

Diagnosis of acute infection and sepsis: the Inflammatrix HostDx™ tests



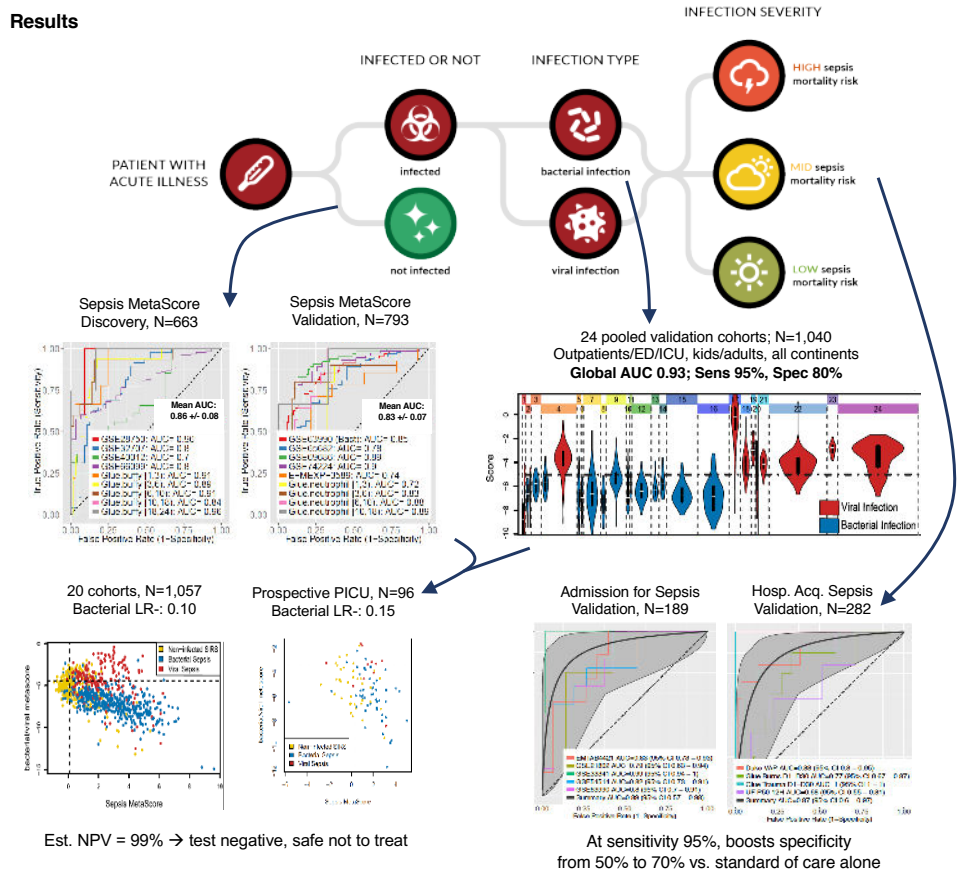
TE Sweeney, MD, PhD, J Romanowsky, MBA, P Khatri, PhD
863 Mitten Ave, Suite 101; Burlingame, CA 94010. info@inflammatrix.com

Overview

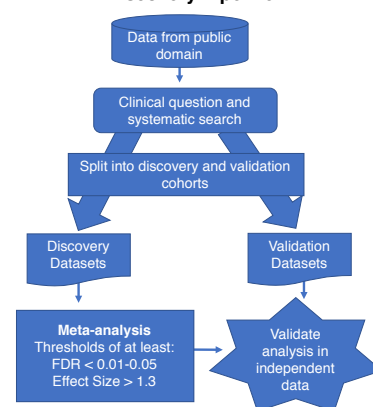
Acute bacterial and viral infections are difficult to diagnose; as many as half of all antibiotics are prescribed inappropriately. Further, some infections lead to sepsis, defined as a dysregulated host response to infections. However, approximately 70% of infections in hospital inpatients are missed by the gold standard (blood culture) since most infections do not result in bacteremia. Infections and sepsis are hard to diagnose, and thus hard to treat.

Using our custom informatics pipeline, we have derived diagnostic gene sets and algorithms that can diagnose the presence, type, and severity of acute infections. Improved diagnosis of infections could decrease hospital/ICU length of stay, improve outcomes, and reduce unnecessary antibiotic administration. We are currently developing the test into a rapid whole blood-based diagnostic for clinical use. Applications are imagined in the clinic, ED, ICU, and in post-surgical care.

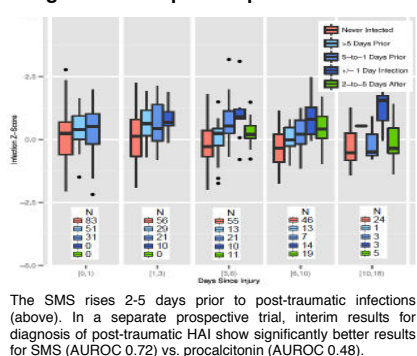
Results



Discovery Pipeline



Diagnosis of Hospital-Acquired Infections



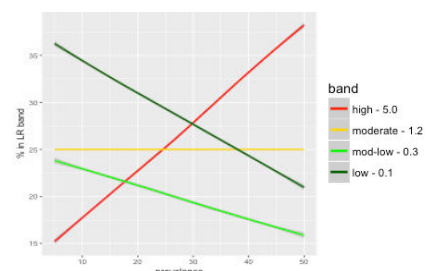
HostDx™ Sepsis

- Multiplex quantitative gene expression
- Rapid TAT (~60 min)
- Sample-to-answer, moderate complexity
- Device/manufacturing partnerships

Example Inpatient Readout: LR band + numeric score

Bacterial Infection		Viral Infection		30-Day Mortality
Low (0.1)		Low (0.1)		Low (0.1)
Low-Mod (0.3)		Low-Mod (0.4)		Low-Mod (0.25)
Moderate (1.2)	1.5 Mod	Moderate (1.4)	6.5 High	Moderate (1.2)
High (5.0)		High (6.0)		High (4.5)
				0.1 Low

Band distribution vs. prevalence @ AUC = 0.85



References

- Sweeney TE, Shidham A., Wong HR & Khatri P. A comprehensive time-course-based multicohort analysis of sepsis and sterile inflammation reveals a robust diagnostic gene set. *Sci Transl Med* 7, 287ra271, (2015).
- Sweeney TE & Khatri P. Benchmarking Sepsis Gene Expression Diagnostics Using Public Data. *Crit Care Med* 45, 1-10, (2017).
- Sweeney TE, Wong HR & Khatri P. Robust classification of bacterial and viral infections via integrated host gene expression diagnostics. *Sci Transl Med* 8, 346ra391, (2016).
- Sweeney TE, Haynes WA, Vallania F, Ioannidis JP & Khatri P. Methods to increase reproducibility in differential gene expression via meta-analysis. *Nucleic Acids Res*, (2016).
- Sweeney TE *et al.* Validation of the Sepsis MetaScore for Diagnosis of Neonatal Sepsis. *J Pediatric Infect Dis Soc*, (2017).
- Sweeney TE *et al.* Mortality prediction in sepsis via gene expression analysis: a community approach. *bioRxiv* (2016).

Acknowledgments

The authors wish to thank their numerous collaborators and co-authors, and the employees of Inflammatrix.

This research was developed with funding from the Defense Advanced Research Projects Agency (DARPA). The views, opinions and/or findings expressed are those of the author(s) and should not be interpreted as reflecting the official views or policies of the Department of Defense or the U.S. Government.