

# Host-Based Approach to Addressing Antibiotic Misuse One Prototype Solution

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Disclosure: Clinical Site for MeMed FDA Study; Participated in Advisory Board Meeting  
Advisory Boards and conducted sponsored research for Roche, Inflammatix, Cepheid, Orasure



# The Challenge: Diagnostic Uncertainty Driving Abx Misuse



## *To Treat or Not To Treat?*

...Because bacterial and viral infections are often clinically indistinguishable



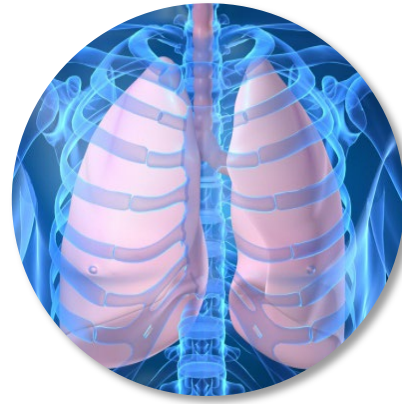
# The Problem: Limitations of Current Diagnostic Solutions



**Prolonged time  
to results**



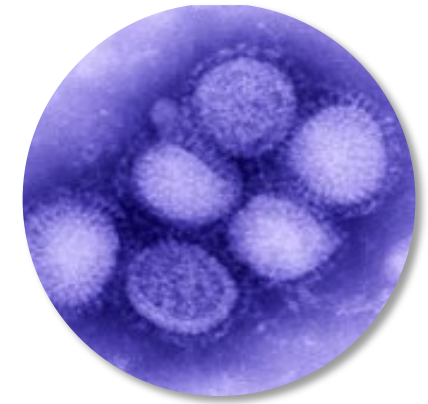
**Difficult to use**



**Require access  
to infection site**

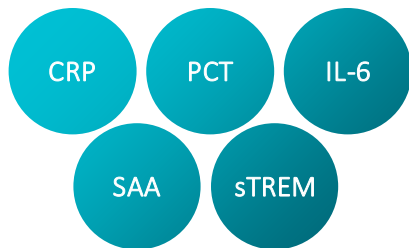


**False alarms due  
to colonizers**

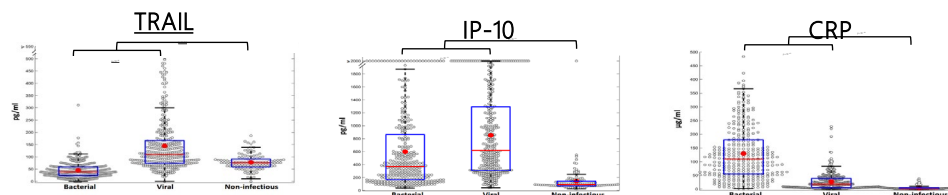
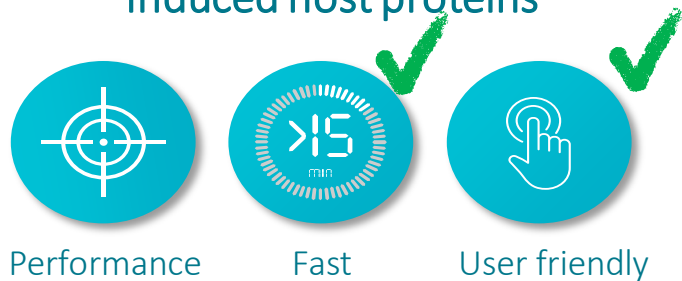


**Poor performance  
to evolving  
pathogens**

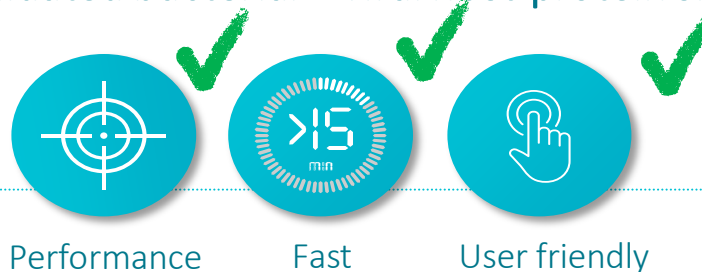
# Leveraging Host Response to Infection Prototype Platform



Individual predominantly bacterial-  
induced host proteins



Validated bacterial + viral host-protein signature



## blood

Gene expression patterns in blood leukocytes discriminate patients with acute infections

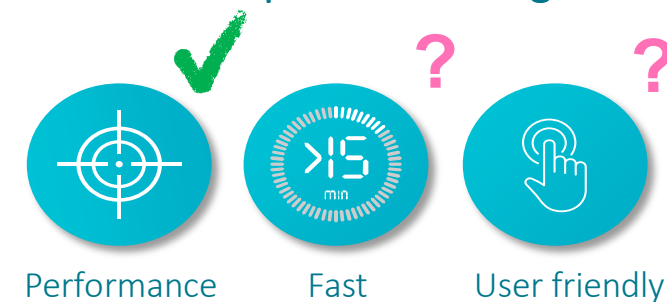
Octavio Ramilo,<sup>1,2</sup> Windy Allman,<sup>1</sup> Wendy Chung,<sup>1,2</sup> Asuncion Mejias,<sup>1,2</sup> Monica Ardura,<sup>1,2</sup> Casey Glaser,<sup>1</sup> Knut M. Wittkowski,<sup>3</sup> Bernard Piqueras,<sup>1</sup> Jacques Banchereau,<sup>1</sup> A. Karolina Palucka,<sup>1</sup> and Damien Chaussabel<sup>1</sup>

## Cell Host & Microbe

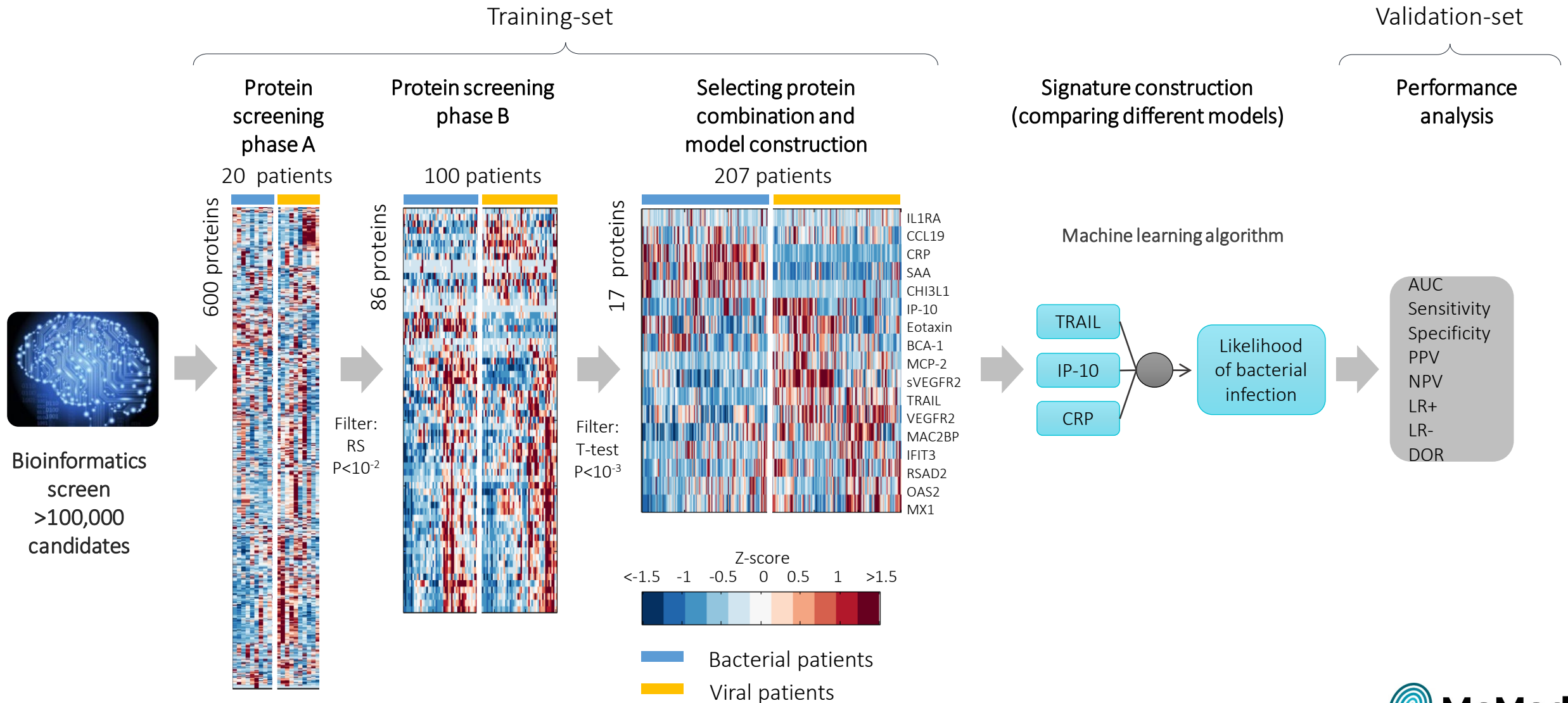
Gene Expression Signatures Diagnose Influenza and Other Symptomatic Respiratory Viral Infections in Humans

Aimee K. Zaas,<sup>1,3,9</sup> Minhua Chen,<sup>2,9</sup> Jay Varkey,<sup>1</sup> Timothy Veldman,<sup>3</sup> Alfred O. Hero III,<sup>4</sup> Joseph L. Yongsheng Huang,<sup>5</sup> Ronald Turner,<sup>2</sup> Anthony Gilbert,<sup>1</sup> Robert Lambkin-Williams,<sup>6</sup> N. Christine Ole Stephen Kingsmore,<sup>7</sup> Lawrence Carin,<sup>7</sup> Christopher W. Woods,<sup>1,3,7</sup> and Geoffrey S. Ginsburg<sup>1\*</sup>

Proof-of-concept host-RNA signatures



# The Curiosity Study (n=1,002, prospective) Discovery and Preliminary Validation of BV™

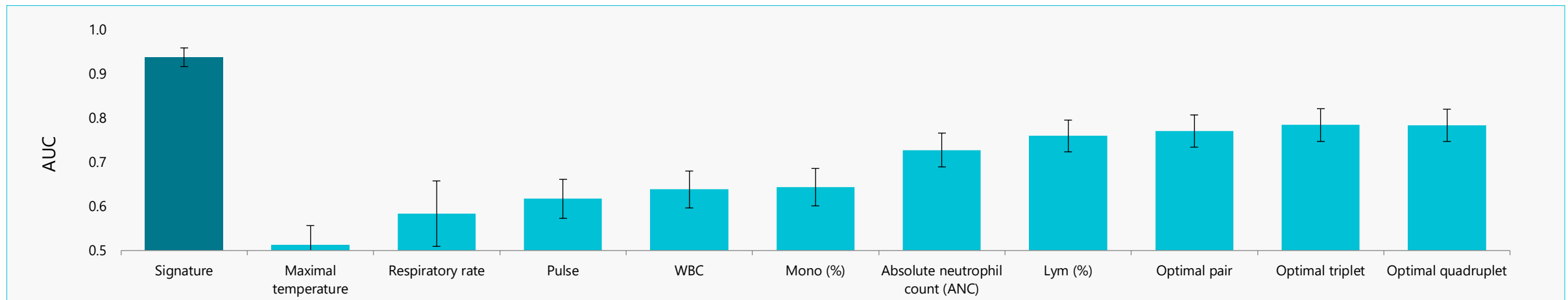
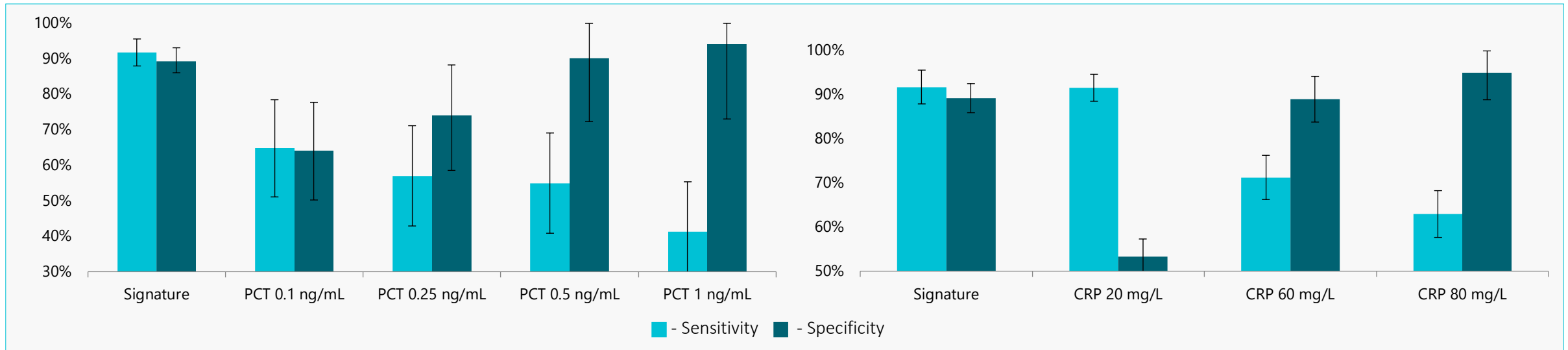




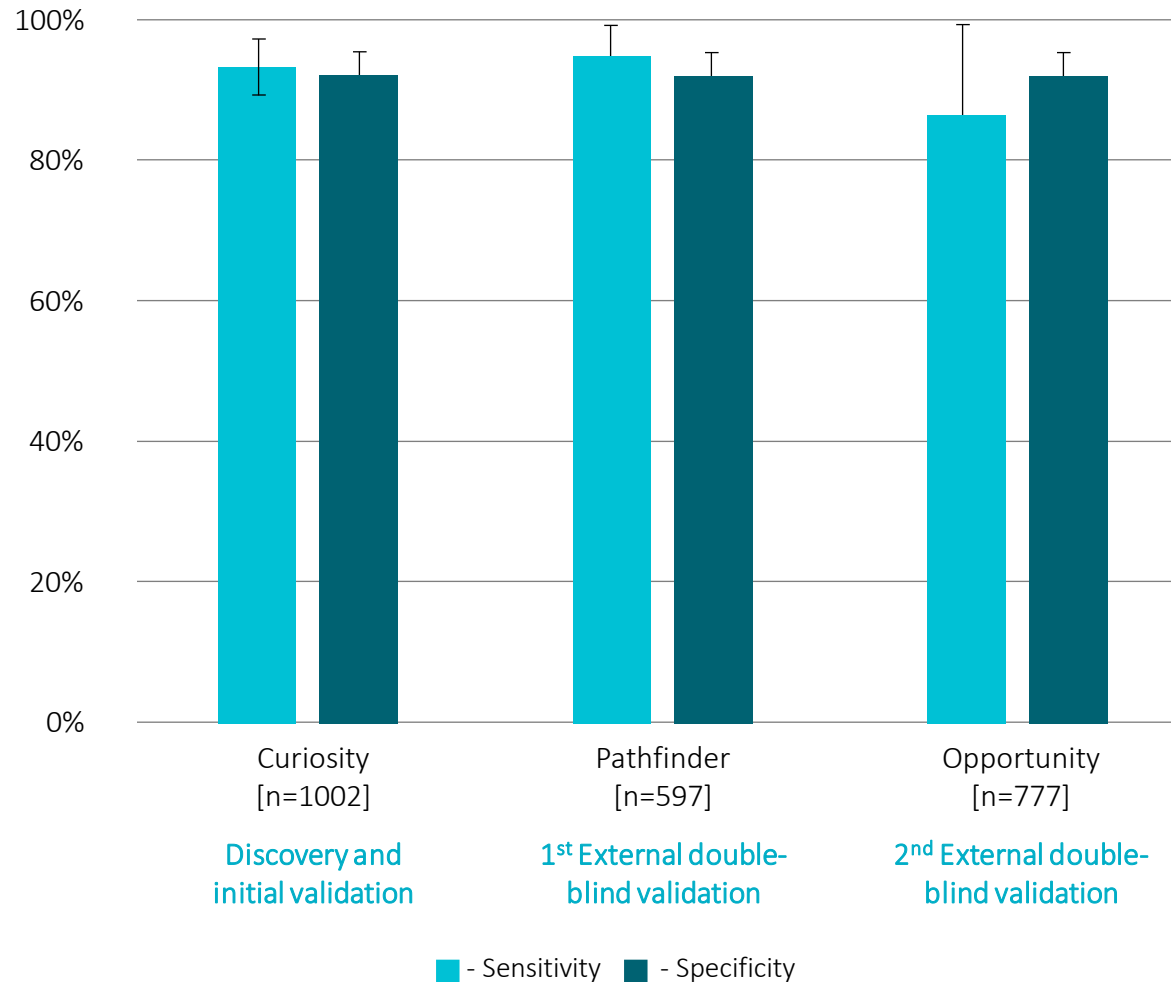
# Comparator Method for Etiology: Adjudication by Expert Panel



# BV™ Outperformed Routine Parameters & Biomarkers



# External Double-Blind Validation >1,300 Patients (2013-2017)



PLOS ONE

RESEARCH ARTICLE

## A Novel Host-Proteome Signature for Distinguishing between Acute Bacterial and Viral Infections

Kfir Oved<sup>1\*</sup>, Asil Cohen<sup>1</sup>, Olga Boico<sup>1</sup>, Roy Navon<sup>1</sup>, Tom Friedman<sup>1,2</sup>, Liat Elshstein<sup>1,3</sup>, Or Kriger<sup>1,4</sup>, Ellen Bamberger<sup>1,3,5</sup>, Yura Fonar<sup>1,6</sup>, Renata Yacobov<sup>1</sup>, Ron Wolchinsky<sup>6</sup>, Gali Denkberg<sup>7</sup>, Yaniv Dotan<sup>3,8</sup>, Amit Hochberg<sup>1</sup>, Yoram Reller<sup>6</sup>, Moti Grupper<sup>3,9</sup>, Isaac Srugo<sup>3,5</sup>, Paul Feigin<sup>10</sup>, Malka Gorfine<sup>10</sup>, Irina Chistyakov<sup>3,5</sup>, Ron Dagan<sup>11</sup>, Adi Klein<sup>1</sup>, Israel Potasman<sup>3,8</sup>, Eran Eden<sup>1\*</sup>

PEDIATRICS

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

## Validation of a Novel Assay to Distinguish Bacterial and Viral Infections

Isaac Srugo, MD,<sup>1,3</sup> Adi Klein, MD,<sup>1</sup> Michal Stein, MD,<sup>7</sup> Orrit Golan Shany, PhD,<sup>7</sup> Noga Kerem, MD,<sup>3,8</sup> Irina Chistyakov, MD,<sup>3,5</sup> Jacob Genizi, MD,<sup>7</sup> Oded Glazer, MD,<sup>7</sup> Liat Yaniv, MD,<sup>3</sup> Alina German, MD,<sup>7</sup> Dan Miron, MD,<sup>1</sup> Yael Shachor-Meyouhas, MD,<sup>1</sup> Ellen Bamberger, MD,<sup>1,3,5</sup> Kfir Oved, PhD,<sup>1</sup> Tanya M. Gottlieb, PhD,<sup>1</sup> Roy Navon, MSc,<sup>1</sup> Mental Pac, MD,<sup>1</sup> Liat Elshstein, MD,<sup>1</sup> Olga Boico, PhD,<sup>1</sup> Gali Kronenfeld, MSc,<sup>1</sup> Eran Eden, PhD,<sup>1</sup> Robert Cohen, MD,<sup>3</sup> Helène Chappuy, MD,<sup>1</sup> François Angoulvant, MD,<sup>1</sup> Laurence Lacroix, MD,<sup>1</sup> Alain Gervais, MD<sup>1</sup>

THE LANCET  
Infectious Diseases

Articles

A host-protein based assay to differentiate between bacterial and viral infections in preschool children (OPPORTUNITY): a double-blind, multicentre, validation study

Charita S van Houten, Joris A M de Groot, Adi Klein, Isaac Srugo, Irina Chistyakov, Wouter de Waal, Giemens S Meijssen, Wim Aerts, Tom F W Weijts, Yael Shachor-Meyouhas, Michal Stein, Elisabeth A M Sanders, Louis J Bont



# BV™ When and Where Needed

## MeMed BV™



One cartridge per patient

Contains all reagents necessary for the test

Easy sample loading

Contains reservoir for the biological waste

Amenable to large scale manufacturing

## MeMed Key™



Central lab precision

Rapid results (<15 min)

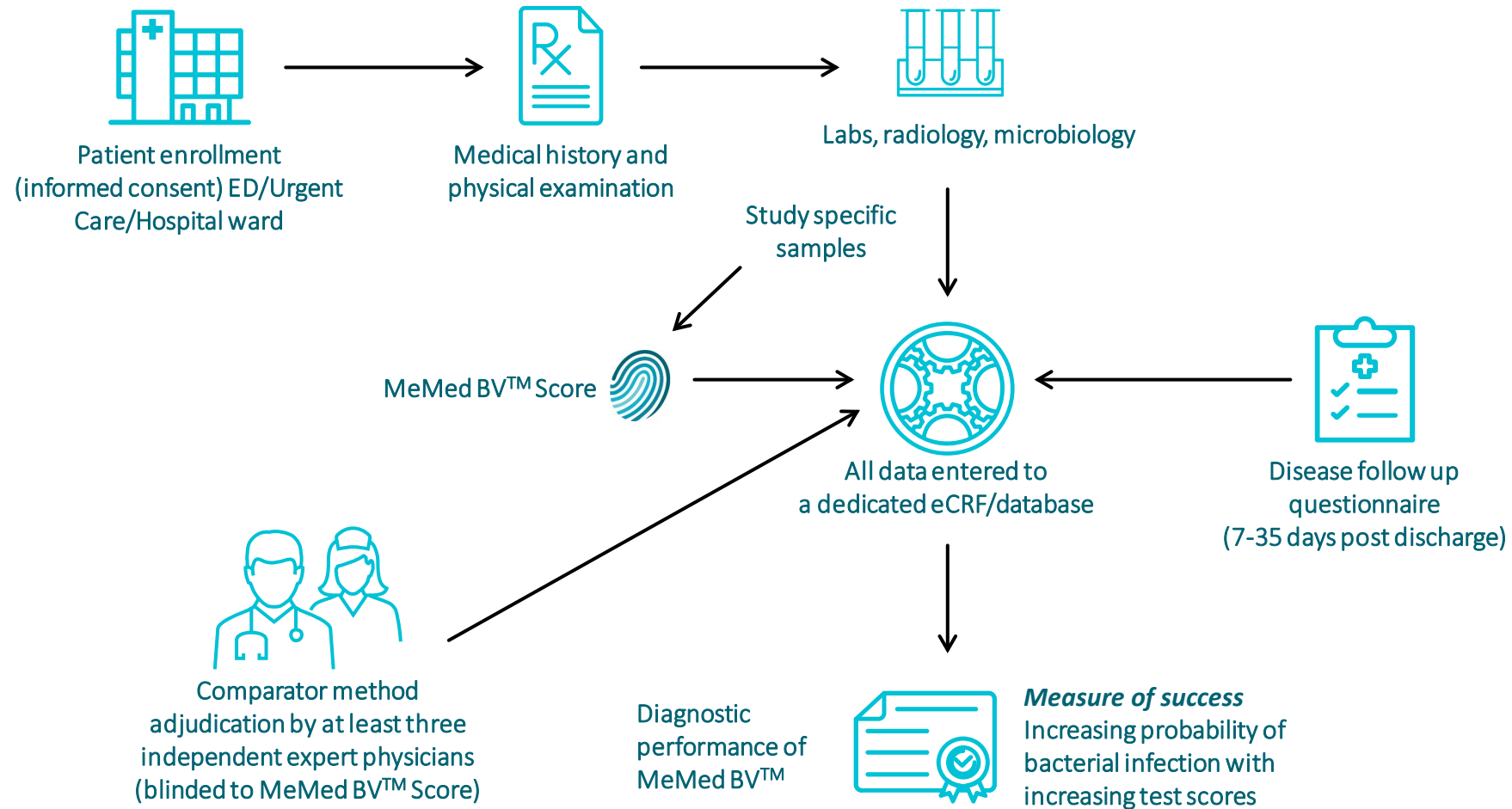
Compatible with multiple sample types

Wide dynamic range (pg/ml to ug/ml)

Easy to use



# Apollo: Clinical Study to Support FDA Clearance (in progress)



# Prototype Solution to address Antibiotic Misuse



***Short time to results***



***Easy to use***



***Inaccessible infection diagnosis***



***Robust to colonizers***



***Robust to evolving pathogens***



***High performance***



***Strain information***





# Multiple Other Promising Assays are in Various Stages of Development: e.g. Inflammatrix

HostDx Sepsis:  
Whole blood testing (B, V and Severity)

Multi-cohort transcriptome analysis



Includes multiple ages, severities, infection types, sampling times, geographies, etc.

Best-in-class gene selection

**SIRS vs Sepsis:**  
11 mRNAs

SCIENCE TRANSL MED 2015

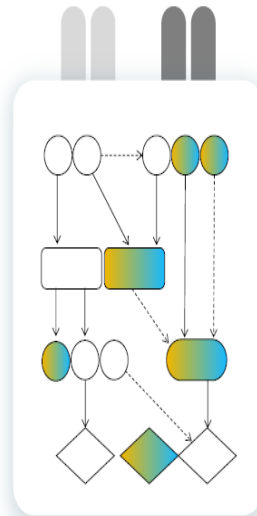
**Bacterial vs Viral:**  
7 mRNAs

SCIENCE TRANSL MED 2016

**Thirty-day Mortality:**  
11 mRNAs

NATURE COMMS 2018

Final HostDx **SEPSIS**  
29-mRNA set



Inflammatrix

## HostDx **FEVER**

Fingerstick testing for outpatient clinics

Test performance at AUROC 0.93 broken down by band (at 30% bacterial prevalence) and recommended actions

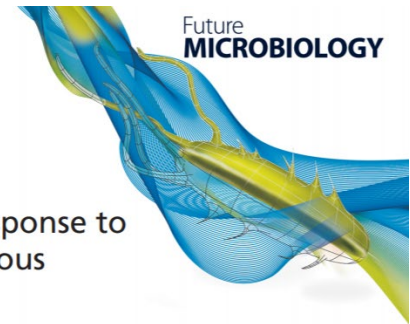


Host Band	Likelihood ratio for bacterial infection	% of patients assigned to band	Recommended action
<b>Viral</b>	0.1	59%	Oseltamivir or home/rest
<b>Equivocal</b>	1.2	14%	Monitor/retest, consider antibiotics
<b>Bacterial</b>	10	27%	Antibiotics recommended

\* *In silico* analysis test performance. Prospective studies and cartridge development in progress  
Shared with permission from O. Lisenfeld, Inflammatrix.

Inflammatrix 25

## Movement of these assays through the FDA clearance and evaluation in real-world practice is the critical next step



Editorial

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## Unlocking the power of the host response to improve the management of infectious diseases

Kfir Oved<sup>\*1</sup>, Eran Eden<sup>1</sup> & Tanya M Gottlieb<sup>\*\*1</sup><sup>1</sup>MeMed, 5 Nahum Het Street, Haifa, Israel<sup>\*</sup>Author for correspondence: [kfiroved@me-med.com](mailto:kfiroved@me-med.com)<sup>\*\*</sup>Author for correspondence: [tanya.gottlieb@me-med.com](mailto:tanya.gottlieb@me-med.com)

“The fundamental value of a diagnostic or prognostic test lies in its ability to accurately and clearly guide patient treatment and improve health outcomes”


First draft submitted: 3 June 2019; Accepted for publication: 28 November 2019; Published online: 18 December 2019

**Keywords:** actionable infectious disease tests • antimicrobial resistance • bacterial versus viral diagnostic • CRP • host biomarker • immune-protein signature • IP-10 • point-of-care platform • sepsis • TRAIL

# Thank you



## Host-Based Peripheral Blood Gene Expression Analysis for Diagnosis of Infectious Diseases

 Zachary E. Holcomb,<sup>a</sup> Ephraim L. Tsalik,<sup>b,c,d</sup> Christopher W. Woods,<sup>b,c,e</sup> Micah T. McClain<sup>b,c,e</sup>

Duke University School of Medicine, Duke University, Durham, North Carolina, USA<sup>a</sup>; Center for Applied Genomics and Precision Medicine, Duke University, Durham, North Carolina, USA<sup>b</sup>; Division of Infectious Diseases, Duke University Medical Center, Durham, North Carolina, USA<sup>c</sup>; Emergency Medicine Service, Durham Veteran's Affairs Medical Center, Durham, North Carolina, USA<sup>d</sup>; Section for Infectious Diseases, Medicine Service, Durham Veteran's Affairs Medical Center, Durham, North Carolina, USA<sup>e</sup>



## Diagnosing and Managing Sepsis by Probing the Host Response to Infection: Advances, Opportunities, and Challenges

Ian L. Gunsolus,<sup>a</sup> Timothy E. Sweeney,<sup>b</sup> Oliver Liesenfeld,<sup>b</sup> Nathan A. Ledebore<sup>a</sup>

<sup>a</sup>Department of Pathology, Medical College of Wisconsin, Milwaukee, Wisconsin, USA

<sup>b</sup>Inflammatix Inc., Burlingame, California, USA

**ABSTRACT** Sepsis is a major source of mortality and morbidity globally. Accurately diagnosing sepsis remains challenging due to the heterogeneous nature of the disease, and delays in diagnosis and intervention contribute to high mortality rates. Measuring the host response to infection enables more rapid diagnosis of sepsis than is possible through direct detection of the causative pathogen, and recent advances in host response diagnostics and prognostics hold promise for improving outcomes. The current review discusses recent advances in the technologies used to probe the host response to infection, particularly those based on transcriptomics. These are discussed in the context of contemporary approaches to diagnosing and prognosing sepsis, and recommendations are made for successful development and validation of host response technologies.