# Development of inexpensive, disposable, pre-symptomatic diagnosis of infectious disease to determine fitness for duty and preempt potential for contagious spread

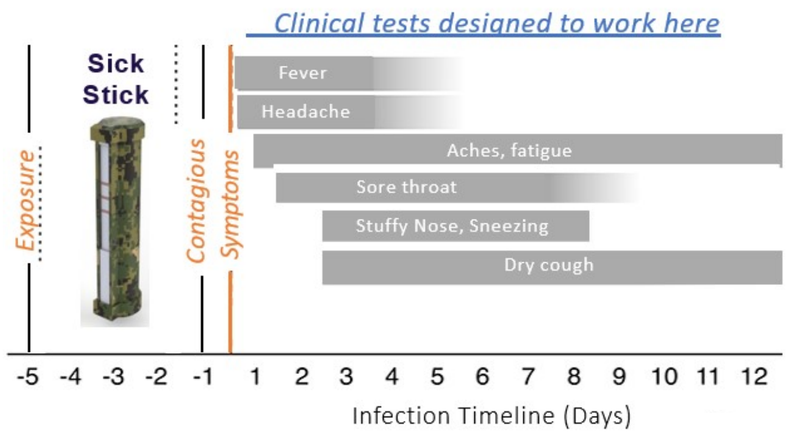
Dr. Stephen Francesconi (1), Dr. Nicholas Meyerson (2), Dr. Sara Sawyer (2,3), Dr. Richard Schoske (1)

Affiliations: 1. Defense Threat Reduction Agency; 2. Darwin Biosciences Inc. ; 3. University of Colorado Boulder

## Introduction

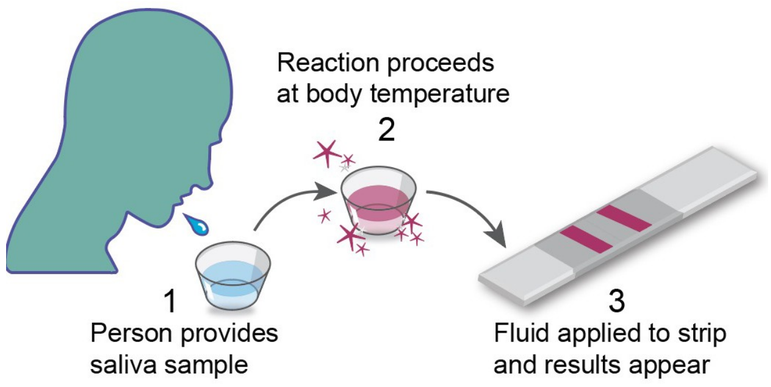
### Objective

This project seeks to identify individuals who have been exposed to infectious agent, before they show symptoms of illness. To enable routine screening of individuals at risk of falling ill, the test needs to be inexpensive, and be easy to perform. The "Sick Stick" is envisioned as an inexpensive lateral flow test, that predicts illness before symptoms appear, from a saliva sample.




### Work Flow

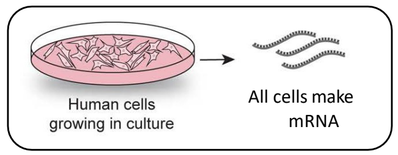
- The SickStick uses a saliva sample. An isothermal amplification assay is used to amplify target RNA molecules in the subjects saliva.
- This reaction product is run on a lateral flow immunoassay. If the mRNA biomarkers associated with oncoming disease are present at sufficient concentrations in the saliva, a visible line appears on the SickStick.

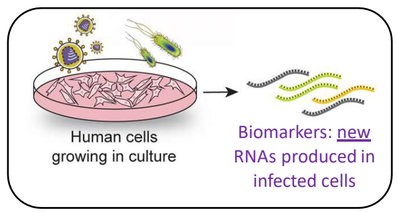


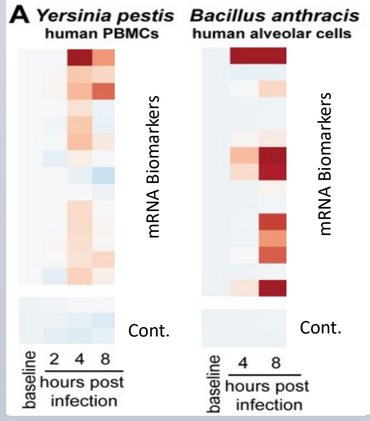

## Biomarker Discovery and Validation

### In Vitro

- For the past 3 years, University of Colorado has discovered and validated biomarkers.
- A panel of mRNA markers were initially identified in tissue culture (Figure A).



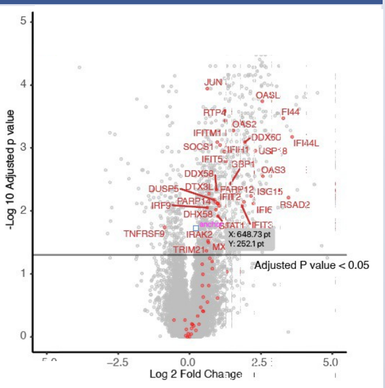



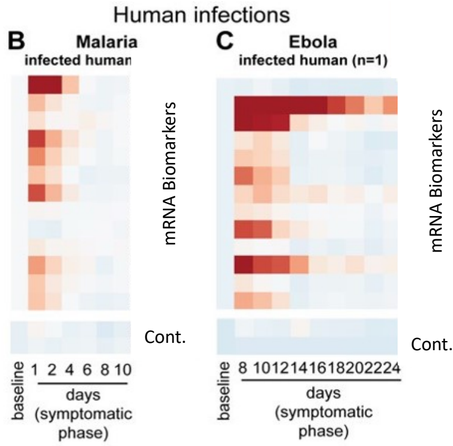




Functional analysis revealed that innate immune response genes are amongst the most consistently expressed early in infection

### In Vivo

- Several human cohorts have since been tested to validate the in vitro identified biomarkers
- In one cohort of 73 SARS-CoV2 positive individuals, many of the same mRNA targets were upregulated, when compared to healthy controls.




We have validated early expression of the markers upon other parasitic (B),viral (C), and bacterial (data not shown) exposures.

## Ongoing Studies

In order to achieve statistically significant results, we need a large population of healthy individuals need to be monitored until a significant number get sick

### Testing at Naval Health Research Center

- A cohort of active duty recruits who will collect saliva routinely.
- This will provide a military relevant dataset.

### Evaluation at NAMRU-6, Iquitos, Peru

- Local population experiences a wider variety of infectious diseases
- Clinical trial infrastructure is very well established

## Military Relevance

- Consider the sailor preparing to board a submarine that feels well but has contracted a respiratory virus. His asymptomatic infection could potentially put the entire crew at risk.
- Think too of the aircrew or platoon member that is exposed and incubating the pathogen. The mission they are on may have already begun once they show symptoms and become infectious to the detriment of themselves and their teammates.
- Moving the diagnostic window to include days prior to symptoms will give the warfighter confidence he or she will be fit to complete the mission.
- Here we are progressing on the development of a rapid test that can quickly mark those that need to seek further medical attention despite feeling healthy that morning, to support these and many other operational scenarios.

**Approved for public release.**

This work is supported in part by the Defense Threat Reduction Agency (DTRA) under the grant HDTRA1-18-1-0032 (FRBAA14-BR-TA7-G15-2-0090) and contract W15QKN-16-9-1002.

The views and conclusions contained in this document are those of the authors and should not be interpreted as representing the official policies, either expressed or implied, of the DTRA or the U.S. government.