Advancing bispecific lead generation through integrated *in vivo*, *in vitro*, and *in silico* approaches to optimize clinical suitability

IMMUNOPRECISE ANTIBODIES

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Introduction

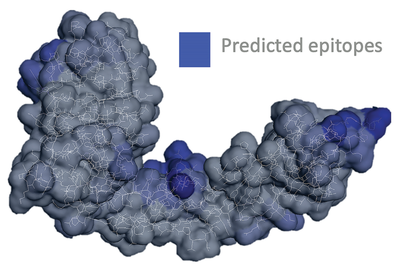
Bispecific antibodies (bsAbs) are increasingly important in today's therapeutic landscape, particularly in cancer immunotherapy and autoimmune diseases, due to their ability to target two distinct antigens simultaneously. However, bsAb lead development presents unique challenges due to their engineered and customized molecular designs consisting of independent binding modules. IPA has a long-standing history in custom Ab discovery and engineering allowing the generation of large panels of target-specific antibodies with broad phenotypes (epitope bins, functionality, binding kinetics). These well-characterized diverse Ab panels can serve as valuable input for the generation of novel bsAbs with unique and clinically-relevant properties. IPA offers a comprehensive and versatile portfolio of capabilities, from robust discovery to high-throughput expression of bsAb combinatorial matrix that enables rapid identification of the most desirable bispecific drug candidates, with a fully integrated multi-parametric *in silico* molecular optimization engine that ensures a successful end-to-end process.

Target/Discovery

Versatile, diversity-driven discovery with high-throughput epitope-clustering boosts lead candidate selection for bsAb development

Antigen Modeling, Design & Epitope Prediction

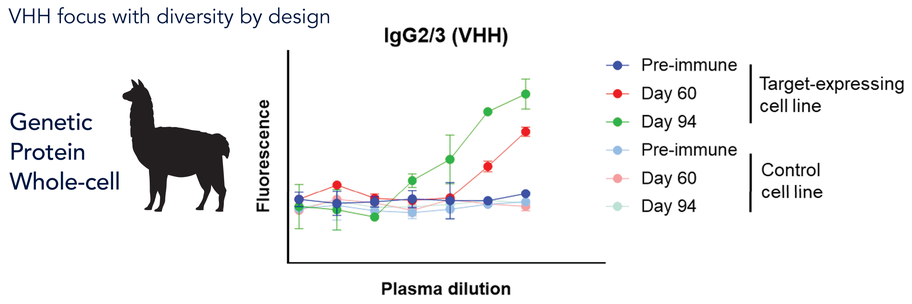
Accuracy that enables design of discovery paths for maximum epitope coverage



AI-based epitope prediction tools enable definition of potential binding areas on the antigen.

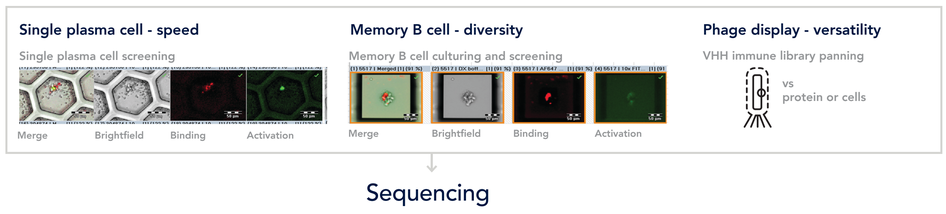
Immunization

VHH focus with diversity by design



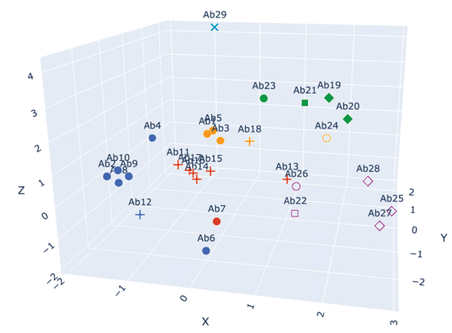
VHH Hit Generation

Rapid, sensitive and high-throughput with diverse output



LENS^{aiTM} Epitope Binning

Rapid candidate selection based on predicted epitope bin from large panel of input sequences without the need for physical material



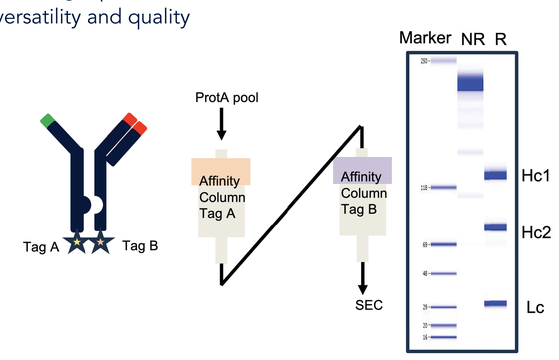
Infinitely scalable epitope binning enables retention of epitope diversity in downstream characterization.

Leads

Efficient bispecific antibody production and candidate characterization enhance precision in therapeutic development

rPEx® high-throughput, recombinant bsAb production

Enabling rapid combinatorial matrix evaluation with built-in versatility and quality



Dual tag recombinant expression and sequential purification ensures high purity while eliminating undesirable byproducts. This method is versatile and agnostic to heterodimerization format and Fc backbone.

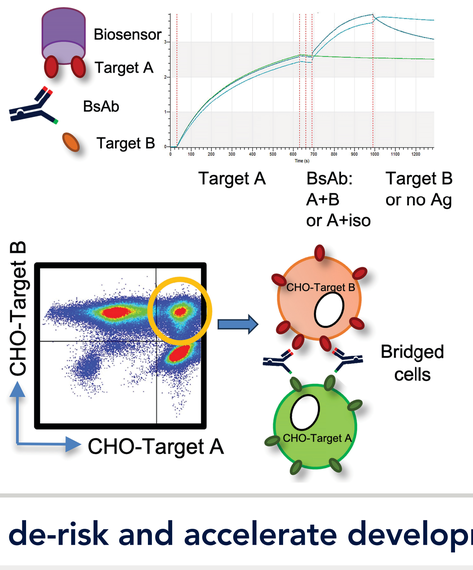
High-throughput *in vitro* characterization

Phenotypically relevant, precise and versatile

Label-free protein-protein interaction analysis

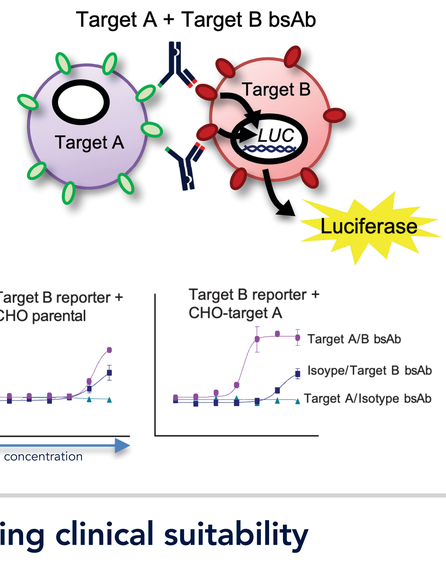
Simultaneous binding to two distinct antigens can be accurately detected with high-throughput label-free protein (top) and cell-based (bottom) assays.

Cell-based bridging assay



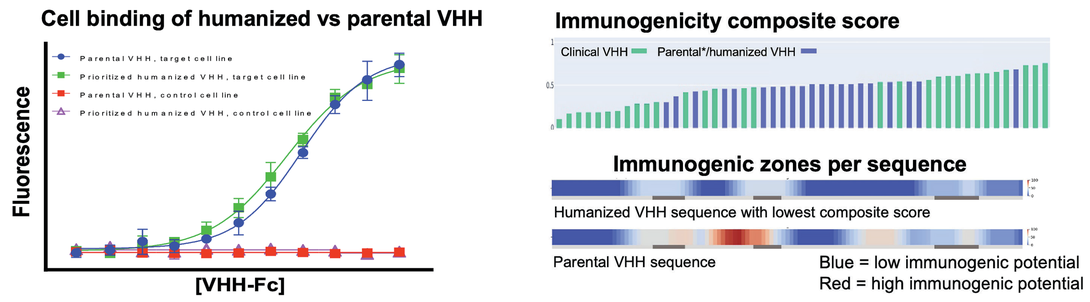
Functional Analysis

High-throughput amenable functional assay demonstrates activation of effector cell line expressing Target B mediated by Target A/B bsAb.



Multiparametric *in silico*-driven humanization is designed to de-risk and accelerate development by enhancing clinical suitability

Rapid and scalable humanization with integrated immunogenicity screening and developability assessment



Species-agnostic, high-throughput humanization (representative binding data on the left) with integrated immunogenicity screening (middle, top/bottom) and developability assessment (AggScore as example on the right) ensures multi-parametric and comprehensive derisking of bsAb lead candidates.

Conclusion

IPA offers a comprehensive **end-to-end solution** for streamlined bsAb discovery and development backed by experience, expertise and innovation. Today's bsAb drug development efforts demand the ability to interrogate large panels of functionally diverse, genetically distinct antibodies. Robust high-throughput and innovative experimental methods combined with cutting-edge *in silico* technologies that are integrated from design to finish provide full versatility and adaptability to suit the needs for each unique project and accelerated therapeutic bsAb lead generation while minimizing risks for downstream clinical development.