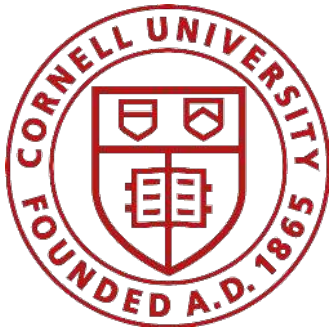
NutriPhone: Mobile Devices for Anaemia Measurement and Iron Deficiency at Home

Saurabh Mehta, M.B.B.S., Sc.D.
Associate Professor of Global Health, Epidemiology, and Nutrition
Director, Program in International Nutrition
Institute for Nutritional Sciences, Global Health, and Technology (INSiGHT)
Division of Nutritional Sciences, Cornell University



CornellNutrition

Disclosure

- Co-Founder and Board Member of VitaMe Technologies dba VitaScan, Inc.
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  - National Institutes of Health
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  - Global Alliance for Improved Nutrition
  - Thrasher Research Fund
  - Micronutrient Initiative/Nutrition International
  - United States Agency for International Development

“Leveraging Advances in Technology To Solve Global Challenges and Bridge Health Disparities.”

MISSION STATEMENT

Precision Crops
Better and Safer

Precision Foods
Accurate Assessment of Quality and Delivery of Nutrients

Precision Nutrition
Better Targeting and Evaluation of Interventions

Precision Health
Earlier Detection of Disease and Improved Prognosis

- 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
- In vitro and in vivo testing for nutrient interactions before programmatic or market implementation
- Incorporate bioavailability and absorption
- Enable POC testing of nutritional status + better functional biomarkers
- Improve resilience and incorporate acceptability (cooking time, taste, etc.)
- 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

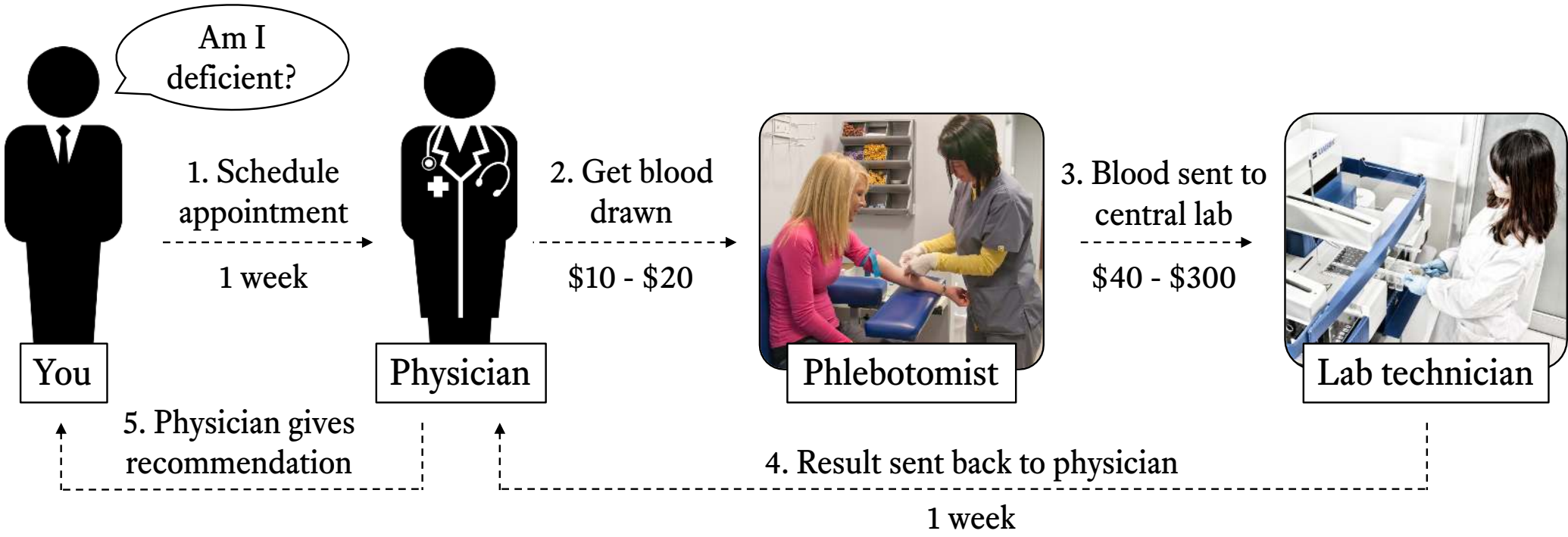
A Brief History…..

Collaboration

Finding the right partner…..

Traditional Lab Testing
Limitations

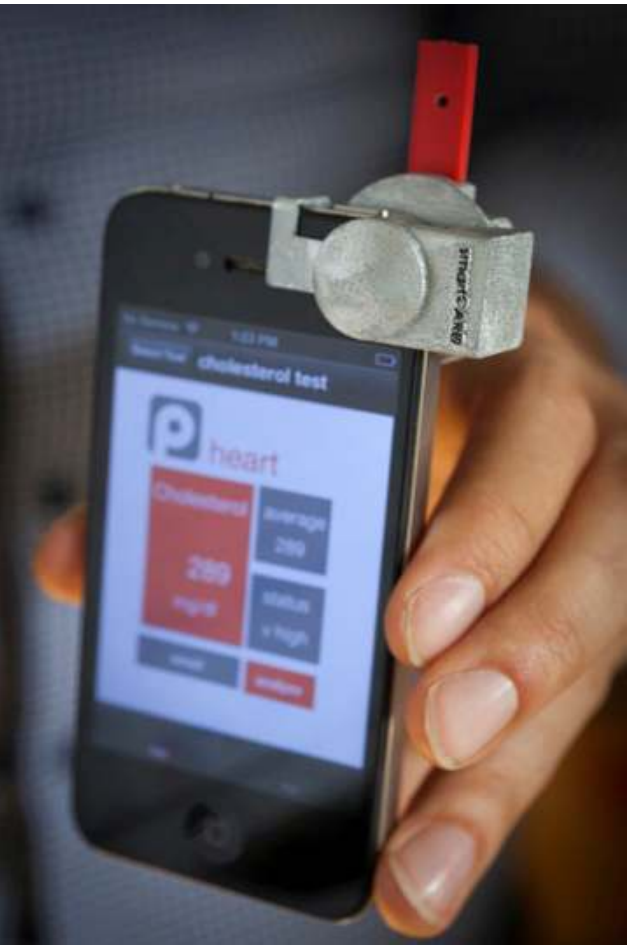
Process for testing takes **weeks**…
And ends up costing **hundreds of dollars per test** (most of which goes to central labs).



Nutritional Status Assessment
Square-ification

We make "Square" for personalized *Nutritional Diagnostics*.

Square



Why Smartphone Enabled Diagnostics?

It has everything

- GPS, High-res, Camera, Email, Facebook, computation, power, etc.
- Extremely rugged

You are already trained on it

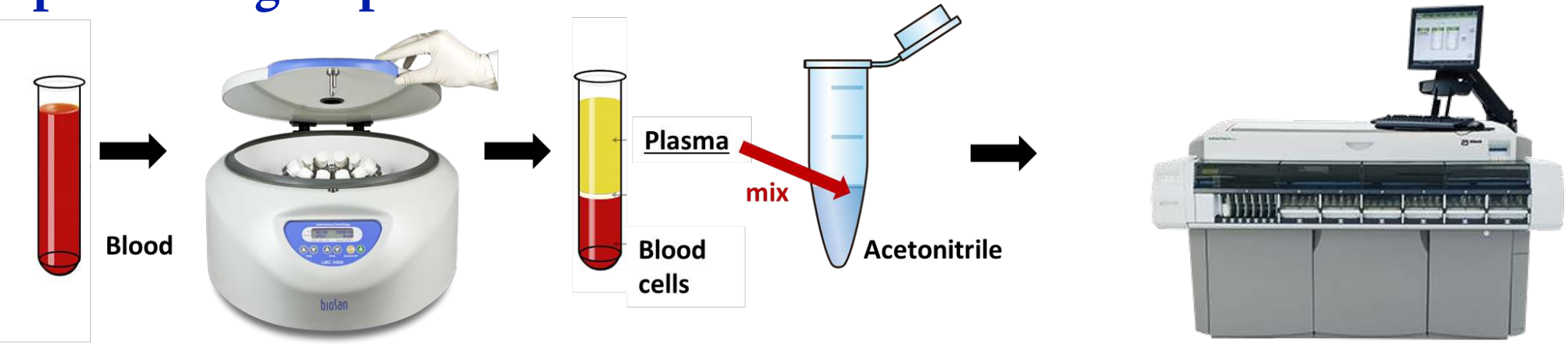
- Technology designed to be easy to use by nearly all age groups

You already own it

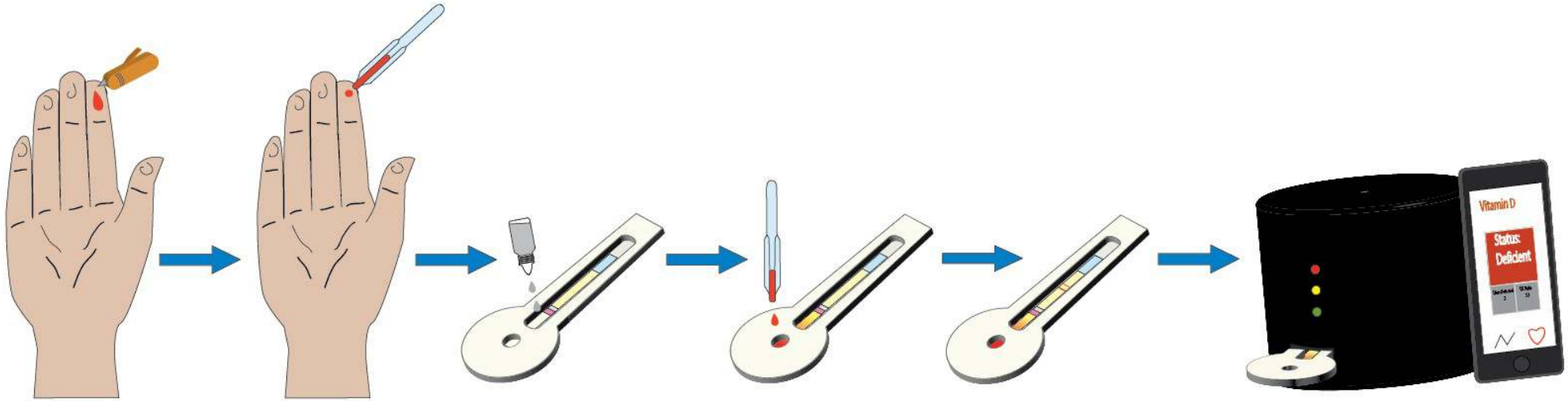
- 81% of US adults have “smartphone”, 96% cellphone
- Everybody is carrying one all the time

Current standard vs. Nutriphone *Vitamin D*

Standard Vitamin D analysis requires extensive equipment and processing steps

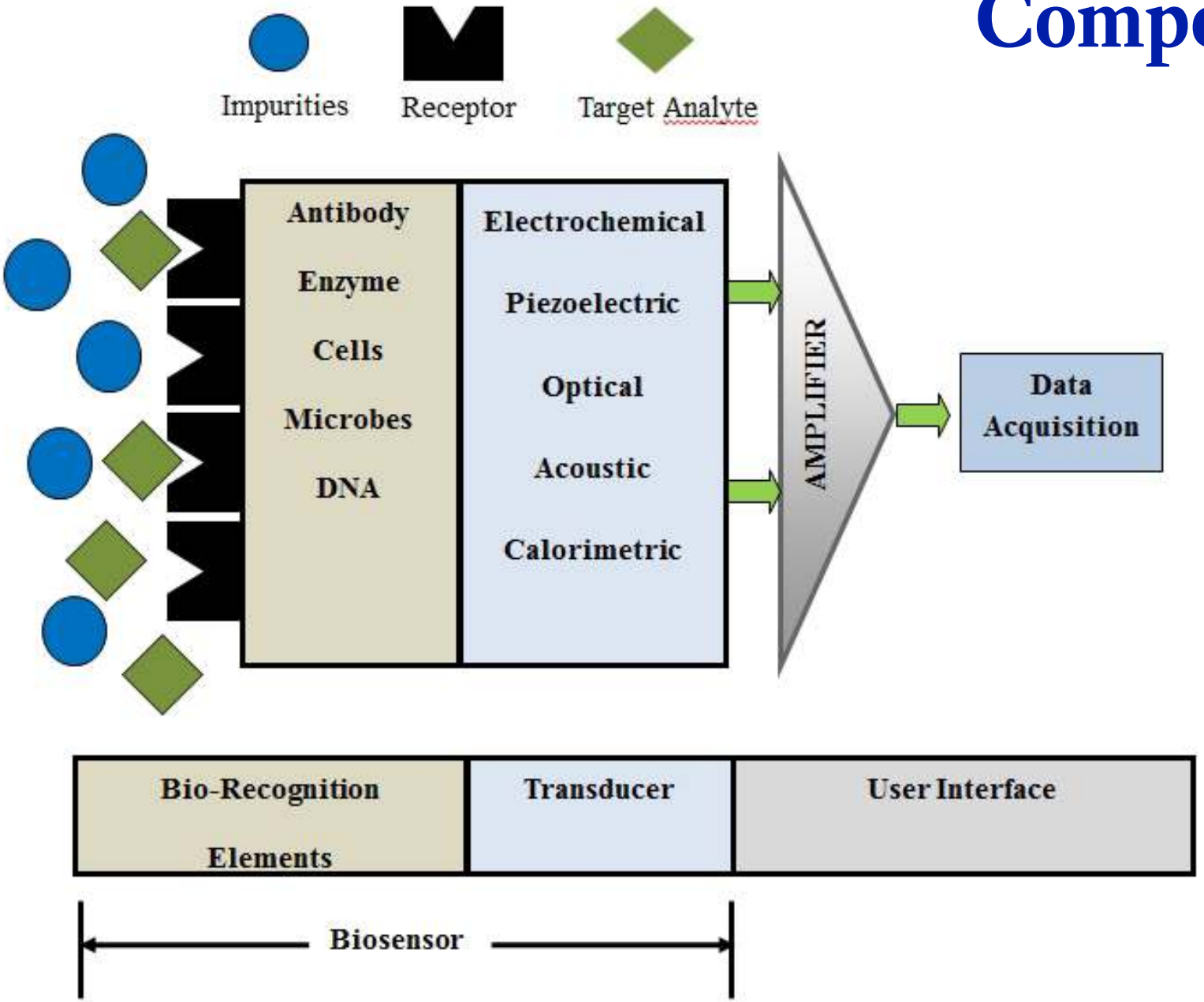


NutriPhone integrates all of this functionality into the test strip

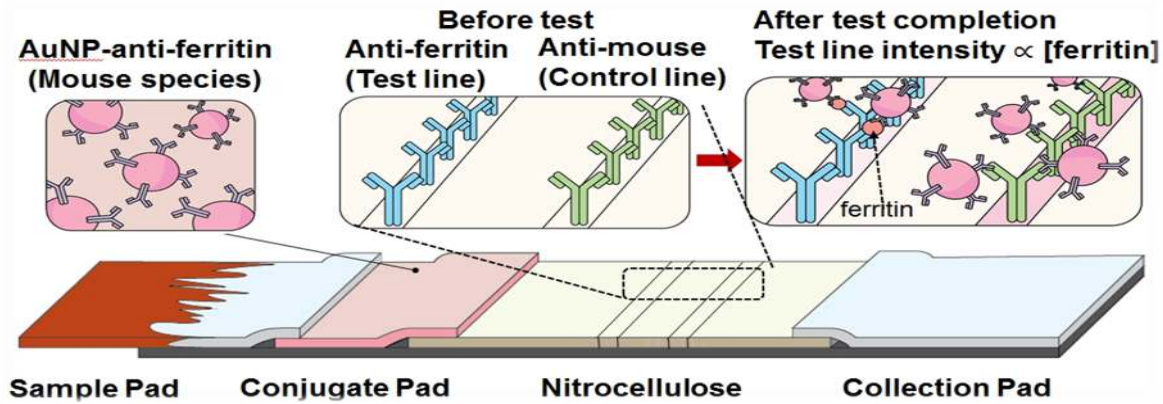


Setup

Biosensor Components



Lateral flow assays
Paper-based Microfluidic device



Advantages

- Low Cost
- Easy to use
- No additional instrumentation
- No moving parts, robust design
- Reagents can be pre-stored in dry form
- Sample moves by wicking- no pump required

Disadvantage

- No flow control, not as intelligent as other microfluidic devices with moving components such as valves, pumps, mixers

NutriPhone Components

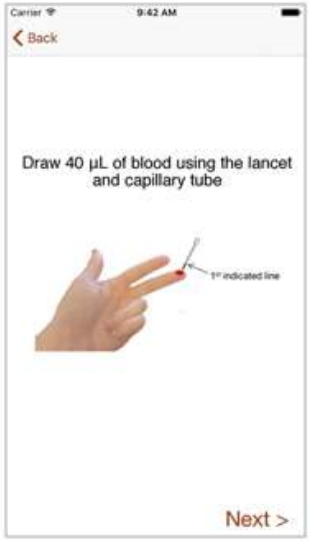
NutriPhone Components

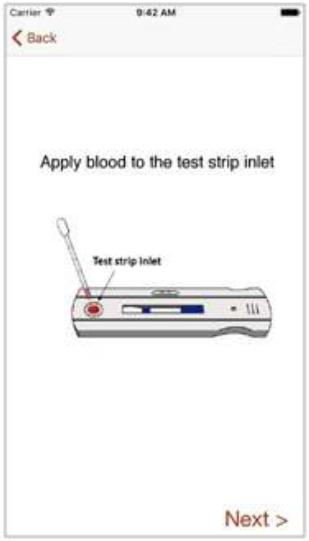
- Custom Test strip
- Mobile device with app
- Chase Buffer

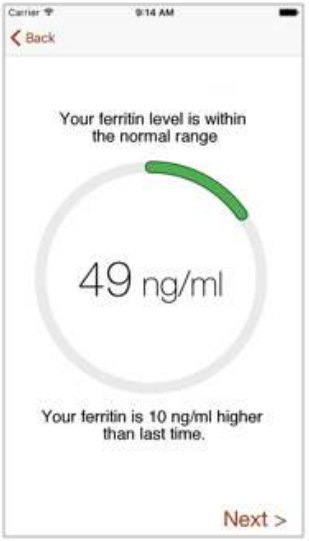
Option 1: Test strip attachment to mobile device camera

Option 2: Standalone portable reader for imaging test strips.

NutriPhone Mobile App







Mobile app provides step-by-step guidance to user

Assay Development Steps

- Determine assay type: Sandwich vs. Competitive
- Target protein chemistry (protein bound/free?)
- Expected detection range

↓

Selection and optimization of test line and control line antibodies/protein

↓

Calibration curve with spiked-buffer sample

↓

Calibration curve with commercial serum-based calibrator or standards

↓

Calibration curve with whole blood samples

Ferritin

- Ferritin molecular weight - 474 kDa, hydrodynamic diameter: 18nm.
  - ✳Multiple epitopes, molecular weight > 1 kDa, commercially available capture-detection Antibody pair => ***Sandwich Assay***

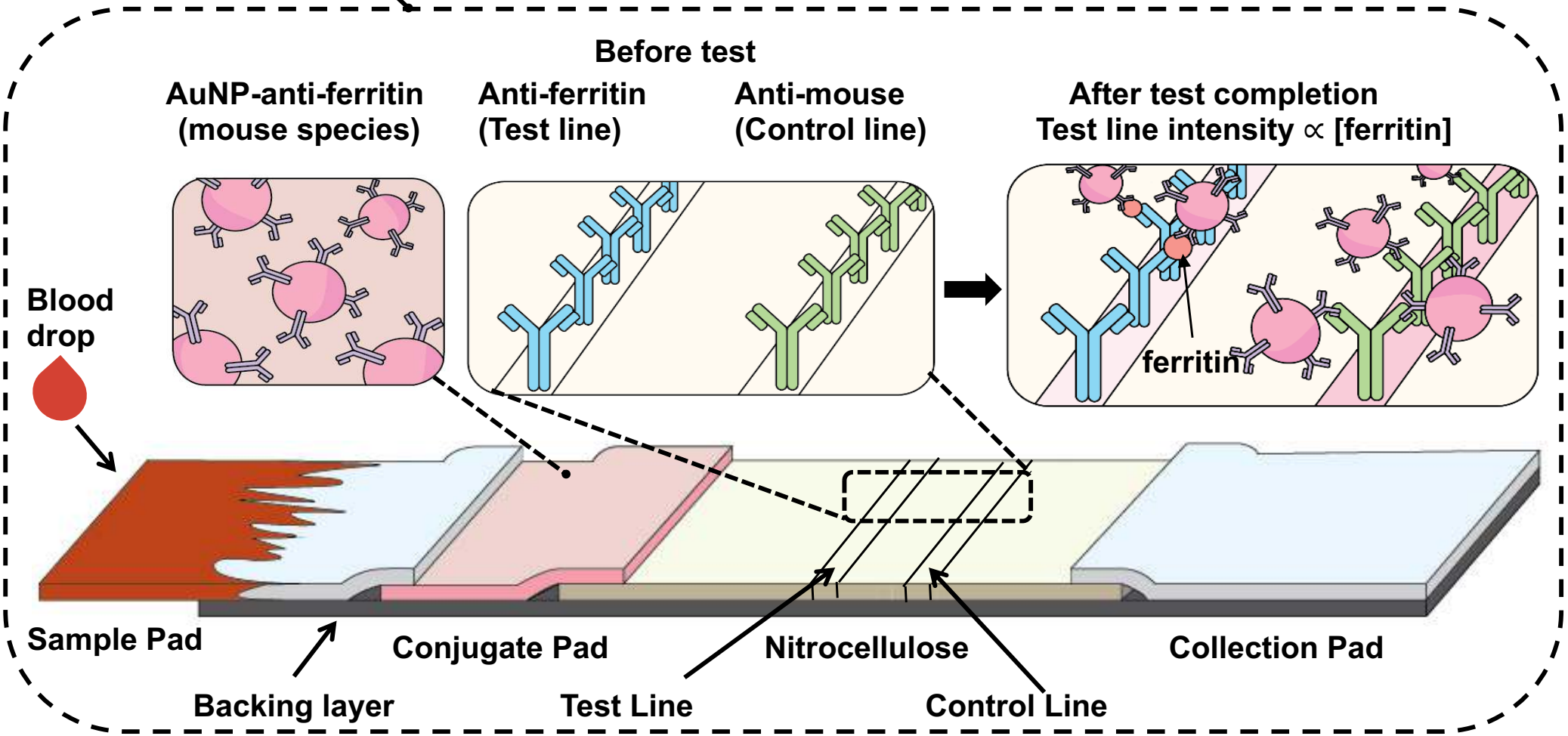
Table 5. Relative extent of iron stores on the basis of serum ferritin concentration Source: WHO 2011

Interpretation	Serum ferritin (µg/L)			
	Less than five years of age		Five years of age or older	
	Male	Female	Male	Female
Depleted iron stores	< 12	< 12	< 15	< 15
Depleted iron stores in the presence of infection	< 30	< 30	-	-
Severe risk of iron overload (adults)	-	-	> 200	> 150

From WHO 2011b

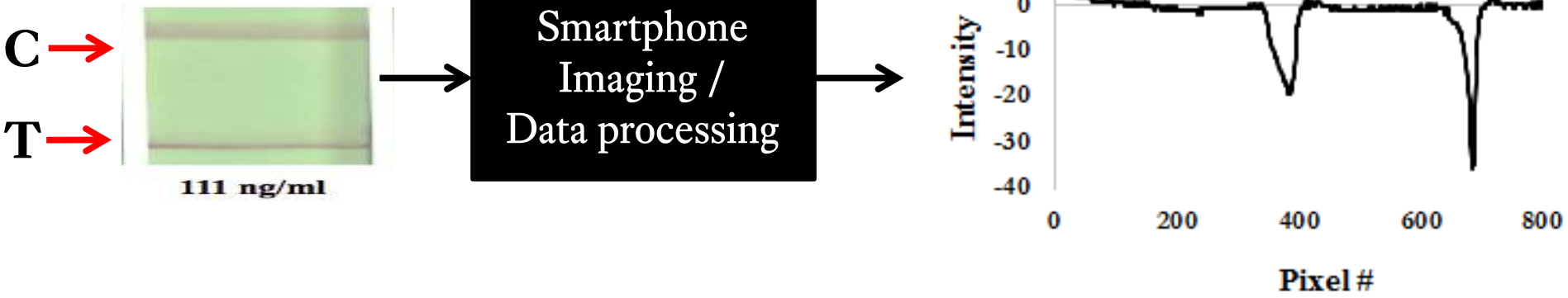
- Assay Detection Range : 10 - 300 ng/ml for iron status

Sandwich Assay
Ferritin



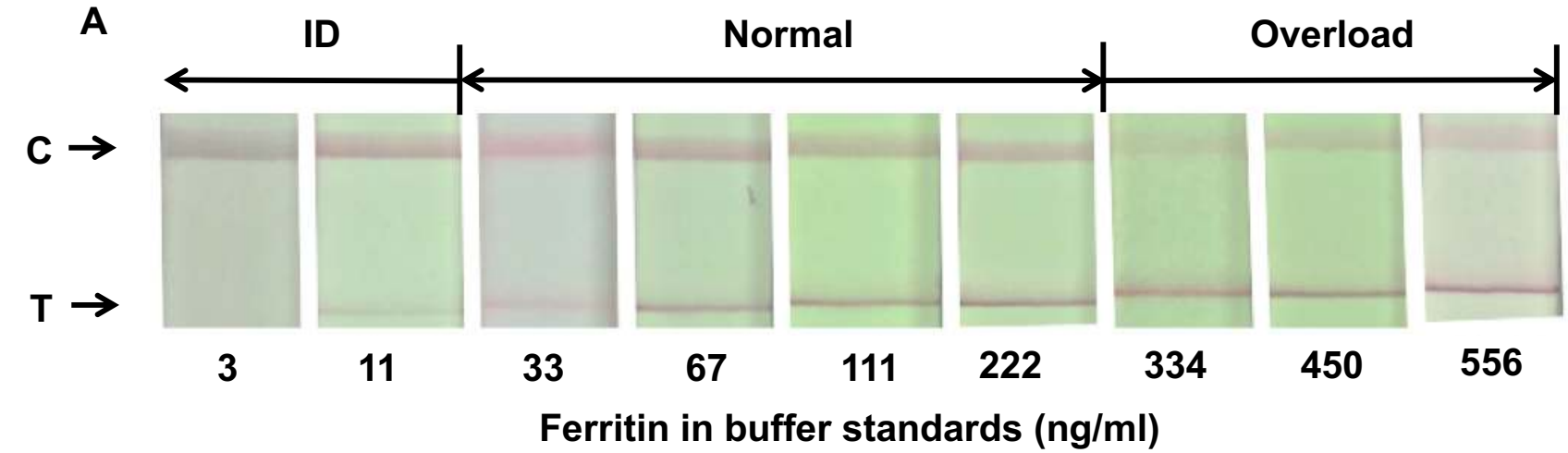
Test Strip *Analysis*

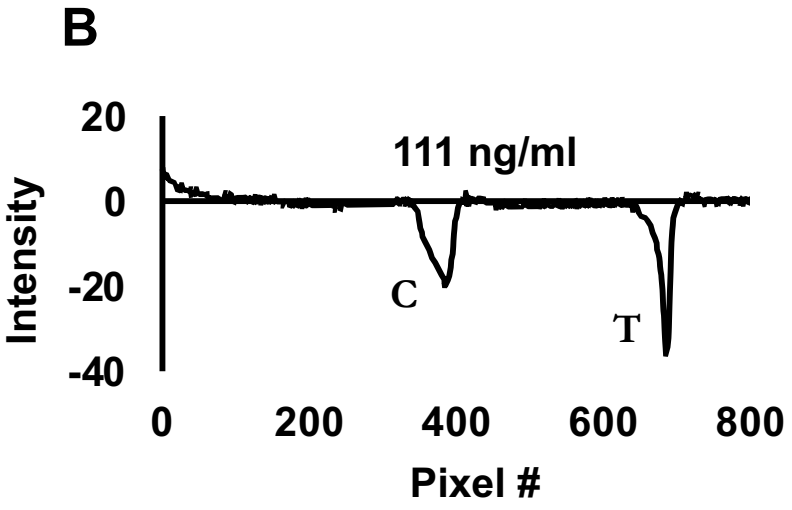
Ferritin concentration based on calibration

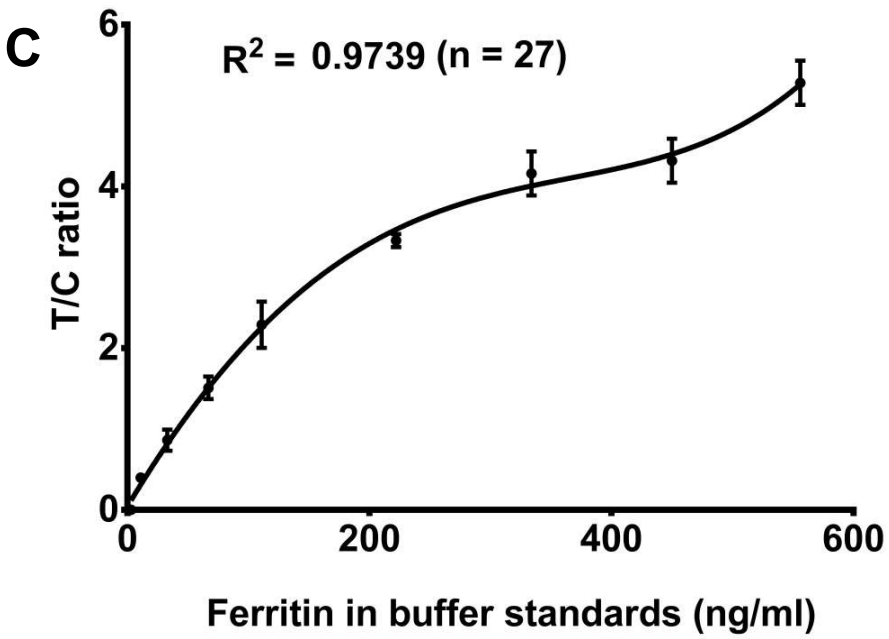


T/C Ratio ~ Ferritin Concentration

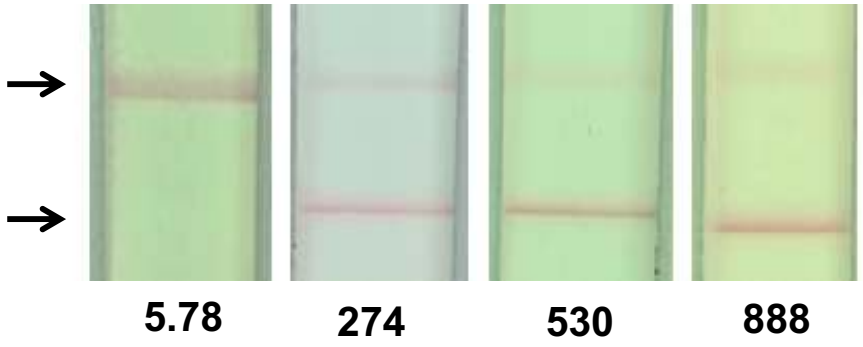
Calibration - Ferritin-Spiked Buffer

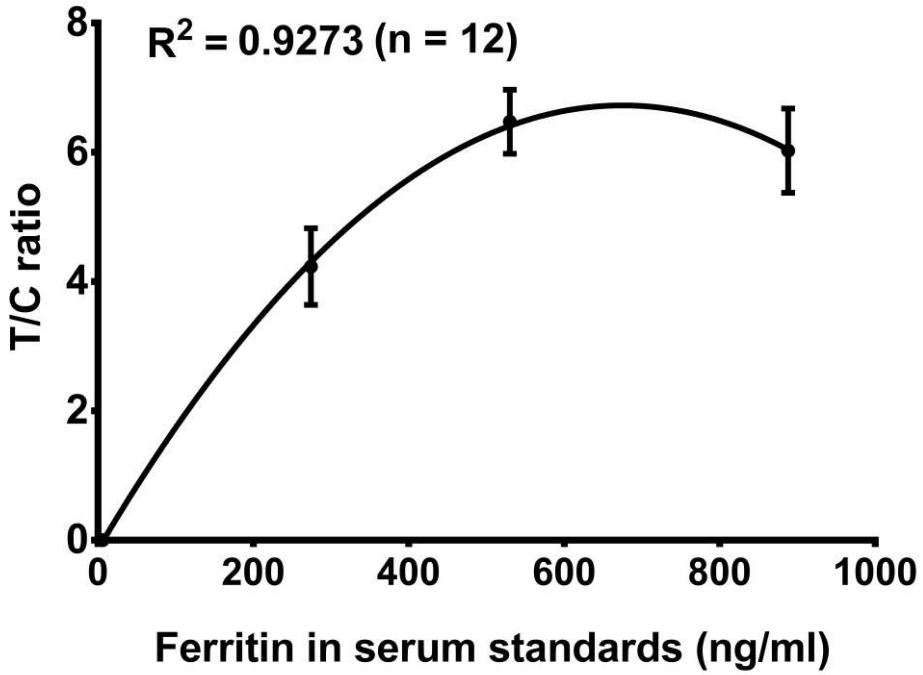




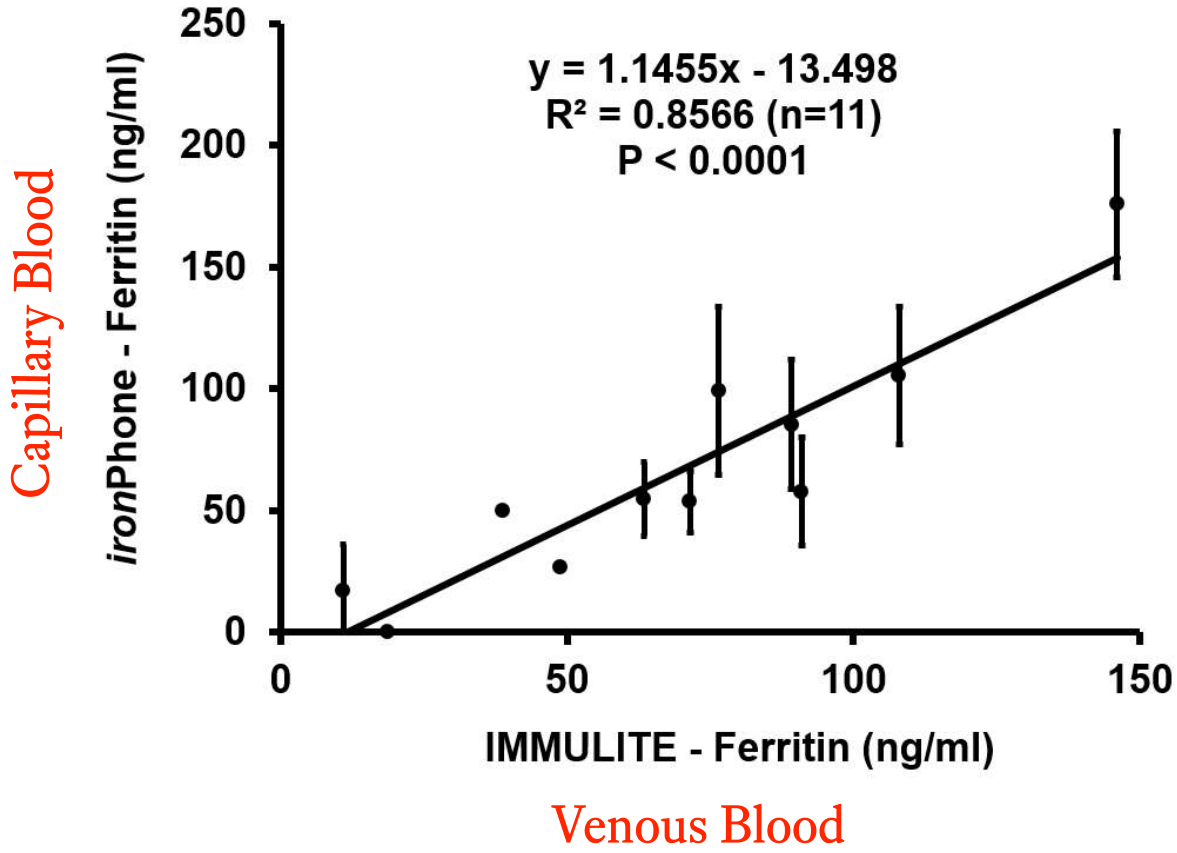


Calibration - Ferritin Serum-based Standard

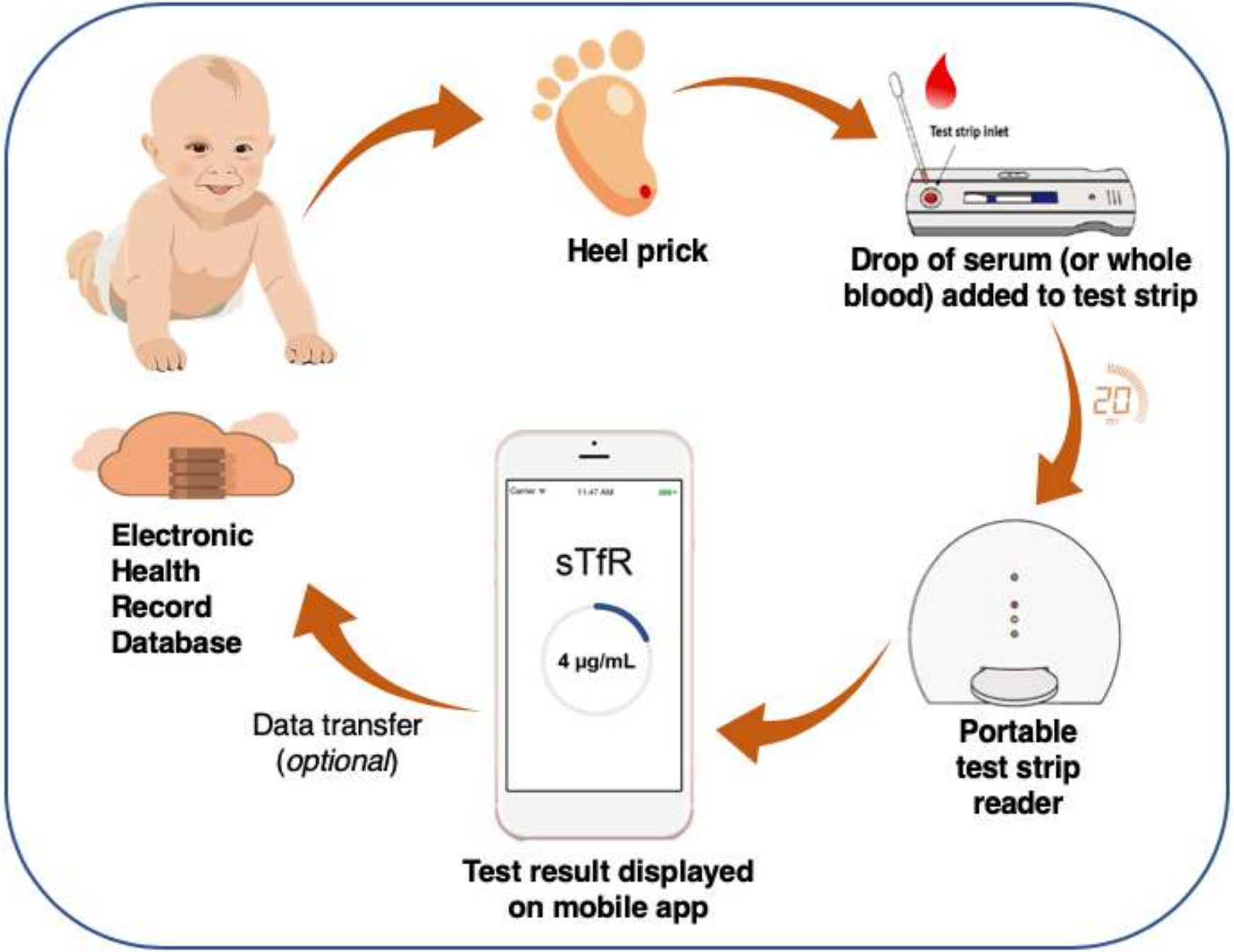




Calibration - Ferritin Whole Blood



Testing Protocol



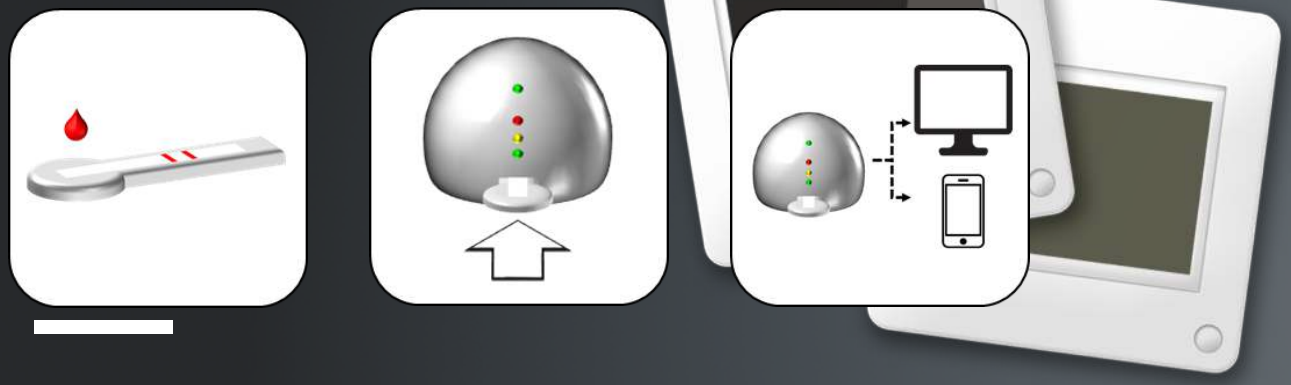
PNAS
Rapid diagnostic testing platform for iron and vitamin A deficiency

NutriPhone bridges the gap

1. Finger-stick applied to custom test-strips

2. Test reaction takes 10 minutes

3. Reader images test and [illegible] to [illegible]



Tests have been developed for: Vitamin D, Vitamin B_{12}, Vitamin A, CRP, Iron, AGP

15+ PEER-REVIEWED SCIENTIFIC PUBLICATIONS
3 ISSUED PATENTS
3 PENDING PATENTS

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

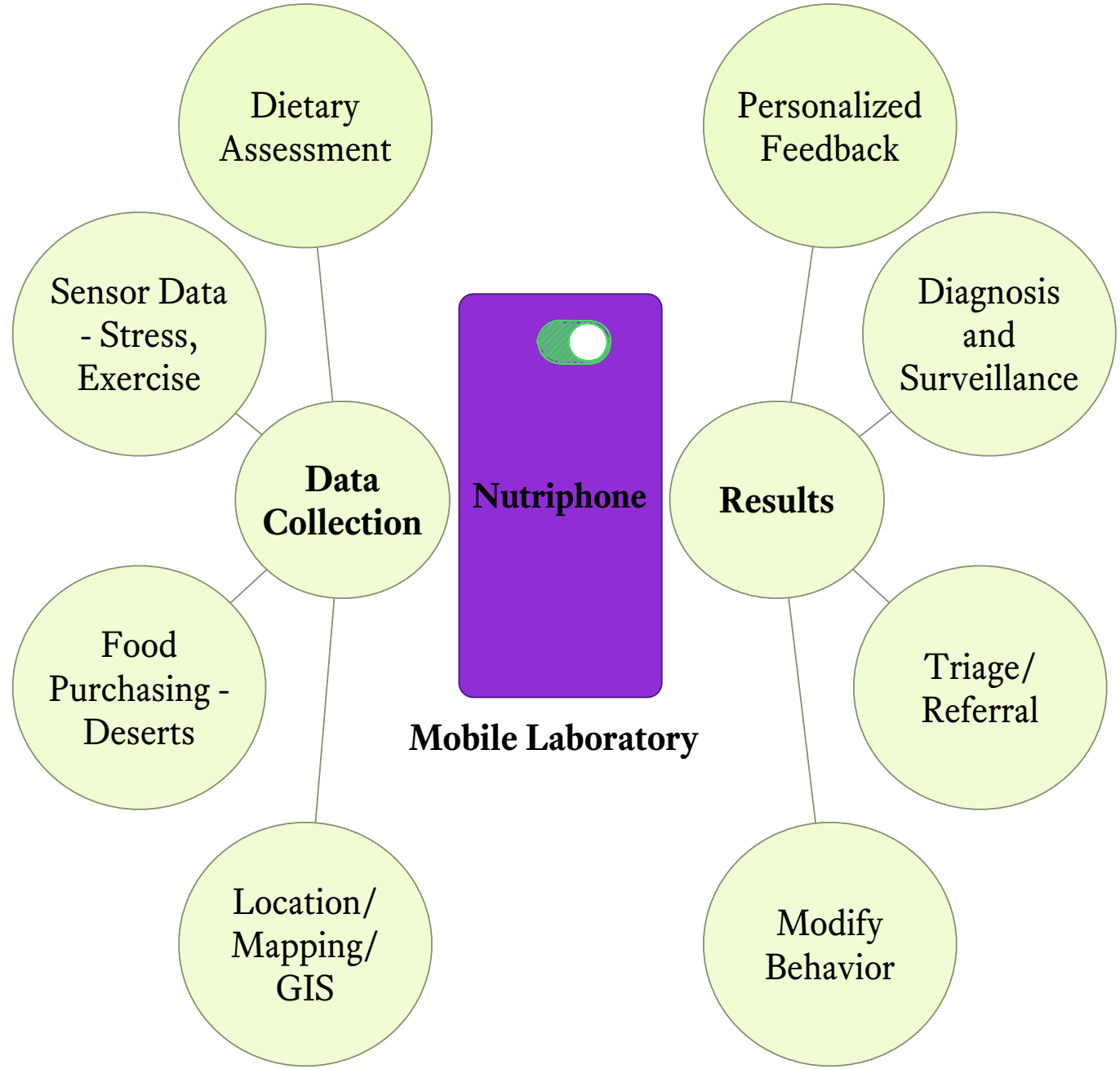
Cancer Biomarkers

- Alpha Fetoprotein (AFP)
- Prostate-specific antigen

Infectious Diseases

- Dengue
- Chikungunya
- Chagas
- Leptospirosis
- Malaria

Cornell Nutriphone



Improve Health

Major Challenge + Current Status: *Bringing to Market*

- Majority of the early stage R&D in universities does not advance beyond the research and small-scale validation phase to reach and truly benefit the end users. This gap is due to gaps in both funding and knowledge transfer.

- Early collaboration with industry will enable identification and scaling up of cutting-edge research into real technologies that could become available to the end user much earlier by shortening the technology and product development cycle.

WHO's ASSURED criteria to evaluate POCT for resource-limited settings

Affordable by those at risk of disease

Sensitive Few false-negative results

Specific Few false-positive results

User-friendly requires minimal training (simple to perform by users with little training)

Rapid (to enable treatment at first visit) and Robust (without the need for special storage)

Equipment free (no large instruments that need external power supply)

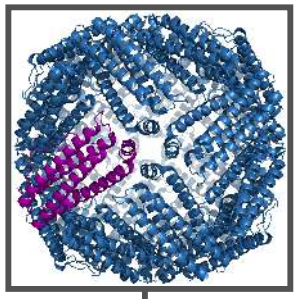
Delivered to those who need it (scale it up with sustainable business model to produce - **most challenging part in meeting ASSURED criteria**)

Path to Commercialization

Our current work addresses these goals…

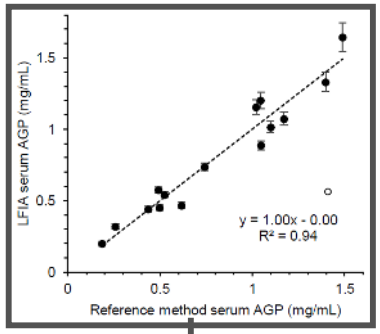
How do we do this?

Identify biomarker with diagnostic need



Optimize assay for required physiological range

Initial small-scale lab validation and performance testing



Commercialize, optimization and manufacturing

Rigorous diagnostic performance evaluation, shelf life, temperature/ humidity effects etc

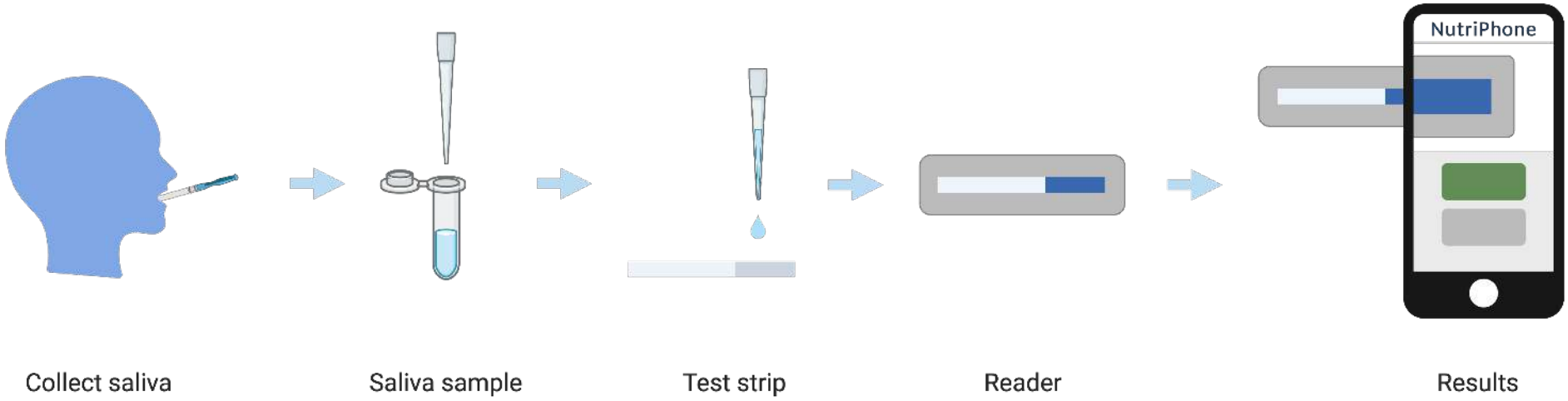
Academic Proof of Concept

Industry Large Scale Production

Images: Siemens, creative-diagnostics, biodot, Vossman

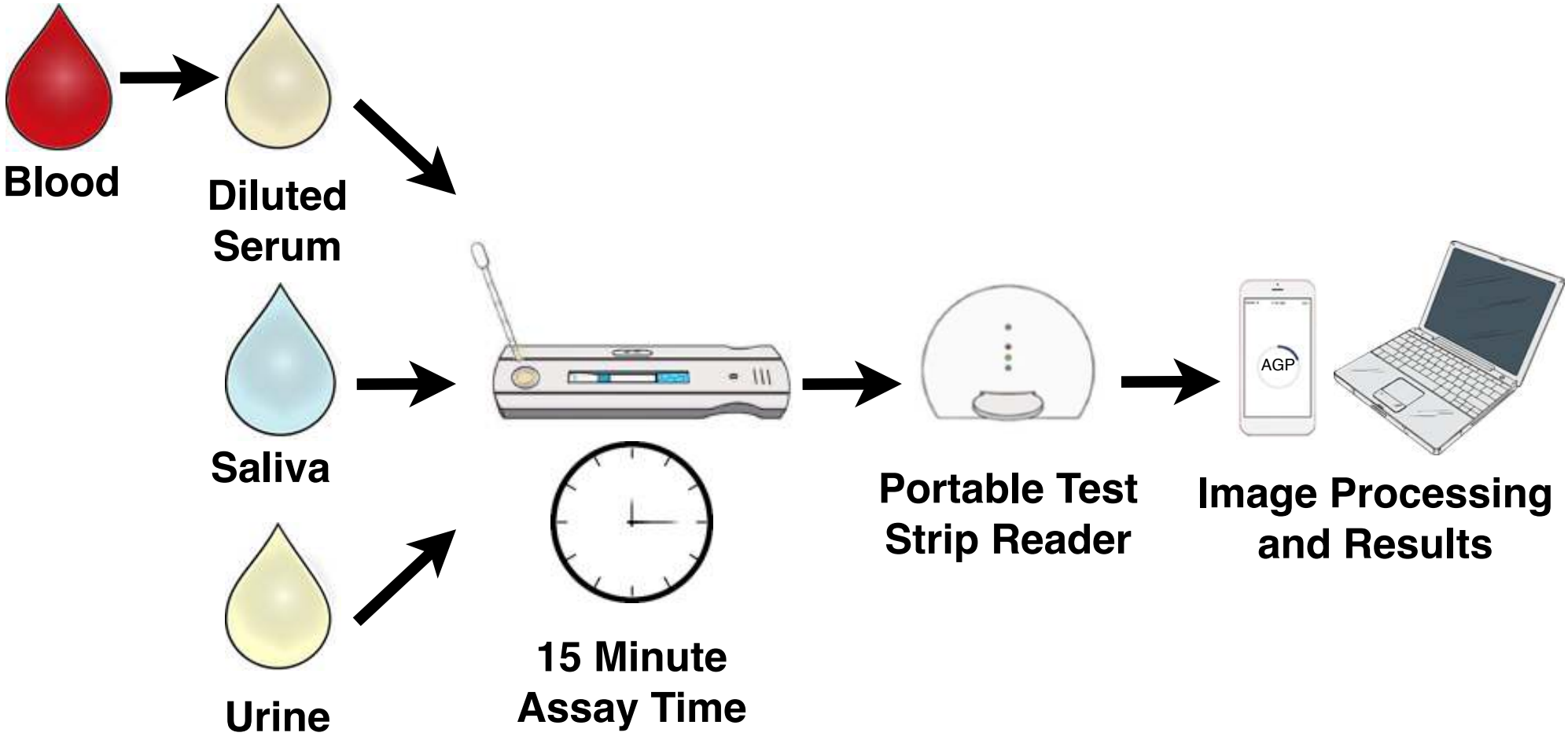
Future plans/challenges: Other biological matrices, Continuous Monitoring

Expanding available sampling sources



Elena Cherchi using biorender.com;
NIH Technology Accelerator Challenge Prize 2020

Expanding available sampling sources



Gannon, Glesby, Finkelstein, Raj, Erickson, and Mehta, 2019, Current Research in Biotechnology

Continuous Monitoring

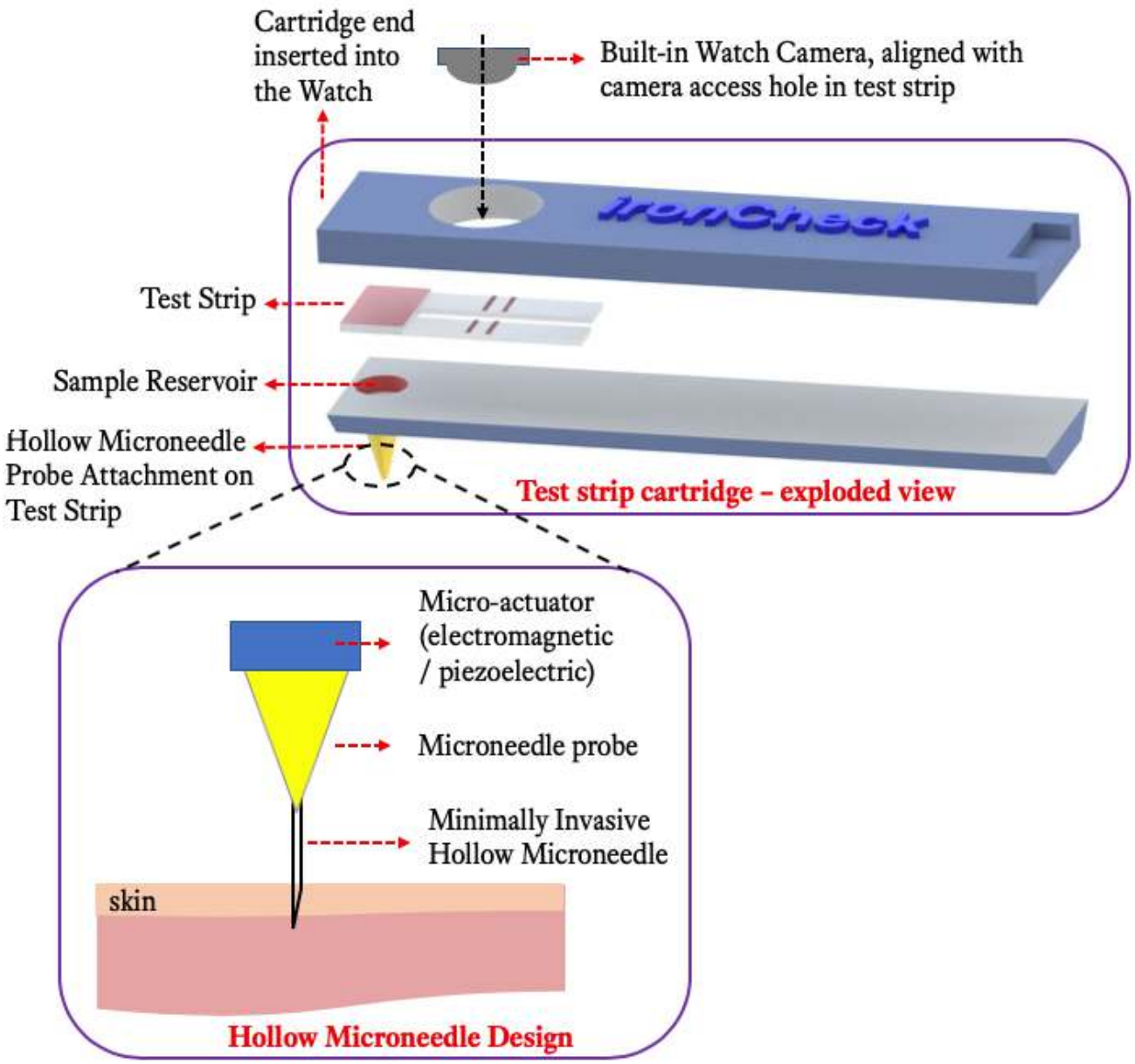
- Is there a need for continuous monitoring of nutritional status / Wearable Technology? What are target biomarkers of interest?

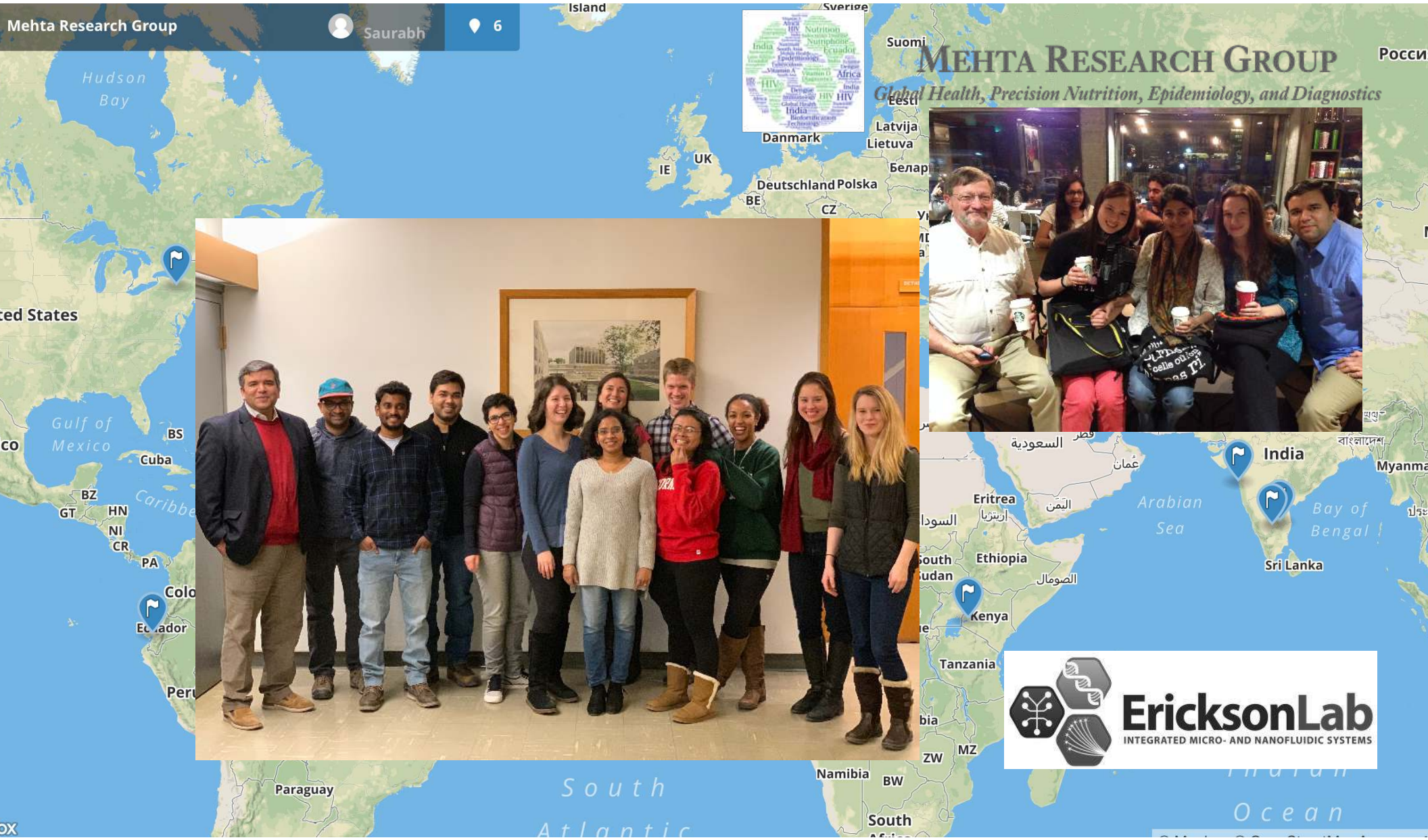
- Current wearable sensors use interstitial fluid as test sample - example: Abbott freestyle *Libre* glucose monitor

NutriWatch


NutriWatch
02-02-2020 7:01pm
Ferritin: 20 ng/ml
sTfR: 6 µg/ml
TBI: 10 mg/kg
Iron Status : Normal
IronCheck


NutriWatch
02-02-2020 7:01pm
Ferritin: 20 ng/ml
sTfR: 6 µg/ml
TBI: 10 mg/kg
Iron Status : Normal


Cartridge end inserted into the Watch
Built-in Watch Camera, aligned with camera access hole in test strip
IronCheck
Test Strip
Sample Reservoir
Hollow Microneedle Probe Attachment on Test Strip
Test strip cartridge – exploded view
Micro-actuator (electromagnetic / piezoelectric)
Microneedle probe
Minimally Invasive Hollow Microneedle
skin
Hollow Microneedle Design



Acknowledgments

Acknowledgments

NSF

HarvestPlus
Better Crops • Better Nutrition

NIH
National Institutes of Health

gain
Global Alliance for Improved Nutrition

Department of Defense
United States of America

Cornell University
David R. Atkinson Center for a Sustainable Future

Micronutrient Initiative

NBTC
Nanobiotechnology Center

CNF
Cornell NanoScale Science and Technology Facility

USAID
FROM THE AMERICAN PEOPLE

CornellEngineering

Cornell University
Division of Nutritional Sciences