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Genome-Wide Association Study of Patients With Sepsis

Sepsis is a systemic inflammatory response to infections accompanied by organ dysfunction. Sepsis has a high mortality rate of about 30%. Approximately 189 cases of sepsis per 100,000 people are reported per year. Many genetic studies have identified gene variants associated with the development and outcomes of sepsis.

In this study, the researchers conduct the first genome-wide association study of 28-day survival in ICU patients with sepsis. The study was conducted in two stages. The first stage included 687 sepsis patients of European ancestry from the GEN-SEP network and 7.5 million imputed variants, while the second stage focused on the prioritised genetic variants and included 2,063 ICU sepsis patients of European ancestry and 701 African-American patients from the MESSI study. A meta-analysis of the two stages was then conducted, along with whole-blood transcriptomic, functional annotations and sensitivity analyses on the identified genes and variants.

Eleven independent variants were prioritised in the first stage. Ten of the 11 prioritised variants were followed up in the second stage. Three of these variants reached the genome-wide significance threshold, including a missense variant in *SAMD9. SAMD9* could play a critical role in the inflammatory response during tissue injury and apoptosis. Study authors hypothesise that *SAMD9* upregulation could potentially activate T cells and produce the accumulation of macrophages, conferring protection against the systemic dysregulation that occurs during sepsis.

The first genomic-wide association study of 28-day sepsis survival identified novel variants associated with reduced survival. However, more studies need to be performed with a larger sample size to better assess the genetic effects on sepsis survival and to validate these findings.

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Source: **Critical Care**

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