MEASUREMENT OF NUTRITION AND FOOD SAFETY BIOMARKERS AT THE POINT-OF-NEED

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<table>
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<tr>
<th>AFFILIATION/FINANCIAL INTERESTS (prior 12 months)</th>
<th>ENTITIES</th>
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<td>Grants/Research Support</td>
<td>National Institutes of Health, National Science Foundation, Global Alliance for Improved Nutrition, United States Department of Agriculture, United States Agency for International Development, HarvestPlus/International Food Policy Research Institute, World Health Organization</td>
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<td>Scientific Advisory Board/Consultant/Board of Directors</td>
<td>VitaScan</td>
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<td>Speakers Bureau</td>
<td>None</td>
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<tr>
<td>Stock Shareholder</td>
<td>VitaScan</td>
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<td>Employee</td>
<td>Cornell University</td>
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<td>Other</td>
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UPDATE ON OUR WORK ON POCT DEVICES

1. Overview and Problem
2. Examples and Patents
3. Multiplexing
4. Different matrices such as Saliva and Urine
5. Moving to Food Testing
6. Target Product Profile
7. Last Mile
**Precision Crops**
Better and Safer
- Scale-up and Efficacy Demonstrations for promising technologies such as Biofortified Crops

**Precision Foods**
Accurate Assessment of Quality and Delivery of Nutrients
- Enable safety assessment via technologies for mycotoxin (aflatoxins) assessment at the point-of-need
- In vitro and in vivo testing for nutrient interactions before programmatic or market implementation
- Incorporate bioavailability and absorption

**Precision Nutrition**
Better Targeting and Evaluation of Interventions
- Enable POC testing of nutritional status + better functional biomarkers
- Improve resilience and incorporate acceptability (cooking time, taste, etc.)

**Precision Health**
Earlier Detection of Disease and Improved Prognosis
- Enable POC testing for illnesses such as Dengue, Zika, and Malaria + Cancer And monitor progress and relapse
- Better methods for diagnosing and preventing antibiotic resistance

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Research, Implementation, and Training in all areas
PROBLEM

1. Access to affordable and reliable micronutrient status testing remains sparse
   
   1.1. Population level
   
   1.2. Personalized
   
   1.3. Food testing

2. Challenges for targeting/designing interventions as well as monitoring response and impact evaluation

3. Can point-of-care devices help?
VISION/GOALS

1. Sensitivity/Specificity - Screening vs. Diagnostic
2. Minimal Sample
3. Minimal Infrastructure
4. Minimal Training
5. Minimal Cost
6. Extend the reach of traditional laboratories
NutriPhone bridges the gap

1. Finger-stick applied to custom test-strips
2. Test reaction takes 10 minutes
3. Reader images test and sends to phone

Tests have been developed for: Vitamin D, Vitamin B₁₂, Vitamin A, CRP, Iron, AGP

More details and list of papers at insight.cornell.edu/projects
Testing Protocol

1. Heel prick
2. Drop of serum (or whole blood) added to test strip
3. Test strip inlet
4. Electronic Health Record Database
5. Data transfer (optional)
6. Test result displayed on mobile app
7. Portable test strip reader

sTfR 4 μg/mL
NutriPhone Mobile App

Mobile app provides step-by-step guidance to user
Current Reader Format and Footprint
Rapid diagnostic testing platform for iron and vitamin A deficiency

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## NutriPhone/FeverPhone Biomarkers

### Nutritional Status
- Vitamin B12
- Vitamin A - RBP
- Ferritin
- Soluble Transferrin Receptor
- Vitamin D - 25(OH)D3
- Folate

### Inflammation Status
- Alpha-1 acid glycoprotein (AGP)
- C-reactive protein

### Cancer Biomarkers
- Alpha Fetoprotein (AFP)
- Prostate-specific antigen

### Food Safety
- Aflatoxin
  - In blood, urine, milk
  - In food
- Fumonisin

### Infectious Diseases
- Dengue
- Chikungunya
- Chagas
- Leptospirosis
- Malaria
SAFE-Phone

Smartphone-Based Aflatoxin Evaluation at the Point-of-Need

Primary Work by:
Balaji Srinivasan, PhD, Research Associate
Zhengda Lu, PhD, Former Graduate Student
Amit Barui, PhD, Former Postdoctoral Associate
SAFE-Phone

- 4” diagonal size, with a touch screen.
- Able to transmit data
- Confocal fluorescence optical sensor
- Europium nanoparticle (EuNPs) lateral flow assay
- Ultra-compact reader
- ~100 times more sensitive than state-of-art technology
SAFE-Phone - BIOMARKERS

AFLATOXIN B1
FOOD

AFLATOXIN M1
URINE

AFLATOXIN B1-ALBUMIN/
AFLATOXIN B1-LYSINE
BLOOD
SAFE-Phone

**FOOD/BLOOD**

Test line- monoclonal anti-aflatoxin (Abcam plc.)

Control line- anti-rat IgG (Jackson ImmunoResearch Inc.)

ELISA Kit- Aflatoxin B1 ELISA Kit (#K4208, BioVision Inc., CA)

**URINE**

Test line- monoclonal anti-AFM1 IgG (Agrisera, Inc.)

Control line- anti-mouse IgG (Jackson ImmunoResearch Inc.)

ELISA Kit- Aflatoxin M1 ELISA (#991AFLM01U, Helica, Inc.)

**REFERENCE**


SAFE-Phone Food

- Latex nanoparticle (400 nm diameter) based lateral flow immunoassay
- USDA cut off for AFB1 in food - 20 ng/ml
- Assay covers the aflatoxin concentration range 5 - 40 ng/ml (ppb)
- Limit of detection as low as 5 ng/ml
SAFE-Phone FOOD

- Selection of antibodies and design and development of test strip for AFB1 in food completed

- Testing of reference standard corn samples and comparison with HPLC results - in partnership with Office of the Texas State Chemist and Texas A&M University.

- Assay development for Fumonisin and multiplexed AFB1, FB1 test strip - in progress
SAFE-Phone - Blood- Challenges

- AFB1 in serum is in a complex adduct form at very low concentrations (pg range)
- Lack of commercial source for reference standard and calibrators for AFB1-lysine or AFB1- human serum adduct
- Lack of commercial sources for antibodies for anti-AFB1-lysine/ anti-AFB1-HSA
- Lack of reference antigen standard (AFB1-lysine) limits outsourcing custom development of antibodies
- Lack of commercial labs for performing gold standard HPLC testing for AFB1 in serum/urine samples
- No prior data on correlation between capillary and venous blood samples
SAFE-Phone - Blood

Next steps

- Substudy - compare capillary vs. venous blood samples for AFB1 concentrations
- Calibration efforts ongoing in partnership with laboratories at UGA and JHU
- Validation in samples collected by the Tufts team in Nepal and Uganda
WHO’S ASSURED CRITERIA/TARGET PRODUCT PROFILE FOR POCT DEVICES

1. Affordable by those at risk
2. Sensitive (Few false-negative results)
3. Specific (Few false-positive results)
4. User-friendly requires minimal training (simple to perform by users with little training)
5. Rapid (to enable treatment at first visit) and Robust (without the need for special storage)
6. Equipment free (no large instruments that need external power supply)
7. Delivered to those who need it (scale it up with sustainable business model to produce)
Our current work addresses these goals...

- Identify biomarker with diagnostic need
- Optimize assay for required physiological range
- Initial small-scale lab validation and performance testing

How do we do this?

- Rigorous diagnostic performance evaluation, shelf life, temperature/humidity effects etc
- Commercialize, optimization and manufacturing

Academic
Proof of Concept

Industry
Large Scale Production

Images: Siemens, creative-diagnostics, biodot, Vossman
ASSAY DEVELOPMENT PIPELINE
ASSAY DEVELOPMENT PIPELINE

ACADEMIA

Biomarker

Feasibility

Development

Lab Validation

INDUSTRY

DTA

Regulatory

Vitamin B12

Vitamin D3

CRP

AGP

Ferritin

sTfR

Folate

Hepcidin-25

MMA

Holo-TC

Zika

Dengue

Chikungunya

SARS-CoV-2

Chagas

Leptospirosis

Malaria

NutriPhone

serum

FeverPhone

nasopharyngeal saliva
ASSAY DEVELOPMENT PIPELINE
Acknowledgments