A Novel Tool to Enable Multivalent Vaccine Development for Influenza and Coronavirus

Jeffrey Call, Chih-lung Fu, Damini Patel, Abeer Al-Ghouleh, Ph. D.

Fig 1. VaxArray Platform and kit

Abstract

Influenza and coronavirus pose unique challenges in vaccine development. Continuous antigenic drift requires new reagents and tools for analytical assessment and this challenge can represent a bottleneck in vaccine production and virus eradication. Improved characterization assays for identity, potency, and stability are needed to replace cumbersome and inefficient methods such as SRID and ELISA, which can cause increased development time and higher manufacturing costs. A lack of standardized assays and reagents also leads to a missed opportunity to compare results across manufacturing sites and products and diminishes a coordinated global effort. InDevR seeks to eliminate these bottlenecks by providing a standardized, ready to use kit with reagents that are versatile for antigenic drift. The VaxArray® Portfolio offers a simple multiplex solution that is validated to ICH guidelines and is manufactured under ISO:13485 quality standards. The VaxArray system has been implemented for bioprocess improvement at several influenza and coronavirus vaccine manufacturing sites and has already gained traction with FDA and Health Canada submissions.

Methods and Materials

The VaxArray platform is a reagent sparing sensitive multiplexed fluorescent immunoassay for detection of antigens or antibodies in a total assay time of 1-2 hours. The assay principles are shown on the right where extremely small volumes of multiple capture molecules can be "printed" and adhered to glass substrate in a small area called an array. The typical linear range for detection is ng/mL – ug/mL. Sample preparation is simply a couple of pipetting steps and a brief rinse of the slides before imaging on the VaxArray system.

Two potential use cases are shown below. On the left, a standard protocol was used to evaluate the potency of a quadrivalent influenza vaccine and accuracy is shown with respect to SRID. The VaxArray solution works well with egg, recombinant, and virus-like-particle vaccine technologies and is compatible with crude and adjuvanted drug substance and product.

The system can also be used to determine pre-immunization status or post-immunization immunogenicity of participants during clinical trials, or can be used to characterize convalescent serum antibodies. On the right, the data shows sero history differences of clinical sample for variants of the coronavirus. The CoV SeroAssay provides a complete picture for understanding prior variant history and potential impact during clinical trials.

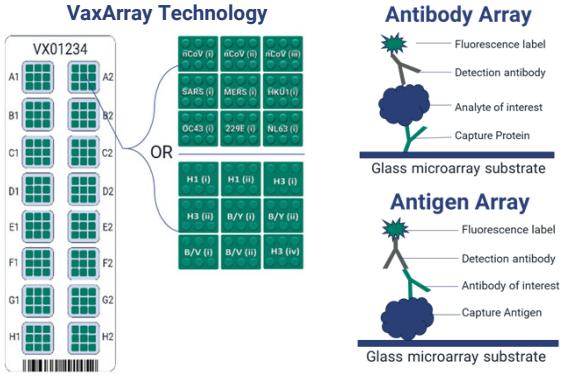

Fig 2. A. VaxArray slide layout. B. VaxArray slide options

Seasonal Influenza Hemagglutinin Assay for Vaccine Development

Simultaneously evaluate potency and subtype specific identity of H1, H3, B/Yamagata-like, and B/Victoria-like HA antigens. All VaxArray Kits contain capture molecules that are both conformational and stability indicating. Strong correlation with SRID was also observed.

Coronavirus SeroAssay for Clinical Evaluation of Sero History

Analysis of pandemic and endemic human antibodies for SARS-CoV printed in replicate in a microarray format shown below, which enables simultaneous analysis of serum antibodies to 9 antigens. Coronavirus SeroAssay shows 98.5 % sensitivity and 100% specificity, when compared to infectivity status by RT-PCR.

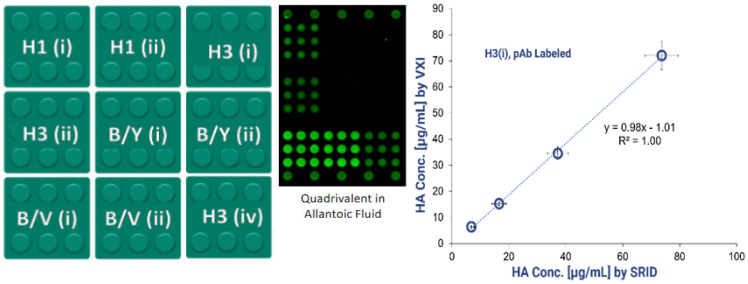

Fig 3. A. Influenza multiplex chip layout; B. Quadrivalent test in allantoic fluid; C. HA concentration correlation as tested by VaxArray vs SRID.

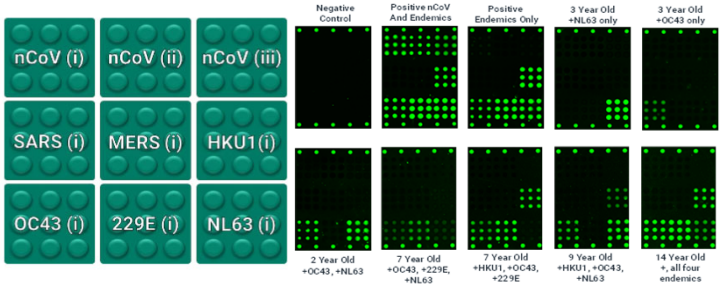

Fig 4. A. Coronavirus SeroAssay multiplex chip layout; B. VaxArray multiplexed results of various patients

Stability Indication

With any vaccine potency assay, it is important to have quantitative analytical methods that can detect stability changes over time during development or storage of the vaccine. A time degradation study using the VaxArray Influenza Neuraminidase kit evaluated the concentration of neuraminidase protein after exposure to 45 Celsius over a several hours time period. Samples from 13 time points were analyzed and showed that increased exposure time at an elevated temperature led to a decreased response from the conformationally degraded protein. This indicates the VaxArray Influenza Neuraminidase kit is able to distinguish between the active and inactive conformational structures of the protein. VaxArray assay kits are configured to be stability indicating which is useful for long term evaluation of the vaccine efficacy.

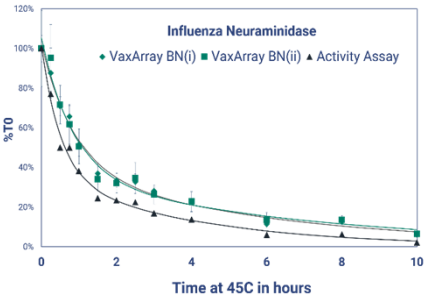

Fig 5. Functional NA vs degradation time

VaxArray Precision

Precision is an important factor when choosing an analytical technique and VaxArray is capable of improved precision when comparing to SRID or ELISA methods. Performance was evaluated using several variables for testing.

Testing Protocol using ICH Guidelines:
3 days
3 operators
3 reagent lots
2 instruments
3 Concentrations
14 variables investigated
Typical CVs ~10%

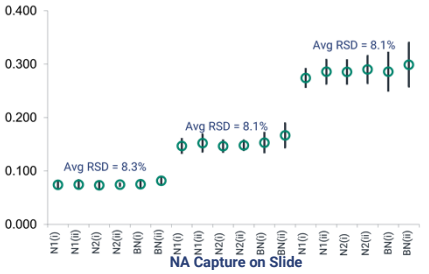

Fig 6. Testing Protocol using ICH Guidelines

Conclusion

The VaxArray platform offers standardized kits for vaccine development and clinical assessment of influenza, coronavirus, measles/rubella, polio, and more. Custom kits can easily be configured for additional vaccine areas and its analytical applicability can extend from vaccine development, bioprocess optimization, manufacturing QC, preclinical/clinical trials, or serosurveillance studies.

The VaxArray kits provide multiple benefits by measuring conformationally correct target analytes with high subtype specificity, and the multiplex assay format provides more answers simultaneously with less labor and reagent. These benefits are helpful as compared to HPLC assays. Faster assay development, with ~30 minutes hands-on time also offers advantages over SRID and ELISA methods.

	VaxArray	SRID	ELISA	HPLC
Time to Result	1-2 hours	2-3 days	8-24 hours	2-3 hours
Multiplexed	√	x	x	x
Ready to Use Kit	√	x	x	x
Functional Assay	√	√	√	x
Stability Indicating	√	√	√	x
Subtype Specific	√	√	√	x
In Process Samples	√	x	x	√
Adjuvated Samples	√	x	x	x
Sensitivity	High	Med	High	Med
Relative Cost	Low	Med	Low	Med

www.InDevR.com
Sales@InDevR.com