WHITE PAPER
VACCINE DEVELOPMENT

Address Key Challenges in Vaccine Development with Antibody Profiling

- Identify five key challenges in vaccine development
- Understand how antibody profiling can streamline every stage of the vaccine development process
- Discover how Sengenics protein microarrays enable accurate antibody profiling to optimize vaccine design and monitoring

Introduction

Vaccines have been the most effective tool in public health, preventing an estimated 154 million deaths worldwide in the past 50 years (1,2). Despite their success, vaccine development still faces major challenges,from managing patient variability to addressing pathogen evolution and ensuring long-term safety (Table 1) (3). This white paper explores how antibody (Ab) profiling can help tackle these obstacles, enabling the design of safer, more effective vaccines while also streamlining the development process.

Identifying Effective Vaccine Candidates

The complexity of immune responses, combined with the constant evolution of pathogens and tumors, makes it challenging to identify the most effective vaccine targets. Ab profiling offers a powerful solution by detecting protective Abs that either already exist or are produced early after exposure—such as those in individuals who are exposed but remain uninfected. It can also identify Abs that increase after exposure or vaccination in protected individuals, acting as key "correlates of protection" (4). Additionally, Ab profiling helps pinpoint immunogenic antigens on the surface of pathogens and confirms the immunogenicity of selected vaccine targets, laying the foundation for more effective vaccine development.

Tackling Host Variability with Molecular Subtyping

Patient variability, driven by differences in genetics, immune history, and human leukocyte antigen (HLA) profiles, complicates the development of universal-

Table 1. How Ab Profiling Can Address Key Challenges in Vaccine Development

Challenges	Antibody Profiling Solutions
Identifying candidates and confirming target immunogenicity	• Discover protective Abs and correlates of protection • Pinpoint immunogenic, disease-associated antigens on the surface of pathogens • Confirm immunogenicity of vaccine target
Understanding patient variability in immune response	• Provide molecular subtyping • Associate with immune-influencing variables (e.g., HLA profile)
Accounting for evolving nature of pathogens and neoplasms	• Evaluate immunogenicity of multiple targets simultaneously • Monitor Ab responses over time • Track Ab responses to emerging pathogens
Understanding the effects of prior immunity and tolerance	• Identify prior seroreactivity to vaccine candidates or vectors
Enhancing and monitoring vaccine safety and efficacy	• Detect unwanted cross-reactions with host molecules early • Monitor and understand vaccine-induced autoimmunity • Track long-term Ab responses and link to protection or harm • Develop surrogate endpoints to speed up clinical trials • Track Ab responses to new attenuated vaccines • Identify optimal vaccination route by analyzing any Ab-containing sample type, from any compartment

ly effective vaccines (5). Ab profiling captures patient-specific immune responses, which can be linked to these variables, enabling population segmentation. This may allow for tailored vaccine designs optimized for at-risk groups like the elderly or immunocompromised, in addition to the general population.

Addressing Pathogen and Tumor Variability

Pathogens and tumors are constantly evolving, creating another major challenge for vaccine developers (6,7). Ab profiling can track immune responses to emerging pathogens and neoplasms over time, ensuring vaccines remain effective even in the face of antigenic variation.

This approach can determine which new pathogen or tumor antigens are immunogenic. It can also identify broadly neutralizing Abs capable of binding to multiple variants.

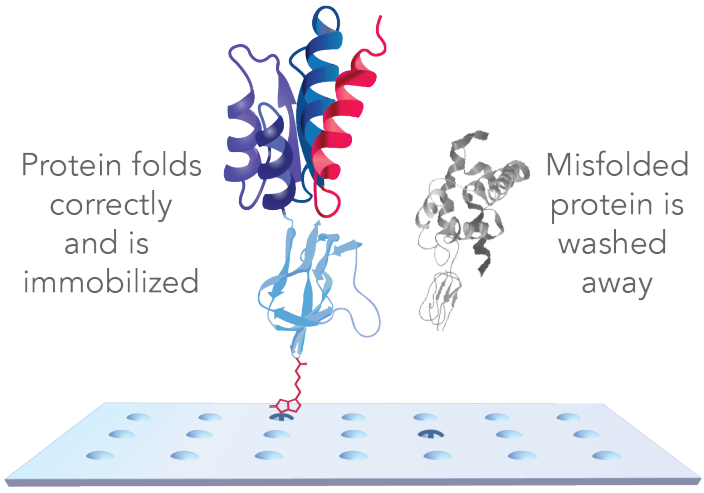

Figure 1. Sengenics protein microarrays feature functional, full-length, and correctly folded proteins for Ab profiling

Managing Prior Immunity and Tolerance

Pre-existing immune memory from previous infections or vaccinations can result in suboptimal responses to new vaccines (8). Ab profiling identifies prior reactivity to vaccine candidates, allowing adjustments to vaccine design or patient selection in clinical trials to improve outcomes.

Enhancing and Monitoring Vaccine Safety and Efficacy

Ab profiling is essential for evaluating vaccine safety and long-term efficacy. In preclinical stages, it helps detect inappropriate cross-reactivity, reducing the risk of autoimmunity. During clinical trials, Ab profiling can provide critical insights regarding safety, dose, and route (9). For instance, profiling across different biological compartments (e.g., oral, respiratory, gastrointestinal) reveals how different vaccination routes impact immune responses. This level of detail helps select the best vaccination route and ensures the immune response is both robust and targeted. Moreover, Ab profiling can help identify correlates of protection, protective Abs produced after vaccination or booster administration, and surrogate endpoints, expediting clinical trials and reducing costs.

Profiling Abs with Protein Microarrays

Protein microarrays offer a fast and cost-effective method to profile Abs against thousands of antigens simultaneously. However, accurate results depend on properly folded proteins since 90% of Abs bind to conformational epitopes *in vivo* (10). This requires both proper protein folding and an array surface

chemistry that preserves the structural integrity of these epitopes.

Sengenics's proprietary KREX® technology ensures that only correctly folded proteins are immobilized on a non-denaturing surface, preserving *in vivo* epitopes for accurate Ab profiling (Figure 1). This technology also addresses a major hurdle in vaccine development: creating stable, biologically relevant protein antigens.

The platform delivers exceptional accuracy, with high reproducibility ($R^2 > 0.95$), picomolar-level sensitivity, and a low sample requirement of less than 50 µL. The i-Ome® Discovery microarray, featuring over 1800 human proteins, has a wide dynamic range spanning over 4 logs. Additionally, Sengenics microarrays allow for the dual analysis of Ab isotypes, providing deeper insights into immune responses, which is critical for enhancing vaccine research and immune system monitoring.

The platform offers flexible solutions, with ready-to-use panels or fully customizable options tailored to specific protein targets. Comprehensive support is provided at every stage, from experimental design through to advanced bioinformatics analysis.

Conclusion

The future of vaccine development will rely more and more on Ab profiling using advanced tools like Sengenics protein microarrays to overcome critical challenges—such as host variability, pathogen evolution, and long-term safety concerns. By allowing for earlier pre-selection of candidates and predicting failures more accurately, Ab profiling can significantly cut down the time spent on ineffective vaccine candidates.

Ab profiling will also enhance clinical trials by broadening patient inclusion and ensuring study populations are more diverse and representative. Real-time immune response monitoring can help optimize vaccine efficacy and allow researchers to adjust strategies as needed, all while accelerating timelines and reducing costs. Ultimately, Ab profiling has the potential to streamline every stage of the vaccine development process, transforming how vaccines are developed and tested.

Contact Us

Sengenics develops key solutions for biological research, specializing in the discovery and validation of autoantibody biomarker signatures. For more information on how Sengenics can advance your research, email us at enquiries@sengenics.com or visit our website at sengenics.com.

Resources

Find out why protein shape matters in antibody binding [White Paper]: https://sengenics.com/wp-content/uploads/2024/04/White-Paper-Antibody-Antigen-Binding-Shape-Matters-vs1pt0.pdf

Watch a 1-minute video to discover why protein shape matters in antibody-antigen binding [Video]: https://www.youtube.com/watch?v=lBEYLlk5Yws

Browse Sengenics protein microarrays, which include custom and ready-to-use panels: https://sengenics.com/services/autoantibody-biomarker-profiling/

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