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)

DCN

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

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

Children's Hospital of Pittsburgh of UPMC
125 YEARS of CARING

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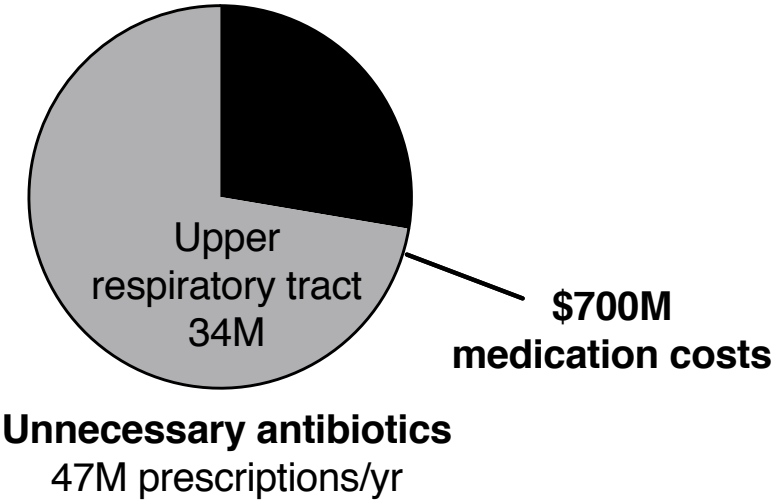
BARDA
BIOMEDICAL ADVANCED RESEARCH AND DEVELOPMENT AUTHORITY

Potential partners for clinical outcomes studies using test prototype

Unmet need

- 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



Unnecessary antibiotics
47M prescriptions/yr

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

Our solution

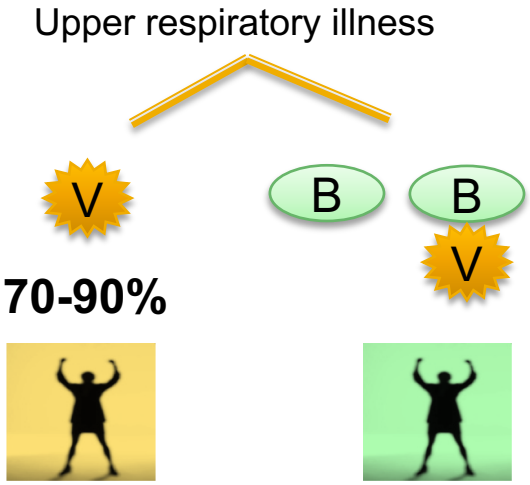
STANDARD OF CARE

- **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

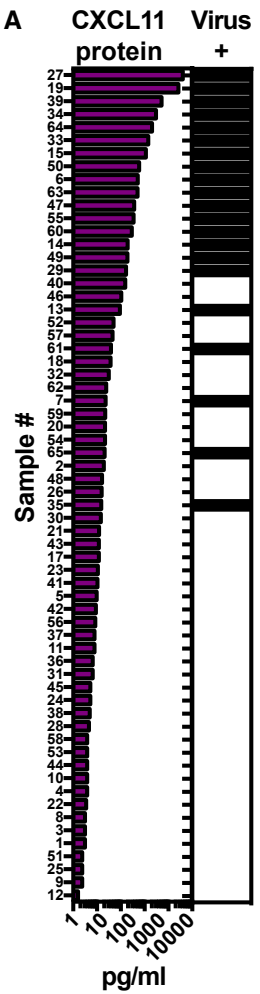
OUR SOLUTION

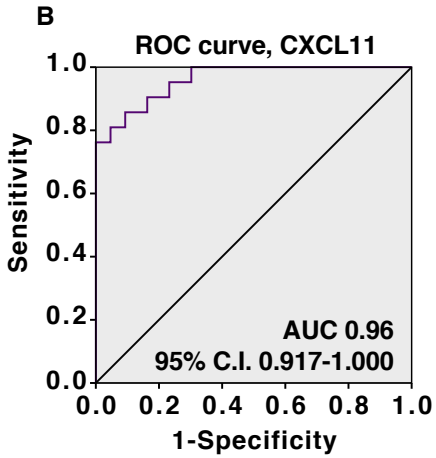
- **Our solution:** Identify the general type of germ the body is fighting by measuring the body's response



Do not prescribe antibiotics

Data and I.P.: Levels of single proteins made by the body identify viral infection in respiratory swabs



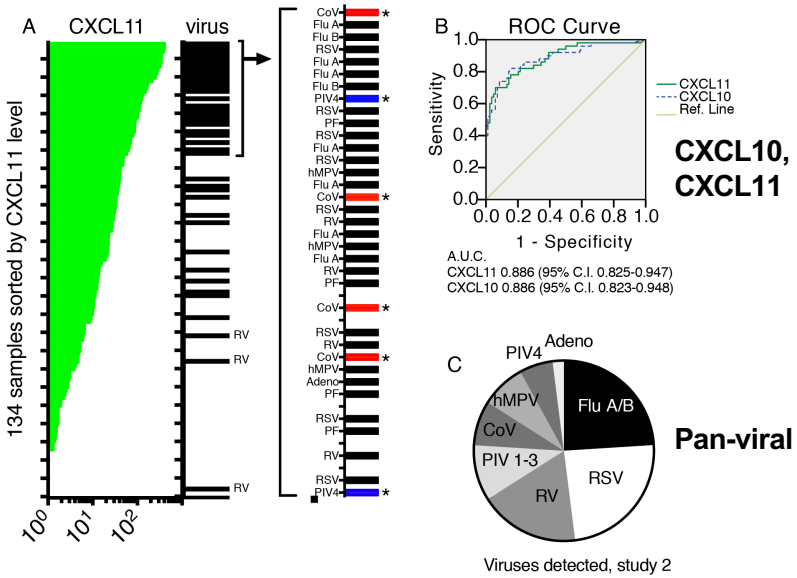


	Sensitivity	Specificity
Single cut-off, all patients	81%	82%
Above high cutoff or below low cutoff, 2/3 of patients	94%	96%

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

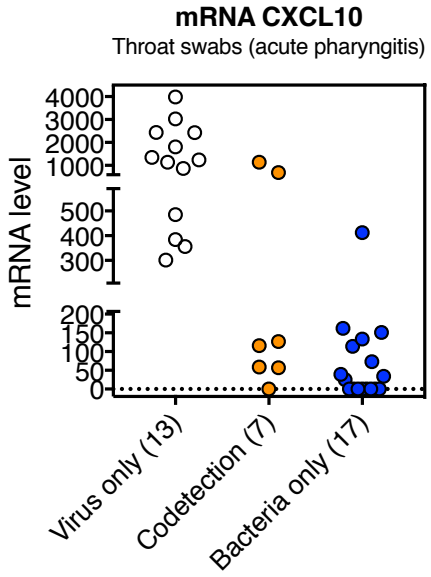


Landry and Foxman, *Journal of Infectious Diseases*, 2018

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

Viral biomarkers distinguish viral-only infection from coinfection



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

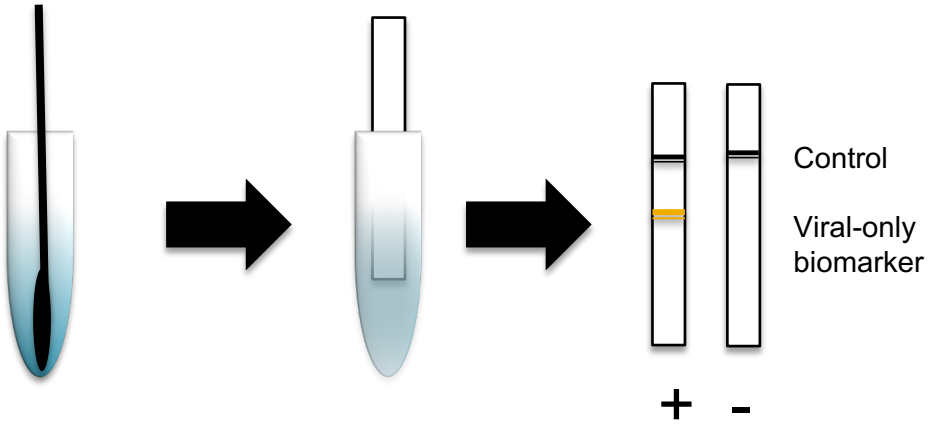
- Methods for distinguishing viral-only infection from bacterial infection or co-infection
- Includes new biomarkers of bacterial/co-infection

Goal of funding: develop prototype point-of-care test

Develop lateral flow point-of-care assay

Nasal swab placed in buffer, then removed

Test strip placed in buffer



<30 minutes
Primary care office visit

Test strip with reader

Pictured: Quidel Sofia system

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

Outcomes data will support changing practice guidelines and physician prescribing behavior

Immediate opportunities to enhance value once we have test prototype

Children's Hospital of Pittsburgh of UPMC
125 YEARS of CARING

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

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Sick patient
Clinical data
Conventional testing
Antibiotics (yes/no)

Outcome study
to determine
health value of
antibiotics

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

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Preliminary talks re: collaboration with Biomarker Discovery Unit

Budget and timeline

- 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

DCN developed Astute Medical's Nephrocheck, now FDA approved

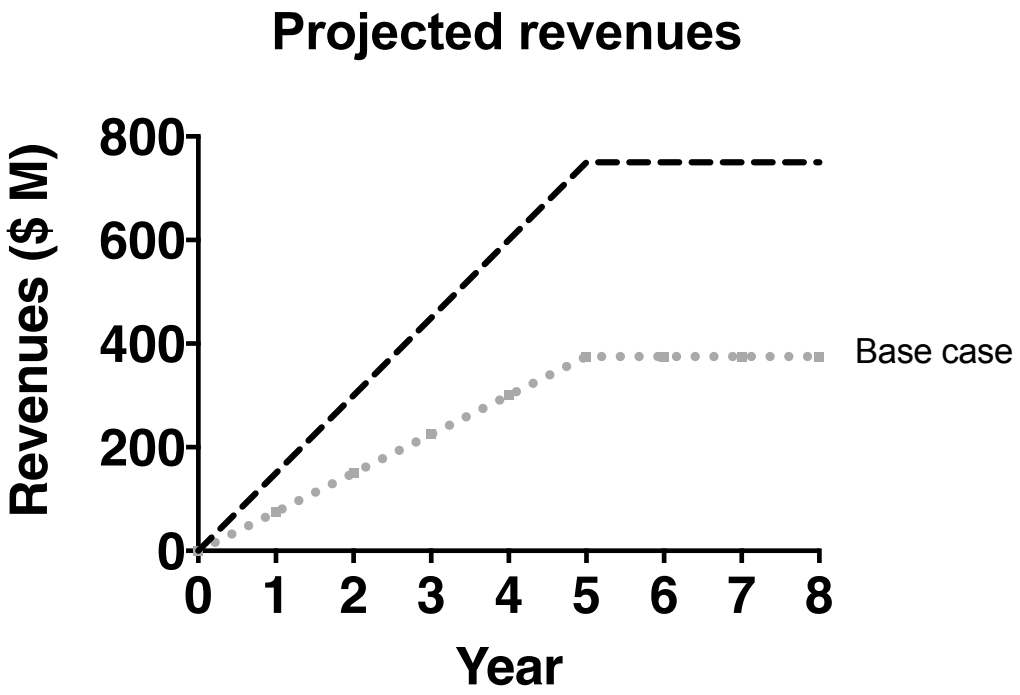
Budget/timeline

$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

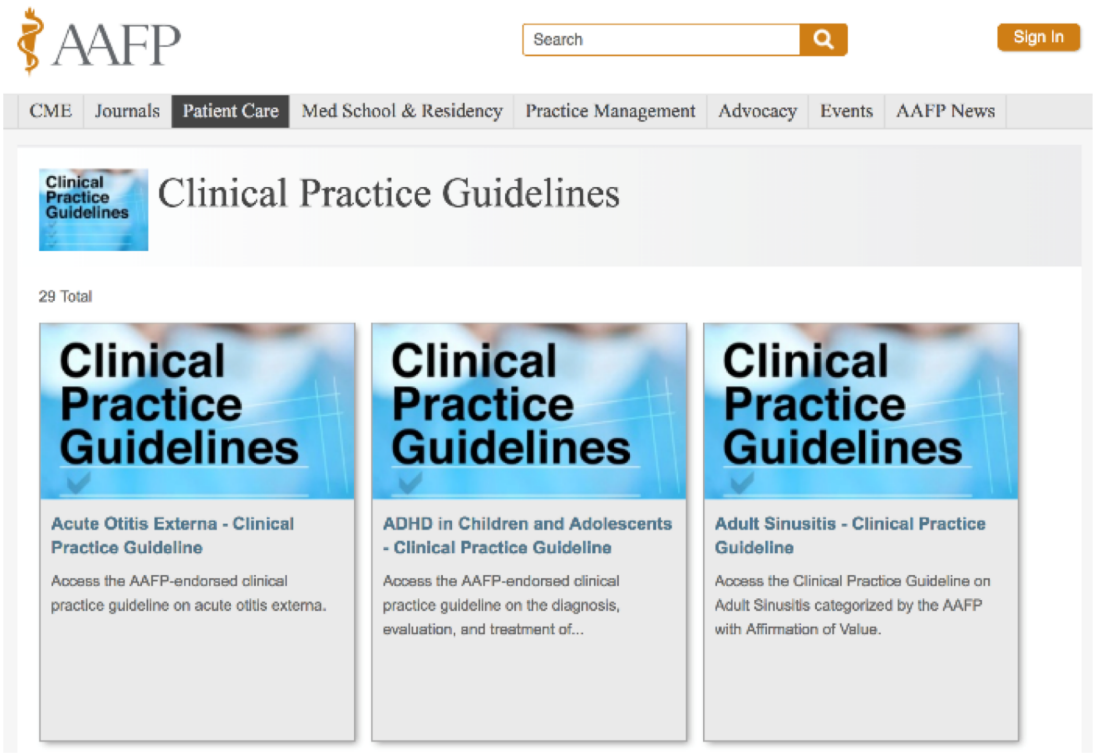
$120K, additional 3 months
Verification and validation
Endpoint: completed device suitable for CLIA-waived use
Suitable prototype for FDA trials, NIH/BARDA phase III challenge

Market potential



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



NATIONAL ACTION PLAN FOR COMBATING ANTIBIOTIC-RESISTANT BACTERIA

White House National Action Plan, 2015

https://www.aafp.org/patient-care/browse/type.tag-clinical-practice-guidelines.html