as a diagnostic and prognostic marker is based on its protein levels in the bloodstream, which correlate with disease severity, organ dysfunction, and patient outcomes.
							PCT, CRP		2. Elevated PTX3 in Septic Patients./protein/gene PTX3 levels were significantly higher in septic patients (median: 22.031 pg/mL) compared to healthy volunteers (median: 438 pg/mL). Non-survivors had higher PTX3 levels (median: 204.879 pg/mL) than survivors (median: 14,893 pg/mL), correlating with disease severity. In septic shock patients 2 hours post-LPS stimulation, while PTX3 mRNA peaked 2 hours post-LPS stimulation, while protein levels increased continuously and peaked at 24 hours. PTX3 protein stability was significantly higher than TNF- α , contributing to sustained circulating levels. PTX3 mRNA expression was maintained in septic patients, with slower decay compared to pro-inflammatory cytokines like TNF- α . PTX3 transcription was less susceptible to endotoxin tolerance, indicating its robust gene-level regulation.
							PCT,CRP		3.PTX3 is a reliable biomarker for the early identification of severe sepsis and prediction /protein of mortality in emergency room patients with suspected infections. Its rapid response to inflammation and strong correlation with sepsis severity make it superior to CRP and comparable to PCT. 4. PTX3's oligomerization state serves as a novel biomarker for resolving inflammation and predicting survival in sepsis./protein The dynamic shift from dimeric to monomeric PTX3 by day 2 post-ICU admission correlates with better outcomes, making it a potential tool for monitoring treatment responses and disease progression.
							PCT,CRP		5. Elevated PTX3 levels are associated with disease severity and mortality in sepsis and infections like pneumonia, tuberculosis, and fungal diseases./protein Persistently high PTX3 levels in sepsis correlate with poor outcomes, organ dysfunction, and coagulation abnormalities. PTX3 outperforms CRP and PCT in predicting mortality and disease severity in septic patients.
							PCT,CRP		6.PTX3 is a robust protein biomarker for diagnosing sepsis and septic shock, with excellent correlation to disease severity and outcomes./protein Its superior diagnostic performance compared to CRP and PCT makes it a valuable tool for early ICU risk stratification and clinical decision-making.
									7. PTX3 protects against sepsis-induced myocardial injury by downregulating apoptosis and autophagy through/protein the inhibition of the PI3K/Akt/mTOR signaling pathway. This suggests PTX3 as a potential therapeutic target for managing sepsis-related cardiac complications.
30.TRAIL	TNFSF10	TNFSF10 TNF Superfamily Member 10 Apo-2L TRAIL CD293 TANCR TL2 Tumor Necrosis Factor (Ligand) Superfamily, Member 10 Tumor Necrosis Factor Ligand Superfamily Member 10 Apo-2 Ligand AF02L Chemokine Tumor Necrosis Factor Ligand Superfamily Memb Tumor Necrosis Factor (Ligand) Family, Member 10 TNF-Related Apoptosis Inducing Ligand TRAIL Tumor Necrosis Factor Superfamily Member 10 TNF-Related Apoptosis-Inducing Ligand Tumor Necrosis Factor Ligand 6A Protein TRAIL CD293 Antigen TNL6A	protein marker	diagnostic/prognostic	triggered by inflammatory signals rather than specific pathogens	Apoptosis and Cell Death Pathways/ immune Cell Apoptosis/Endothelial Cell Apoptosis Inflammatory and Immune Pathways/ Immune Dysregulation/ Cytokine Storm Vascular and Endothelial/ Endothelial Dysfunction		GeneCards/ NO MalaCards/ NO	1. Identifies TRAIL as a key mediator of immune suppression during sepsis. /protein contributing to impaired bacterial clearance and reduced CD8 T-cell responses. Targeting the TRAIL pathway may have therapeutic potential to restore immunity and reduce mortality associated with secondary infections in septic patients.
									2. TRAIL Levels and Organ Dysfunction./protein Lower TRAIL levels (<28.6 pg/mL) were associated with: Increased organ dysfunction (higher SOFA scores). Greater incidence of septic shock in all cohorts. Lower TRAIL levels were associated with higher lactate levels and greater vasopressor use, reflecting hemodynamic instability. Diagnostic: TRAIL differentiates septic shock from sepsis and non-infectious critical illness. Potential use as a marker of immune dysfunction in septic patients. Prognostic: Low TRAIL levels predict higher mortality and severe organ dysfunction, making it a candidate for risk stratification.
									3. TRAIL Levels and Sepsis Severity./protein Plasma TRAIL levels were significantly lower in septic and septic shock patients compared to controls TRAIL levels were associated with sepsis severity and could serve as a biomarker for distinguishing sepsis and septic shock from non-septic critically ill patients.
									4. Downregulated Genes (Pro-Apoptotic Pathways) /gene/protein TRAIL (TNF-related apoptosis-inducing ligand): Reduced expression (0.65-fold) in LPS-stimulated macrophages. TRAIL is involved in apoptosis induction, and its downregulation correlates with increased macrophage survival. FASL (Fas ligand): Downregulated to 0.67-fold. FASL plays a role in intrinsic apoptotic signaling, and its suppression helps protect macrophages.
							FASL, Caspase 3		Downregulated (0.65-fold) Caspase 3 is a key executor of apoptosis, and its reduced expression decreases apoptotic activity in macrophages.
									5. Mean plasma sTRAIL levels were significantly lower in septic patients compared to healthy controls (16.9 ± 8.3 vs. 68.3 ± 8.6 pg/mL, p < 0.01). Severe sepsis and septic shock patients had lower sTRAIL levels than patients with milder sepsis (p < 0.05). Diagnostic: sTRAIL levels differentiated septic patients from healthy controls and distinguished sepsis severity (sepsis, severe sepsis, septic shock). Prognostic: Lower sTRAIL levels were associated with worse outcomes, including higher APACHE II scores and mortality, suggesting its potential as a prognostic biomarker. sTRAIL could serve as a biomarker for assessing immune status and guiding treatment decisions in sepsis
									6. Elevated TRAIL levels and increased T-cell apoptosis could serve as early markers of trauma-induced immunosuppression./protein
									7. TRAIL and IP-10 were particularly useful in distinguishing viral infections, while CRP, IL-6, and PCT were more indicative of bacterial infections./protein
31.MMP8	MMP8	MMP8 Matrix Metalloproteinase 8 CLG1 Matrix Metalloproteinase 8 (Neutrophil Collagenase) Matrix Metalloproteinase-8 Neutrophil Collagenase PMNL Collagenase PMNL-CL MMP-8 PMN Leukocyte Collagenase Collagenase 2 EC 3.4.24.34 EC 3.4.24.47 HNC	protein/gene	diagnostic/prognostic	not pathogen-dependent	Inflammatory and Immune/ Cytokine Storm/ Neutrophil Activation Vascular and Endothelial/ Endothelial Dysfunction Extracellular Matrix/ ECM Degradation and Remodeling		GeneCards/ NO MalaCards/ NO	1. Serum levels of MMP-8, MMP-9, and TIMP-1 were significantly higher in sepsis patients compared to healthy controls./protein Elevated MMP-8 and TIMP-1 levels upon ICU admission are associated with poor outcomes, indicating their potential utility as prognostic biomarkers. The findings support the role of MMP-8 in the inflammatory response during sepsis and its excessive upregulation in severe cases. High MMP-8 and TIMP-1 levels are associated with increased mortality in severe sepsis and septic shock, highlighting their potential as prognostic biomarkers.
									2. This study identifies MMP-8 as a key player in the inflammatory response to sepsis and a potential therapeutic target./protein/gene MMP-8 Gene: Expression increased in septic and septic shock patients; higher levels correlate with worse outcomes. Elevated MMP-8 levels in blood correlate with increased disease severity, organ failure, and mortality, suggesting its use as a biomarker for risk stratification in sepsis.

42.CCL2												
43.ARG1	ARG1	ARG1 Arginase 1 Arginase-1 Liver-Type Arginase Arginase, Liver Type I Arginase EC 3.5.3.1	protein/gene	diagnostic/prognostic			IL1R2, ELANE, MPO, MMP9	GeneCards/NO MalaCards/ Bacterial Sepsis	1. ARG1, IL1R2, ELANE, MPO, MMP9./gene Associated with immune dysregulation and oxidative stress during sepsis.			
							IL10		2. Elevated IL-10 expression suggests a biomarker for immunosuppressive phases in sepsis./gene Ratio of MD5 (M1) and ARG1 (M2) could be diagnostic markers for macrophage polarization states. 3. ARG1 emerges as a multifunctional biomarker in sepsis for (yellow)/gene Diagnosis: Differentiating sepsis severity and related conditions. Prognosis: Predicting treatment response and survival outcomes.			
44.IL1R2	IL1R2	IL1R2 Interleukin 1 Receptor Type 2 CD121b IL1RB CD121 Antigen-Like Family Member B Interleukin-1 Receptor Type II Interleukin-1 Receptor Type 2 Interleukin-1 Receptor Beta IL-1 Type II Receptor IL-1R-Beta IL-1RT2 CDw121b IL-1R2 IL-1R2 Type II Interleukin-1 Receptor, Beta Interleukin 1 Receptor, Type II Antigen CDw121b CD121b Antigen IL1R2c	protein/gene marker	diagnostic/prognostic	distinguished sepsis from bacterial infections			GeneCards/ NO MalaCards/ Bacterial Sepsis	1. IL1R2 offers a non-invasive, rapid diagnostic tool for sepsis and pathogen identification./gene/protein It could improve early diagnosis, guide antibiotic selection, and enhance sepsis management.			
							IGHG1, LCN2, LTF, MMP9, OLFM4		2. In sepsis, IL1R2 transcription was significantly increased in monocytes, aligning with the higher plasma sIL-1R2 levels./gene/protein sIL-1R2 distinguished sepsis from bacterial infections and could differentiate sepsis based on the Sepsis-2 and Sepsis-3 criteria. 3. Differentially expressed genes included: Upregulated in septic shock: IGHG1, IL1R2, LCN2, LTF, MMP9, OLFM4. These genes showed significant ability to distinguish septic shock from non-septic shock based on ROC analysis.			
IL1B	IL1B	Interleukin 1 Beta IL1F2 IL-1BETA Interleukin-1 Beta IL-1 Beta Catabolin IL-1B Pro-Interleukin-1 Beta Prointerleukin 1 Beta Interleukin 1beta IL1beta IL-1	protein gene marker	diagnostic/prognostic			IL-6, TNF-α	GeneCards/ Septic Shock MalaCards/ Bacterial Sepsis	1. The findings indicate potential biomarkers of immune dysfunction in late sepsis (IL-1β, IL-6, TNF-α)/gene These genes may reflect the extent of immunosuppression during sepsis.			
							IL-1R2		2. PMNs from sepsis patients exhibited a marked reduction in IL-1β mRNA and protein synthesis in response to endotoxin stimulation compared to controls./gene Elevated IL-1R2 expression on PMNs and tolerance to endotoxin-induced IL-1β expression may serve as markers for sepsis.			
45.CD177	CD177	CD177 Molecule PRV1 NBI CD177 Antigen HNA2A Polycythemia Rubra Vera Protein Human Neutrophil Alloanigen 2a NBI Glycoprotein HNA-2a NBI GP PRV-1 Polycythemia Rubra Vera 1 Cell Surface Receptor	protein/gene marker	diagnostic/prognostic				GeneCards/ NO MalaCards/ NO	1. CD177 proposed as a marker for sepsis, reflecting changes in neutrophil function during the disease./gene(yellow) The study investigates both gene-level (CD177 mRNA expression) and protein-level (CD177 surface expression) changes, providing a comprehensive view of the biomarker's potential			
46.OLFM4		Olfactomedin 4 GW112 OID GC1 G-CSF-Stimulated Clone 1 Protein Antiapoptotic Protein GW112 Olfactomedin-4 Olfactomedin Tiam HCC-1 HCLD PQF4 OLM4 BA209/19.1 UNC292	protein/gene marker	more prognostic marker				GeneCards/ NO MalaCards/ NO	1. OLFM4+ neutrophil percentage is strongly linked to mortality and could serve as a prognostic biomarker for sepsis severity and outcomes.			
							CD177, MAPK14		2. Diagnostic Value: OLFM4 is a promising biomarker for distinguishing between severe and mild infectious diseases, including sepsis and ARDS./protein/gene Prognostic Value: Higher OLFM4 expression indicates poor prognosis in sepsis and other diseases. 3. Plasma Olfm4 is elevated in septic shock but lacks specificity as a diagnostic marker./protein			
47.MAPK14	MAPK14	Mitogen-Activated Protein Kinase 14 PRKM14 PRKM15 CSBP1 CSBP2 CSBP1 Mx2 P38 Mitogen-Activated Protein Kinase P38 Alpha MAX-Interacting Protein CSAID-Binding Protein MAP Kinase P38 Alpha P38 MAP Kinase 2 MAP Kinase 14 EC 2.7.11.24.4 SAPK2A.3 CSBP Cytokine Suppressive Anti-Inflammatory Drug Binding Protein P38 Mitogen Activated Protein Kinase Stress-Activated Protein Kinase 2A Stress-Activated Protein Kinase 2a MAP Kinase Mx2 MAP Kinase MX2 P38alpha Exp EC 2.7.11 P38ALPHA MAPK 14 SAPK2a EXIP MX2 RK	gene marker	diagnostic/prognostic	Epigenetic and Transcriptionic Regulation Pathways/Immune Gene Transcription Hypoxia and Metabolic Pathways/ Metabolic Shift	PID1, CS, CYP11B1, FLVCR1, IFT2	GeneCards/ NO MalaCards/ NO	1. Diagnostic Biomarkers: PID1, CS, CYP11B1, FLVCR1, IFT2, MAPK14 were identified as diagnostic genes for sepsis. Validation: These genes demonstrated high sensitivity and specificity for diagnosing sepsis across datasets and experimental models.				
48.VCAM1/ ICAM1	VCAP1/ICAM1	Vascular Cell Adhesion Molecule 1 CD108 Vascular Cell Adhesion Protein 1 CD108 Antigen NCAM-100 VCAM 1 VCAM-1/ Intercellular Adhesion Molecule 1 CD54 BB2 Major Group Rhinovirus Receptor ICAM-1 Intercellular Adhesion Molecule 1 (CD54), Human Rhinovirus Receptor Epitope-Specific Secretory Sperm Binding Protein Cell Surface Glycoprotein P3.58 Human Rhinovirus Receptor CD54 Antigen P3.58	protein/gene marker	more prognostic	Vascular and Endothelial Pathways/ Endothelial Activation	VCAM1+ EC-EVs	GeneCards/NO MalaCards/Bacterial sepsis Septic Arthritis	1. Diagnostic: Elevated levels of VCAM1+ EC-EVs can serve as a biomarker for sepsis-related ARDS. Prognostic: VCAM1+ EC-EVs could potentially predict the severity and progression of lung injury in septic patients.				

50.SOC53	OC53	Suppressor Of Cytokine Signaling 3 SOCS3 SSI-3 CIS3 Csa3 Cytokine-Inducible SH2 Protein 3 STAT-induced STAT Inhibitor 3 SSI ATOD4 CIS-3				Epigenetic and Transcriptional Regulation Pathways/ Gene Expression Modulation Inflammatory and Immune Pathways/ Anti-inflammatory Signals		GeneCards/ NO MalaCards/ Septic Arthritis	
51.GATA3	GATA3	GATA Binding Protein 3 HDR Trans-Acting T-Cell-Specific Transcription Factor GATA-3 GATA-Binding Factor 3 GATA-Binding Protein 3 HDR6				Inflammatory and Immune Pathways/ Immune Cell Recruitment Adaptive Immune Pathways/ T-cell Activation/Regulation of Differentiation		GeneCards/ NO MalaCards/ Bacterial sepsis	
52.CCR7/8	CCR7	C-C Motif Chemokine Receptor 7 CD197 BLR2 CMKBR7 CD197 EBI1 Epstein-Barr Virus-Induced G-Protein Coupled Receptor 1 Chemokine (C-C Motif) Receptor 7 C-C Chemokine Receptor Type 7 MIP-3 Beta Receptor CC-CKR-7 CCR-7 Lymphocyte Specific G Protein-Coupled Peptide Receptor EBV-Induced G Protein-Coupled Receptor 1 EBV-Induced G Protein-Coupled Receptor 1 Epstein-Barr Virus Induced Gene 1 Burkitt's Lymphoma Receptor CC Chemokine Receptor 7 CD197 Antigen C-C CKR-7 EVI1	protein/ gene marker	diagnostic/prognostic		Adaptive Immune Pathways/ Regulation of Differentiation Inflammatory and Immune Pathways/ Immune Cell Recruitment		GeneCards/ NO MalaCards/ Bacterial sepsis	
53.CCR2	CCR2	C-C Motif Chemokine Receptor 2 CC-CKR-2 MCP-1-R CMKBR2 CD192 CCR2 Monocyte Chemoattractant Protein 1 Receptor Chemokine (C-C Motif) Receptor 2 C-C Chemokine Receptor Type 2 FLJ17032 CCR-2 Monocyte Chemoattractant Protein 1 Receptor MCP-1 Receptor CD192 Antigen C-C CKR-2 CCR2A CCR2B CCR2A CCR2B PCLUD	protein/gene marker	diagnostic/prognostic		Inflammatory and Immune Pathways/ Immune Cell Recruitment		GeneCards/ NO MalaCards/ No	
54.HIF1a	HIF1A	Hypoxia Inducible Factor 1 Subunit Alpha BHLHE78 PASB8 MOP1 Class E Basic Helix-Loop-Helix Protein 78 PAS Domain-Containing Protein 8 Member Of PAS Protein HIF-1alpha HIF1 Hypoxia Inducible Factor 1, Alpha Subunit (Basic Helix-Loop-Helix Transcription Factor) Basic-Helix-Loop-Helix-PAS Protein MOP1 Hypoxia-inducible Factor 1 Alpha HIF-1-Alpha Hypoxia Inducible Factor 1 Alpha Subunit Hypoxia-inducible Factor1alpha Member Of PAS Superfamily 1 ARNT Interacting Protein ARNT Interacting Protein HIF-1-ALPHA HIF-1alpha BHLHE78 HIF-1A	protein/ gene marker	diagnostic/prognostic		Vascular and Endothelial Pathways/ Vascular Integrity Hypoxia and Metabolic Pathways/ Metabolic Shift Epigenetic and Transcriptional Regulation Pathways/ Gene Expression Modulation		GeneCards/ NO MalaCards/NO	1. Diagnostic Biomarker: HIF-1a alone and as part of a composite measure was effective in distinguishing septic from non-septic patients (gene/protein Prognostic Biomarker: HIF-1a levels were predictive of ICU mortality and disease severity.
IKZF1									2. HIF-1a mRNA levels in leukocytes show potential as a diagnostic biomarker for sepsis severity (gene