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Mechanistic clues from urinary trypsin inhibitor in sepsis research

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Sepsis remains one of the greatest challenges in modern intensive care medicine, marked by severe systemic inflammation and multi-organ failure [1]. Despite years of research, effective targeted treatments are still unavailable, and death rates are still very high [2, 3]. This urgent, unmet need highlights the importance of new approaches that not only reduce excessive inflammation but also protect organ function.

In this context, the study by Dongmei Zhu, Binghui Yin, Danying Wu, Min Huang, and Suming Zhou, published in this issue of the *Central European Journal of Immunology*, provides strong evidence that urinary trypsin inhibitor (UTI, ulinastatin) could be a promising therapeutic option. UTI, a natural serine protease inhibitor already used in some inflammatory and critical care settings, was shown to reduce organ damage in a murine model of cecal ligation and puncture-induced sepsis and to inhibit the release of inflammatory cytokines in human THP-1 cells stimulated with bacterial lipoproteins.

The authors combined *in vivo* and *in vitro* approaches to analyze the molecular basis of UTI protective effects. Their results show that UTI reduces the release of pro-inflammatory mediators like TNF-α and IL-1β, while also modulating important intracellular signaling pathways, specifically the NF-κB/IκB and p38/MAPK pathways. By maintaining mitochondrial integrity in septic hearts and decreasing neutrophil infiltration in the lungs, UTI showed histological and biochemical evidence of organ protection. These findings broaden our understanding of UTI anti-inflammatory properties by emphasizing their effect on bacterial lipoprotein-driven innate immune activation. This study strongly aligns with earlier papers published in CEJI that highlighted the crucial role of these signaling pathways in sepsis and inflammatory responses, and it broadens our knowledge of sepsis immune mechanisms [4-7].

By elucidating how urinary trypsin inhibitor interferes with NF-κB and p38/MAPK signaling in experimental models of sepsis, this study provides valuable mechanistic insight that complements previous CEJI contributions on the regulation of inflammatory responses. On this basis, it has been selected as this issue's *Editor's Pick*.

References

1. Lelubre C, Vincent JL (2018): Mechanisms and treatment of organ failure in sepsis. Nat Rev Nephrol 14: 417-427.
2. Venet F, Monneret G (2018): Advances in the understanding and treatment of sepsis-induced immunosuppression. Nat Rev Nephrol 14: 121-137.
3. Giamarellos-Bourboulis EJ, Aschenbrenner AC, Bauer M, et al. (2024): The pathophysiology of sepsis and precision-medicine-based immunotherapy. Nat Immunol 25: 19-28.
4. Zhao Y, Li Y, Su M, Cai X (2024): Predictive value of miR-582-5p for onset of sepsis-induced acute kidney injury and its functional role during disease development. Cent Eur J Immunol 49: 383-392.
5. Zhang D, Cheng J, Cao D, Sheng K (2025): Innate immunosenescence and sepsis in the elderly: mechanisms and innate immune modulation strategies. Cent Eur J Immunol 50: 3-10.
6. Hu X, Hu A, Luo Y, et al. (2024): LncRNA HCP5 acts as a potential diagnostic biomarker and attenuates the inflammatory response in neonatal sepsis by targeting miR-138-5p/SIRT1. Cent Eur J Immunol 49: 216-226.
7. Fan H, He X, Tong H, Chen K (2024): Preventive effect of hyperforin on lipopolysaccharide-induced acute kidney injury and inflammation by repressing the NF-κB/miR-21 axis. Cent Eur J Immunol 49: 169-186.

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