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Role of Immune-Endothelial Cell Crosstalk in the Pathogenesis of Multiple Organ Dysfunction Syndrome (MODS): From Molecular Mechanisms to Therapeutic Targets

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1.1. Body Text

Multiple organ dysfunction syndrome (MODS) remains a leading cause of death among critically ill patients despite major advances in intensive care. Classical models have emphasized uncontrolled systemic inflammation as the predominant driver of organ failure. Accumulating evidence, however, indicates that dynamic, bidirectional interactions between immune cells and the vascular endothelium constitute a central pathogenic mechanism that initiates and sustains MODS (1).

Rather than serving as a passive barrier, the endothelium functions as an active immunological interface. In response to sepsis, trauma, major surgery, or ischemia-reperfusion injury, endothelial cells undergo rapid activation. This response promotes leukocyte adhesion and transmigration, local cytokine release, disruption of the coagulation cascade, degradation of the endothelial glycocalyx, and widespread microvascular dysfunction (2). Concurrently, activated neutrophils, monocytes, macrophages, platelets, and lymphocytes exacerbate endothelial injury by releasing proinflammatory mediators, extracellular vesicles, and neutrophil extracellular traps. The resulting feed-forward loop results in tissue hypoxia, mitochondrial dysfunction, impaired cellular bioenergetics, and progressive organ failure (3).

Recent advances in single-cell transcriptomics, multiomics profiling, and computational approaches have substantially refined our understanding of these cellular networks (4). Novel circulating biomarkers reflecting endothelial injury and immune activation are emerging as tools for earlier diagnosis, risk stratification, and individualized therapy. In parallel, interventions aimed at endothelial protection, immune modulation, glycocalyx preservation, restoration of mitochondrial function, and recovery of microcirculatory flow are being explored (5).

As critical care evolves toward precision medicine, elucidating the molecular circuits governing immune-endothelial crosstalk will be essential for translating mechanistic insights into effective clinical strategies. Future research should integrate advanced molecular profiling with computational modeling and rigorous prospective validation to identify actionable targets and refine patient-specific management (6).

A systems-level perspective that considers immune cells, the endothelium, metabolism, and the microcirculation as an interconnected network may shift critical care from purely supportive measures toward mechanism-based therapeutics, thereby improving outcomes in life-threatening critical illness.

Footnotes

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References

1. Xu X, Chen J, Feng Y, Zou C, Peng X, Wang Z, et al. Multiple organ dysfunction syndrome: molecular mechanisms and therapeutic strategies. *Signal Transduct Target Ther*. 2026;**11**(1). 274. [PubMed ID: 42443151]. [PubMed Central ID: PMC13365620]. https://doi.org/10.1038/s41392-026-02782-6.
2. Wang Y, Guan QN, Zhang ZJ, Zhang YM. Interaction between endothelial injury and immune response in septic shock: from basic research to clinical applications. *Front Physiol*. 2025;**16**. 1627008. [PubMed ID: 40980807]. [PubMed Central ID: PMC12443731]. https://doi.org/10.3389/fphys.2025.1627008.
3. Ardic N, Dinc R. Neutrophil extracellular traps and microglia/macrophages interactions in stroke: from thromboinflammation to immunotherapy. *Front Immunol*. 2026;**17**. 1752471. [PubMed ID: 41710878]. [PubMed Central ID: PMC12909230]. https://doi.org/10.3389/fimmu.2026.1752471.
4. Dabbagh A. Anesthesiomics: could a new name be coined for anesthesia? *Anesth Pain Med*. 2020;**10**(1). e100988. [PubMed ID: 32337174]. [PubMed Central ID: PMC7158238]. https://doi.org/10.5812/aapm.100988.
5. Zhang Z, Qiu X, Zeng X, Liu X, Lu J, Xu C, et al. Integrated multiomics and machine learning reveal mitochondrial immunometabolic networks in sepsis-associated encephalopathy. *Sci Rep*. 2025;**15**(1). 33572. [PubMed ID: 41023055]. [PubMed Central ID: PMC12480024]. https://doi.org/10.1038/s41598-025-18650-2.
6. Saavedra-Torres JS, Pinzón-Fernández MV, Nati-Castillo HA, Cadena Correa V, Lopez Molina LC, Gaitán JE, et al. Immunodynamic disruption in sepsis: mechanisms and strategies for personalized immunomodulation. *Biomedicines*. 2025;**13**(9):2139. [PubMed ID: 41007702]. [PubMed Central ID: PMC12467355]. https://doi.org/10.3390/biomedicines13092139.