A simple test to predict benefit of antibiotics for upper respiratory tract infections

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Introduction

Ellen Foxman, M.D., PhD.

• My research lab studies how airway cells defend the body against respiratory infections

• Professional training at Stanford (MD/PhD), Harvard (Pathology), and Yale (Immunology postdoc)

Yale collaborators
• Dr. Marie Landry, Yale Dx Virology Lab
• Dr. David Peaper, Yale Dx Microbiology Lab

9 diagnostics through PMA or 510k approval process for medical devices

Potential partners for clinical outcomes studies using test prototype
We are lacking a fundamental tool to guide treatment of one acute upper respiratory infection: a test to show whether antibiotics will benefit patient.

- 75% of antibiotic overuse is for upper respiratory tract illness

- Antibiotic overuse has huge financial & health costs

Antibiotic overuse leads to:

- **Health problems for patient (esp. kids)**
  - Immediate side effects
  - Alters microbiome/long term health impact

- **Promotes antibiotic resistant bacteria**
  - $20B in health care costs/yr (US)
  - 23,000 deaths/yr (US)

_Fleming-Dutra et al, JAMA, 2016_
STANDARD OF CARE

- **Standard of care**: point-of-care tests for individual viruses/bacteria
- Too many different viruses and bacteria cause similar symptoms
- Patients and physicians know these test miss many infections

OUR SOLUTION

- **Our solution**: Identify the general type of germ the body is fighting by measuring the body’s response

Upper respiratory illness

- 70-90%
- Do not prescribe antibiotics
Data and I.P.: Levels of single proteins made by the body identify viral infection in respiratory swabs

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<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tbody>
<tr>
<td>Single cut-off, all patients</td>
<td>81%</td>
<td>82%</td>
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<tr>
<td>Above high cutoff or below low cutoff, 2/3 of patients</td>
<td>94%</td>
<td>96%</td>
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Landry and Foxman, *Journal of Infectious Diseases*, 2018
Data & I.P.: We have discovered biomarkers that (1) distinguish viral-only from bacterial or viral/bacterial infection and (2) are detectable on nasal or throat swabs.

A single nasal biomarker rules in diverse virus infections

Viral biomarkers distinguish viral-only infection from coinfection

Landry and Foxman, *Journal of Infectious Diseases*, 2018

U.S. Patent Pending, filed Oct. 2017

24 claims related to methods for detecting a respiratory virus infection in a patient using mRNA or protein biomarkers of host antiviral response using diverse platforms

U.S. Provisional Patent Filed (May 7, 2018)

- Methods for distinguishing viral-only infection from bacterial infection or co-infection
- Includes new biomarkers of bacterial/co-infection
Develop lateral flow point-of-care assay

Nasal swab placed in buffer, then removed

Test strip placed in buffer

Control
Viral-only biomarker

<30 minutes
Primary care office visit

If viral-only biomarker level is high, supports decision not to prescribe antibiotics

Outcomes data will support changing practice guidelines and physician prescribing behavior

Test strip with reader
Pictured: Quidel Sofia system
Immediate opportunities to enhance value once we have test prototype

Prospective study of sinusitis in which children are randomized to receive antibiotics and followed for outcomes, >600 patients

- Collaborator: Judy Martin, M.D., Associate Professor of Pediatrics
- 4 other ongoing studies of acute respiratory infection outcomes

Provide our test free of charge (piggyback onto study)
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1. Antimicrobial Resistance Diagnostic National Challenge
   - This project won Phase I, March 2017
   - Phase II: Due September 4, 2018: Description of Prototype, SOP, Video, supporting data; 10 winners
   - Phase III: Phase II winners submit device in December 2018; BARDA will finance device validation by 2 independent CLIA labs

2. BARDA: pre-symptomatic detection of virus infection study, with 4 clinical cohorts with longitudinal sampling, we provide device/testing

Preliminary talks re: collaboration with Biomarker Discovery Unit
CRO: DCN diagnostics offers full-service development of lateral immunodiffusion assay

- GLP/GMP
- Record keeping meets criteria for FDA approval process
- 9 products through 510k or PMA process for medical devices

Budget/timeline

$300K budget:

$180K, 4-5 months
Feasibility testing
Endpoint: Working prototype for scientific collaborators including test strips
Suitable to gather data on intended use in research setting

$120K, additional 3 months
Verification and validation
Endpoint: completed device suitable for CLIA-waived use
Suitable prototype for FDA trials, NIH/BARDA phase III challenge

DCN developed Astute Medical’s Nephrocheck, now FDA approved.
Based on current influenza virus point-of-care test market
Price/test $29-185,
Cost to manufacture: $1.00/test
Ultimate goal: improve standard of care for acute respiratory infections and change clinical practice