

In Silico-Driven Strategies to Unlock the Therapeutic Potential of Rabbit- Derived Antibodies

Intersection of phenotypically
rich B cell Select[®] discovery
and highly scalable and
multidimensional LENS^{ai™}
applications

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ImmunoPrecise Antibodies

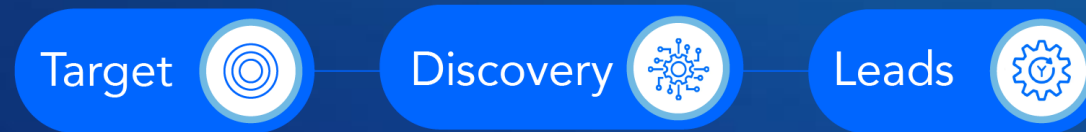


Connect insight to impact

Advance *in vivo* success with accurate, scalable, and multi-modal *in silico* intelligence

Fully integrated end-to-end therapeutic workflow.

Early-stage actionable insights. Better leads, faster.



Application Scenarios

Engineered for clarity, depth, accuracy and speed.

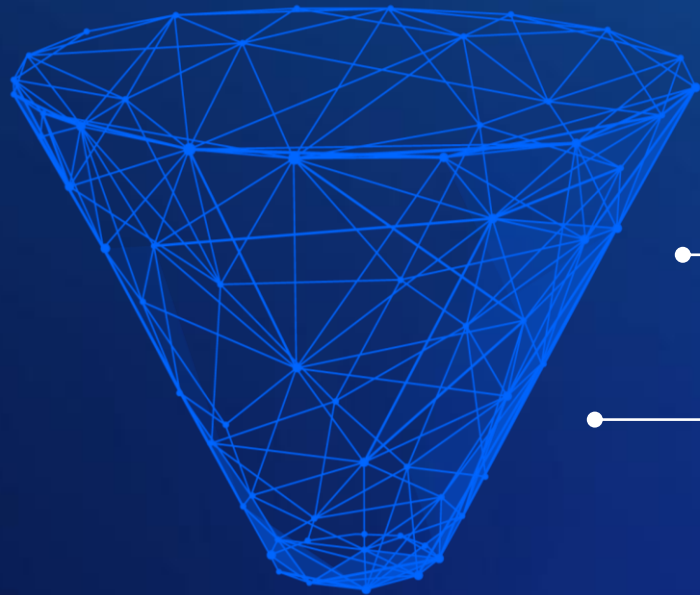
1. Unlock Hidden Epitopes on Complex Targets
2. Maximize Diversity with High-Throughput AI Screening
3. Find Functional Antibodies Faster
4. Reduce Risk Early in Discovery
5. Expand Antibody Design Possibilities

In silico insight in antibody discovery and development

Enabling data-driven decision making at early stages to accelerate timelines

LENS^{ai} Integrated Intelligence Platform

End-to-End Analysis



Target

Target Analysis

- Antigen Modeling & Design
- Epitope Prediction
- Epitope Specificity



Discovery

Hit Selection

- NGS Data Processing
- Hit Expansion
- Epitope Binning
- Epitope Mapping



Leads

Candidate Characterization

- Developability
- Off-target Screening

Lead Optimization

- Humanization
- Immunogenicity Screening
- Affinity Maturation
- De-risk Engineering
- pH Selectivity/Sensitivity

Accurate modeling with versatility to tackle challenging targets

AI-augmented search across structured and unstructured data to build confidence



Target

Discovery

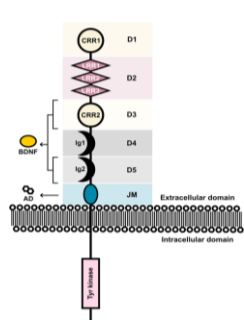
Leads

Modeling based on a combination of technologies is the foundation of accurate predictions

Multimer & Complex Proteins

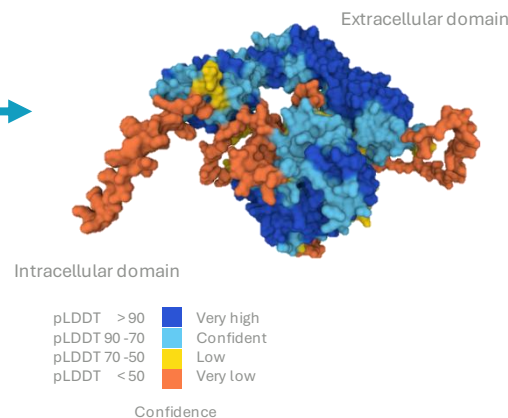
Challenging Target

- multi-domain
- heavily glycosylated



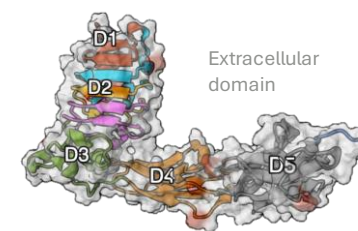
De novo structure prediction

De novo AlphaFold structure prediction can (in some cases) show low to very low model confidence. Resulting in unusable models.

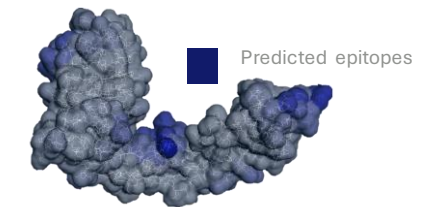


Toolset to create suitable models

Utilizing hybrid approaches to model atomic interactions and to estimate stability of multimeric protein complexes.

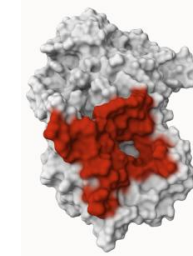


Epitope Prediction

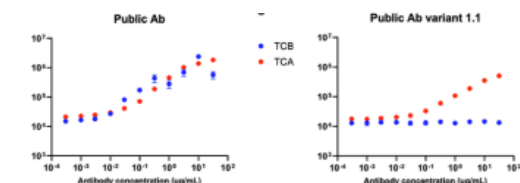


Epitope Mapping

Applications



Optimization & Engineering



Key advantages of rabbit antibodies

Underexplored path to clinical success

- 2 approved rabbit-derived humanized mAb therapeutics (10 to 15 more in clinical trials)
- 11+ approved for diagnostics
- High affinity and exquisite specificity
- Phylogenetically distinct host from rodents



Superiority of Rabbit Antibody Discovery at IPA

Successes of Rabbit B Cell Select[®]

IPA's proprietary Rabbit B cell Select[®] workflow success

A versatile solution that is unmatched in the industry, **with a >98% program success rate** in therapeutics, anti-drug/anti-id and diagnostics.

IPA discovers rabbit anti-LILRB2 antibodies for OncoResponse

Best-in-class anti-LILRB2 mAb to reverse macrophage-mediated immunosuppression in cancer patients showed durable monotherapy responses with excellent safety profile.

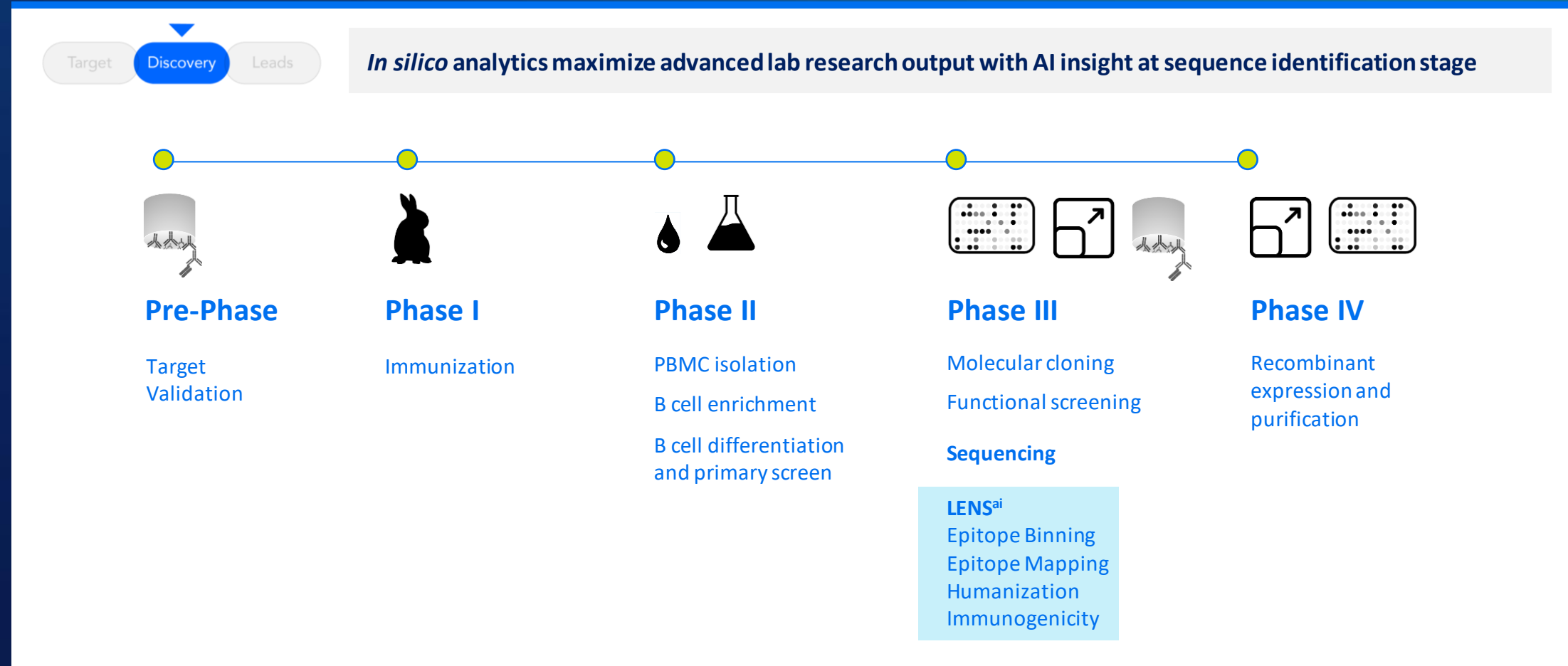
Recombinant mAbs with rich phenotypic properties

Diverse output with rich phenotypic characterization leads to **early sequence identification as the footprint for insightful *in silico* analytics** to accelerate the path to the clinic.



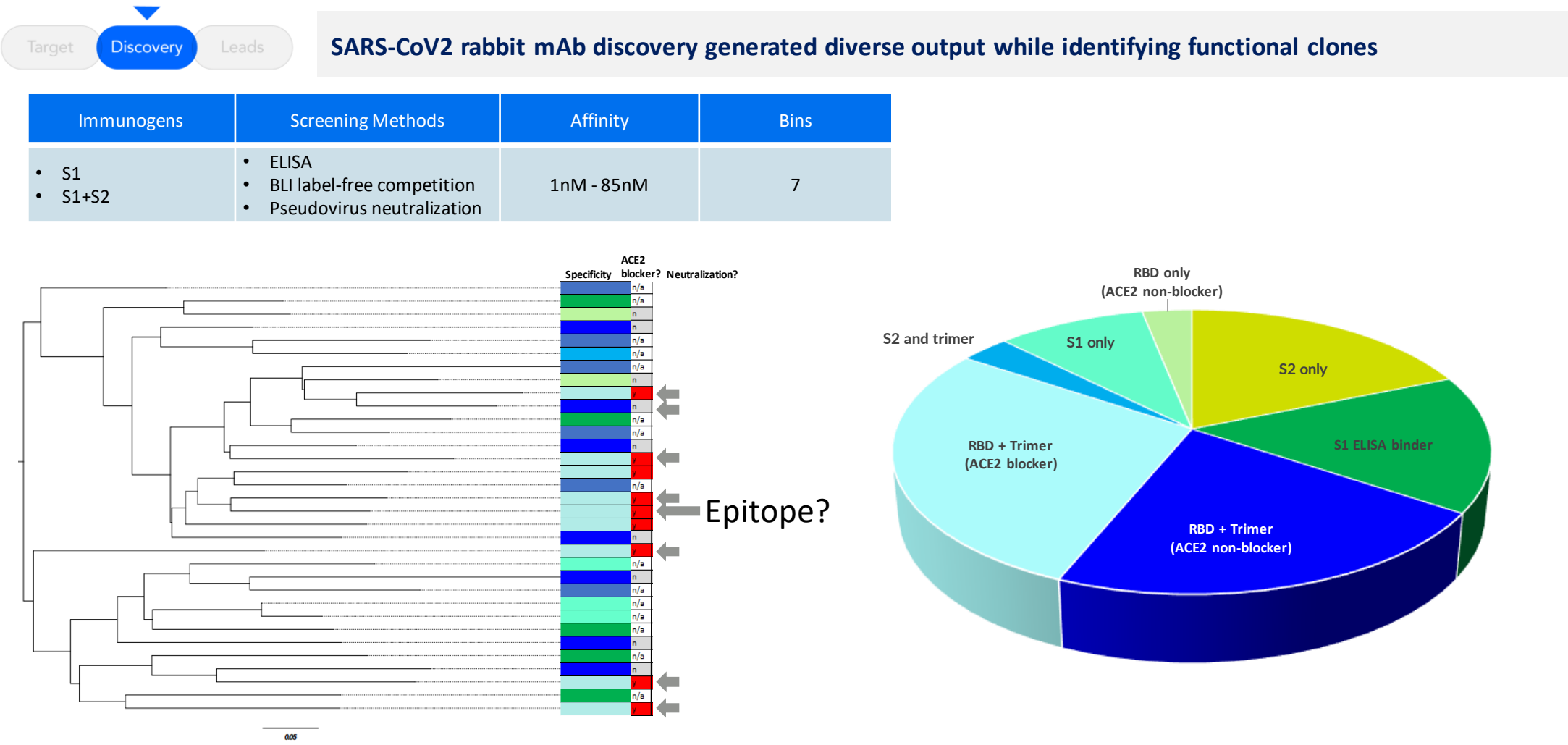
Rabbit B cell Select[®] drives robust *in vivo* discovery

Depth from high efficiency (~500-fold higher efficiency than hybridoma) combined with **breadth** from versatility



Rabbit B cell Select[®] discovery delivers diversity by design

Phenotypically rich, multilayer screening uncovers functional clones at an early stage



LENS^{ai} Epitope Mapping reveals functionally relevant binding

Accurate, rapid and scalable mapping enables visualization of MOA



Target

Discovery

Leads

Neutralization-sensitive and ACE2-competing epitope is revealed in the absence of any physical material produced

Input

Amino acid sequences of:

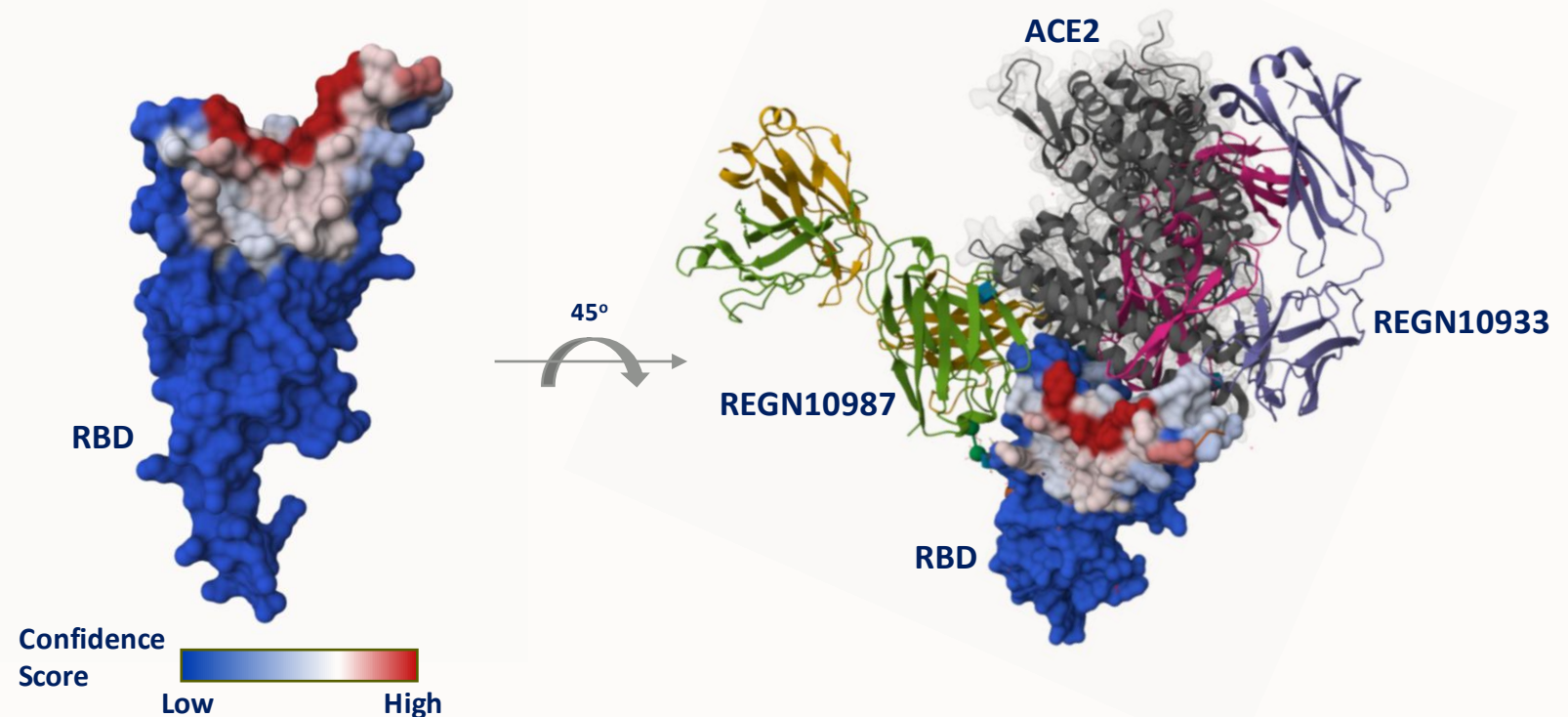
- antibody hits and benchmark molecules
- target

Output

Multi-feature-based

Epitope Mapping:

Based on syntactical-, structural profiling and, atomic interactions to enable affinity propagation clustering. Function-driven information package to select potential lead candidates.



LENS^{ai} Epitope Mapping benchmarking against existing technologies

Accuracy that matches x-ray crystallography precision



Target

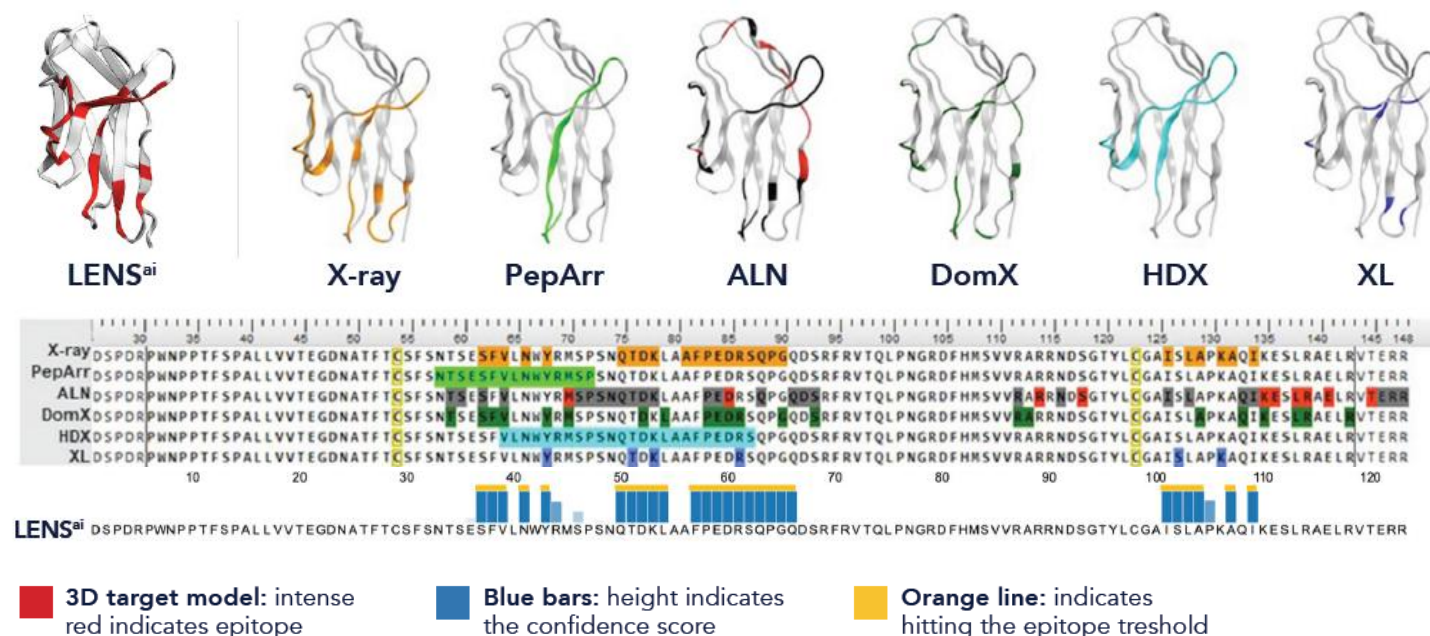
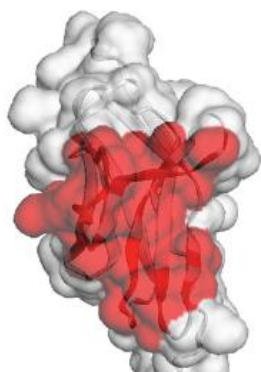
Discovery

Leads

LENS^{ai} identifies specific epitope residues more accurately than well-established techniques

PD1 + Pembrolizumab

LENS^{ai} AUC = 0.80



AUC - measure of prediction accuracy

True Positive Rate vs False Positive Rate = prediction's ability to distinguish between epitope and non-epitope residues.

AUC = 1: perfect prediction

AUC = 0.5: no better than random

AUC = 0.8-0.9: high predictive accuracy

Reference: MABS 2023, VOL. 15, NO. 1, 2285285

<https://doi.org/10.1080/19420862.2023.2285285>

LENS^{ai} Epitope Mapping benchmarking against existing technologies

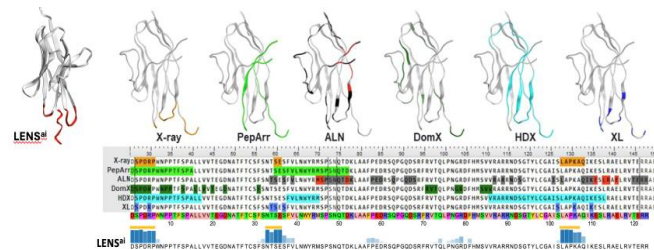
Accuracy that matches x-ray crystallography precision



LENS^{ai} identifies specific epitope residues more accurately than well-established techniques

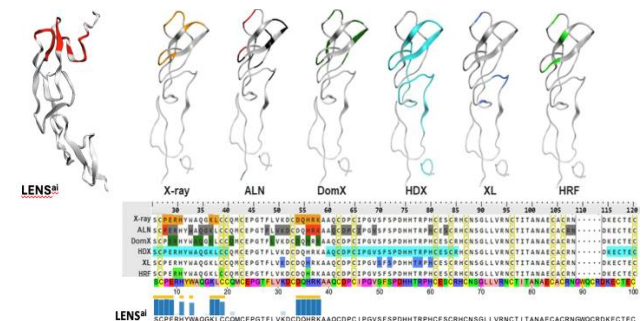
PD1 + nivolumab

AUC = 0.79



CD27 + MK-5890

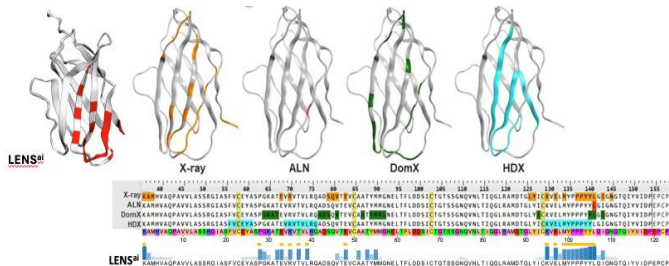
AUC = 0.89



The CD27 + MK-5890 complex was NOT part of the original AF training set.

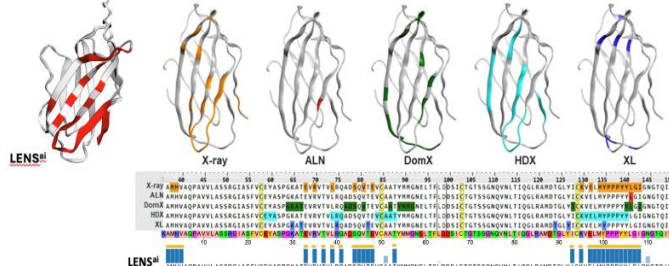
CTLA4 + tremelimumab

AUC = 0.83



CTLA4 + ipilimumab

AUC = 0.84



LENS^{ai} Epitope Mapping:

- Matches x-ray crystallography precision: AUC $\geq$ 0.8 for majority
- Unmatched speed and scalability:
 - 15h for ~500aa target
 - 34h for ~1300aa target
 - Throughput - 50+ mAbs
- Reduced cost: no need for physical material; timeline compression
- Not limited by target type

Additional validation:

- 30 known complexes (half of which were not part of AF training set) yielded similarly high AUC.

AUC - measure of prediction accuracy

True Positive Rate vs False Positive Rate = prediction's ability to distinguish between epitope and non-epitope residues.

AUC = 1: perfect prediction

AUC = 0.5: no better than random.

AUC = 0.8-0.9: high predictive accuracy.

Reference: MABS 2023, VOL. 15, NO. 1, 2285285

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Multiparametric de-risking of lead candidates ensures clinical confidence

High-throughput *in silico* humanization and risk assessment of top leads



Target

Discovery

Leads

Humanization on a panel of candidates efficiently accomplished in a single round of design

LENS^{ai} Immunogenicity Prediction

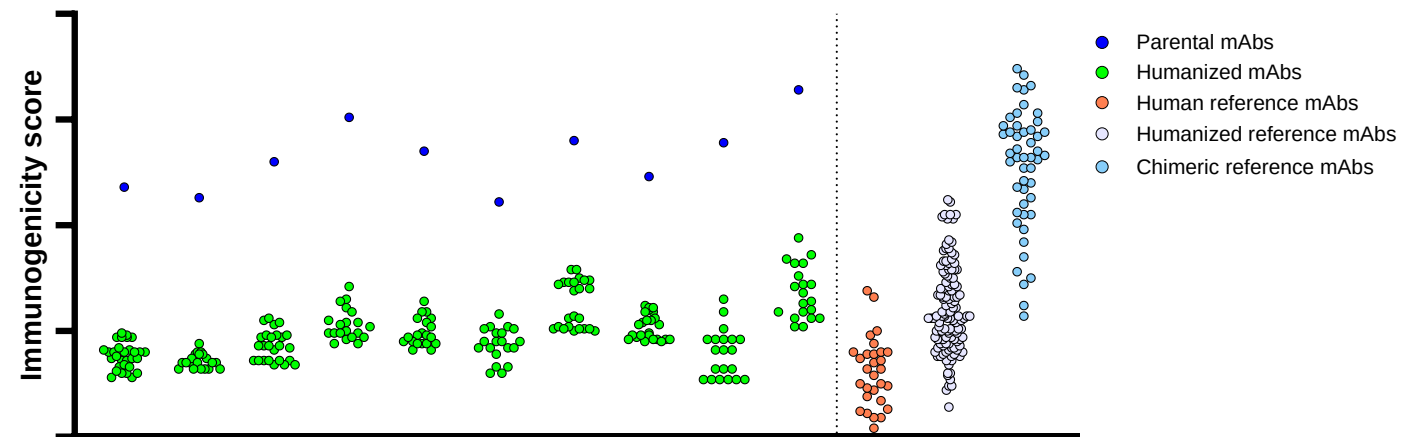
Binding Affinity Peptide – MHC II

- Based on artificial neural networks
- Predictions: Strong – medium – weak binding
- Position of peptide parts in Ab sequence

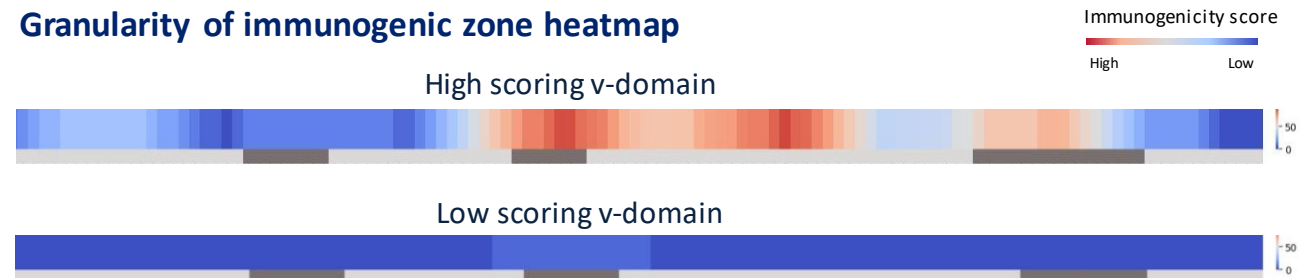
Humanness

- Check presence of (binding) peptides in **full proteome reference**

Immunogenicity assessment of multi-parametric humanization design



Granularity of immunogenic zone heatmap



Clinical utility of LENS^{ai} Immunogenicity in predicting ADA incidences

Clear positive correlation in classification of mAbs with 10% or greater ADA occurrence



Target

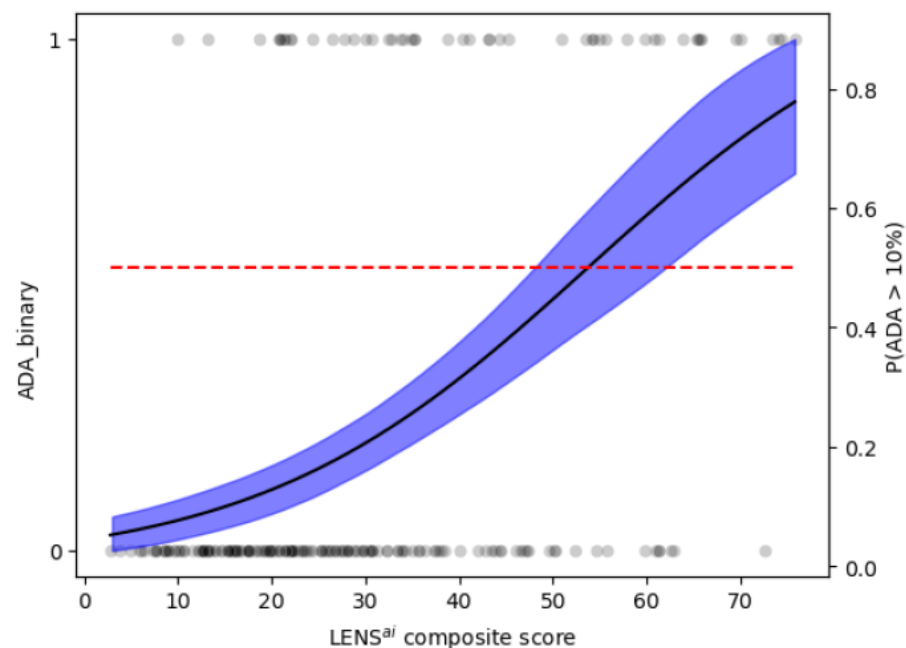
Discovery

Leads

Predictive power of LENS^{ai} to enable risk-associated decision making with greater confidence

LENS^{ai} Immunogenicity ADA prediction, n = 217

(ADA data compiled by Marks *et al.* 2021)

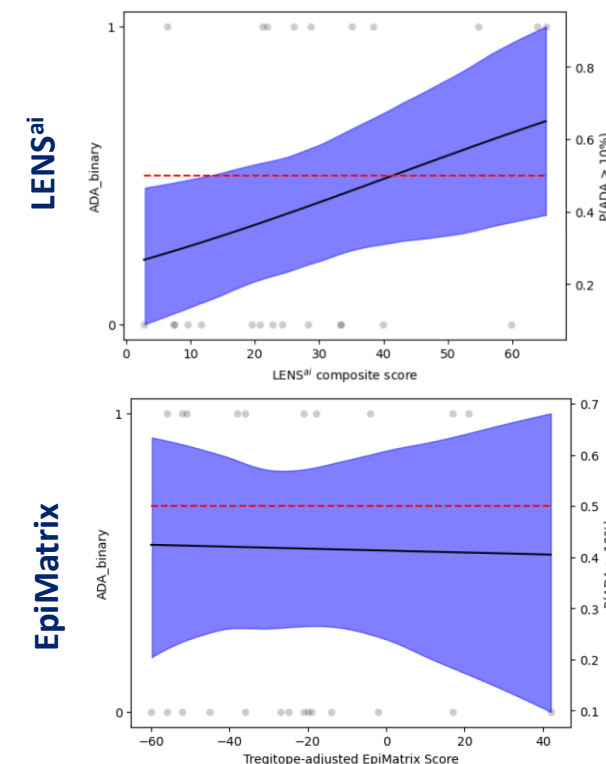


Binary logistic regression fit

- Individual therapeutic mAbs grouped by:
 - Class 0 = ADA < 10% ; Class 1 = ADA > 10%
- Mean predicted probability of ADA% > 10%
- Model uncertainty p(ADA > 10%) 89% HDI
- P(ADA > 10%) = 0.5

LENS^{ai} vs EpiMatrix ADA prediction, n = 24

(data points based on AAPS NBC 2024 poster)



See you at booth #406, Posters C047/048

All-in-one bio ecosystem

Disruptive AI-driven biotherapeutic discovery potential

- *De novo* sequence generation
- Integration of multi-omics data
- Benchmarking potential candidates
- Discover hidden candidates
- Allowing unprecedented insight, accuracy, speed and efficiency.



**Collaborative planning
and design for success**



High client retention