IntelliSep®

Read more about IntelliSep Biological Underpinnings Study

IntelliSep Biological Underpinnings Study

Biophysical Changes of Leukocyte Activation (and NETosis) in the Cellular Host Response to Sepsis

Study Objective

The objective of this study was to investigate the underlying mechanisms by which the biophysical measurements of leukocytes obtained in a new cellular host response test, the IntelliSep test, relate to the biology of immune dysregulation associated with sepsis, such as neutrophil extracellular trap (NET) formation.

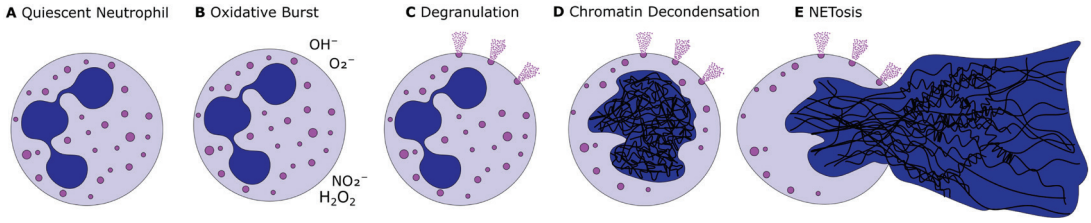


Diagram of neutrophil activation leading to neutrophil extracellular traps (NET)osis. Quiescent neutrophils **(A)** are stimulated by an agonist, resulting in the formulation of reactive oxygen species, known as oxidative burst, that aid in host defense **(B)**. Neutrophils undergo degranulation, resulting in the release of a variety of anti-microbial proteins from granules **(C)**. As activation proceeds, the nuclear chromatin of neutrophils decondenses from packed lobes into loosely arranged DNA **(D)**, and the neutrophil cell membrane eventually ruptures, releasing the DNA as NETs into the extracellular environment **(E)**.

Study Approach

In-vitro Studies

Phorbol myristate acetate (PMA), an agonist of neutrophils known to induce NET formation, was added to whole blood of healthy volunteers at concentrations of 0, 200, and 400 nM. Samples were then evaluated using the IntelliSep test.

Clinical Studies

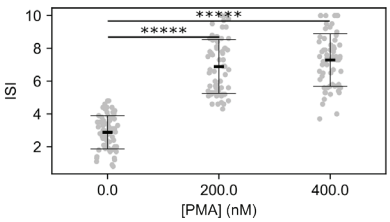
Plasma from a cohort of subjects was segregated into Control and Diseased populations and tested for levels of NET components (citrullinated histone (Cit-H3) DNA and neutrophil elastase (NE) DNA) using customized ELISA assays and correlated with the ISI (IntelliSep Index) scores from the same patient samples.*

* Lefrancais, *JCI Insight*, 2018.

IntelliSep Observations

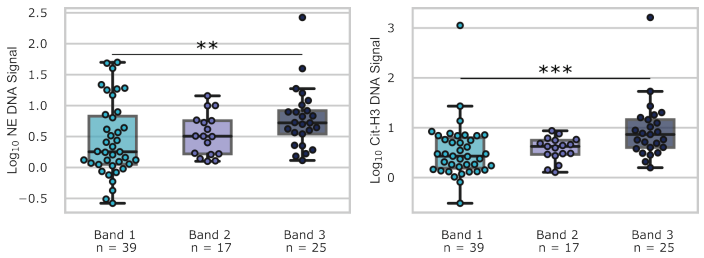
In-vitro Studies

Significant 2.3 and 2.5-fold increases in ISI values were observed when increasing concentrations of PMA in healthy blood from 0-200 nM and 0-400 nM, respectively (*****$p < 10^{-10}$).



Clinical Studies

Significant increases in NE DNA and Cit-H3 DNA were observed across ISI Interpretations Bands from Band 1 (low sepsis probability) to Band 3 (high sepsis probability) (**$p < 0.01$, *** $p < 0.001$).



Study Conclusions

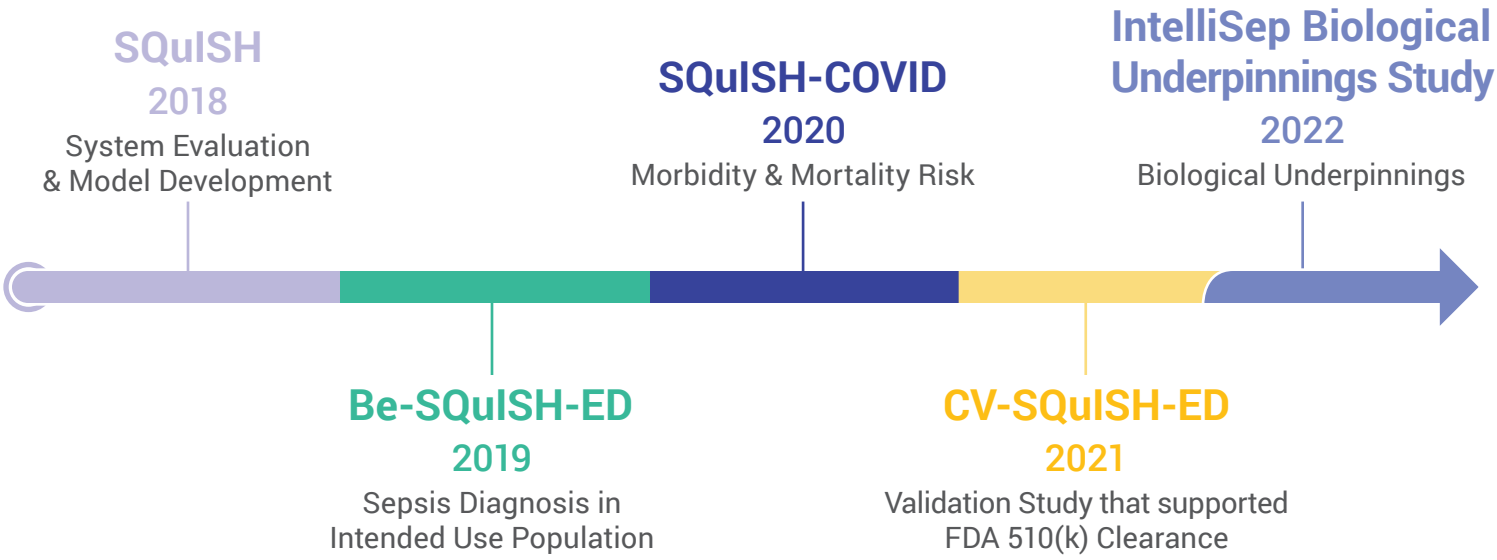
The IntelliSep test is associated with the biological processes of leukocyte activation and NETosis, providing a window into a patient's state of dysregulated immunity. As such, it may have the potential to aid ED physicians in early diagnosis of sepsis.

Sorrells M, Seo Y, Magnen M, et al., Biophysical Changes of Leukocyte Activation (and NETosis) in the Cellular Host Response to Sepsis. *Diagnostics* 2023; 13(8):1435.

IntelliSep®

IntelliSep Clinical Data

Supported by clinical studies* of over 2000 subjects, the FDA-cleared IntelliSep test is a first-of-its-kind host immune response diagnostic helping clinicians identify sepsis and get the right care to the right patients at the right time.



*Key Publications

Crawford K, et. al., Rapid Biophysical Analysis of Host Immune Cell Variations Associated with Sepsis. *Am J Respir Crit Care Med* 2018; 198: 280-282.

Guillou L, et al., Development and validation of a cellular host response test as an early diagnostic for sepsis. *PLoS One* 2021; 16: e0246980.

O'Neal HR, Jr., et. al., Assessment of a Cellular Host Response Test as a Sepsis Diagnostic for Those With Suspected Infection in the Emergency Department. *Crit Care Explor* 2021; 371 3: e0460.

O'Neal HR, Jr., et. al., Assessment of a cellular host response test to risk-stratify suspected COVID-19 patients in the Emergency Department setting. *PLoS One* 2022; 17(3): e0264220.

Sorrells M, Seo Y, Magnen M, et al., Biophysical Changes of Leukocyte Activation (and NETosis) in the Cellular Host Response to Sepsis. *Diagnostics* 2023; 13(8):1435.

U.S. Food and Drug Administration. IntelliSep test decision summary, 510(k) number K220991, December 20, 2022. https://www.accessdata.fda.gov/cdrh_docs/pdf22/K220991.pdf.

Cytovale®

Cytovale
150 Executive Park Blvd., Suite 4100
San Francisco, CA 94134 USA

cytovale.com