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PLENARY SESSION 5: INNOVATIVE METHODS AND METRICS FOR NUTRITION RESEARCH AND PROGRAMMING

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

Saurabh Mehta, M.B.B.S., Sc.D.
The Janet and Gordon Lankton Professor

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Department of Population Health Sciences | Weill Cornell Medicine
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Director, Program in International Nutrition
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Disclosure

AFFILIATION/FINANCIAL INTERESTS (prior 12 months)	ENTITIES
Grants/Research Support	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
Scientific Advisory Board/Consultant/**Board of Directors**	VitaScan
Speakers Bureau	None
Stock Shareholder	VitaScan
Employee	Cornell University
Other	N/A

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

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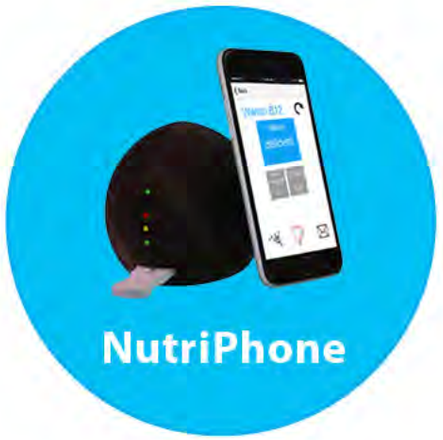
Precision Crops
Better and Safer

- Scale-up and Efficacy Demonstrations for promising technologies such as Biofortified Crops
- Enable safety assessment via technologies for mycotoxin (aflatoxins) assessment at the point-of-need

Precision Foods
Accurate Assessment of Quality and Delivery of Nutrients

- 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

Research, Implementation, and Training in all areas

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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

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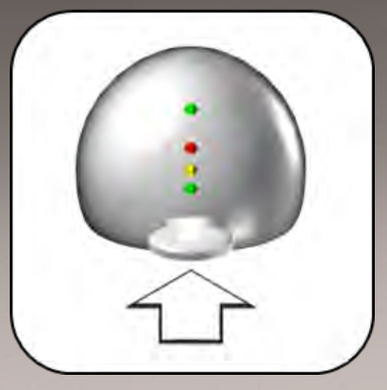
NutriPhone bridges the gap

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 B_{12}, Vitamin A, CRP, Iron, AGP

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

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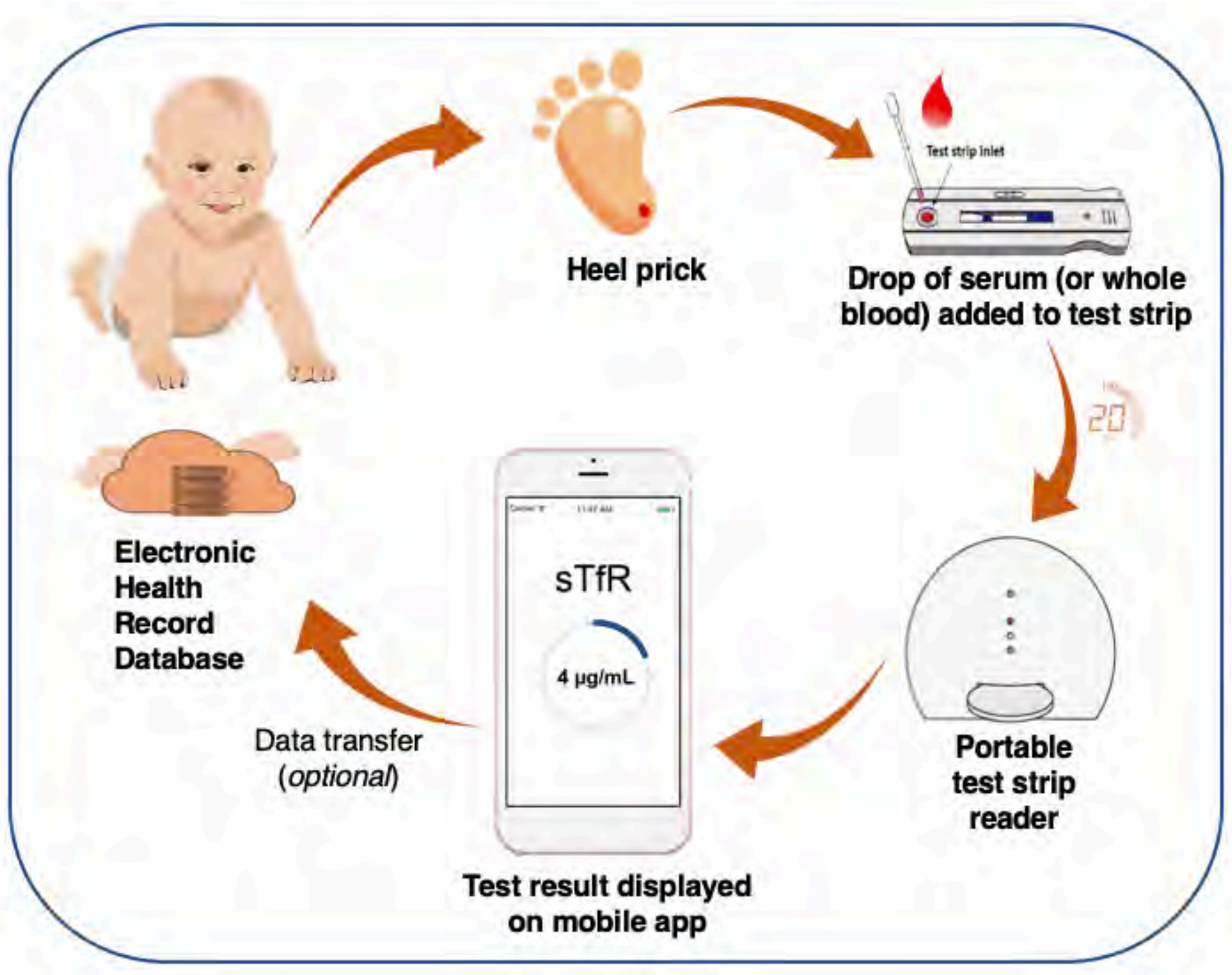
Testing Protocol



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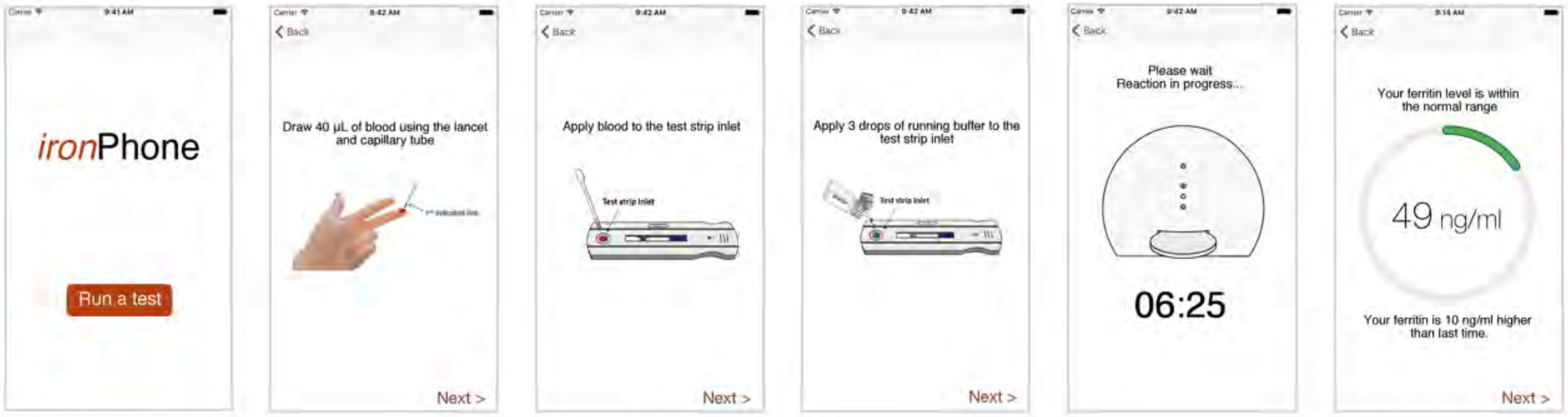
NutriPhone Mobile App



Mobile app provides step-by-step guidance to user

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Current Reader Format and Footprint

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PNAS

Rapid diagnostic testing platform for iron and vitamin A deficiency

Zhengda Lu[a], Dakota O'Dell[b], Balaji Srinivasan[c], Elizabeth Rey[a], Ruisheng Wang[d], Sasank Vemulapati[a], Saurabh Mehta[c,e,1], and David Erickson[a,c,e,1]

[a]Sibley School of Mechanical and Aerospace Engineering, Cornell University, Ithaca, NY 14853; [b]Applied and Engineering Physics, Cornell University, Ithaca, NY 14853; [c]Division of Nutritional Sciences, Cornell University, Ithaca, NY 14853; [d]Meinig School of Biomedical Engineering, College of Engineering, Cornell University, Ithaca, NY 14853; and [e]Institute for Nutritional Sciences, Global Health, and Technology, Cornell University, Ithaca, NY 14853

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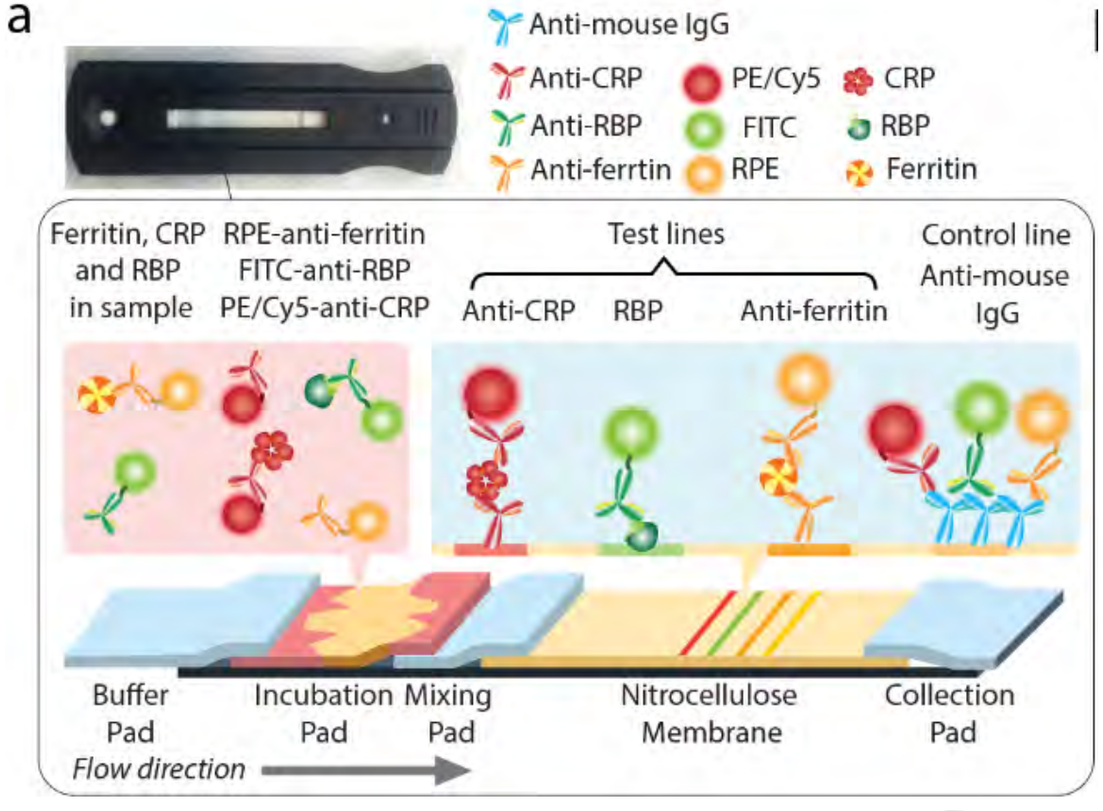

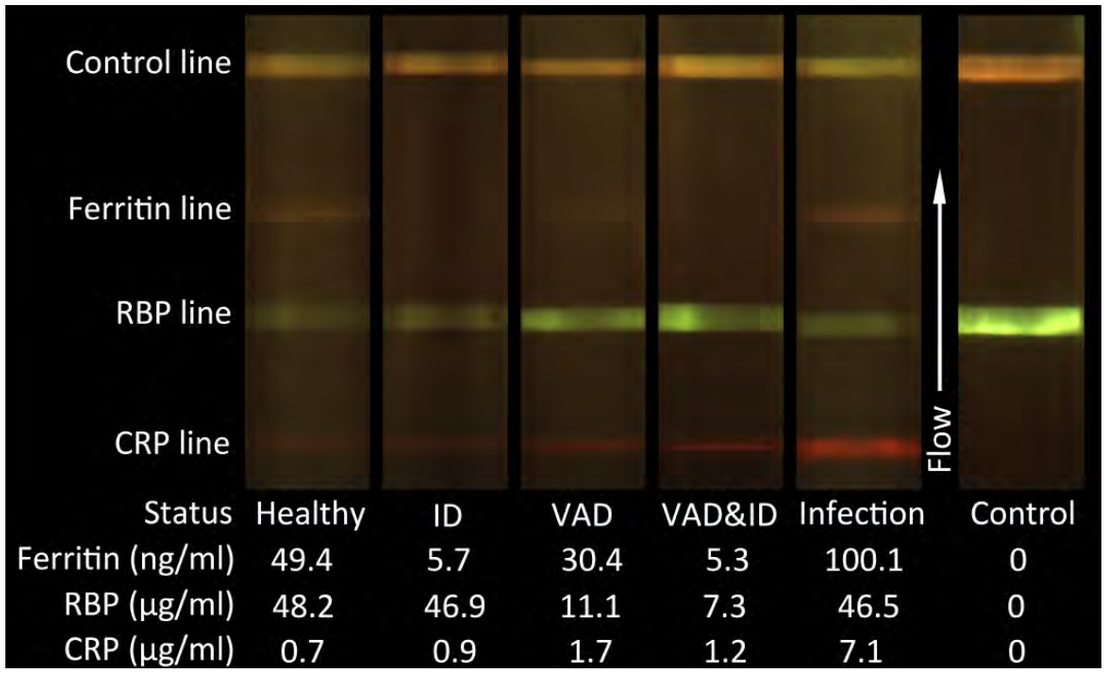

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NutriPhone/FeverPhone Biomarkers

Nutritional Status

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

Food Safety

- Aflatoxin
  - In blood, urine, milk
  - In food
- Fumonisin

Inflammation Status

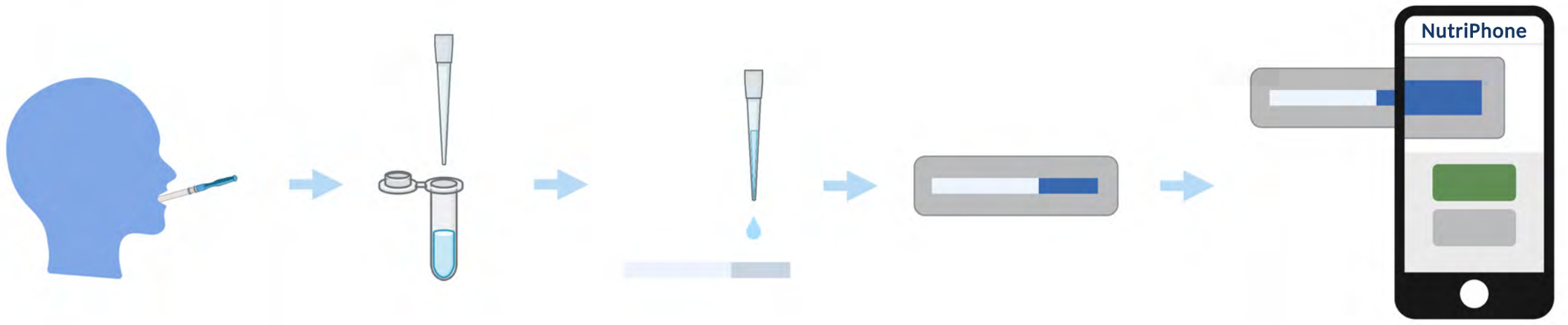
- Alpha-1 acid glycoprotein (AGP)
- C-reactive protein

Cancer Biomarkers

- Alpha Fetoprotein (AFP)
- Prostate-specific antigen

Infectious Diseases

- Dengue
- Chikungunya
- Chagas
- Leptospirosis
- Malaria



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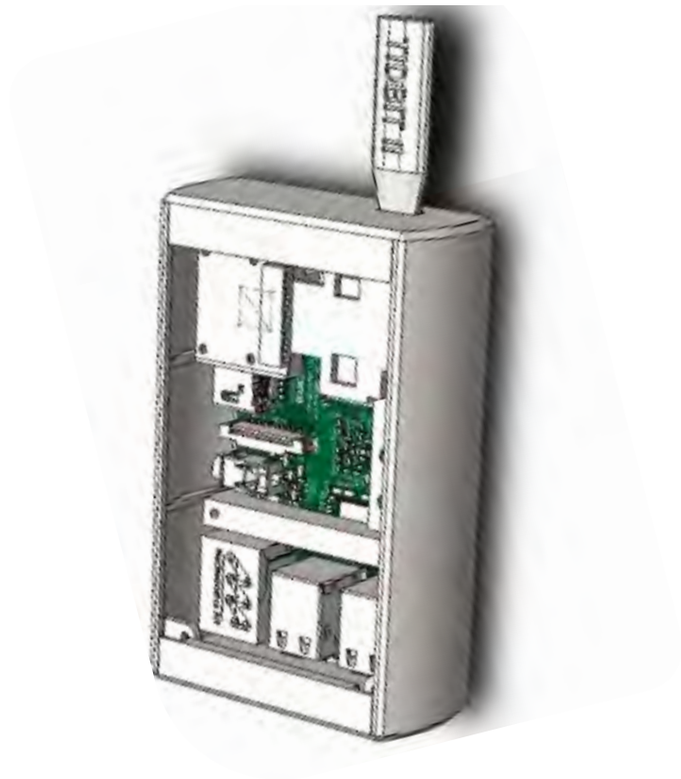
SAFE-Phone

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



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Amit Barui, PhD, Former Postdoctoral Associate

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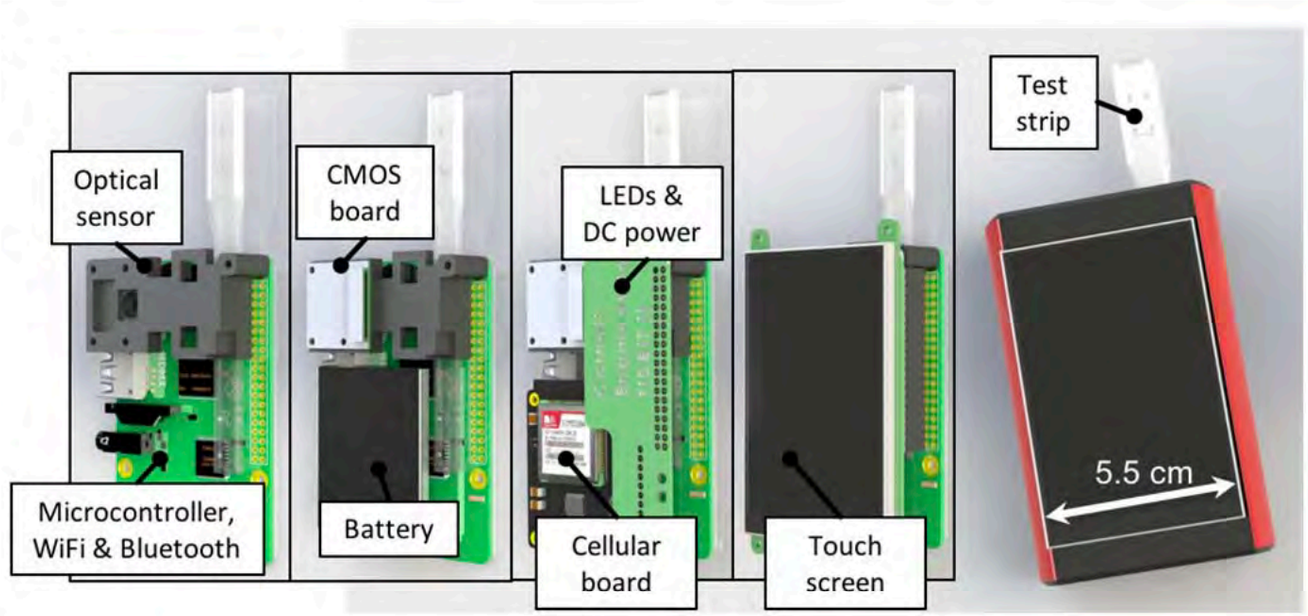
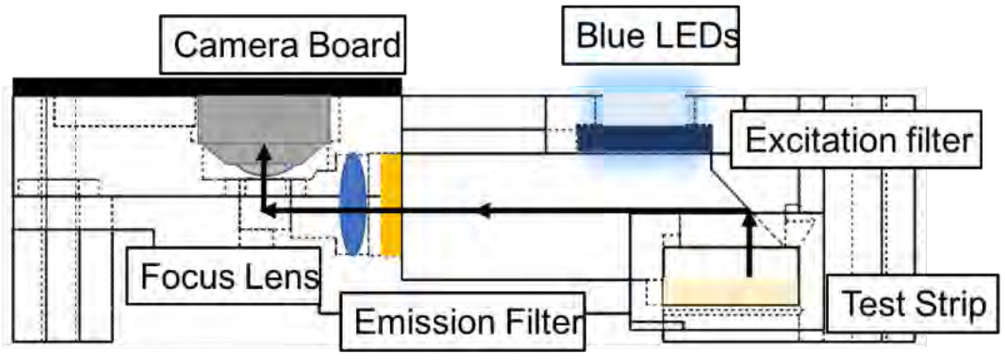
SAFE-Phone

- 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





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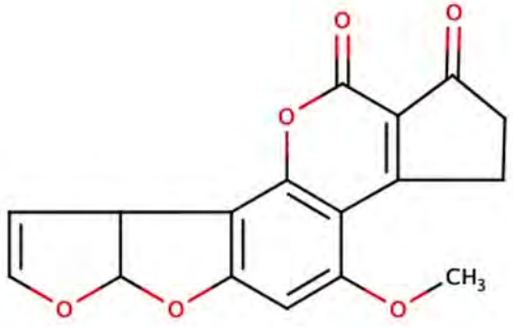
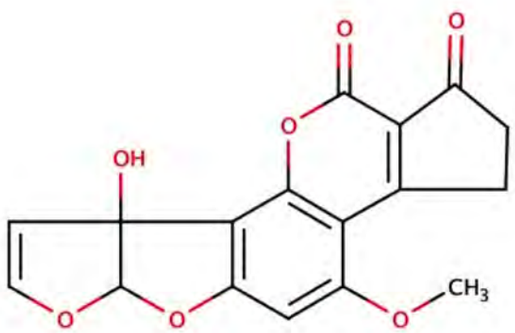
SAFE-Phone - BIOMARKERS



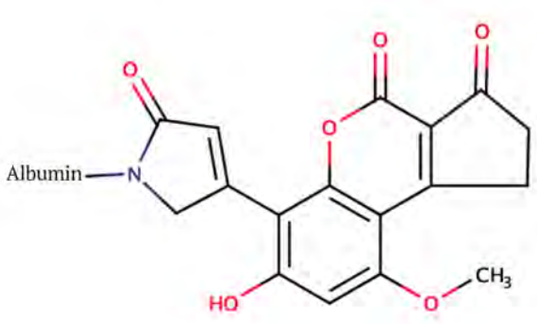
AFLATOXIN B1

FOOD



AFLATOXIN M1

URINE



AFLATOXIN B1-ALBUMIN/ AFLATOXIN B1-LYSINE

BLOOD

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FOOD/BLOOD

Test line- monoclonal anti-aflatoxin (Abcam plc.)[1-3]

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

1. Kanungo L & Bhand S Fluorimetric immunoassay for multianalysis of aflatoxins. J Anal Methods Chem 2013:584964 (2013).
2. Parker CO & Tothill IE Development of an electrochemical immunosensor for aflatoxin M1 in milk with focus on matrix interference. Biosens Bioelectron 24:2452-7 (2009).
3. Parker CO et al. Electrochemical immunochip sensor for aflatoxin M1 detection. Anal Chem 81:5291-8 (2009).

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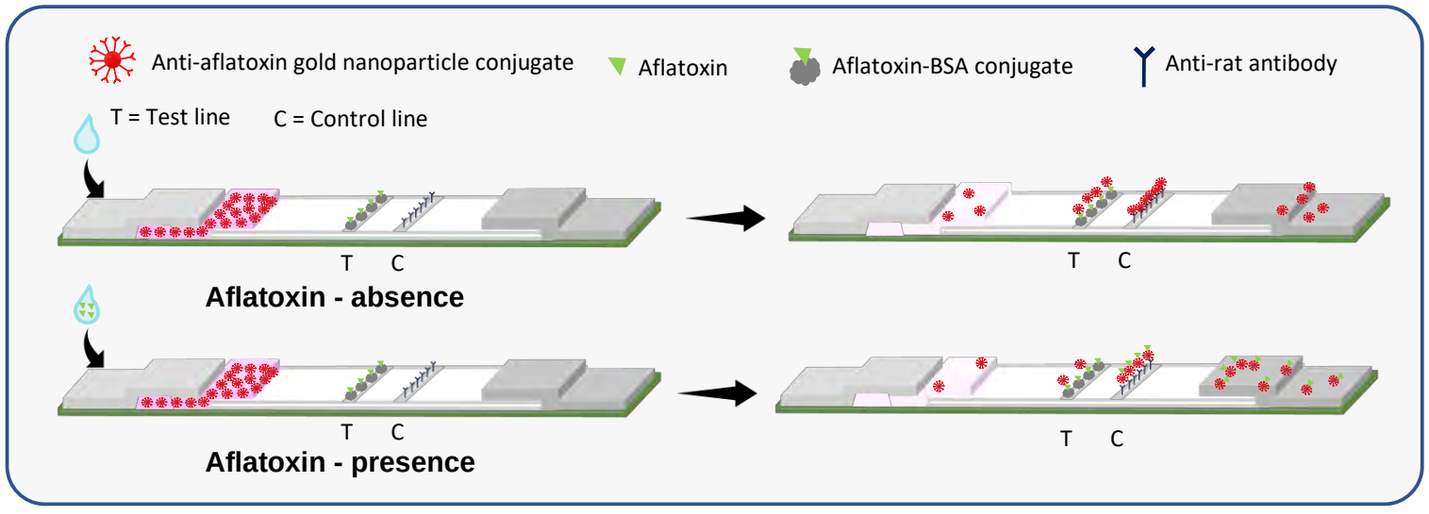
SAFE-Phone Food

- 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



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- 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

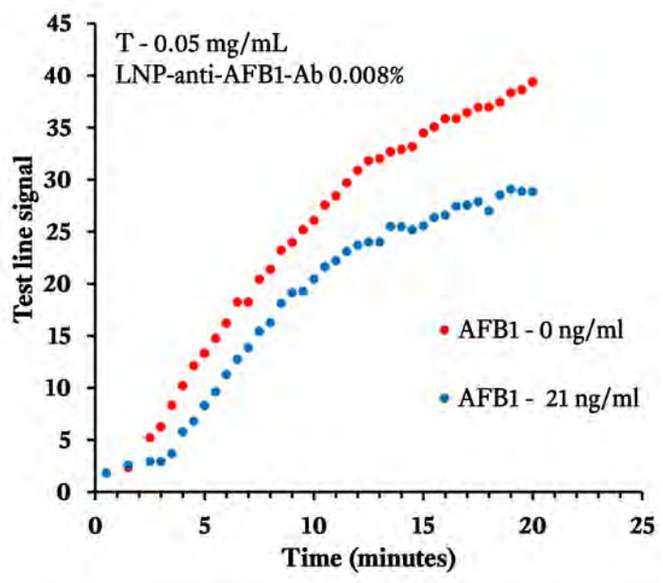

Figure: Analytics - variation of test line signal with time at various concentrations

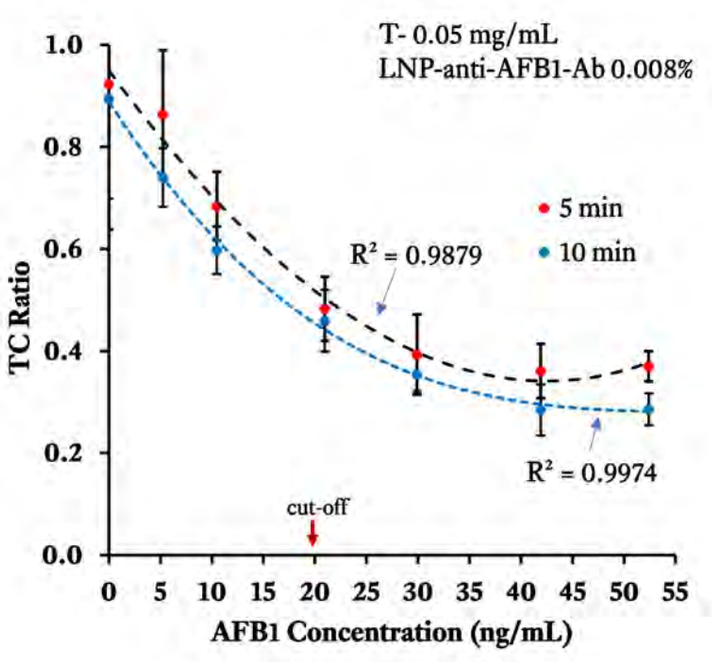

Figure: calibration curve for measurements at t = 5 min and 10 min.

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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

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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)**

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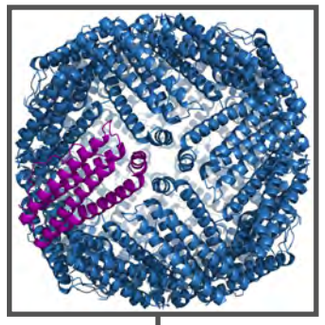
Our current work addresses these goals…

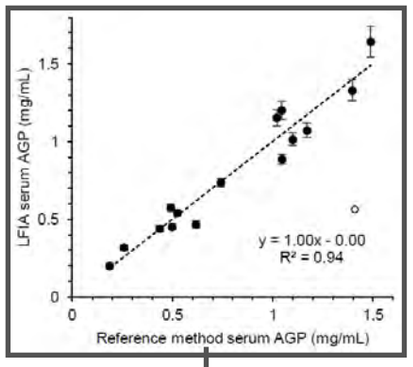
How do we do this?

Identify biomarker with diagnostic need



Optimize assay for required physiological range

Initial small-scale lab validation and performance testing



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

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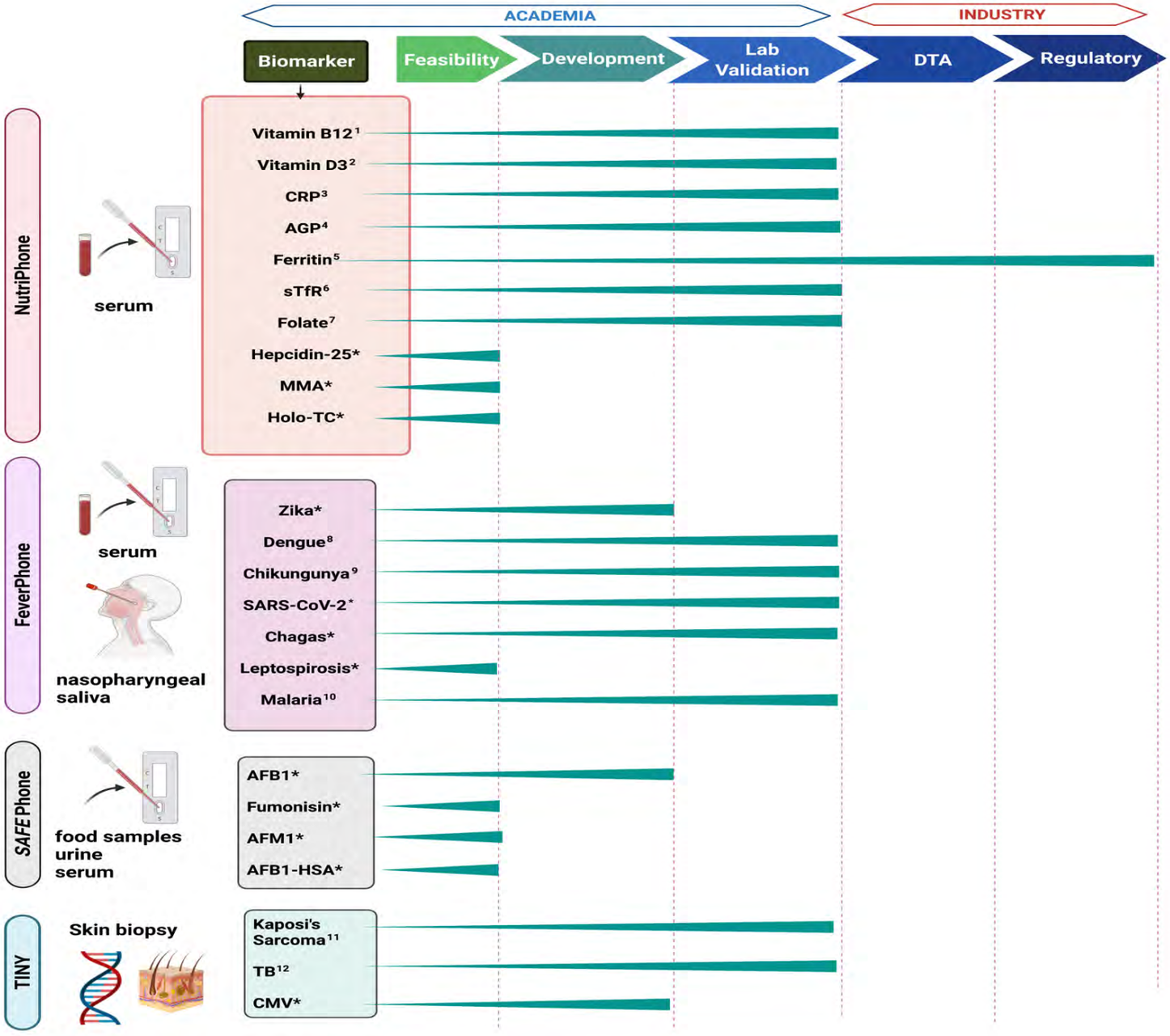
ASSAY DEVELOPMENT PIPELINE



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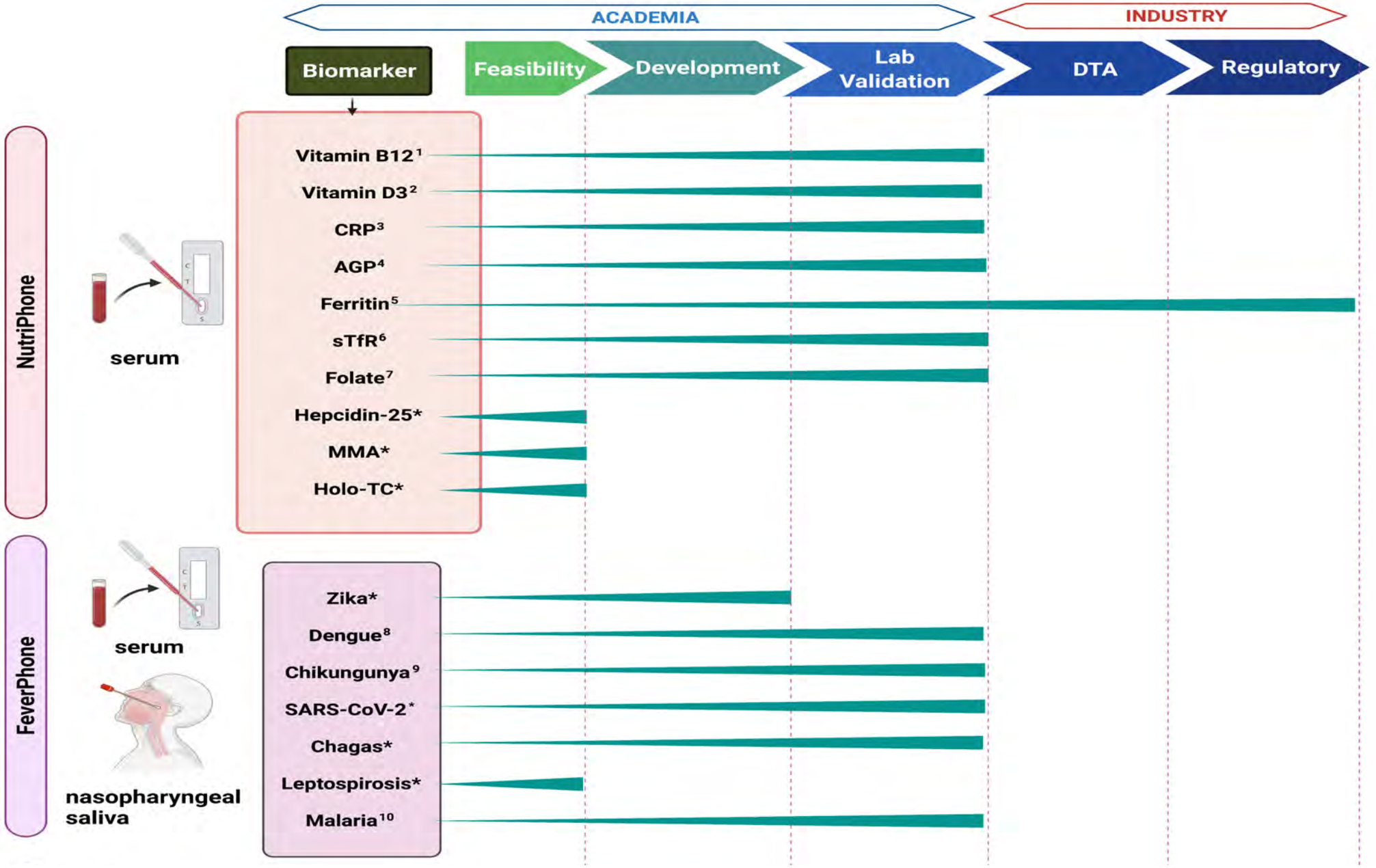

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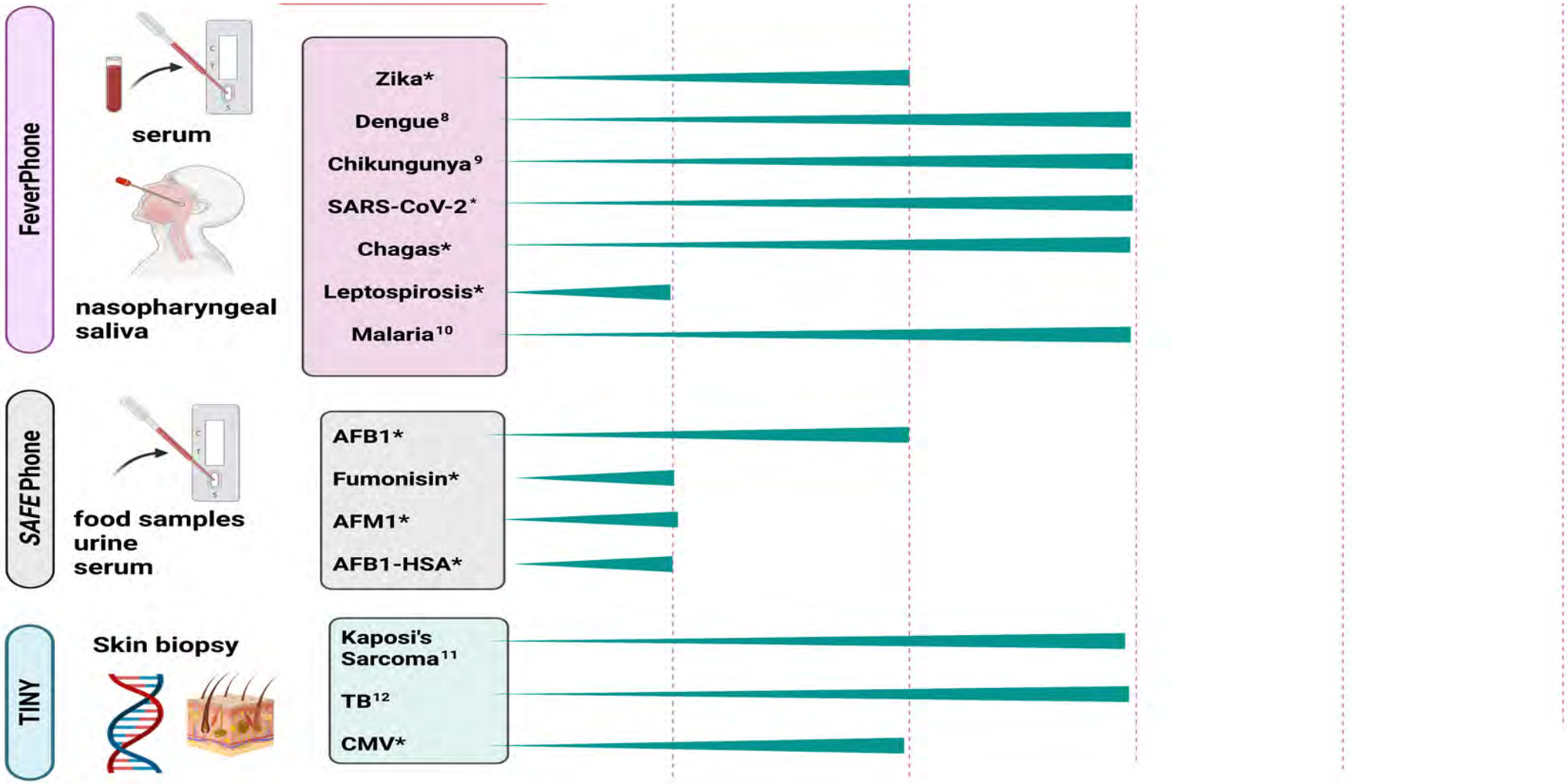
ASSAY DEVELOPMENT PIPELINE



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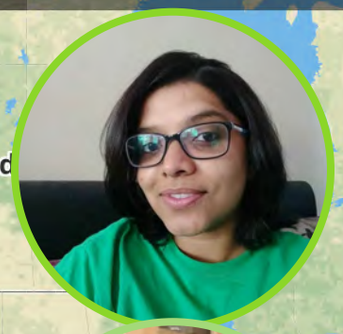

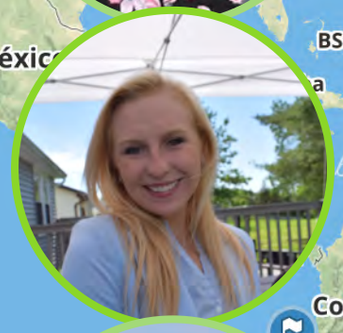

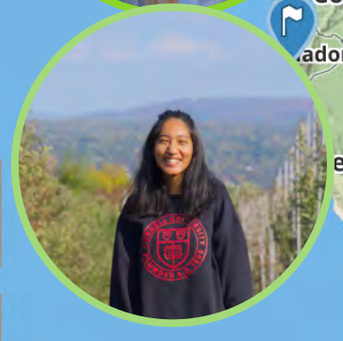

EricksonLab
INTEGRATED MICRO- AND NANOFLUIDIC SYSTEMS

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CNF
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