



# Bioelectronic Platform with Point-of-Care Applications

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## Abstract

### Background

A new bioelectronic platform is described that is designed for multiple Point-of-Care (POC) diagnostic applications, including protein, DNA and small molecule diagnostics. A self-assembled monolayer (SAM) technology is presented that demonstrates quantitative, ultra-sensitive, precise and accurate measurement of a number of clinical analytes in biological samples (e.g. whole blood, urine, semen, prostatic fluid, saliva etc). Cyclic voltammetry techniques measuring a ratiometric signal allow for a rapid, self-calibrating, fully quantitative dose response with broad dynamic range (over 4 logs of analyte concentration). This capability lends itself to any applicable clinical assays to be executed on the Ohmx platform, with a minimal sample volume (1-50 uL), resulting in performance level similar to reference lab tests. The analytical performance of the sensor, and the clinical validation for multiple analytes (Hemoglobin A1c, hs Troponin I, TSH, hs CRP, DNA and lactate) are discussed.

### Methods

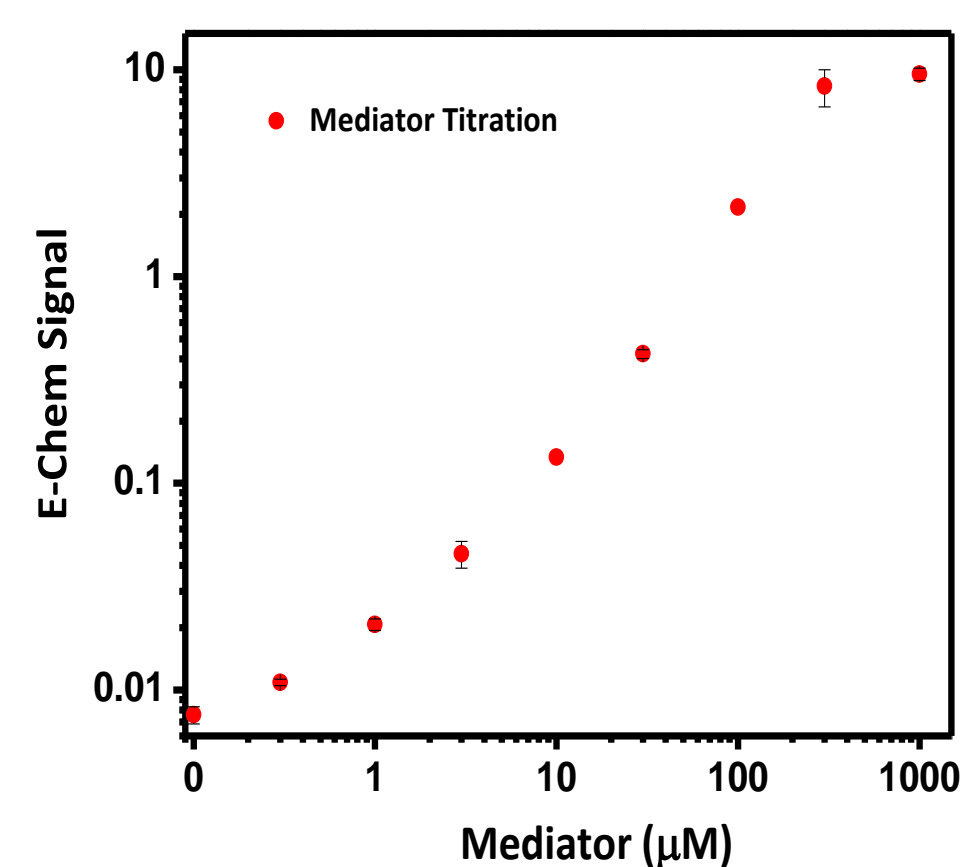
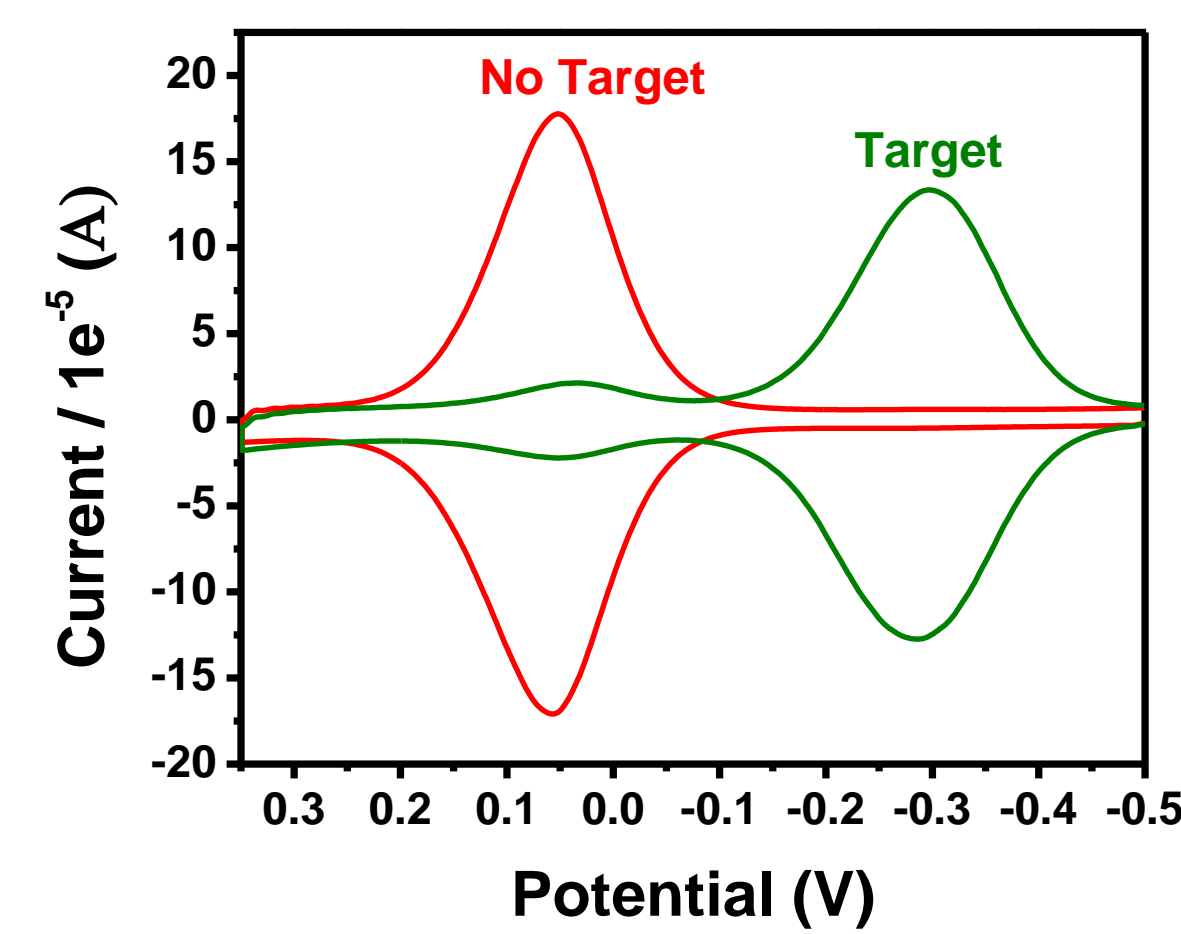
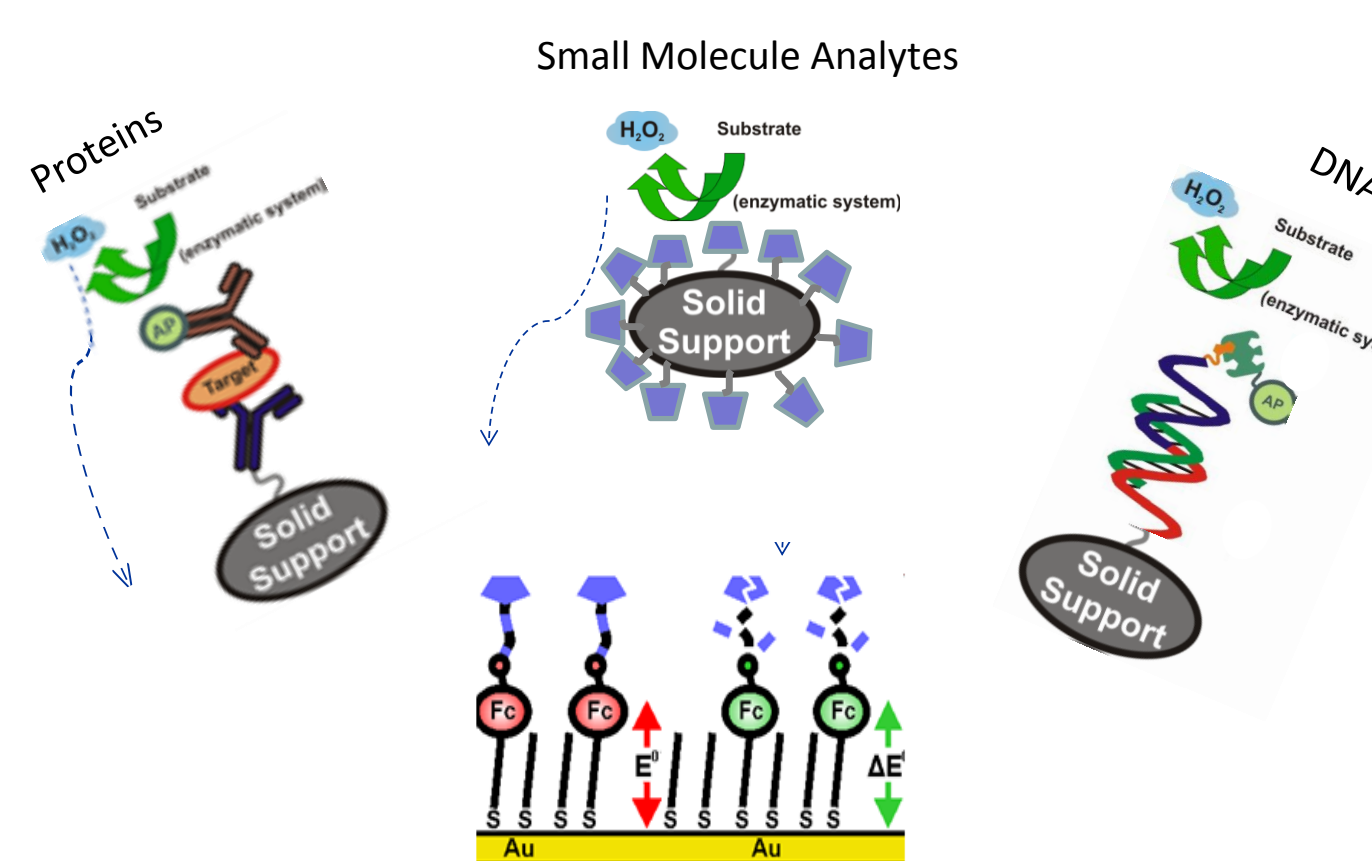
Following standard solution bioassays (immunoassays, hybridization or enzymatic reactions) a chemical mediator specifically reacts with the monolayers on the gold micro-electrodes. For all assays, a dose response from commercially available calibrators that spans the analytes' clinical relevant range was obtained. Further clinical validation is presented with 50 clinical samples tested for A1c, 65 samples tested for Lactate, 72 samples tested for Troponin I and 50 samples for TSH. The clinical samples were provided by hospital collaborators and pre-tested with clinical immunoanalyzers. A correlation statistical study is shown between the Ohmx test and reference methods.

### Results

The Ohmx HbA1c is a single measurement test in 2 uL of whole blood, a TAT of 3 minutes with a linear response ranging from 2.7% (6.0 mmol/mol) to 19.8% (192.9 mmol/mol), an intraday precision of CV less than 3% and with R<sup>2</sup>=0.93 linear correlation with BioRad clinical immunoanalyzer. The Ohmx troponin I assay is a high sensitivity assay that has a LOD of 1 pg/mL with a TAT of 15 min, with CVs from 1-10% and a linear correlation with R<sup>2</sup>=0.95 with Siemens immunoanalyzers. The TSH Ohmx test has an LOD of 0.0024 uIU/mL, a TAT of 15 min and R<sup>2</sup>=0.9 correlation with clinical the Beckman Coulter DXI. SNP differentiation is shown for DNA factors II, IV and MTHFR and a lactate test with a linear range from 0.2 to 28 mM.

## Technology Overview

Assays use standard bioassay procedures (immunoassays, hybridization or enzymatic reactions) where a tagged probe / antibody, or a mediator specifically interact with nanolayers on independent gold micro-electrodes.



### Platform Benefits

- Proven bioelectronic technology
- Rapid signal detection
- Broad dynamic range
- Fully quantitative results
- Accurate and precise assays
- Sensitive detection
- Minimal sample volume (1-50uL)

Platform Features	Benefits to the POC
Bioelectronic	Robust - Portable - Easy to use No optics /lenses - Low Cost instrument
Quantitative	Broad Dynamic range, Sensitive, Precise, Accurate and Reproducible
Ultrasensitive	High Sensitivity testing for Troponin I and Thyroid Stimulating Hormone
Rapid Assays	MD Intervention during patient visit
Versatile	Measure Proteins, Small molecules, DNA
Small sample (1-50 uL)	Fingerstick based; Patient and RN benefit. Also: Whole Blood, Plasma, Urine, PF, Saliva

## System Development

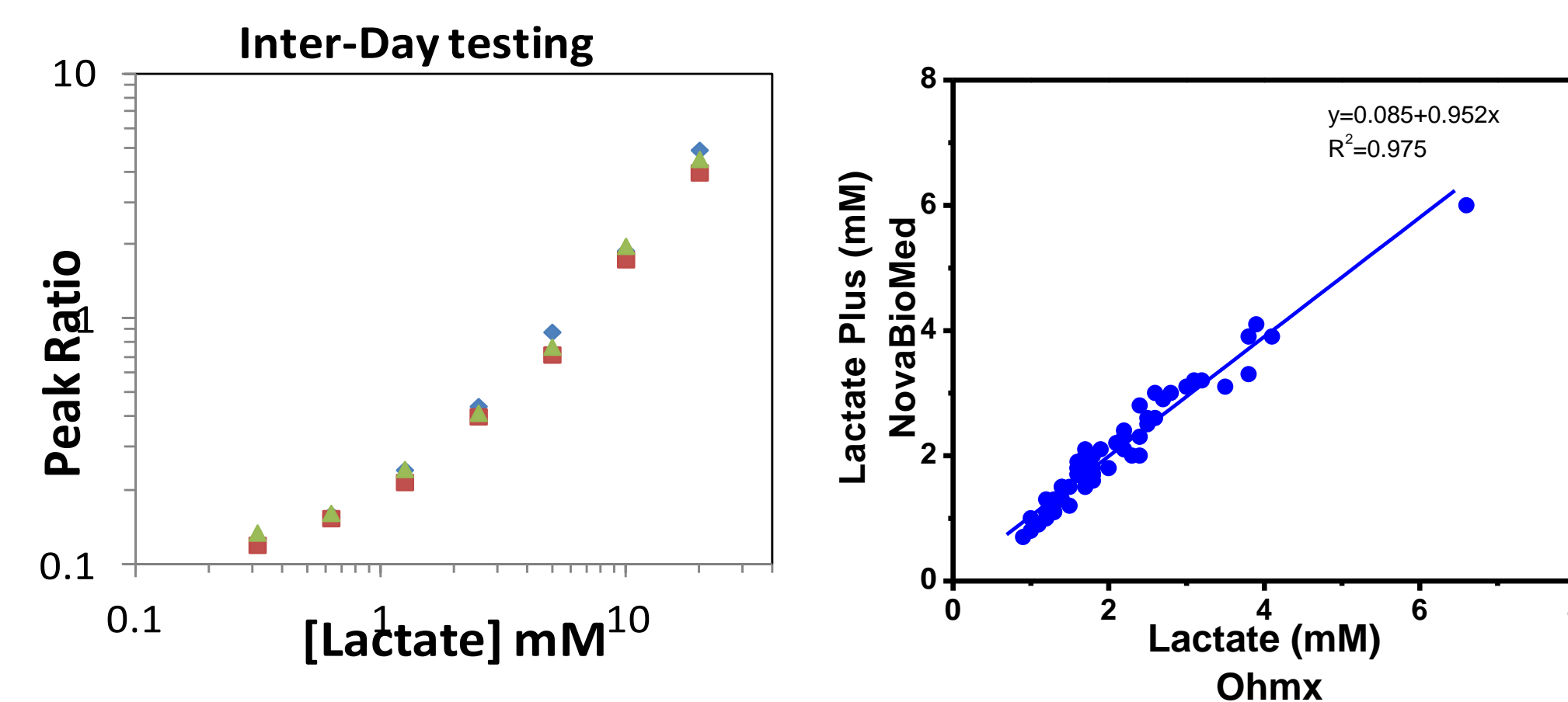
Prototype software, electronic reader, and disposable cartridge development complete  
ISO 13485 compliant Quality System

- Alpha system is fully developed as a programmable automated system for 'sample to result'
- Ohmx products include potentiostat reader and disposable cartridge.
- CE Mark for Lactate test scheduled for Q4 2014
- Alpha system uses liquid handler for verification and validation testing.



## Small Molecule Test: Lactate Detection for Sepsis

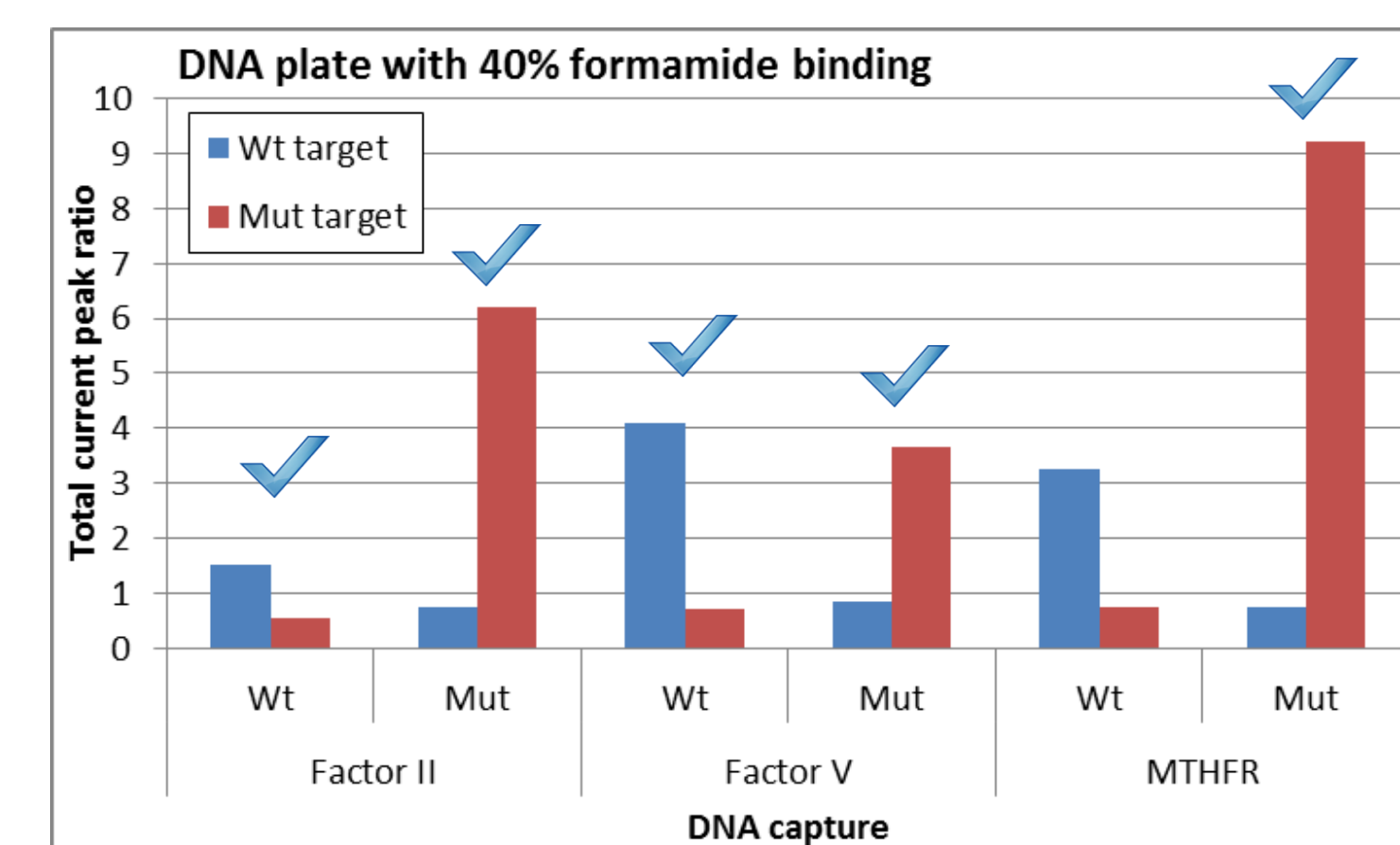
Lactate is the most prescribed test in hospitals for Sepsis testing. Sepsis is the 10th leading cause of death in the US (CDC) and the leading cause of death in non-coronary ICU patients.



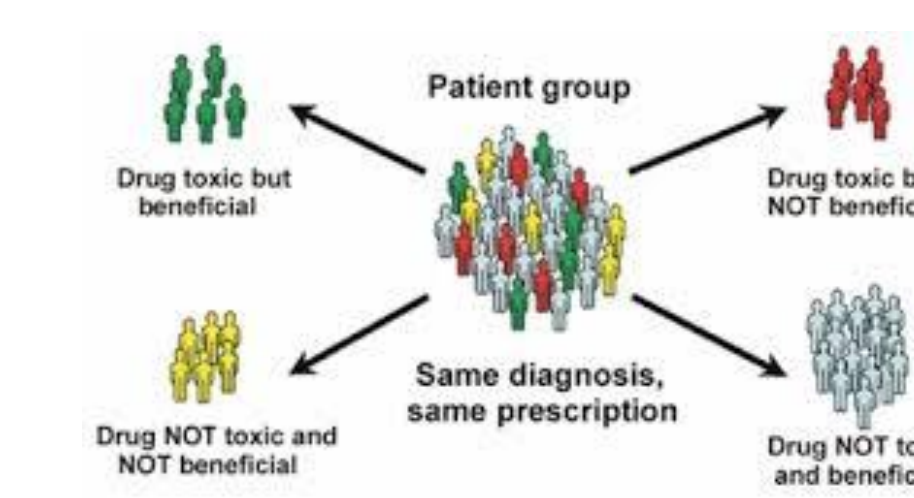
- Results:**
- CV= <3%
  - LOD = 0.01 mmol/L
  - TAT= 3 min
  - Very good correlation with predicate for n=65
  - R<sup>2</sup>=0.975 with NovaBiomed Lactate Plus

## DNA –SNP detection for Hypercoagulation

Three different SNP tests for three different mutant genes differentiating from wild-type gene for a single pair mismatch can indicate predisposition for Hypercoagulation and Deep Vein Thrombosis (Travelers test)



- Results:**
- DNA Mutant Factors: Type II, Type IV and MTHFR
  - TAT = 8 min, C= 10 nM
  - Single base pair differentiation
  - Complementary Diagnostics capability



## Ohmx Tests Developed to Date

Target	Analytical Performance	Assay Validation
<b>Proteins</b>		
Troponin I	LOD = 1 pg/mL	72 clinical samples; R <sup>2</sup> =0.95 correlation
Hemoglobin A1c (Quantitative)	Range = 2.7% - 19.8%	50 clinical samples; R <sup>2</sup> =0.93 correlation
Hemoglobin A1c (Screening)	Range: Above/Below 6.5%	TBD
<b>Thyroid Stimulating Hormone (TSH)</b>		
TSH	LOD = <0.0024 uIU/mL	50 clinical samples R <sup>2</sup> =0.9 correlation
hs-CRP	LOD = 1 pg/mL	Ongoing
BNP	LOD = 10 pg/mL	Ongoing
PSA	LOD = 1 pg/mL	Ongoing
HSP70	LOD = 32 pg/mL	In cell lysates
ALT	LOD = 10 mU/mL	Ongoing
<b>Small Molecules</b>		
Lactate	LOD = 0.1 mmol/L	65 clinical samples R <sup>2</sup> =0.975 correlation
Cholesterol	Range = 10 - 1300 uM	High Precision
Glucose	Range = 0.3 - 10 mM	Broad Dynamic Range
FAD metabolite	LOD = 10 pM	High Reproducibility
NADH	LOD = 0.7 nM	In cell lysates for drug discovery
ATP	LOD = 5 nM	
<b>DNA</b>		
DNA Co-Ag Factors (II, V, MTHFR)	Yes / No (Qualitative)	Ongoing

## Acknowledgements



### Collaborators:

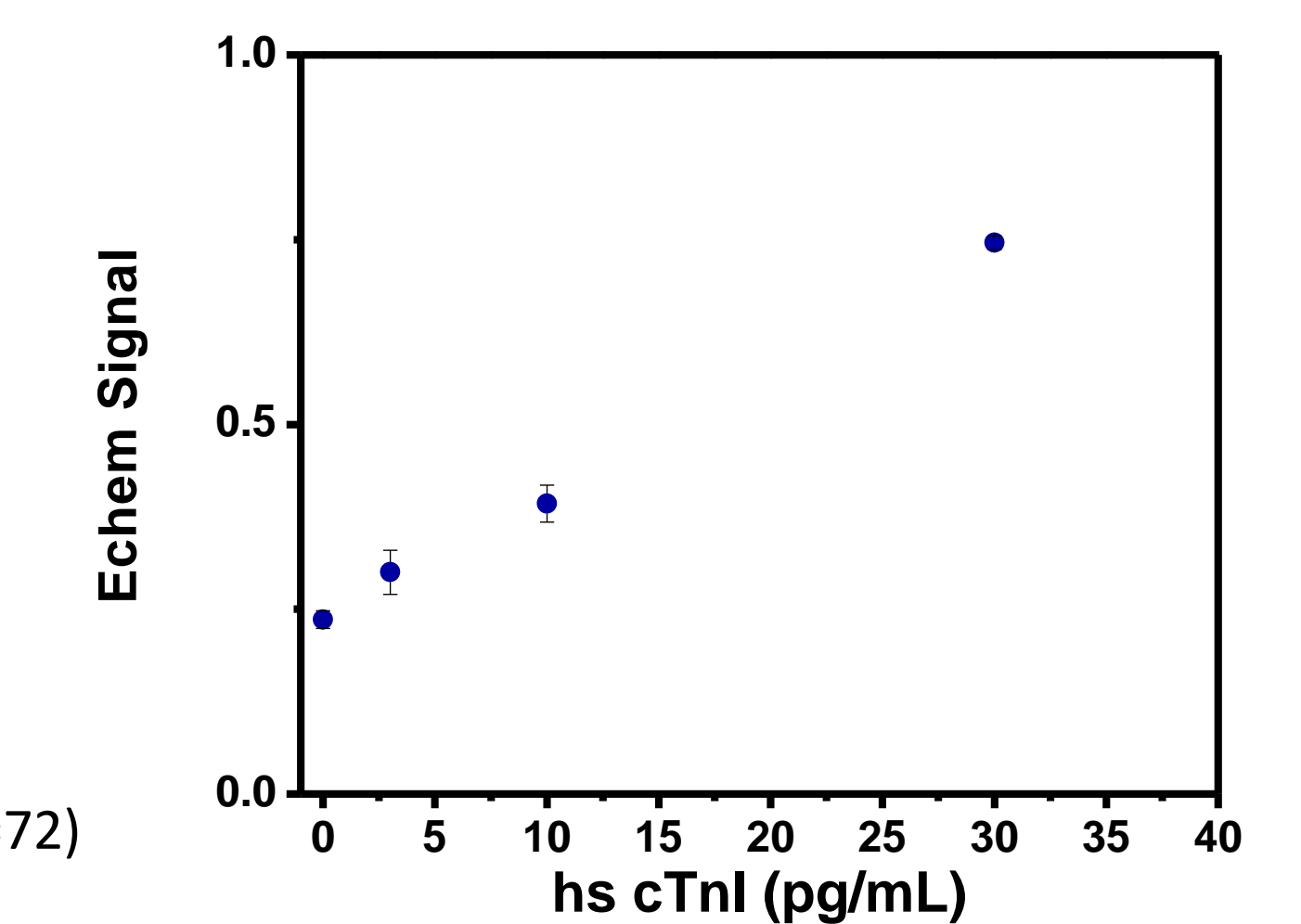
Dr. William Catalona (NU)  
Dr. Steve Smith (COH)

## Proteins: High Sensitivity Troponin I - AMI

- There is a need for accurate rapid Rule In/Rule Out for MI patients in the ED
- Ohmx will provide a High sensitivity cTnI assay < 15 mins; with low cost disposable

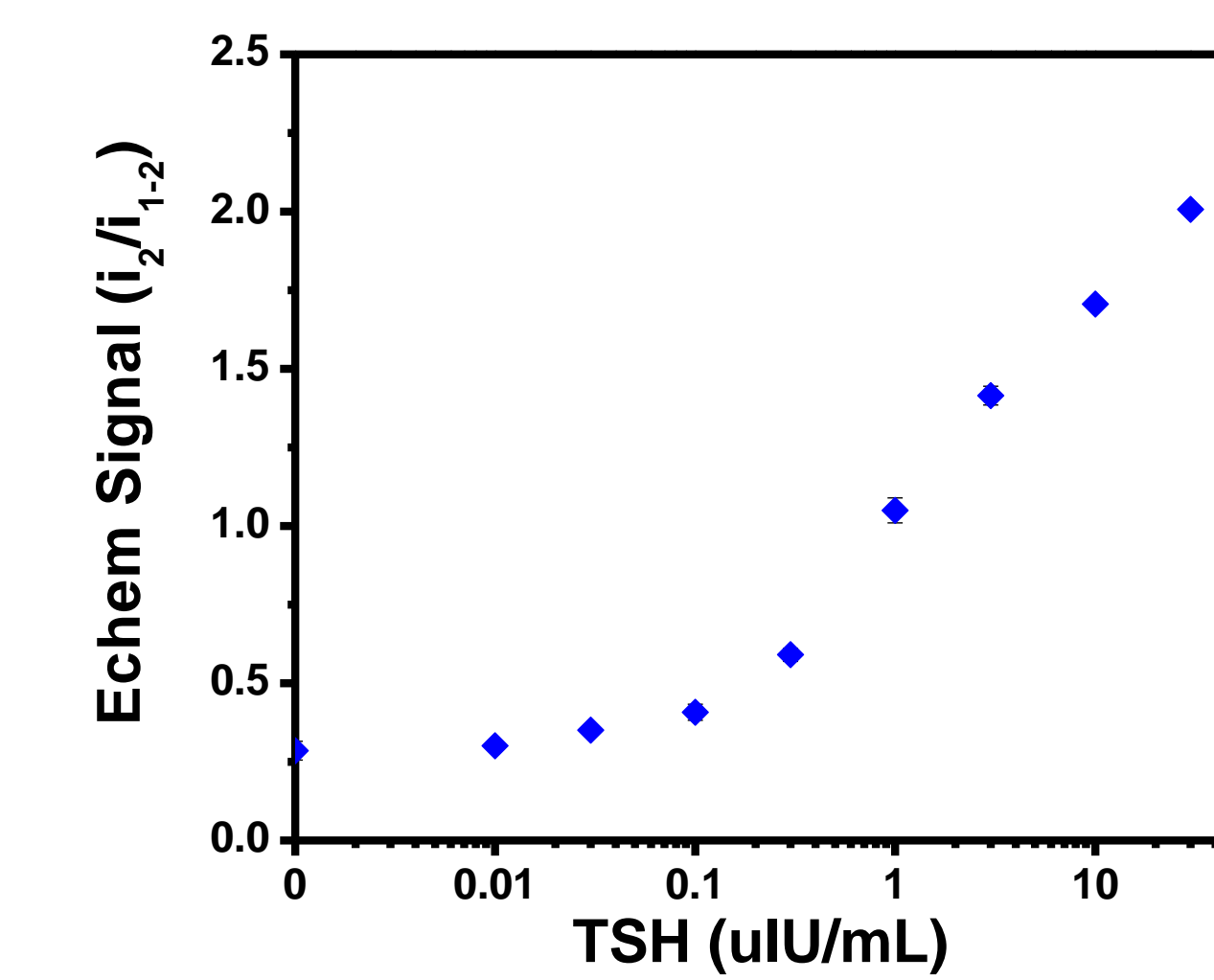
cTnI pg/mL	Signal	CV%
0	0.236	5.1%
3	0.300	9.8%
10	0.393	6.3%
30	0.746	1.1%

- CV% at 99 Percentile
- CV= 6.3% at ~10 pg/mL
- LOD = 1 pg/mL, CVs = 1-10%
- TAT= 15 min
- R<sup>2</sup>=0.95 with Siemens Analyzers (n=72)

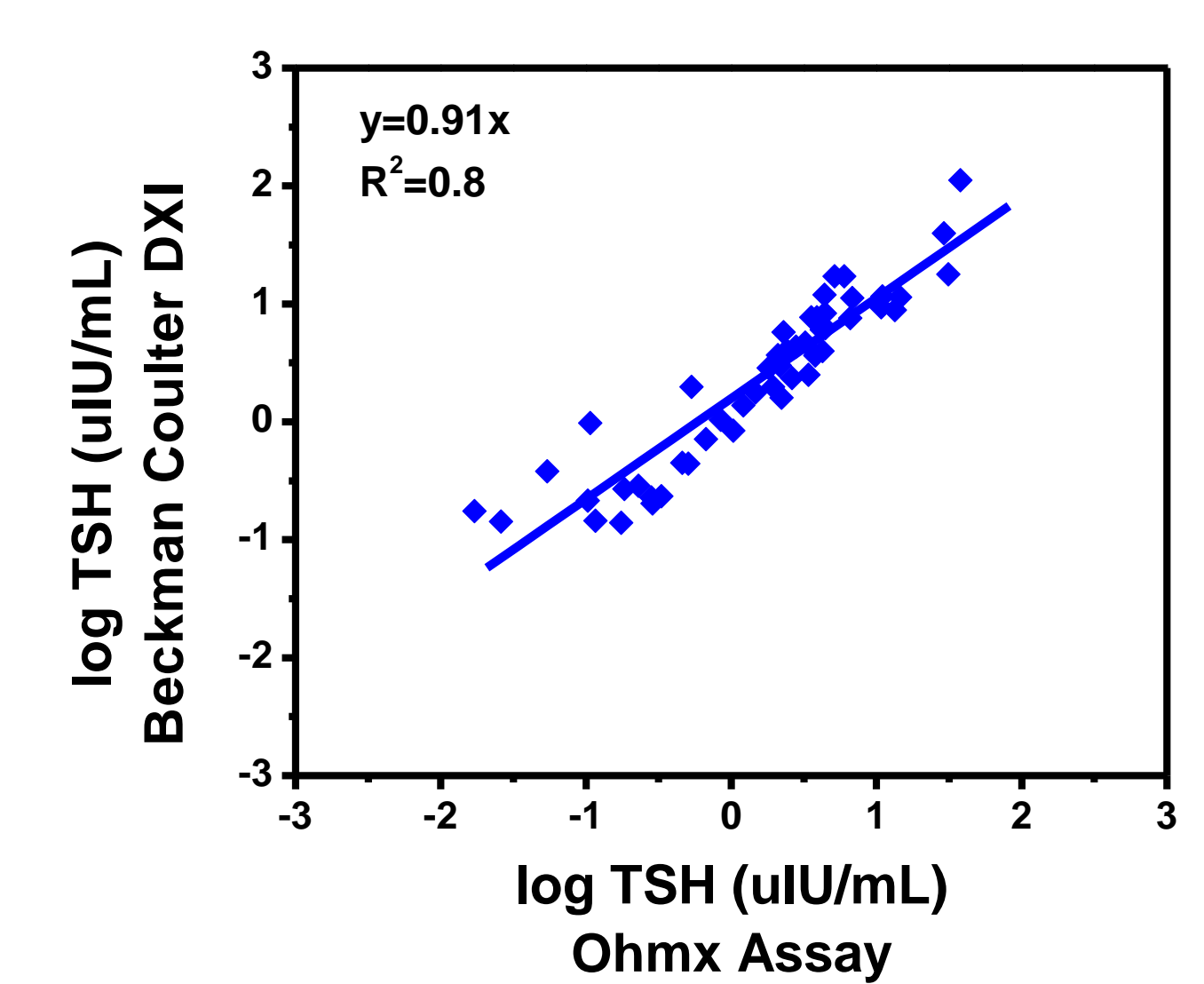


## hs-Thyroid Stimulating Hormone (TSH) Assay

- Thyroid Stimulating Hormone triggers the thyroid to release hormones that affect carbohydrate and lipid metabolism, cardiovascular, reproductive and central nervous systems.



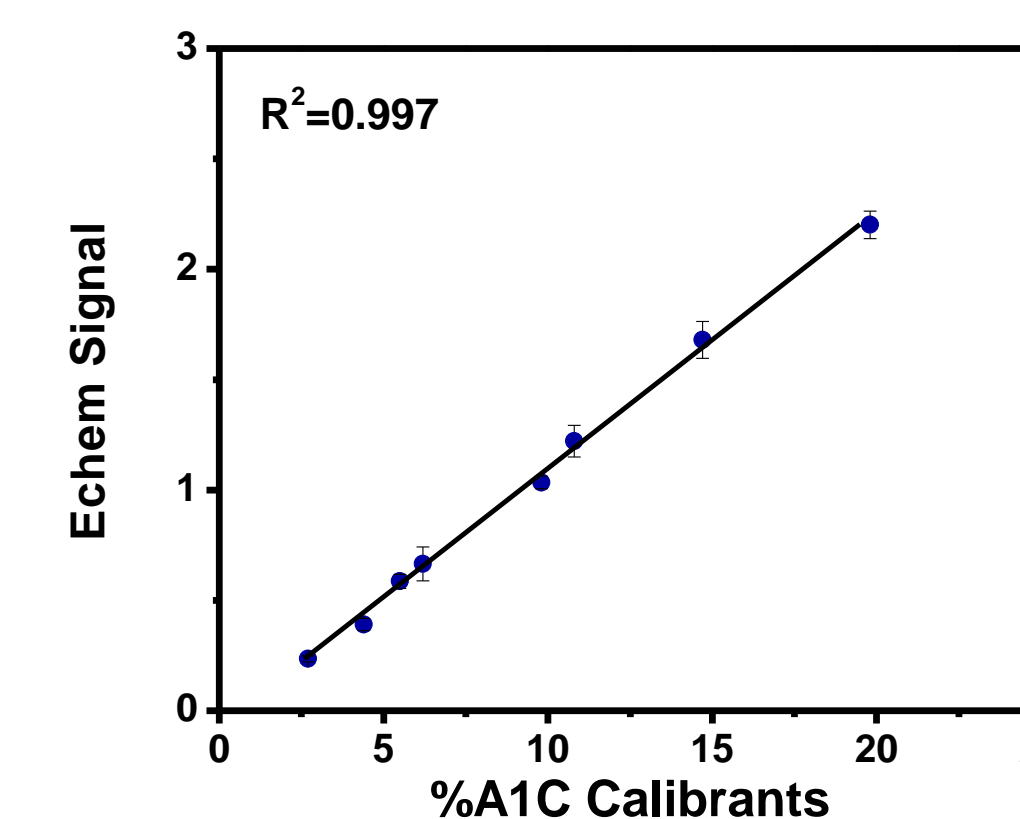
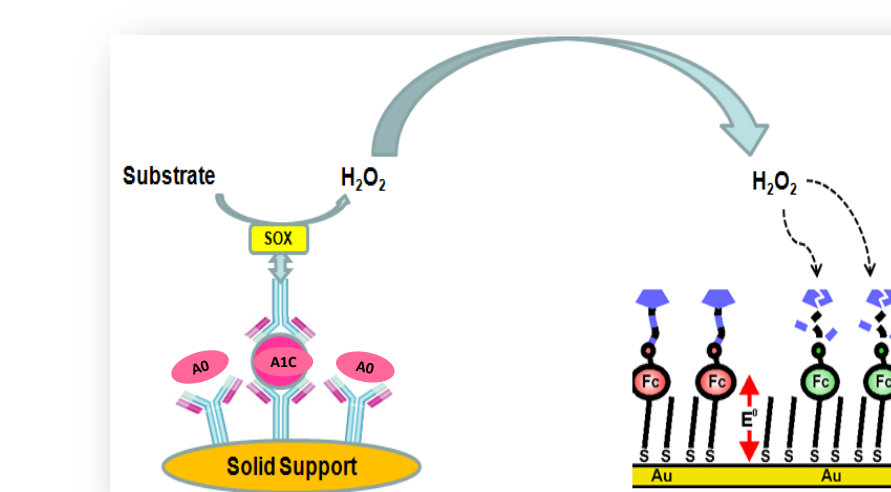
TAT= 15 min  
hs LOD=0.0024 uIU/mL



Good correlation with Beckman Coulter DXI R<sup>2</sup>= 0.9 (n=50)

## A1C – Type II Diabetes

- The American Diabetes Association recommends A1c "as a means of diagnosing diabetes and identifying pre-diabetes." Ohmx is developing its POC device for an indication of use for diagnosis and monitoring.
- Single measurement assay for Hemoglobin A1C ensures accuracy & precision.



### Results:

- Assay time is ~3 min . Single measurement of A1c ratio (not separate measurements for total Hb/glycated Hb)
- LOQ = 2.7% Dynamic range 3%-20%
- Intraday CV <3%, n=50
- R<sup>2</sup>=0.93 correlation with BioRad clinical analyzer
- Better correlation with than the A1cNow POC device

Ohmx LDT	BioRad Immunoanalyzer	Bayer POC A1c-Now
5.1	5.6	4.9
6.7	6.0	4.9
4.9	5.5	5.0
5.1	5.3	5.1
4.7	5.6	4.8
4.1	5.5	5.0
5.1	5.5	4.8
4.8	5.6	4.8
5.9	5.5	4.7
5.6	5.8	5.7
5.5	5.4	4.8
6.2	5.8	5.1
5.8	5.8	5.1
5.8	5.8	4.8
5.6	5.8	5.3
5.0	5.1	4.7

## Summary

Ohmx test performance was confirmed with strong correlation with and clinical immunanalyzers of predicate devices. The analytical and clinical performance for all POC tests offered that rivals reference labs. The platform versatility is shown with tests that include proteins, DNA and small molecule with a cartridge that has a COGS of \$0.40.

The Ohmx bioelectronic system is a powerful comprehensive platform developed for POC (Physician Office Lab, Pharmacy Clinic, Acute Care Settings etc) with the sensitivity and accuracy needed for most POC tests prescribed today, which can evolve to be a mobile diagnostic platform.

\*Assays currently under development and not for clinical use