# ACCURACY OF SEPTICYTE® FOR DIAGNOSIS OF SEPSIS ACROSS A BROAD RANGE OF PATIENTS

Krupa Arun Navalkar, Dayle Sampson, Roy Davis, Thomas Yager, Richard B. Brandon
Immunexpress, Seattle, WA

Immunexpress
*the signature diagnostics for sepsis*

## INTRODUCTION

The purpose of the study was to demonstrate sepsis diagnostic performance of the biomarkers of SeptiCyte® across a broad range of critically ill patients, including adults, children and neonates, and in hospital locations other than ICU. SeptiCyte® LAB was the first immune-response sepsis diagnostic assay to gain FDA-clearance (K163260) and, as part of gaining this clearance, clinical validation was performed on adult patients admitted to intensive care (ICU) only [1]. We therefore performed an *in silico* analysis across a broad range of patients using the SeptiCyte® host immune response biomarkers and algorithm.

## METHODS

Peripheral blood gene expression data, including public and private datasets, were chosen based on quality, annotation, and clinical context for the intended use of SeptiCyte®. Multiple comparisons were performed within datasets to better understand the diagnostic performance in certain cohorts including healthy subjects. Diagnostic performance was determined using Area Under Curve (AUC).

## RESULTS

Table 1 shows a summary of the selected datasets and patients, including number of datasets (N=22) and comparisons (N=55), number of cases (N=2234) and controls (N=2089) used in comparisons, patient category and hospital location. SeptiCyte® AUCs for the three groups of adults, pediatric / neonates and adult / pediatric and were 0.88, 0.87, and 0.85 respectively, which is similar to that previously reported for adults only (0.82 – 0.89) [1].

Table 2 shows more details of the patient population comparisons made and the AUC results, including sepsis vs SIRS, sepsis vs healthy, bacterial sepsis vs control, severe viral infection (ICU) vs control, Gram positive sepsis vs control and Gram negative sepsis vs control. Respective mean AUCs for these comparisons were 0.87, 0.88, 0.86, 0.97, 0.84 and 0.88. In this instance "Control" samples consisted of a mix of patients without sepsis, including healthy subjects.

Figures 1 and 2 show box and whisker plots (A) and ROC curves (B) for example datasets, including E-MTAB1548 [2] and GSE69528 [3]. The plots demonstrate good differentiation of adult patients with sepsis from those with SIRS (E-MTAB1548), and from healthy subjects with diabetes (GSE69528) using SeptiCyte® biomarkers.

**Figure 1 – Example Dataset – E-MTAB1548**

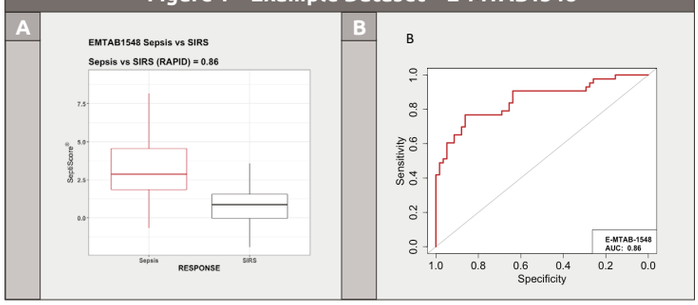


**Figure 1**
Box and whisker plot (A) and ROC curve (B) demonstrating SeptiCyte® performance in dataset E-MTAB1548. Comparison was 43 adult post-surgical ICU patients with septic shock vs 58 ICU adult patients with SIRS.

**Figure 2 – Example Dataset – GSE69528**

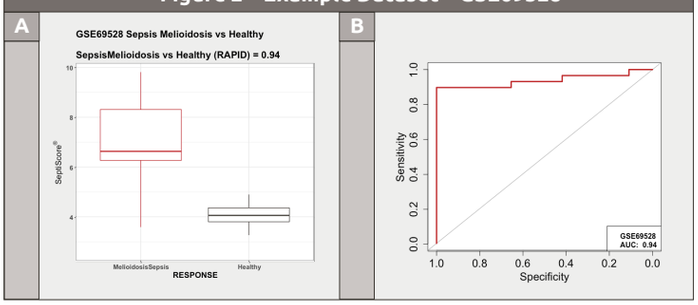


**Figure 2**
Box and whisker plot (A) and ROC curve (B) demonstrating SeptiCyte® performance in dataset GSE69528. Comparison was 29 adult patients with melioidosis vs 55 diabetic (healthy) subjects (hospital location not known).

| Table 1: Summary of Datasets, Patients and SeptiCyte® Diagnostic AUC | | | | |
|---|---|---|---|---|
| **# Datasets / Comparisons** | **Case / Control** | **Patients** | **Location** | **Mean AUC** |
| 13 / 35 | 1640 / 987 | Adults | ICU, Ward, ED | 0.88 |
| 7 / 16 | 417 / 589 | Neonatal / Pediatric | ICU, Ward, ED | 0.87 |
| 2 / 4 | 177 / 513 | Adults+Pediatric | Ward | 0.85 |
| **22 / 55** | **2234 / 2089** | | | **0.87** |

| Table 2: Detail of Comparisons, Datasets, Patients and SeptiCyte® Diagnostic AUC | | | | |
|---|---|---|---|---|
| **Comparisons** | **# Datasets** | **# Case / Controls** | **Patients** | **Mean AUC** |
| **Sepsis vs SIRS** | 6 | 670 / 516 | Adults | 0.84 |
| | 2 | 114 / 293 | Pediatric / Neonates | 0.91 |
| | 2 | 177 / 513 | Adults / Pediatric | 0.85 |
| | | | | **0.87** |
| **Sepsis vs Healthy** | 9 | 970 / 471 | Adults | 0.92 |
| | 5 | 303 / 296 | Pediatric / Neonates | 0.84 |
| | | | | **0.88** |
| **Bacterial Sepsis vs Control** | 8 | 511 / 399 | Adults | 0.86 |
| | 7 | 375 / 513 | Pediatric / Neonates | 0.86 |
| | 2 | 177 / 513 | Adults / Pediatric | 0.85 |
| | | | | **0.86** |
| **Severe Viral vs Control** | 3 | 41 / 99 | Adults | 0.95 |
| | 1 | 5 / 29 | Pediatric / Neonates | 0.99 |
| | | | | **0.97** |
| **Gram Positive vs Control** | 1 | 17 / 16 | Adults | 0.83 |
| | 2 | 79 / 144 | Pediatric/ Neonates | 0.82 |
| | 1 | 52 / 282 | Adults / Pediatric | 0.87 |
| | | | | **0.84** |
| **Gram Negative vs Control** | 2 | 47 / 71 | Adults | 0.88 |
| | | | | **0.88** |

## References


[1] Miller III, R. R. et al. AJRCCM 198: 903–913, 2018.

[2] Almansa, R. et al. Transcriptomic evidence of impaired immunoglobulin G production in fatal septic shock. Journal of Critical Care 29, 307–309 (2014).

[3] Conejero, L. et al. The Blood Transcriptome of Experimental Melioidosis Reflects Disease Severity and Shows Considerable Similarity with the Human Disease. The Journal of Immunology 195, 3248–3261 (2015).




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## CONCLUSIONS

- **Similar mean AUCs in adult and pediatric patients, across hospital locations and with various sepsis etiologies, suggests that the SeptiCyte® signature has broad diagnostic utility in this heterogenous sepsis patient population.**
- **The SeptiCyte® signature has now been translated to the near-patient testing platform Biocartis Idylla™ (as SeptiCyte® RAPID) which promises rapid (~1 hour) diagnosis of sepsis in a broad patient population following further validation.**