Three-dimensional label-free morphology of CD8+ T cells as a sepsis biomarker

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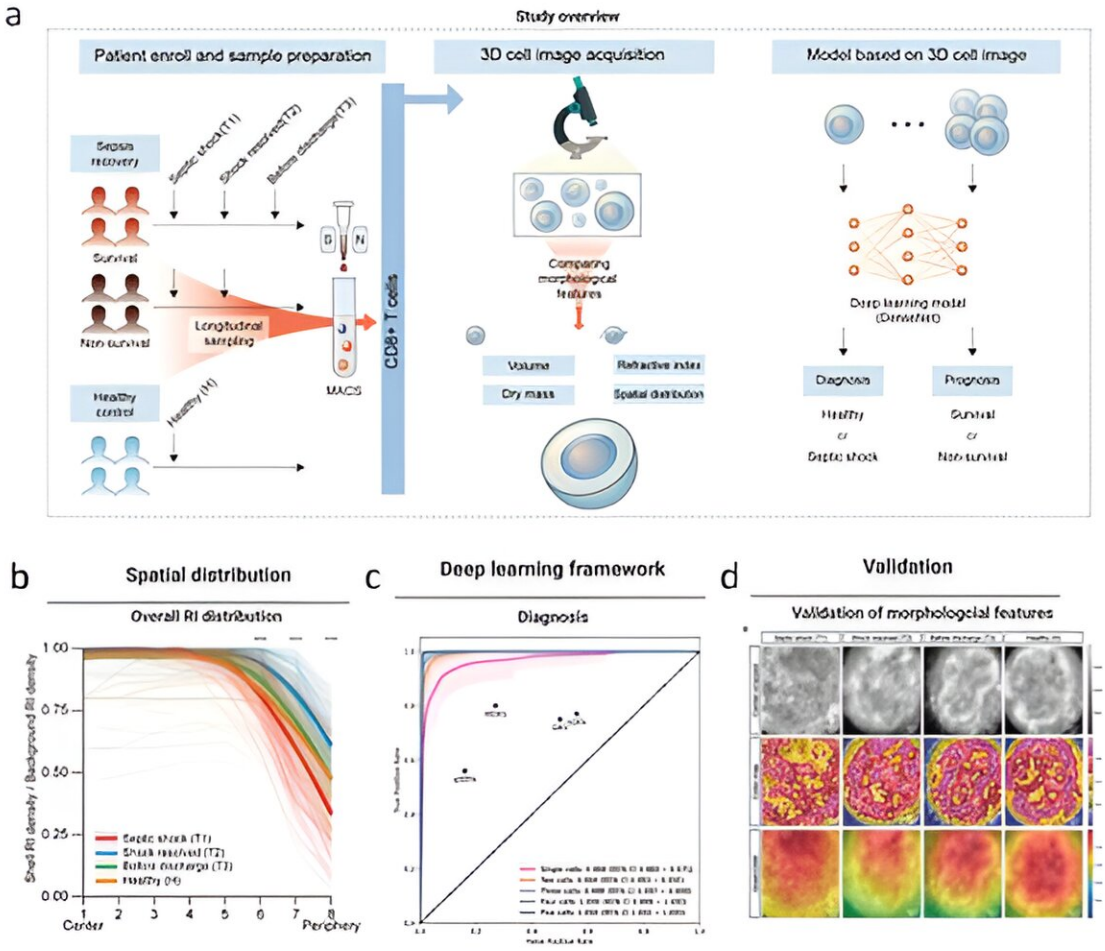

a, Schematic overview of the study workflow. Blood was sampled three times in the sepsis recovery cohort and once in the healthy control cohort. CD8+ T cells were extracted from the blood using a Magnetic Cell Separator (MACS). 3D cell images were acquired using holotomography. The morphological features of the

3D cell and the 2D sectioned images were obtained and compared. The spatial distribution within the cell was compared with that of the shell structure. Deep learning models for predicting the diagnosis and the prognosis of sepsis were developed and validated based on internal cell structure. PBMCs, peripheral blood mononuclear cells; ICU, intensive care unit. b, Spatial distribution within cells at each time point in longitudinal sepsis recovery and healthy control. Spatial distribution within cells in survival and non-survival groups at the first time point of sepsis recovery (T1) with the density of shell structure. c, The receiver operating characteristic (ROC) curve of the proposed method with one–five cells in predicting diagnosis and prognosis models. d, Validation of the morphological feature through correlation with clinical features and the visual explanation. Credit: MinDong Sung, Jong Hyun Kim, Hyun-Seok Min, Sooyoung Jang, JaeSeong Hong, Bo Kyu Choi, JuHye Shin, Kyung Soo Chung,Yu Rang Park

Sepsis is a life-threatening condition with high mortality rates due to the complex and variable immune response. Early diagnosis and prompt intervention are essential. Existing biomarkers such as CRP and PCT have limitations, including delayed responses. Efforts to address this delay include using RNA levels and single-cell sequencing, but these methods are time-consuming.

Immune cell morphology shows promise as a rapid biomarker. Morphological changes occur rapidly during inflammation and can provide an immediate insight into the immune response. However, the complexity of human immune responses is lacking in most studies using cell lines or healthy cells. Comprehensive investigations are needed to overcome these limitations and accurately capture immune cell dynamics in sepsis.

In a new paper published in *Light: Science & Applications*, a team of scientists led by Professor Yu Rang Park and Kyung Soo Chung from

Yonsei University College of Medicine, South Korea, and co-workers developed an artificial intelligence model using label-free 3D imaging to analyze changes in immune cell structure during healthy conditions, sepsis diagnosis, and sepsis recovery.

By comparing data between healthy controls and sepsis patients at different stages of recovery, the team identified significant changes in morphological characteristics such as $CD8^+$ T-cell volume and dry mass. More interestingly, this suggests that 3D label-free $CD8^+$ T cell structures can complement traditional diagnostic tools and provide valuable insights for clinical decision-making in sepsis cases.

Moreover, their suitability for periodic and repeated testing, requiring only a small blood sample, makes them a promising candidate for routine monitoring of sepsis patients.

"The technology developed in this study can be applied to a variety of patients with poor immune status as a model for predicting patient health. By using this breakthrough technology as a fast and highly accurate model to measure patient condition based on a small blood sample, it can be applied to various diseases, opening a new chapter in precision measurement and diagnosis," the scientists predict.

More information: MinDong Sung et al, Three-dimensional label-free morphology of CD8 + T cells as a sepsis biomarker, *Light: Science & Applications* (2023). DOI: 10.1038/s41377-023-01309-w

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