A 29-mRNA host response signature accurately distinguishes bacterial and viral infections among Emergency Department patients

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Introduction

Rapid diagnosis of acute infections and sepsis is critical in Emergency Departments (EDs). Current tests have slow turnaround times, low sensitivities, and/or signals from contaminant or commensal organisms. Empirical antimicrobial treatment may result in severe adverse events and contributes to antimicrobial resistance. Inflammatix's HostDx Sepsis is a novel host response assay which aims to address this unmet need. HostDx Sepsis measures 29 human mRNA targets and employs advanced machine learning to predict the likelihoods of both bacterial and viral infections.

Methods

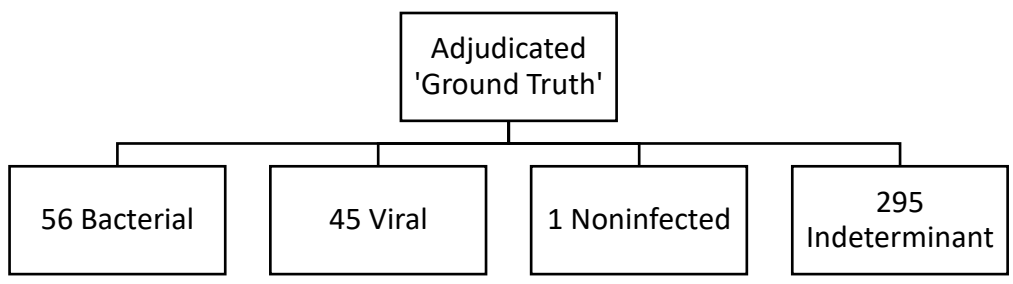
We evaluated HostDx Sepsis in a prospective, non-interventional study in the EDs of 6 sites in Greece (PROMPT study NCT03295825). 397 adult patients presenting with suspected acute infection and at least one vital sign change were enrolled. Whole blood RNA was quantified using NanoString nCounter. Predicted probabilities of bacterial and viral infection were calculated (BVN-2 algorithm). Patients were adjudicated in a retrospective chart review by 3 independent infectious disease specialists blinded to HostDx Sepsis results.

Results

Patient Characteristics

Characteristic	No. Patients (%)
Sex	
Female	203 (51%)
Male	194 (49%)
Mean Age	62.1 (SD 21.9)
Ethnicity	
White, Non-Hispanic	397 (100%)
Immune Status	
Immunocompetent	330 (83%)
Immunocompromised	63 (16%)
Unknown	4 (0.01%)

Results of Physician Chart Review



HostDx Sepsis and Procalcitonin Performance

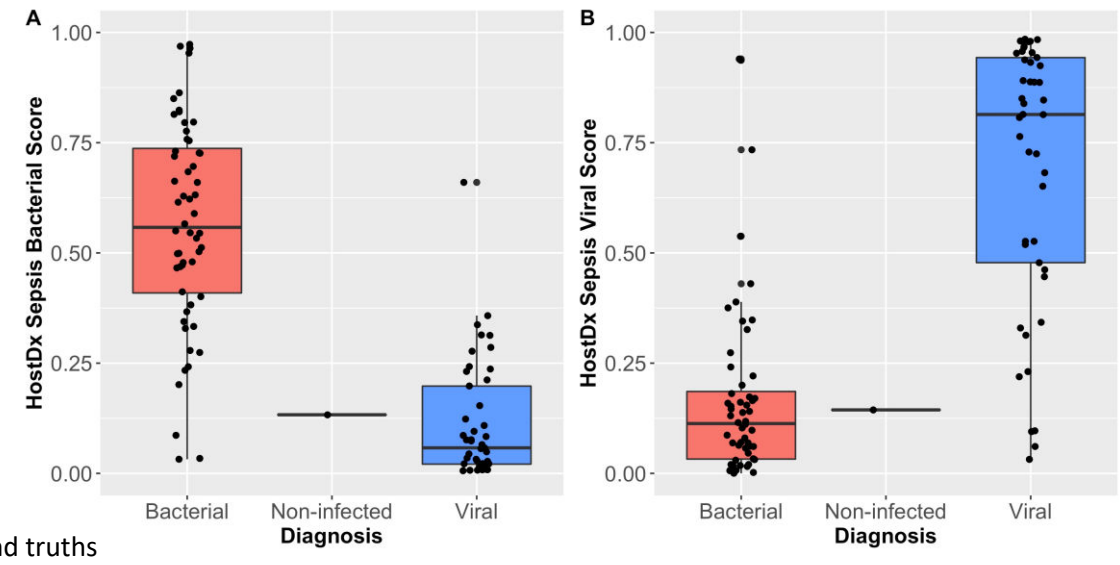
Among Patients with Known Ground Truths (n=102)

	Bacterial AUROC[1]	Viral AUROC[2]
HostDx Sepsis	0.94 (95%CI 0.90-0.99)	0.89 (95% CI 0.83-0.96)
Procalcitonin[3]	0.88 (95% CI 0.79-0.96)	N/A

[1]Bacterial vs. Viral and Non-infected
[2]Viral vs. Bacterial and Non-infected
[3]Procalcitonin results available for only 69/102 patients with known ground truths

HostDx Sepsis Bacterial and Viral Scores

Among Patients with Known Ground Truths (n=102)



HostDx Sepsis Performance Segmented by Prediction Bands Using Previously-Established Cutoffs (BVN-2 Algorithm)

Among Patients with Known Ground Truths (n=102)

		Adjudicated Ground Truth		HostDx Sepsis Performance Characteristics Per Band			
		Bacterial	Not Bacterial	% in Band	Sens.	Spec.	LR
HostDx Sepsis Predictions	Very Likely Bacterial	31	1	**31%**	55%	**98%**	**25**
	Possibly Bacterial	17	2	19%	30%	96%	7.0
	Unlikely Bacterial	5	13	18%	91%	28%	0.32
	Very Unlikely Bacterial	3	30	**32%**	**95%**	65%	**0.082**

Procalcitonin Performance Segmented by Prediction Bands Adopted from ProACT Study (Huang et al., *NEJM*, 2018)

Among Patients with Known Ground Truths and Procalcitonin Results (n=69)

		Adjudicated Ground Truth		Procalcitonin Performance Characteristics Per Band			
		Bacterial	Not Bacterial	% in Band	Sens.	Spec.	LR
Procalcitonin Predictions[1]	>0.5	22	2	**35%**	59%	**94%**	**9.5**
	0.25-0.5	7	0	10%	19%	100%	∞
	0.1-0.25	3	3	8.7%	92%	9.4%	0.86
	<0.1	5	27	**46%**	**86%**	84%	**0.16**

[1]Procalcitonin results available for only 69/102 patients with known ground truths

Discussion

Our results indicate that HostDx Sepsis identifies bacterial and viral infections with high accuracy. HostDx Sepsis is currently developed as a rapid point-of-care device with a turnaround-time of less than 30 minutes. HostDx Sepsis may therefore assist ED doctors in making appropriate treatment decisions earlier, towards the ultimate goal of antimicrobial stewardship.

Further Reading

1. Sweeney TE et al.. "Robust classification of bacterial and viral infections via integrated host gene expression diagnostics." *Science Translational Medicine.* Jul 2016.
2. Mayhew MB et al. "A generalizable 29-mRNA neural-network classifier for acute bacterial and viral infections." *Nature Communications*. In Press.
3. Gunsolus et al., "Diagnosing and Managing Sepsis by Probing the Host Response to Infection: Advances, Opportunities, and Challenges." *Journal of Clinical Microbiology*. Jul. 2019

Acknowledgments

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