

LENS^{ai}[™]

Empowering Diversity-Driven Discovery, Intelligent Lead Selection and Optimization

LENS^{ai} Integrated Intelligence Platform
Universal Foundation AI model for life sciences

A layered solution: 3 Levels of data Analytics

Capturing all granularities



- **Democratizing Innovation**
Empowering researchers across organizations to run and interpret cutting-edge tools in a secure, scalable environment.
- **Integrated Insight Pipelines**
Enabling researchers to run complex workflows that reveal molecular interactions and profiles, helping de-risk molecules early in development.
- **Multimodal engineering**
Leveraging our proprietary toolbox to optimize and engineer protein therapeutics within scenario specific constraints.

Technology designed to solve the complex

A toolbox to cater to every question

Fee-for-service
Tools



Engineering
&
Optimization

Software
Platform
UI/API



Characterization
&
Analytics

End-to-end
Partnerships



From target
to
molecule

Antibody Discovery and Development

Inform-select-optimize



Antibody Discovery and Development

Data-driven down selection



Target Analysis

- Antigen Modeling & Design
- Agentic Interactions

Immunogenicity

- Proven candidate de-risking based on scoring function

Epitope Mapping

- X-ray Precision in epitope residue recall. Maintained on novel protein complexes. (~0,8AUC)

Epitope Binning

- Near perfect agreement with in-vitro competition assays

Protein Affinity Engineering

- GLP1 optimization, receptor activation at 2-fold lower EC50 compared with therapeutic.

Ph-selectivity Engineering

- 3 FOLR2 binding Ph selective Abs retaining target specificity in a single engineering round

LENS^{ai} Protein Structure Prediction

Foundation of antibody development: from high-throughput to detailed refinements

Target design & analysis

●●● Target | Discovery | Leads

(De-Novo) protein structure prediction tools

AlphaFold and AlphaFold successor structure prediction pipelines integrated in a user-friendly UI. Quick, easy and secured environment to predict structures for any protein sequence.

- Integrated quality metrics
- Optimized for various inputs
- User friendly 3D-model interactions

Example scenarios

- Custom antigen domain design
- Antibody agnostic target analysis
- Target feature characterisation
- ...

Agentic Interactions

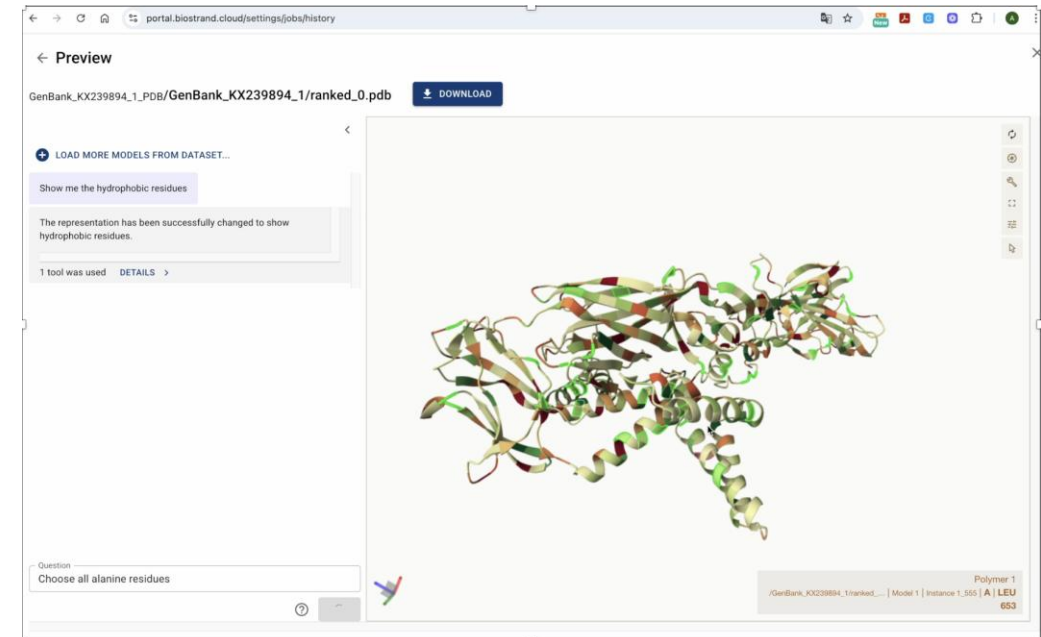
Sentence – to feature

Use free text to perform complex protein analytics for an intuitive protein analysis experience. Enabling any researcher to extract the full value out of a structural model.

Protein Simulations

Push button Molecular Dynamics

Fully automated workflows to perform various environment specific simulations to enable and facilitate the analysis of even the most challenging proteins.

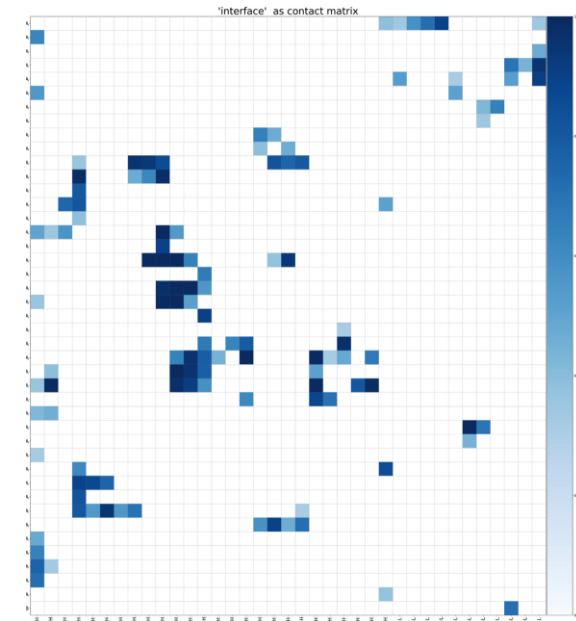


LENS^{ai} Protein Structure prediction tools

Optimized MD workflows

BioStrand implementation – Ready to go Gromacs (GMX) MD pipelines

- Various implementations:
 - **GMX Protein Molecular Dynamics:**
 - **GMX Membrane-protein Molecular Dynamics:** performs MD simulations of transmembrane proteins (and peripheral proteins)
 - **GMX Glycoprotein Molecular Dynamics:** performs MD simulations of glycosylated proteins
 - **GMX Constant-pH Protein Molecular Dynamics:** performs MD simulations of proteins in explicitly modelled solvent at constant pH level. The main difference with the standard MD pipeline is that the protonation state of titratable residues are dynamically adjusted during the simulation based on environmental pH and local electrostatics.
 - **GMX Protein – Ligand Molecular Dynamics:** Performs MD simulations of protein-ligand complexes.
- All fully automated pipelines:
 - Preprocessing – Equilibration – MD – Post processing automated
- Parallelized pipelines: designed for scalability
- API & UI ready
 - Contact maps, Affinities, trajectories,...



MD output example - Contact map

LENS^{ai} Epitope Binning:

More-informed early triaging of lead candidate panel

Discovery

LENS^{ai} Epitope Binning

Rapid and early-stage epitope landscape profiling

Input

Combination of sequence and structural features and LLM embeddings to identify main bins

Antibody sequence input:

- from single cell sequences up to full immune repertoires
- target-agnostic

Output

- Highly scalable clustering of antibody sequences (> 5000 sequences)
- Rapid and early-stage epitope landscape profiling of large panels of hits
- No need for physical material

Case Study: Comparing LENS^{ai} binning with classical competition assays

Scale:

29 antibodies

Type:

Blinded

Method:

Cohen's Kappa Test using a majority consensus label mapping

Near perfect agreement between LENS^{ai} Epitope Binning and classical wet-lab binning results.

LENS^{ai} Epitope Binning matches in vitro competition assays with high confidence

Label mapping

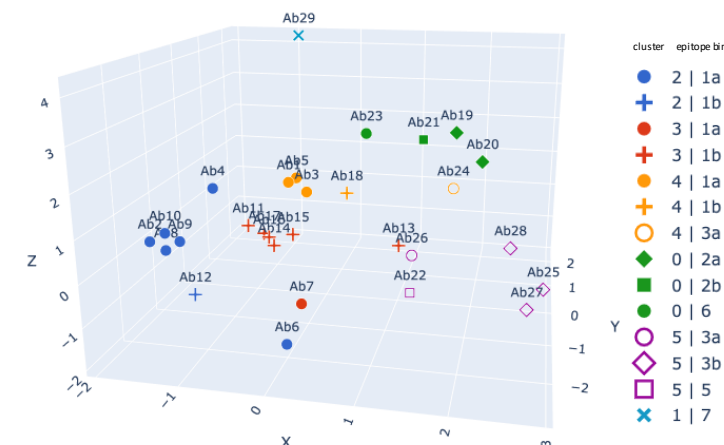
LENS^{ai} cluster > Wet lab bin

K
0,925

Wet lab bin > LENS^{ai} cluster

0,842

Cohen's Kappa Coefficient (-1 to 1)
> 0,8: near perfect agreement



LENS^{ai} Epitope Binning relies on a multi-modal prediction engine for optimal results without the need for physical material

LENS^{ai} Hit Selection Analysis

Multi-modal clustering of antibody sequences

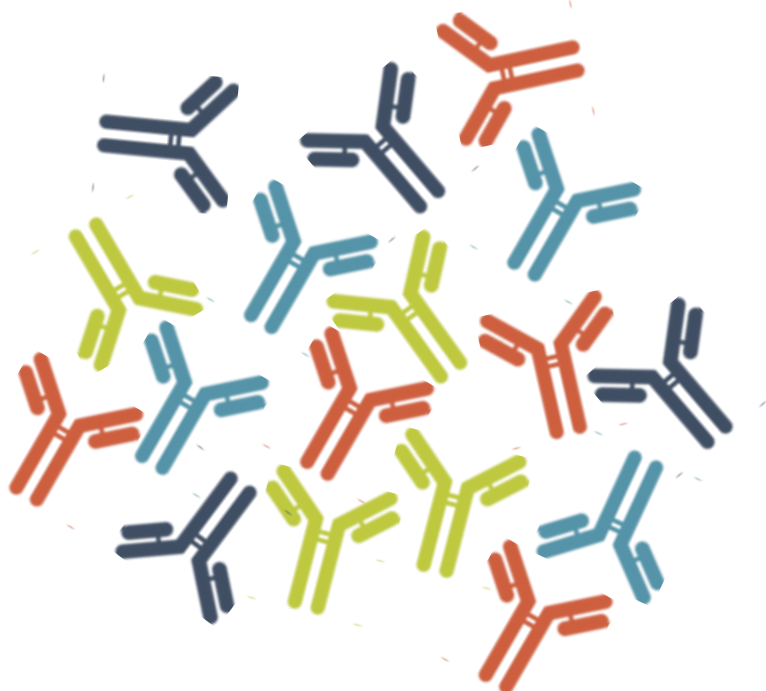
Discovery

LENS^{ai} Hit Selection

Optimize clustering through multi-modal feature extraction

Input

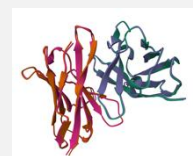
(NGS) antibody repertoire or Library



LENS^{ai}

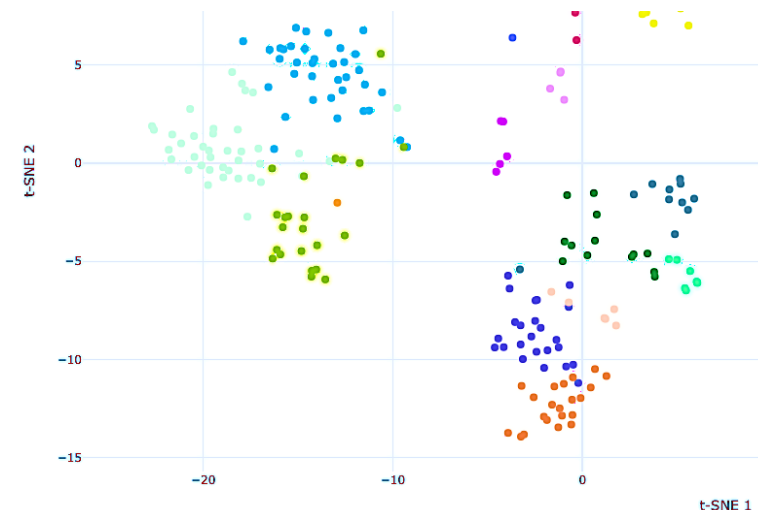
Multi-dimensional analysis

Q L V E S G G G L V Q F
Q M T Q S P S S L S A S
Q L V E S G G G L V K F
I Q M T Q T T S S L S F
V Q P G G S L L R L S C
V L T Q S P G T L S L S
Q L Q Q S G T V L A R F
V S T Q S P A I M S A S



Output

Multimodal clustering based on
sequence | structure | LLM embeddings



LENS^{ai} Hit Selection pipeline is similar in algorithm to Epitope Binning, but has NGS specific settings – including an optional pairing step

LENS^{ai} Hit Expansion Analysis

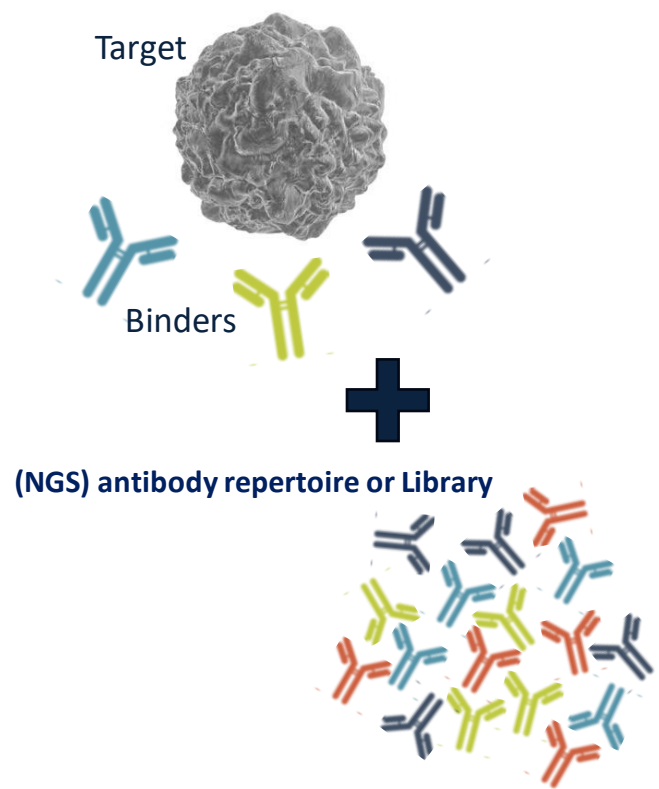
Mining complete repertoires to extract ALL relevant clones

Discovery

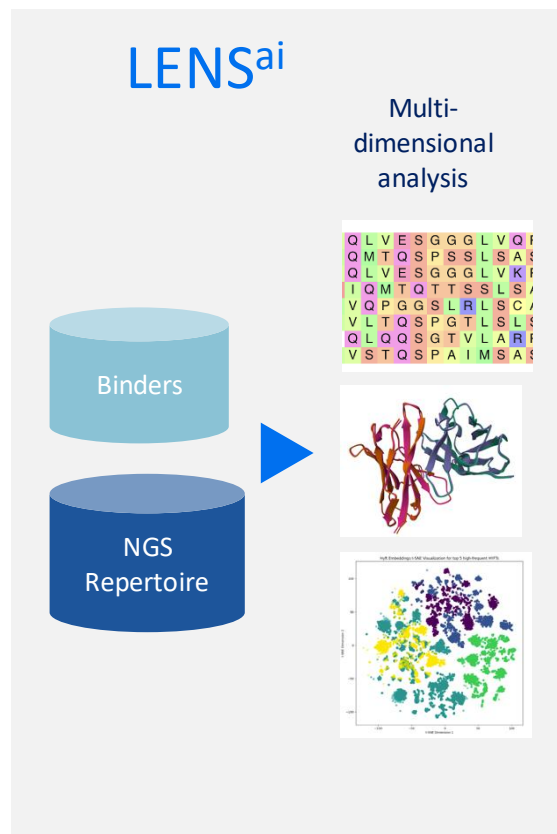
LENS^{ai} Hit Expansion

Phage display, B-cell, and Hybridoma output as *seed* sequences

Input



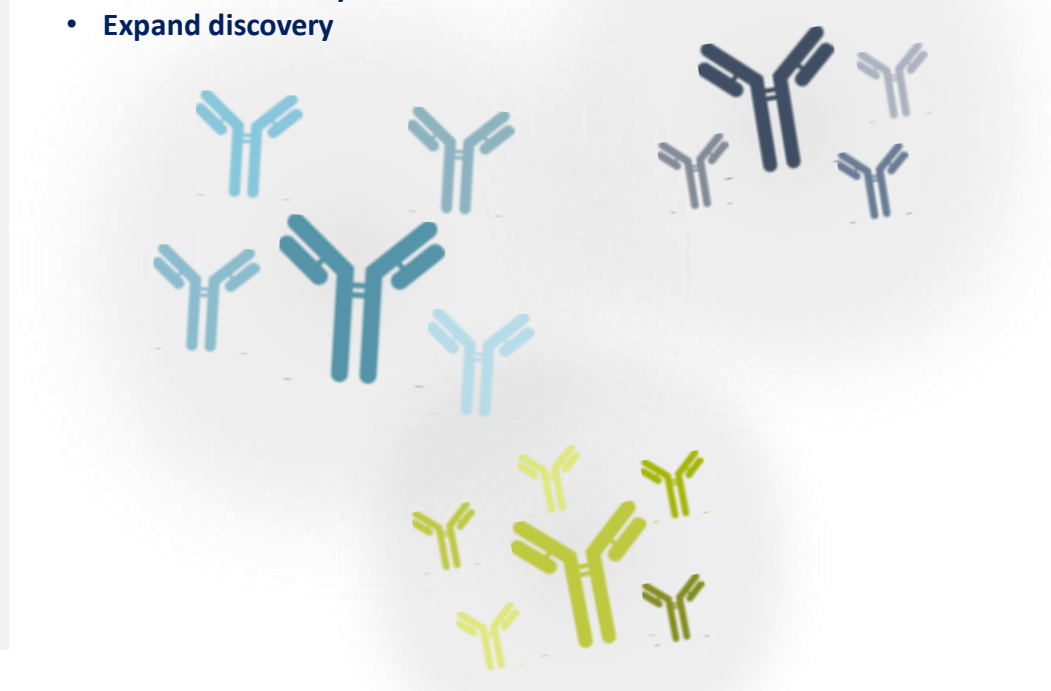
LENS^{ai}



Output

Hit expansion

- Multi-modal analyses to retrieve additional hits
- Expand discovery



LENS^{ai} Hit expansion pipeline is an end-to-end workflow built to extract all relevant hits for downstream analysis.

LENS^{ai} Epitope Mapping: Informed lead selection

Leads

LENS^{ai} Candidate Characterization Epitope Mapping

Input

Amino acid sequences of:

- hits or candidates
- target

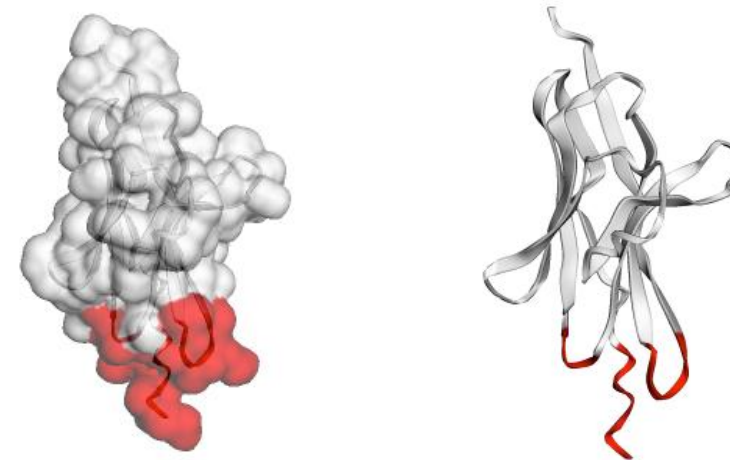
Output

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 of PD1 + nivolumab

LENS^{ai} epitope mapping 3D view
Red indicates epitope region



LENS^{ai} epitope mapping Sequence view

Blue bars represent the confidence score, which varies between 0-1.
If this confidence score hits a set threshold (orange line above blue bars)
the residue is classified as being a part of the predicted epitope.



LENS^{ai}'s Differentiator

X-ray crystallography is considered as gold standard for identifying epitope regions, yet the method is time consuming, costly and with feasibility that is highly dependent on target type.

LENS^{ai} Epitope mapping, our **proprietary algorithm**, offers a fast, high throughput alternative identifying epitope residues with high sensitivity while maintaining high precision and minimizing false positive rates.

LENS^{ai} showcases reliable epitope identification; the benefits for a drug developer are:

- Early-stage identification of epitope diversity
- Accelerated decision making and risk reduction

Key differentiators:

- Near x-ray accuracy, more reliable than all other in vitro methods
- Fast (hours) and infinitely scalable, analyze multiple candidates at once
- Only requires sequences, not reliant on physical material

LENS^{ai} Epitope Mapping:

Benchmarking LENS^{ai} against established techniques: Reliable, Rapid, Insight-driven

Leads

LENS^{ai} Epitope mapping benchmarking
AUC calculated vs X-ray crystallography

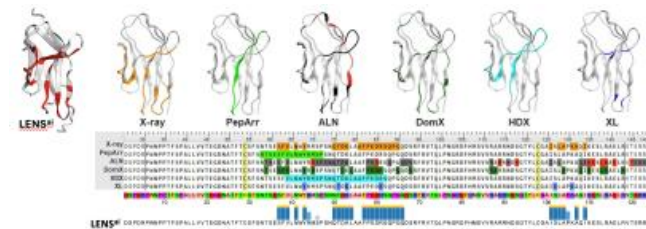
Reference: MABS 2023, VOL. 15, NO. 1, 2285285

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

Epitope mapping data and diagrams based on X-ray crystallography, peptide array, alanine scanning, domain exchange, HDX and XL-MS were published in the above article.

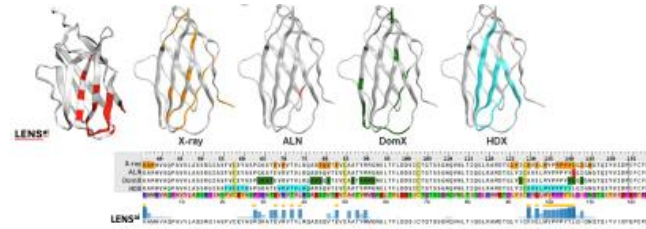
PD1 + pembrolizumab

AUC = 0.80



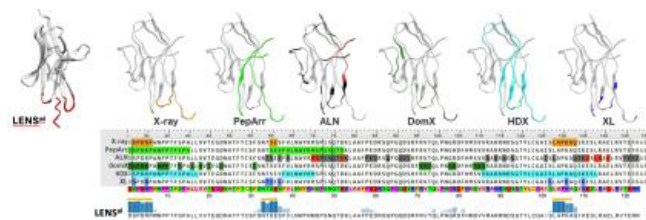
CTLA4 + tremelimumab

AUC = 0.83



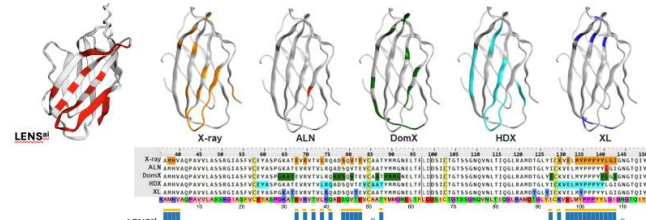
PD1 + nivolumab

AUC = 0.79



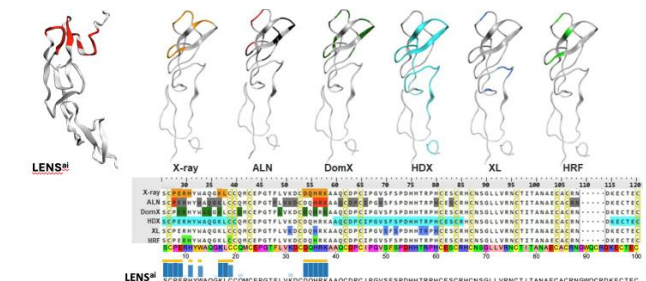
CTLA4 + ipilimumab

AUC = 0.84



CD27 + MK-5890

AUC = 0.89



LENS^{ai} epitope mapping

3D target model: intense red indicates epitope

Blue bars: height indicates the confidence score

Orange line above indicates hitting the epitope threshold

AUC is derived from the ROC curve, which plots the True Positive Rate against the False Positive Rate and demonstrates the prediction's ability to distinguish between epitope and non-epitope residues.

AUC = 1 is a perfect prediction, AUC = 0.5 is not better than random. AUC = 0.8-0.9 is excellent.

The CD27 + MK-5890 complex was not part of the original training set. LENS^{ai} Epitope prediction quality is unaffected.

LENS^{ai} epitope mapping:

- X-ray crystallography precision
- rapid results: within hours
- reduced costs: no need for physical material timeline compression
- unmatched scalability
- works for almost all target types

Additional validation on +35 known complexes yields similar AUC ranges (half of complexes not part of training set)

Coming soon: LENS^{ai} Clash Matrix

In silico equivalent of in vitro competition assay
Extension of LENS^{ai} mapping
Checks whether 2 antibodies can simultaneously bind to a target

LENS^{ai} Epitope Mapping:

Benchmarking LENS^{ai} against established techniques: Reliable, Rapid, Insight-driven

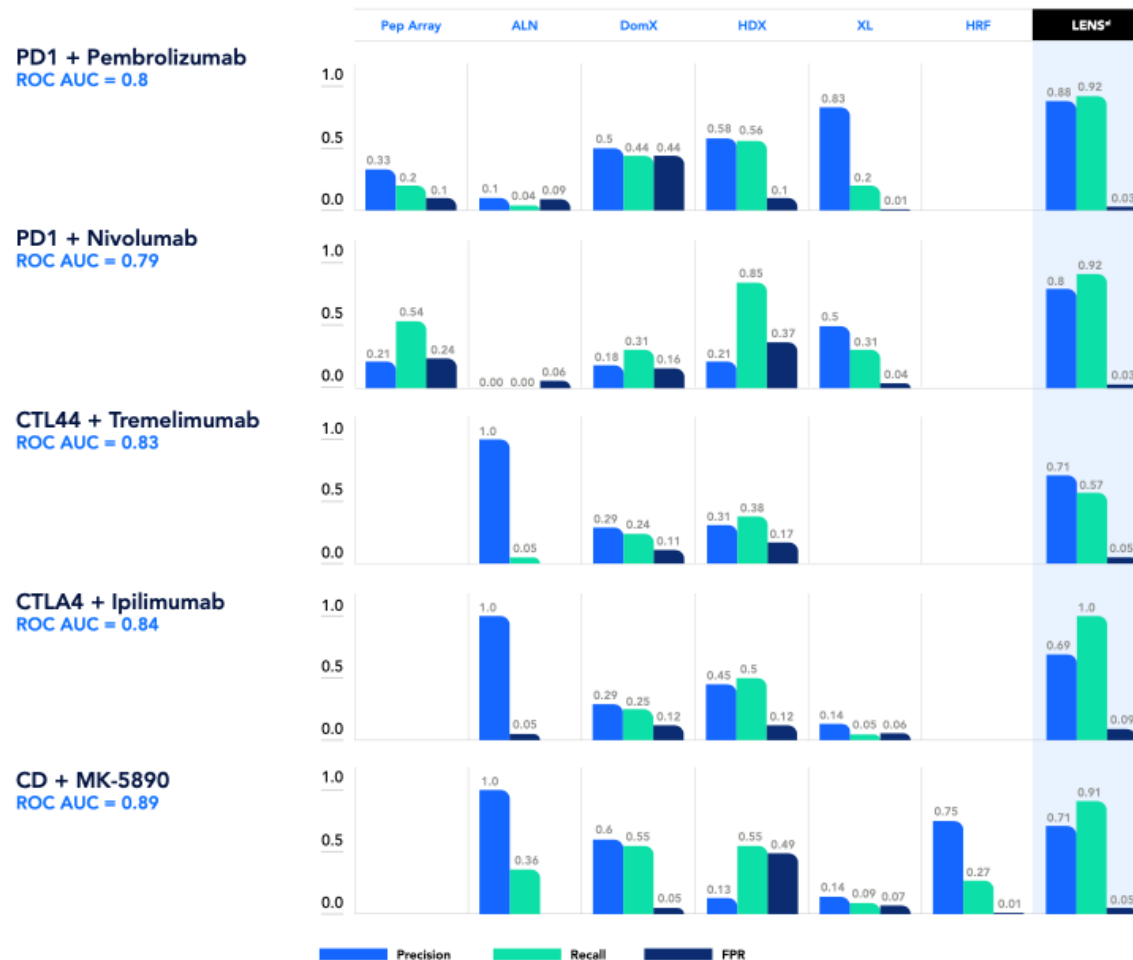
Leads

LENS^{ai} Epitope mapping benchmarking
AUC calculated vs X-ray crystallography

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

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

Epitope mapping data and diagrams based on X-ray crystallography, peptide array, alanine scanning, domain exchange, HDX and XL-MS were published in the above article.



LENS^{ai} clearly outperforms all wet-lab based methods and shows a near x-ray crystallography performance.

LENS^{ai} can accurately identify true epitope residues (high recall or sensitivity) while minimizing wrong predictions (high precision and low FPR).

Precision

$$TP = \frac{TP}{(TP+FP)}$$

measures how many of the residues predicted to be part of the epitope are correctly predicted

Recall

$$TPR = \frac{TP}{(TP+FN)}$$

measures the proportion of residues being part of the true epitope that are correctly identified

False Positive Rate

$$FPR = \frac{FP}{(FP+TN)}$$

is the proportion of residues not being part of the true epitope that are incorrectly predicted as part of it

LENS^{ai} Immunogenicity & Developability profiling:

Compare your antibodies against a database of all therapeutic antibodies



Leads

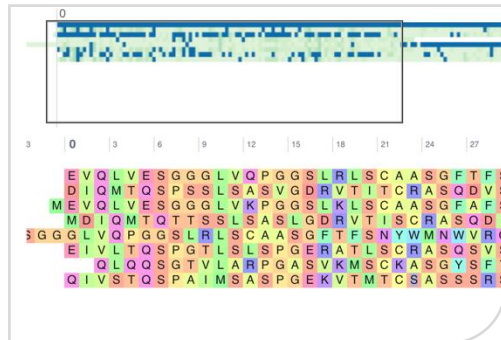
LENS^{ai} Lead Optimization

Immunogenicity Screening
Affinity Maturation

De-risk Engineering
pH Optimization
Humanization

Input

Amino acid sequences of
lead candidates

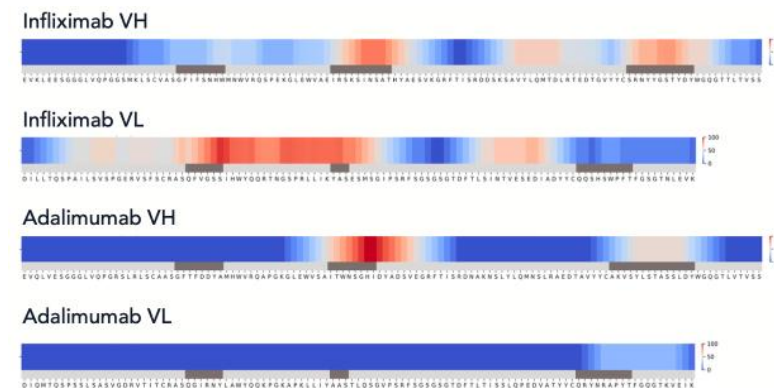


Output

Multi-parameter optimization to create therapeutic leads

Analyse candidates to gain 360-degree insight in developability and immunogenicity profiles to guide engineering. Easily humanize and optimize candidates to become leads.

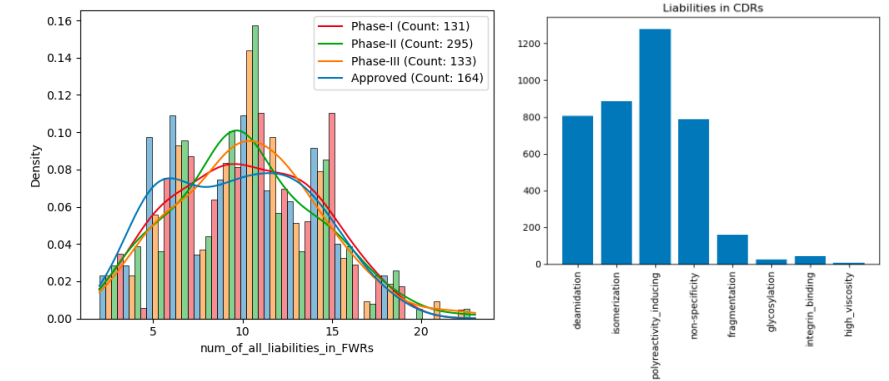
Immunogenic heat maps illustrating hotspots



Immunogenicity and Developability profile

Data are compared with clinical reference sets.

Designed for throughput, speed, scalability and insights
Applicable to all Ab formats (mAb, VHH, multispecifics...)



LENS^{ai}'s Differentiator

In silico MHCII-complex binding predictors are reliable tools that mimic *in vitro* assay outcomes yet tend to overpredict immunogenic risk.

LENS^{ai} immunogenicity screening combines gold standard MHCII-binding prediction tools with a **proprietary algorithm** and demonstrates reliable ADA risk classification.

Our tool showcases reliable risk classification; a drug developer could use this tool to:

- Focus on candidates with lower scores
- Apply caution on higher scoring candidates

Key differentiators:

- Full (transcriptome-based) human proteome scanning
- Expanded coverage with ~900 additional alleles beyond the MHCII Allele superfamily
- Customizable for regional-, genotype-, and indication-specific patient populations.

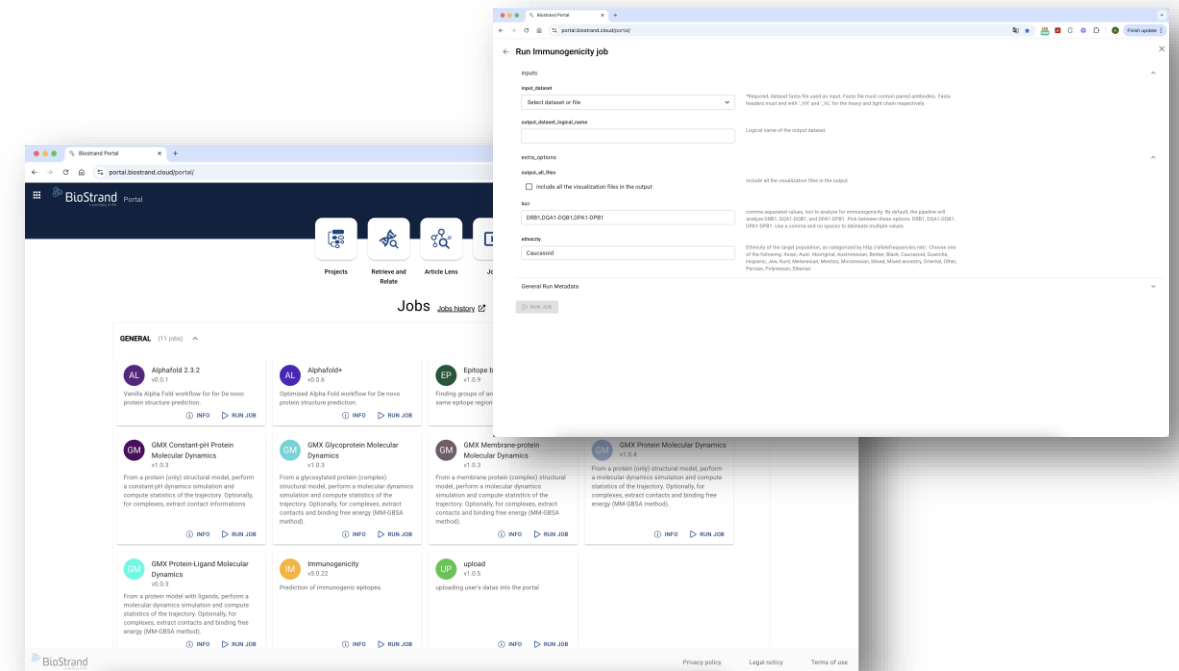
Easily accessible intelligence

LENS^{ai} Immunogenicity screening

Empower Your Decisions Anywhere, Anytime:

Run your analytics, set your own parameters, explore trends and get answers from a single, web-based platform.

- Start from any popular sequence format, .csv, .fasta
- No limit on number of input sequences
- Custom data-connectors possible



LENS^{ai} platform: Multi-level interactive data reporting

Ability to rank and compare multiple levels of detail

Analytical results

- Global statistics
- Sequence level overview

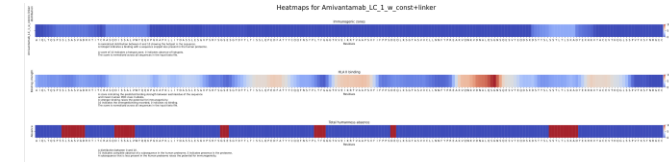
← Preview

FC_immunogenicity_run12/report_summary.csv [DOWNLOAD](#)

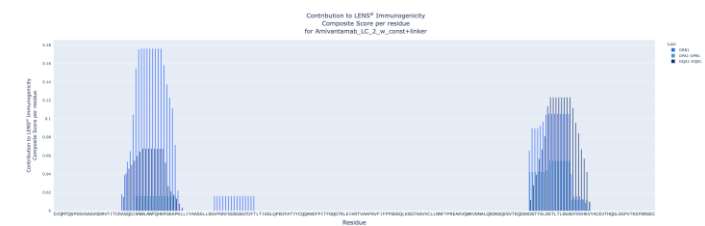
COLUMNS **FILTERS** **COLUMNS SETTINGS** **EXPORT**

#	☐	Name of the sequence	Total score per sequence	Name of the protein	Total score per protein	Path to the r...
#1	☐	Alefacept_sequence_Heavy_chain__subunit_1	2.095	Alefacept	2.596	/Report...
#2	☐	Alefacept_sequence_Light_chain__subunit_2	0.502	Alefacept	2.596	/Report...
#3	☐	Amivantamab_HC_1_w_const+linker	10.893	Amivantamab	41.538	/Report...
#4	☐	Amivantamab_HC_2_w_const+linker	15.005	Amivantamab	41.538	/Report...
#5	☐	Amivantamab_LC_1_w_const+linker	7.859	Amivantamab	41.538	/Report...
#6	☐	Amivantamab_LC_2_w_const+linker	7.781	Amivantamab	41.538	/Report...
#7	☐	Blinatumomab_+_Tarlatamab_Blinatumomab__BsAb_	38.062	Blinatumomab_+_Tarlatamab	47.882	/Report...
#8	☐	Blinatumomab_+_Tarlatamab_Tarlatamab__BsAb_	9.82	Blinatumomab_+_Tarlatamab	47.882	/Report...
#9	☐	Cinrebafusp__sequence_Heavy_chain__subunit_1	86.53	Cinrebafusp__	98.889	/Report...
#10	☐	Cinrebafusp__sequence_Light_chain__subunit_2	1.96	Cinrebafusp__	98.889	/Report...
#11	☐	Conbercept_sequence_Heavy_chain__subunit_1	24.152	Conbercept	46.664	/Report...
#12	☐	Conbercept_sequence_Light_chain__subunit_2	22.511	Conbercept	46.664	/Report...
#13	☐	Efmorotocog__sequence_Heavy_chain__subunit_1	11.135	Efmorotocog__	11.137	/Report...
#14	☐	Efmorotocog__sequence_Light_chain__subunit_2	0.002	Efmorotocog__	11.137	/Report...
#15	☐	Romiplostim_Amino_acid_sequence_for_Fc_fusion_compound	13.026	Romiplostim	13.508	/Report...
#16	☐	Romiplostim_Thrombopoietin_receptor_binding_domain_amino_acid_sequence	0.482	Romiplostim	13.508	/Report...

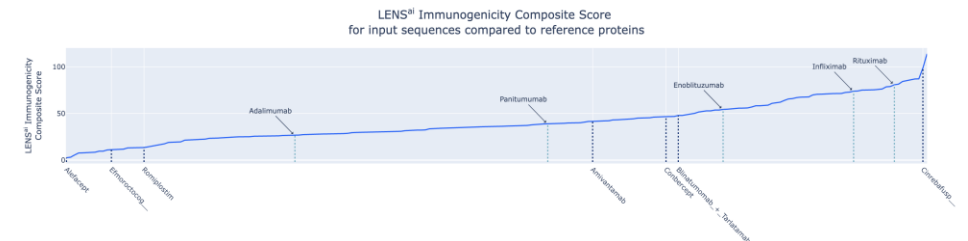
Sequence based evaluation:



Epitope level- and AA-level scoring:

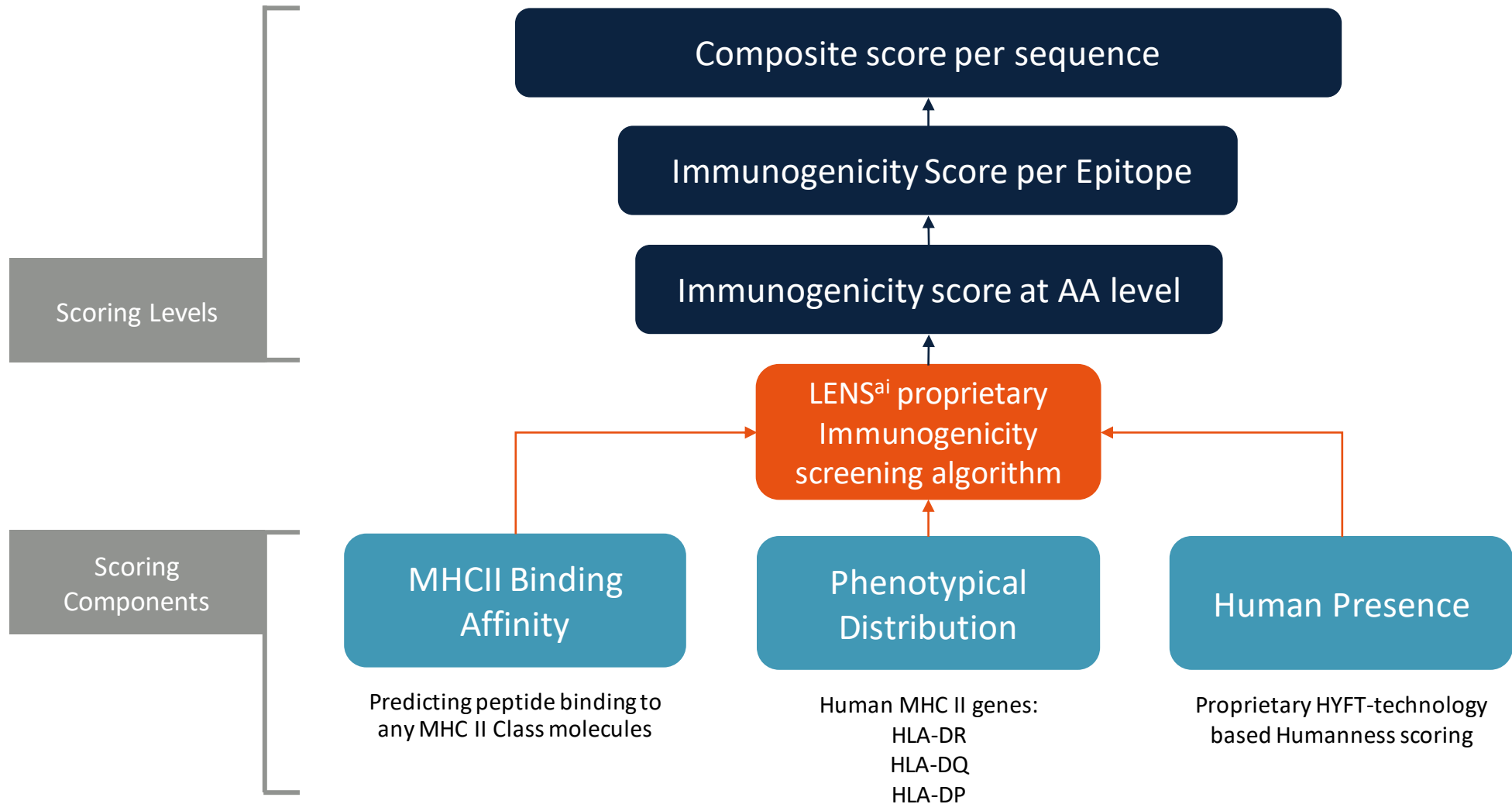


Benchmark based comparisons; candidates of interest vs clinical reference



LENS^{ai} Immunogenicity Scoring mechanism

Breakdown of components



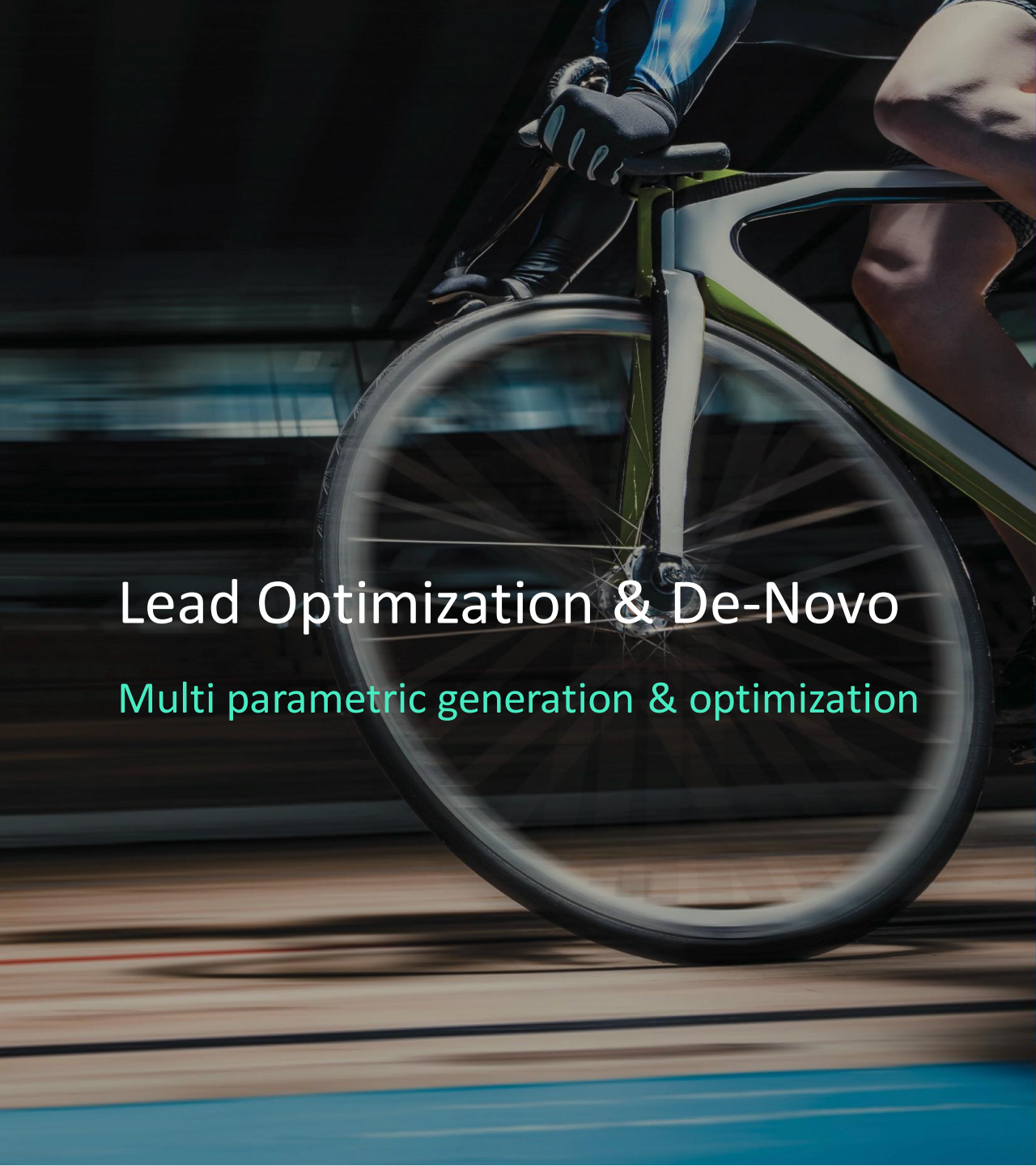


BioStrand showcases evidence for clinical utility of ADA risk assessment

Performance comparison in classifying candidates at risk (>10% ADA)

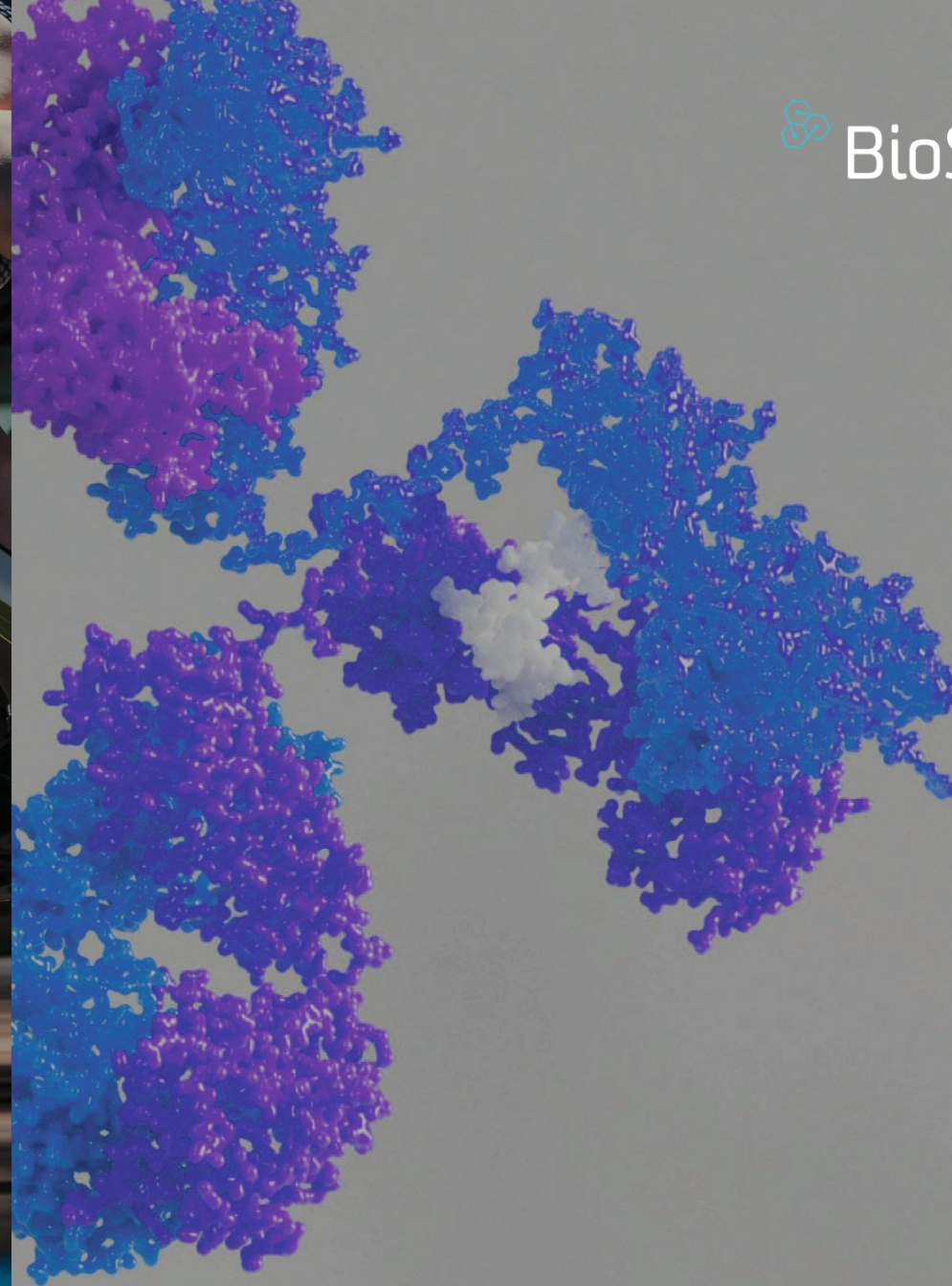
*Values from Merck/BioPhi 2021 publication

Feature	LENS ^{ai} Immunogenicity
Trend	✓ Clear positive correlation
Binary logistic model Gray dots represent individual therapeutic mAbs grouped by class Class 0= ADA < 10% ; Class 1= ADA >10% Black line shows mean predicted probability of ADA% > 10% Blue shaded area indicates model uncertainty	
Prediction Pattern	✓ The higher the LENS ^{ai} scores the more likely antibody belongs to high ADA class
Confidence Interval	✓ Narrower 89% HDI (more certain)
Clinical Utility	🌀 Effective for ADA risk stratification
Threshold	🌀 Can identify high-risk therapeutics



Lead Optimization & De-Novo

Multi parametric generation & optimization



End to End De-Novo pipeline

Powerful post filtering

Ready to run De-Novo pipeline

- Proprietary in-house Fine-tuned generative model(s)
- Access to public pipelines
- Advanced proprietary post filtering
 - Pipeline with proven success in engineering workflows
 - Extremely accurate filtering and selecting is critical for successful De-Novo design.

De-Novo generation for various scenarios:

(synthetic) Protein design

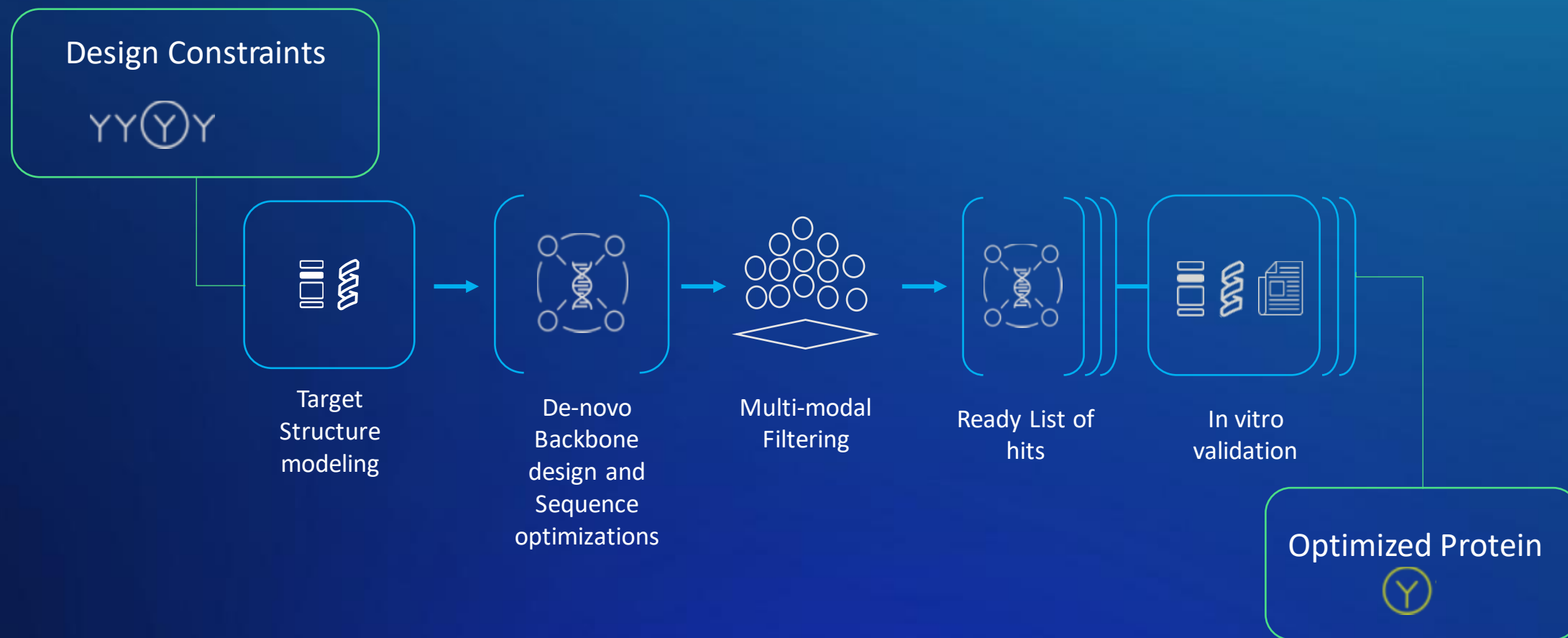
Protein – Protein

Protein – Antibody

Protein – Ligand

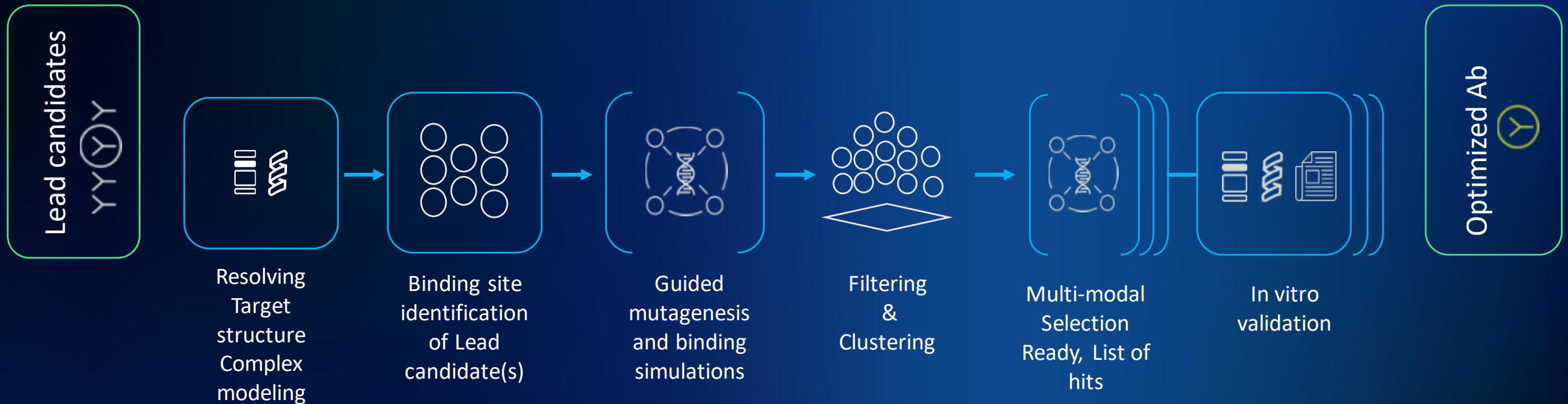
Technology designed to solve the complex

Overview of the *De-Novo* molecular design workflow



Technology designed to solve the complex

Overview of the *in silico*-only molecular engineering workflow



Antibody engineering for Tumor MicroEnvironment Targeting (pH selective)

Project overview

Objective

Achieve engineered variants with the following characteristics:

- Preferential binding to target FOLR2 in Acidic pH condition (pH 6.0)
- Reduced or negative binding to FOLR2 in Neutral pH condition (pH 7.4)
- Removed cross-reactivity with FOLR3

Input Sequences

- Publicly disclosed FOLR2 binding mAb sequences: $n = 3$
- Panel of FOLR2 binding mAb sequences internally sourced: $n = 12$

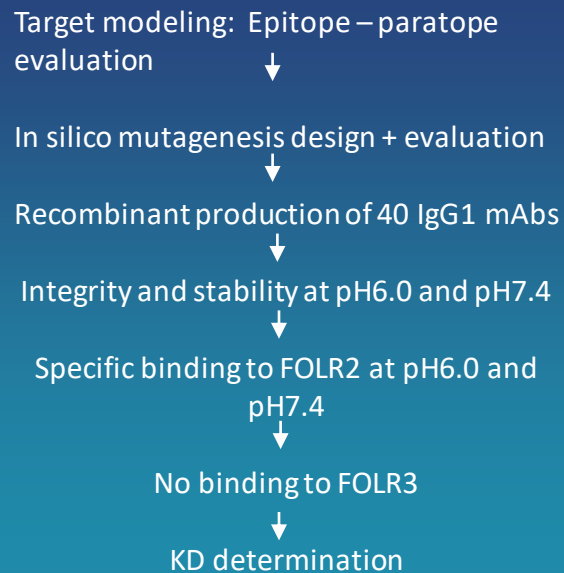
Starting position

No crystal structure for the following:

- hFOLR2 in acidic conditions
- hFOLR3 in acidic and neutral conditions
- mAb-Ag complex for human FOLR2

Antibody engineering for pH selective FOLR2 antibody

Overview workflow



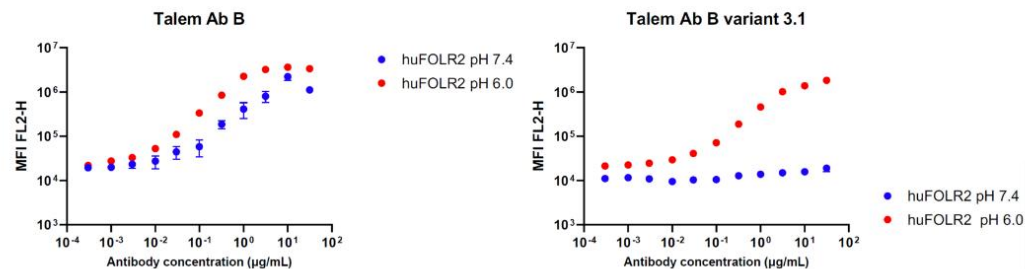
40 mutants with highest predicted pH6.0 specificity and low off-target interaction were selected for in vitro validation. Each mAb variant had up to 5 amino acid substitutions, mostly across CDRs and predominantly in the heavy chain.

- All 40 mutants were successfully produced recombinantly.
- HP-SEC analysis indicated that integrity and stability was not impacted by either pH condition.
- Reactivity profiling using both plate- and flow-based assays indicated that 3 mAbs had the desired characteristics.
- Affinity determination using high-throughput SPR was performed to determine KD under both conditions.

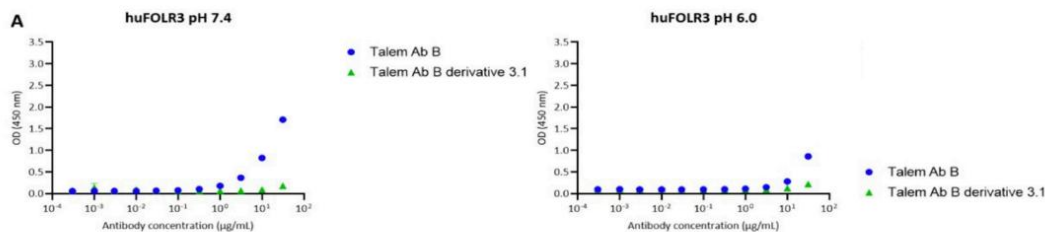
Antibody engineering for Tumor MicroEnvironment Targeting

Experimental validation

Talem B 3.1 maintains binding strength with hFOLR2 at pH 6.0, but not at pH 7.4, demonstrating its pH-selective feature



Talem B 3.1 showed differentiated binding to hFOLR2 at different pH conditions



Binding of Talem B3.1 with hFOLR3 was significantly reduced in both pH conditions compared to parental Talem B.

- An example of one engineered clone, Talem Ab B 3.1 showed preferred binding to hFOLR2 at pH6.0 but not pH7.4.
- This engineered clone also showed significantly decreased cross reactivity to FOLR3.
- Talem Ab B 3.1 also shows solid developability and low immunogenicity.
- Talem Ab 3.1 maintains the binding affinity as its parental clone.

Conclusion:

LENSai in silico platform achieves successful molecular engineering of pH selective antibodies. Despite the absence of crystal structures. This innovative approach demonstrates the potential for rationally engineering pH-selective antibodies while maintaining specificity and favorable developability.

Technology designed to solve the complex

A toolbox to cater to every question



Fee-for-service
Tools



Software
Platform
UI/API



End-to-end
Partnerships

LENS^{ai} Integrated
Intelligence Technology

Unlocking growth: The power of a (Machine) learning organization



Extend workflow beyond
In vitro screening



Effortless integration of
workflows in a
unified data ecosystem



Easy to deploy internal
analytical workflows with
LENS^{ai} BioIntelligence cloud



Innovative potential: Combining
capabilities to become the
world's fastest platform from
concept to clinic



IpA



BioStrand

a subsidiary of IPA

Let's solve the complex through
collaboration

Thank you

Contact

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www.biostrand.ai