

## COST EFFECTIVE DRUG DISCOVERY AT NCATS

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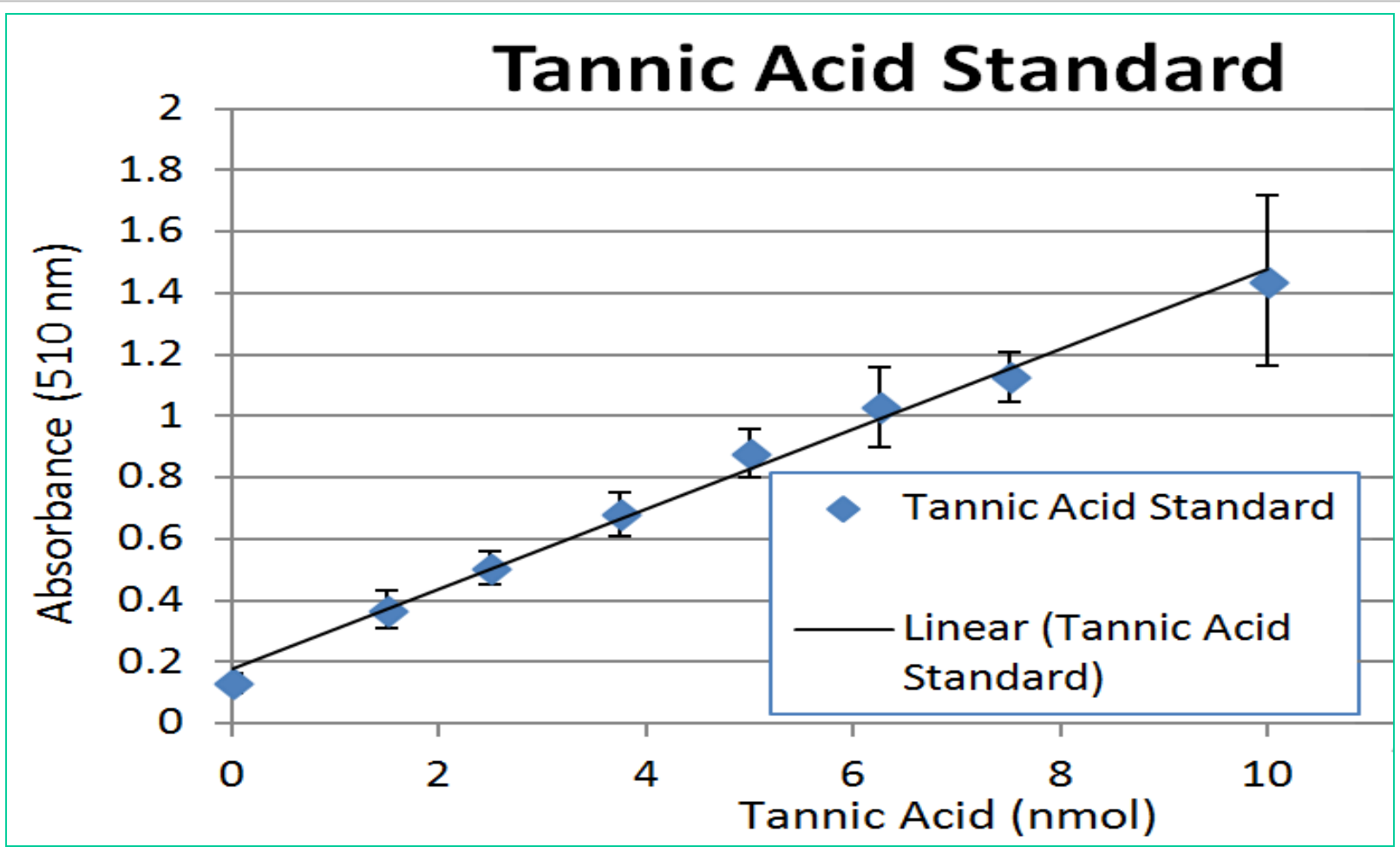
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### ABSTRACT

The National Center for Advancing Translational Sciences (NCATS) is the newest of 27 Institutes and Centers (ICs) at the National Institutes of Health (NIH). A major focus of NCATS is to lead innovation – the validation of novel drug targets and novel screening strategies to enable effective and efficient discovery campaigns for the next generation of pharmaceutical scientists. We will describe the development of NCATS, providing examples of novel assay systems, ongoing discovery campaigns and innovative technologies. We are on a path to decrease assay costs at NCATS to refurbish and reuse standard laboratory plastic ware. We will discuss our preliminary efforts using standard wash protocols and recent work by IonField Systems showed that room temperature plasmas can be employed to decontaminate micropipette tips using TipCharger, cleaning surfaces of detectible DNA, protein and small organic molecules. And new results supported by an SBIR grant awarded to IonField Systems for an instrument using plasma to clean microplates. We will describe our experience with this technology, and will outline the Phase 2 plans of IonField for inclusion in a commercial system. We believe this technology will dramatically decrease costs and improve assay method robustness throughout the biotechnology and pharmaceutical community.

Ferric chloride reacts with phenolic compounds in solution to form complexes with the general formula  $\text{Fe}(\text{OR})_6^{-3}$  where -OR- represents the ionized phenol -  $\lambda_{\text{max}}$  510 in alkaline solution.



### INTRODUCTION

A source of high cost and inefficiency in high throughput screening protocols is the utilization of single-use plastic labware. At the NCATS Division of Pre-Clinical Innovations, screening activities require 1500-2000 microplates per screen and 50 screens per year. Adding to this cost of labware, the waste stream resulting from the use of biohazard materials in plastic labware is a significant outlay.

For some experimental systems, the NCATS team has developed plate cleaning protocols that enable plastic assay plates to be reused. Since 2011, NCATS has screening ~50,000 plates of experiments using only ~1400 plates, with a significant saving in both cost and solid waste. The protocol is limited to certain assay systems, however.

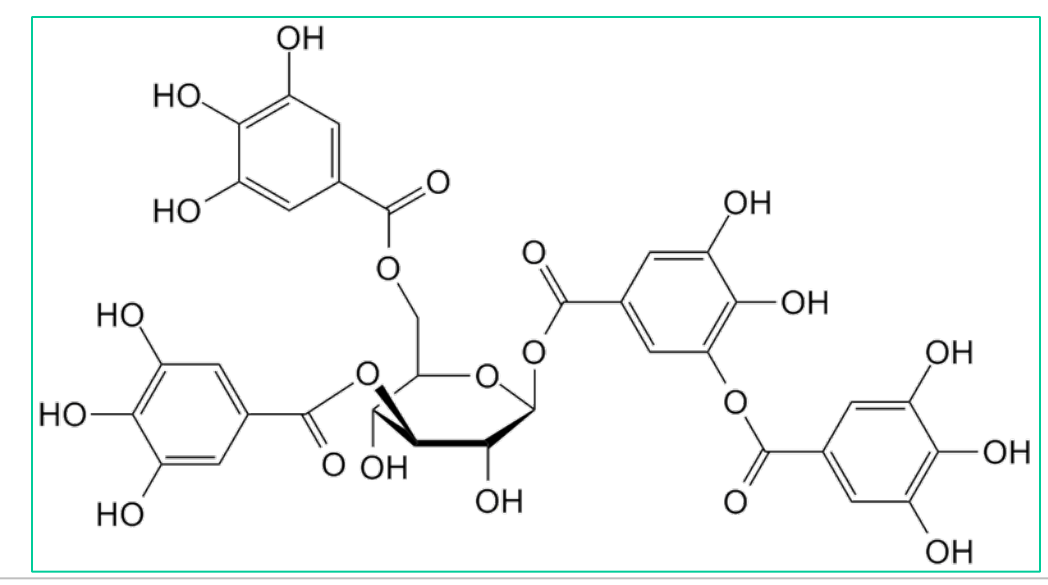
Employing the Small Business Innovation Research program, NCATS is working to develop a microplate cleaning system with IonField Systems, LLC. The company utilizes cold plasma to clean plastic pipette tips with TipCharger – the company is now working to adopt this technology microassay plates for all assay technologies.

### METHODS

#### TANNIC ACID AS TEST SUBSTRATE

- Tannic acid is a basic ingredient in the chemical wood stains and a common fixative for fabric dyes
- In foods, tannic acid is used as a clarifying agent, colour stabilizer and taste enhancer in beer and wine.

• Polyphenolic compounds like tannic acid often contaminate natural product libraries used in drug screening



#### TANNIC ACID ASSAY

10 nmol tannic acid (in methanol) deposited onto wells of Corning 3072 white 384-well plate

Samples **DRIED** to insure surface binding

Plates washed in 20% ethanol (30 seconds)

Where specified, plates treated with plasma using PlasmaKnife

Add 40 ul 1% SDS Buffer C + 6 ul 10 mM  $\text{FeCl}_3$   
Incubate 15' at RT, Quantitate A510 nm

Figure 1: Spray wash and plasma treatment removes tannic acid

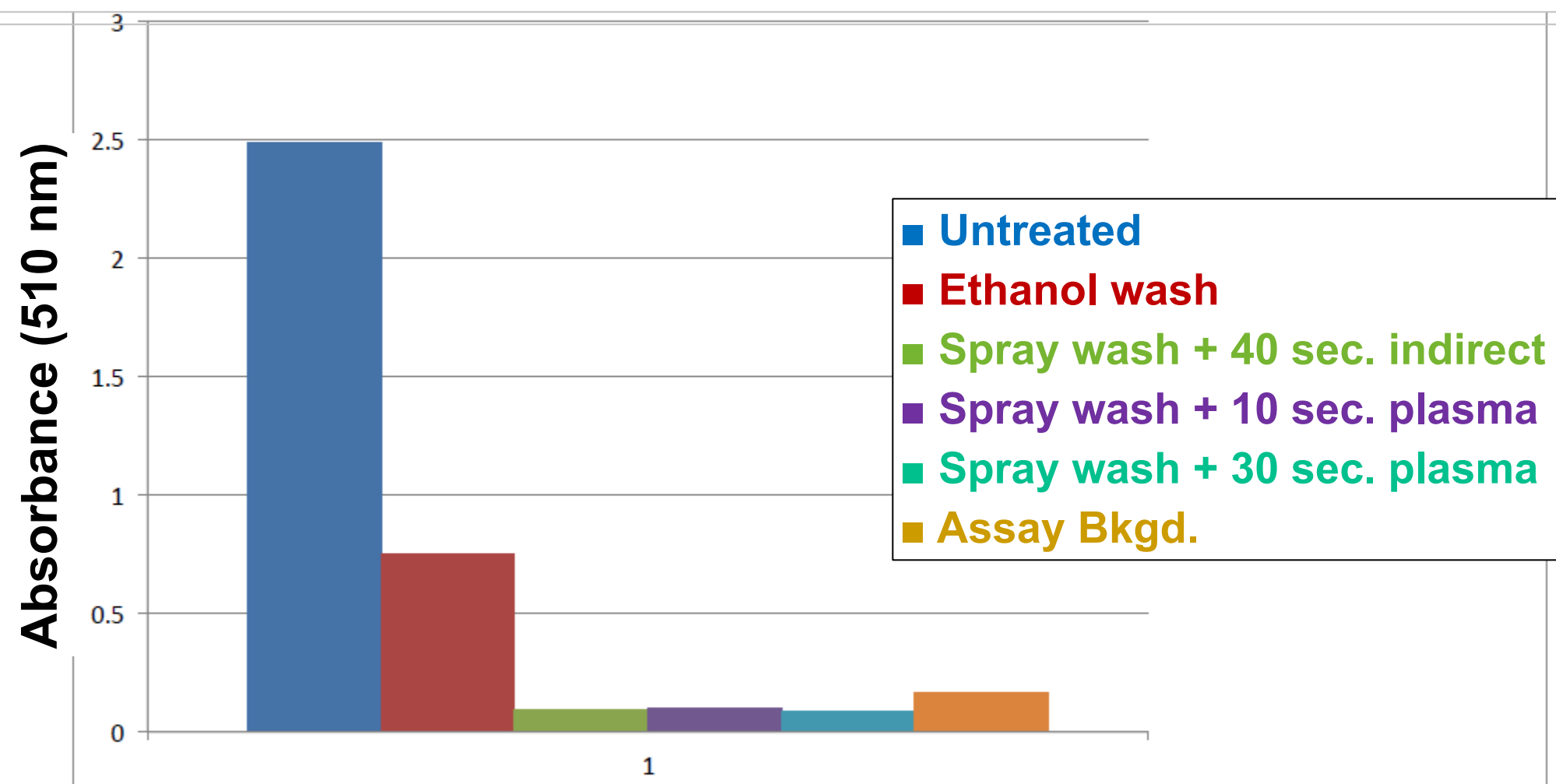
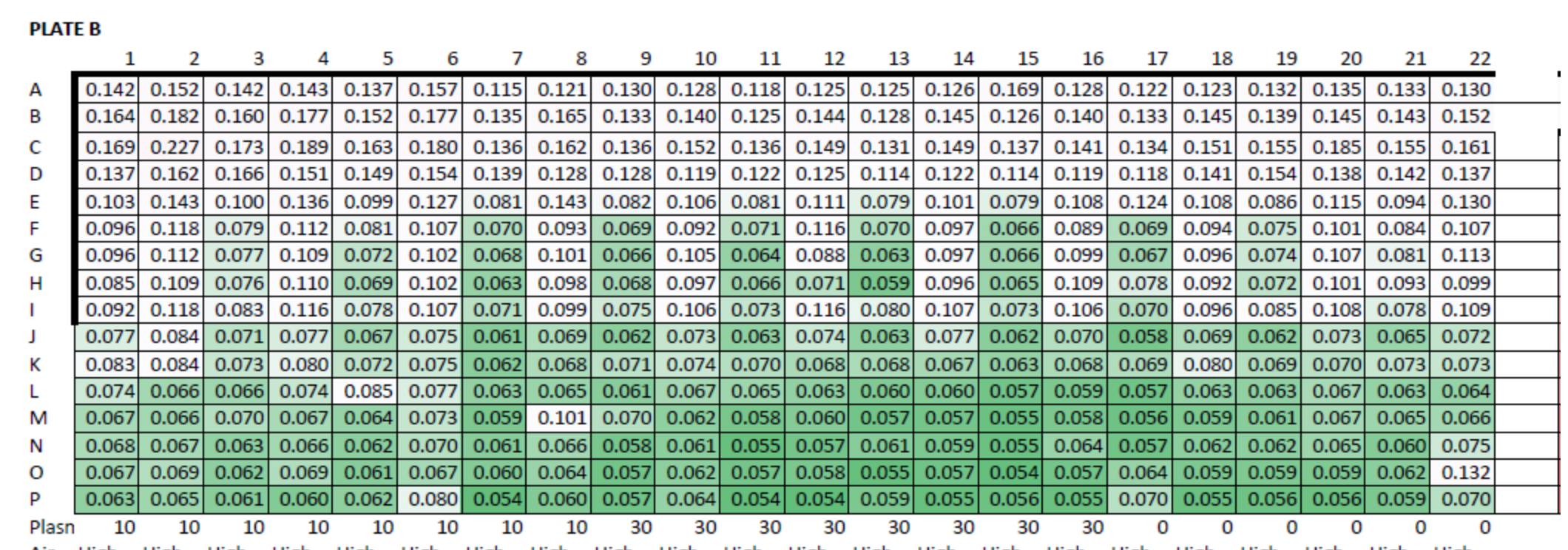


Figure 2: Spray wash uniformly removes tannic acid from plate



NOTE: Uniform cleaning to assay background with no outliers at concentration tested

### METHODS

#### NCATS CELL ASSAY PLATES

Used plates stored in moist bag at RT, for month

Plates washed with 20 % ethanol (30 sec.)  
Plates treated with PlasmaKnife (60 sec.)

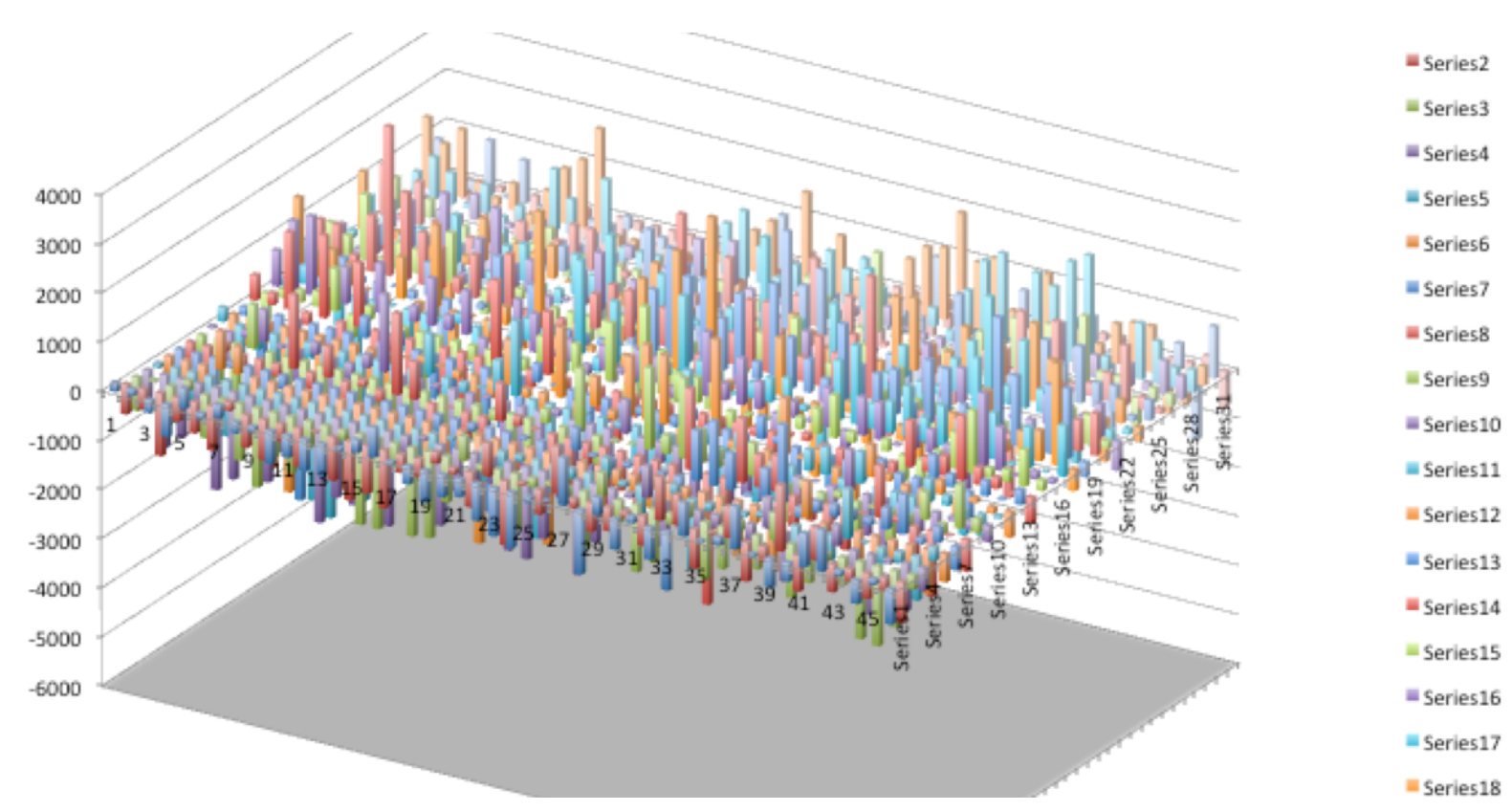
Compare with unwashed plates for residual luminescence

Unwashed 1536-well plate used for CellTiter-Glo® Luminescent Cell Viability



Figure 3: Residual luminescence after plasma cleaning used plates

- Used plates were stored as described, then processed using PlasmaKnife and analyzed for residual luminescence



Data presented as difference between untouched plate and cleaned microassay plate. Data shows uniform cleaning to detection background.

### CONCLUSION

- IonField Systems constructed prototype of PlasmaKnife cleaning station as defined by SBIR proposal PHS 2013-1 NCATS No 003: “Automated Instrument to Clean Microtiter Plates”
- PlasmaKnife prototype successfully removed tannic acid dried onto 384-well polystyrene assay plates
- PlasmaKnife successfully cleaned undefined residual biologic material from 384-well assay plates
- Phase 2 funding for development of PlasmaKnife awarded to IonField Systems.