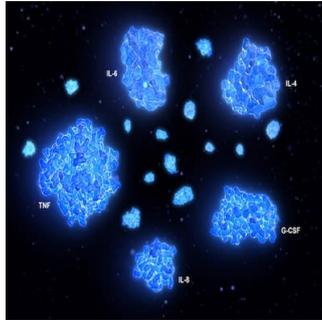


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## Decoding the Cytokine Storm in Sepsis



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Sepsis is a prominent cause of mortality in ICUs. Despite extensive research on the dynamics leading to sepsis, the role of cytokines—immune system molecules that can cause substantial harm to the body—has remained inadequately understood. While these proteins typically regulate inflammation, an overly aggressive immune response can result in a cytokine storm, leading to tissue damage, organ failure, and, ultimately, death.

Researchers from the University of Chicago Pritzker School of Molecular Engineering delved into a comprehensive exploration of sepsis and cytokine involvement by assessing gene expression across tissues and organs affected by sepsis in a mouse model. The study identified three specific pairs of cytokines responsible for the body's detrimental response to sepsis.

According to the Centers for Disease Control, one in three hospital deaths can be attributed to sepsis. Therefore, the importance of understanding the intricate factors of a dysregulated immune response like sepsis to comprehend the broader functioning of the immune system is critical to improve outcomes.

To gain insights into the body-wide response to sepsis, the research team measured gene expressions across various tissues in mouse models, spanning organs such as the brain, heart, and skin over multiple time points. The analysis revealed over 10,000 expressed genes across the body, encompassing nearly half of the mouse genome. The researchers then focused on six cytokines associated with sepsis, discovering that the damaging effects across tissues could be attributed to three specific cytokine pairs (IL-18, IFN- $\gamma$ , IL-1 $\beta$ ) when paired with TNF.

The team utilised whole-tissue gene expression analysis, termed PME-seq, and spatial transcriptomic analyses to map the effects of these cytokine pairs on almost 200 cell types throughout the body. The findings indicated a profound impact of sepsis on tissues, with non-lymphoid tissues recovering faster than lymphoid tissues—a potential explanation for lower survival rates in the subsequent years for sepsis survivors due to impaired immune system functioning.

The next research phase for the researchers involves investigating whether the identified cytokine pair principle holds true in human tissue. If confirmed, this insight could open up new avenues for sepsis therapy, potentially involving combinations of blockers specifically targeting these cytokines—a departure from previous unsuccessful attempts with single cytokine blockers.

Source: [Nature](#)

Image Credit: iStock

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