

absci.

```
from absci import de_novo_model
model = de_novo_model.load_latest()
antigen = model.load_pdb("7olz.pdb",
chain="A")
antibodies = model.predict(antigen, N=300000)
```

```
from absci_library import codon_optimizer
library
= codon_optimizer.reverse_translate(library)
library.to_csv("covid-antibody-designs.csv")
library.to_wet_lab(assay="ACE")
```

```
from absci import lead_opt_model
lead_optimizer = lead_opt_model.load_latest()
library.naturalness =
lead_optimizer.naturalness(library)
lead_optimizer.optimize(library).to_wet_lab(assay="SPR")
```

DRUG CREATION



Carterra Boston Symposium
June 2024

```
from absci import genetic_algorithm; parameters=["maximize(binding_affinity:pH=7.5", "minimize(binding_affinity:pH=6.0",
"maximize(human_naturalness)"]; library = genetic_algorithm.multiparametric_optimization(library, parameters, evolutions=100);
library.to_wet_lab(assays=["ACE", "SPR", "Bioassays"])
```

Disclaimers

Market and Statistical Information

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other industry data. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. We have not independently verified the data generated by independent parties and cannot guarantee their accuracy or completeness.

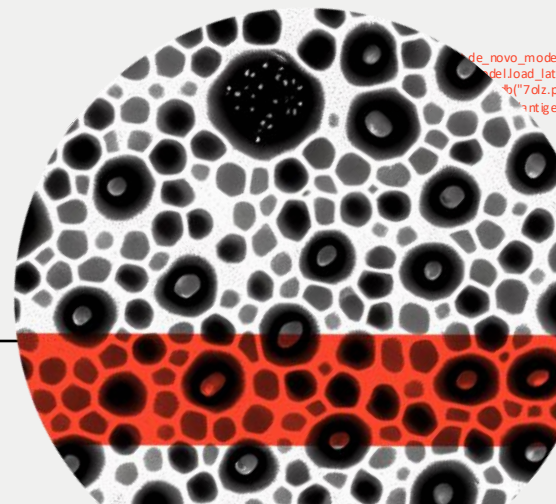
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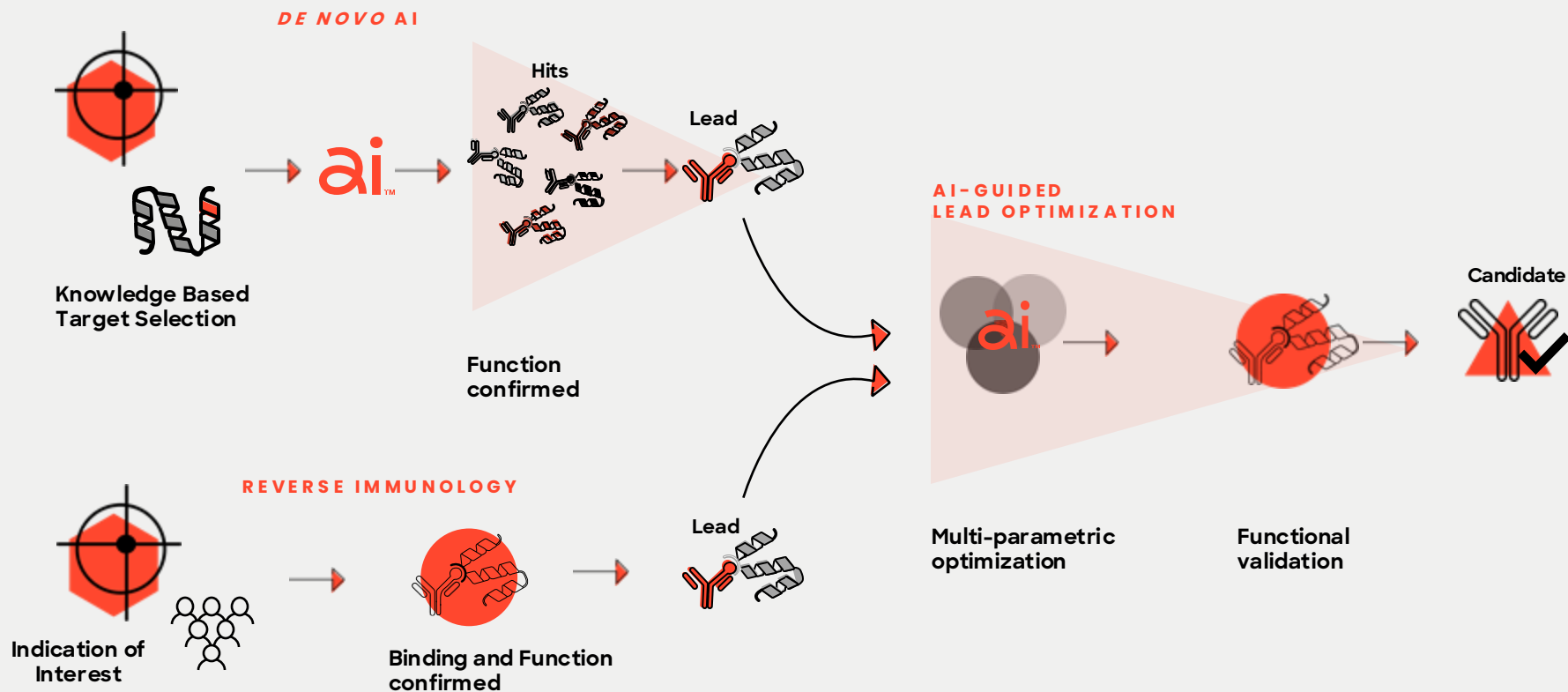
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abscli_library import codon_optimizer
r = codon_optimizer.reverse_translate(library)
r.to_csv("covid-antibody-designs.csv")
r.to_wet_lab(assay="ACE")
```

Outline

1. AI Drug Creation™ platform
2. IgDesign™: Absci's wet lab-validated generative inverse folding model for designing CDRs from antibody-antigen complexes
3. Functionality and Developability Assessment of Zero-Shot Trastuzumab Designs: Going beyond binding affinity to assess drug-like properties.



Integrated Drug Creation™ platform



Integrated Drug Creation™ platform

DATA TO TRAIN

Proprietary wet-lab assays generate large quantities of high-quality data a week for generative AI model training



aiTM

AI TO CREATE

Generative AI engine to create new antibodies and next-gen biologics



WET LAB TO VALIDATE

Scalable wet-lab infrastructure capable of validating millions of unique AI-generated designs a week



Iterative cycles enable rapid validation of *de novo* designs

+

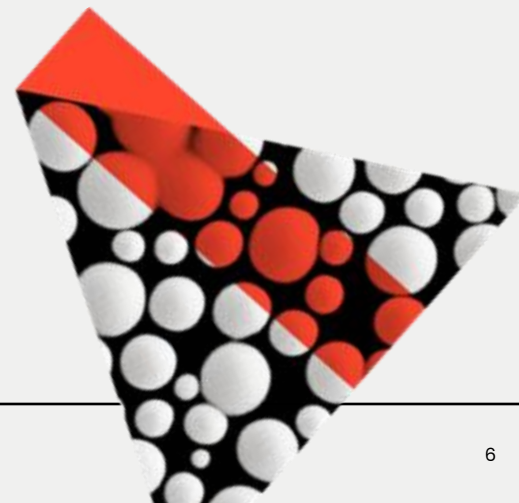
continuous improvements to generative models

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optimizer = codon_optimizer.reverse_translate(library)
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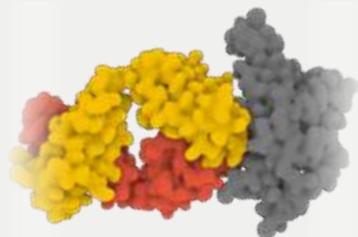
IgDesign™

A deep learning method for
antibody CDR design

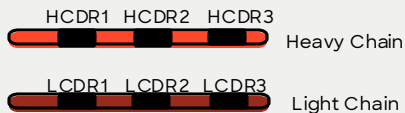
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IgDesign™ - Antibody Inverse Folding

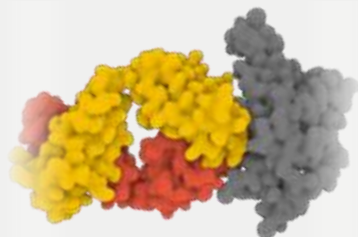


Bound Structure

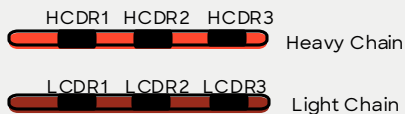


Antibody Sequence (CDRs)

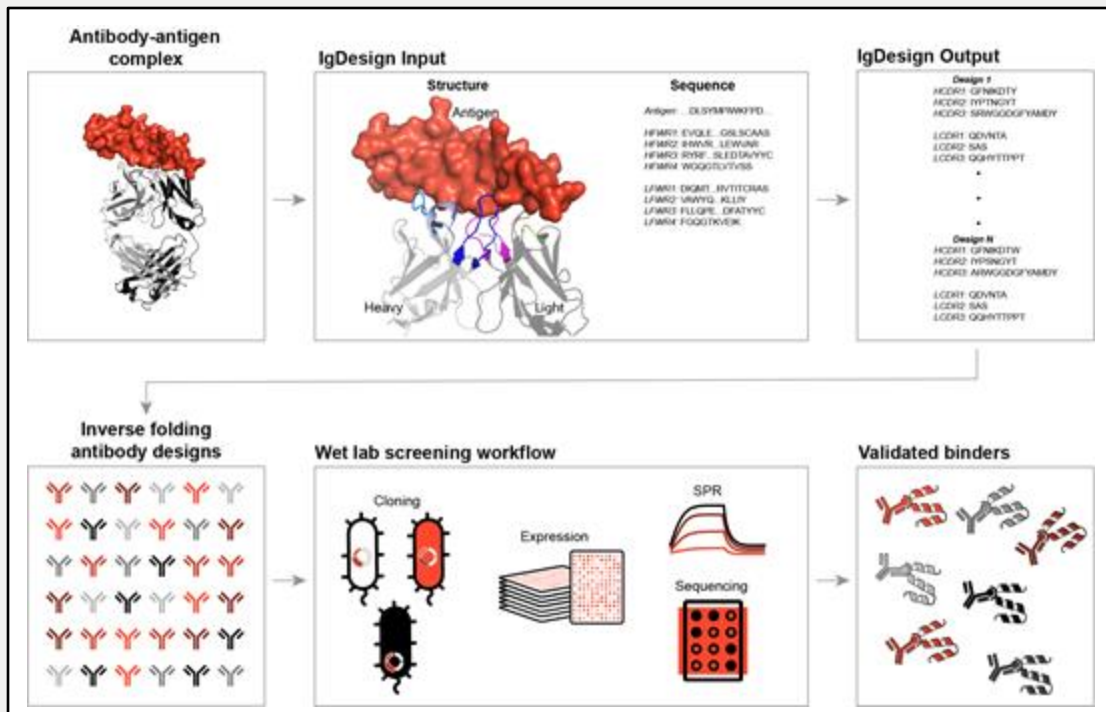
IgDesign™ - Antibody Inverse Folding



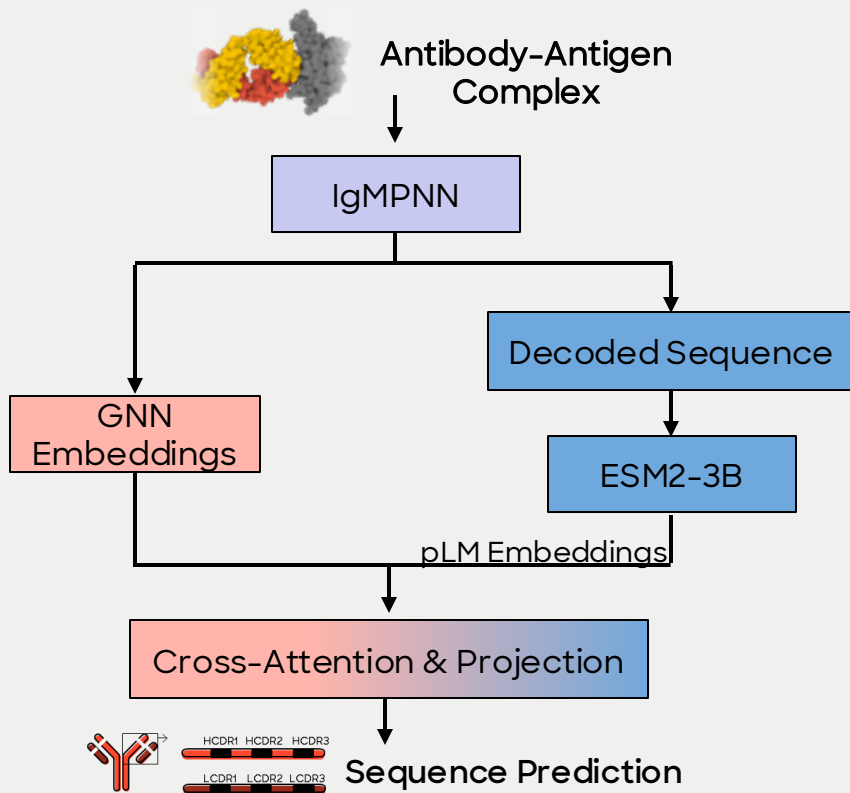
Bound Structure



Antibody Sequence (CDRs)



IgDesign™ Model¹



- IgDesign: IgMPNN structure encoder combined with protein language model as sequence decoder (LM-Design strategy²)
- IgMPNN: Graph-neural network (GNN) antibody-antigen structure encoder based on ProteinMPNN³
- ESM2-3B: 3 billion parameter protein language model (pLM) used as sequence decoder⁴

¹Shanehsazzadeh et al. bioRx preprint Dec 2023

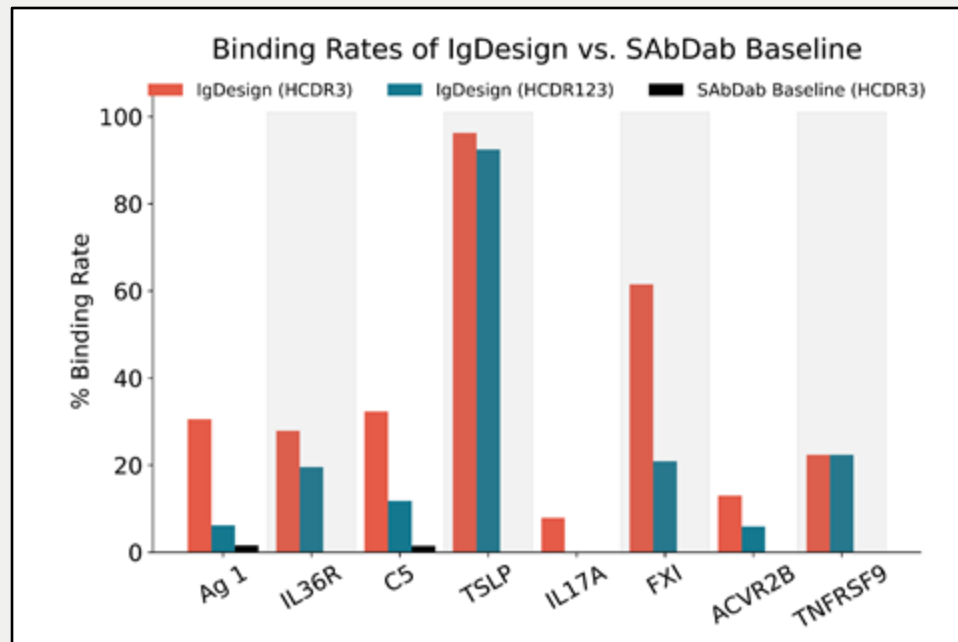
²Zheng et al. <https://doi.org/10.48550/arXiv.2302.01649>

³Dauparas et al. <https://doi.org/10.1126/>

⁴Lin et al. <https://www.biorxiv.org/content/early/2022/12/21/2022>

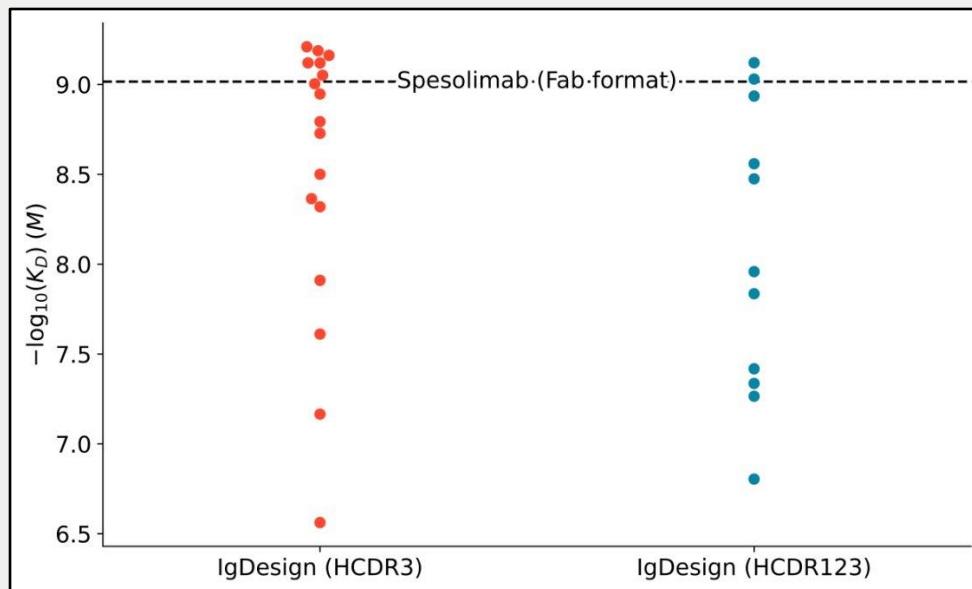
IgDesign™ experimentally outperforms baseline

- Ab-Ag complexes (PDBs) selected for 8 diverse therapeutic targets
- Designed libraries for each target. Each library consisted of:
 - IgDesign™: 100 HCDR3 designs
 - IgDesign™: 100 HCDR123 designs
 - Baseline: 100 HCDR3 samples from the training set (SAbDab) with matching HCDR3 length
- Libraries screened against respective targets using surface plasmon resonance (SPR)



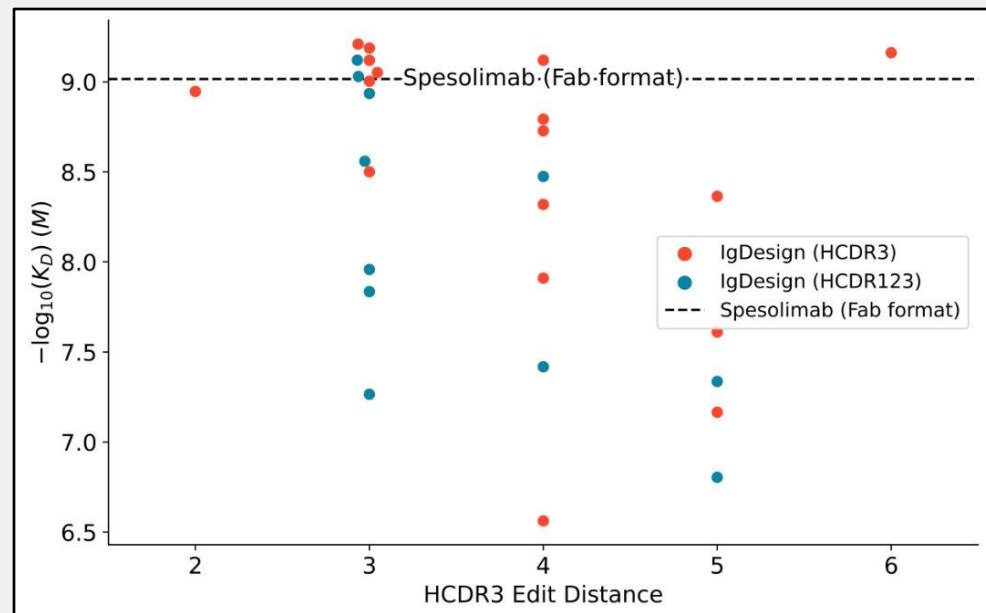
Affinity Data for IL36R-Spesolimab HCDRs

- IgDesign is able to design high affinity binders for the IL36R-Spesolimab system
- Many variants are competitive with spesolimab, with some having subnanomolar affinity



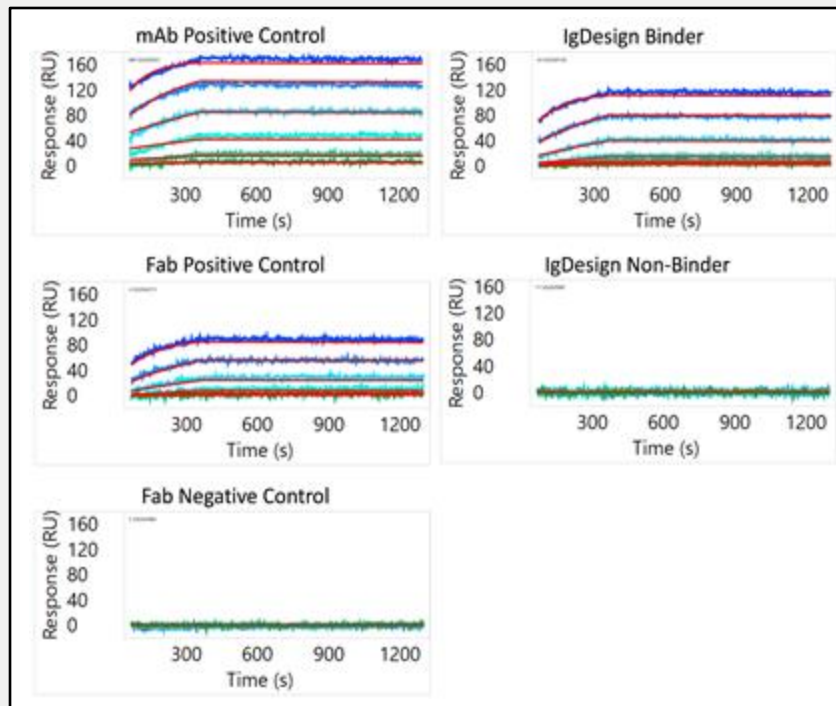
Diversity Data for IL36R-Spesolimab HCDRs

- IgDesign is able to design diverse, high-affinity HCDR3 variants of spesolimab
- Spesolimab HCDR3 has length 12



Sensorgrams for IL36R-Spesolimab HCDRs

- Absci's HT-SPR is powered by the Carterra LSA platform
- Able to screen thousands of antibody designs on a weekly basis
- HT-SPR enables rapid assessment of models with high quality data

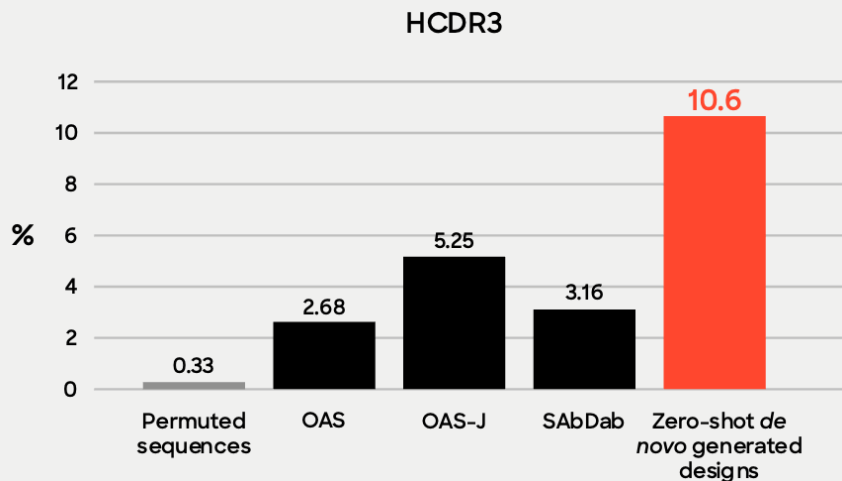


IgDesign™: An Experimentally-Validated Inverse Folding Approach to Antibody Development

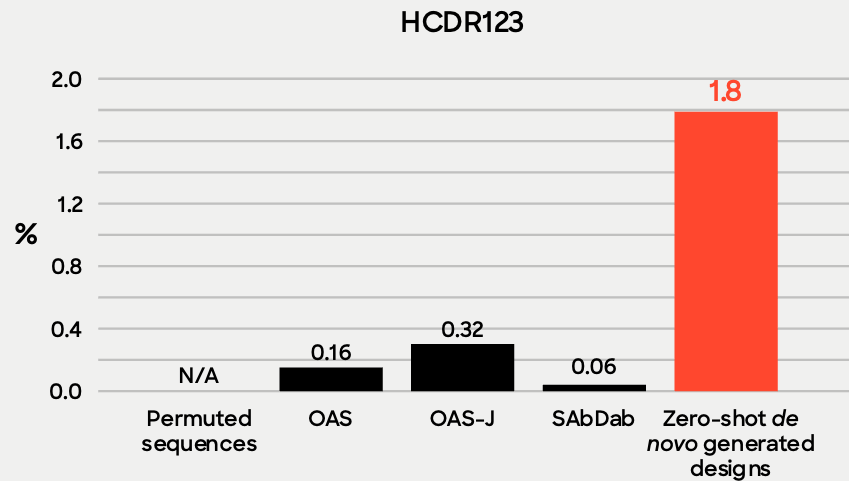
1. IgDesign™ is an antibody inverse folding model developed by combining:
 - Ideas from protein inverse folding models and language models such as LM-Design, ProteinMPNN, and ESM2
 - An antibody-specific framing of the problem with antigen and antibody framework (FWR) sequences provided as context
 - Fine-tuning on antibody-antigen complexes
2. IgDesign™ is able to consistently design binders against a diverse set of therapeutic antigens with confirmation using SPR via Carterra LSA platform
3. Demonstrating the success of antibody inverse folding is key to advancing the field since models such as IgDesign™ can be broadly applied to antibody development efforts

Trastuzumab-HER2 zero-shot binder design

HER2 BINDING RATE (%)

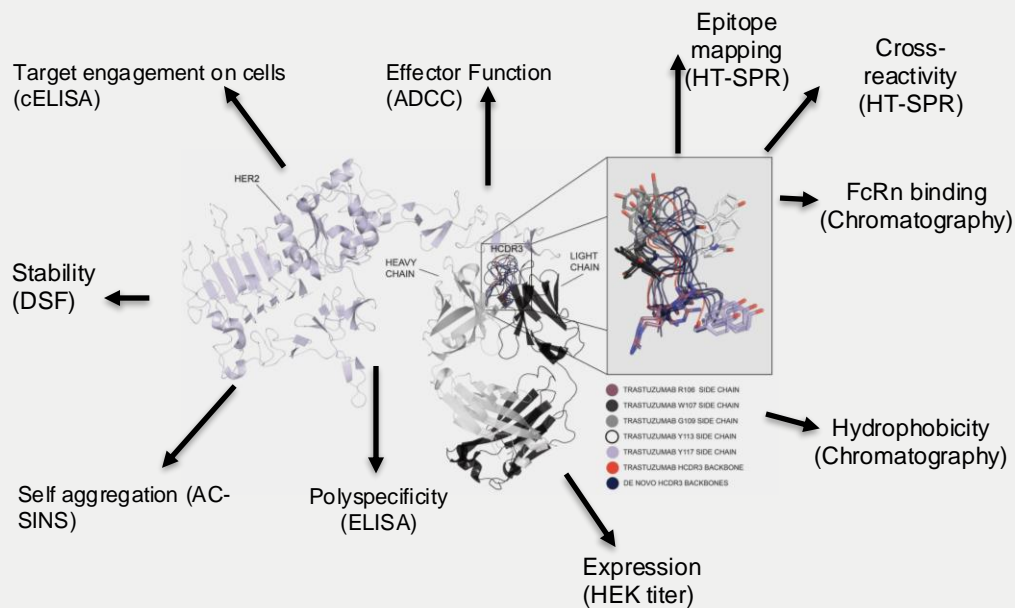
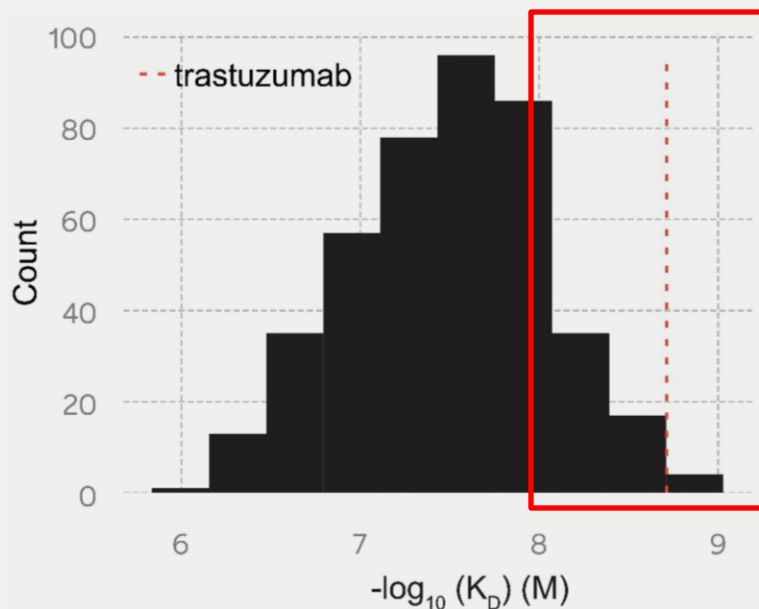


De novo designed HCDR3s achieve a **4-fold improvement** over random OAS baseline



De novo designed HCDR123s achieve an **11-fold improvement** over random OAS baseline

Therapeutic and functional benchmarking of AI designed libraries



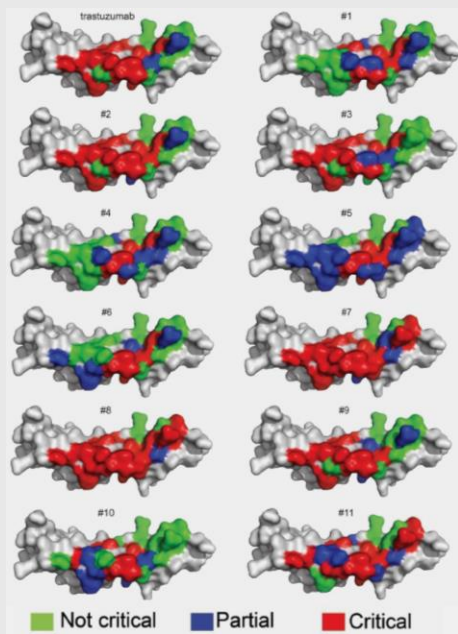
- We took 11 candidate HCDR3 trastuzumab variants with high affinity to HER2 and screened them as mAbs for functionality and developability
- Epitope mapping via alanine scanning HT-SPR was enabled by Carterra LSA platform

AI designs are generally developable with comparable or better potency than trastuzumab

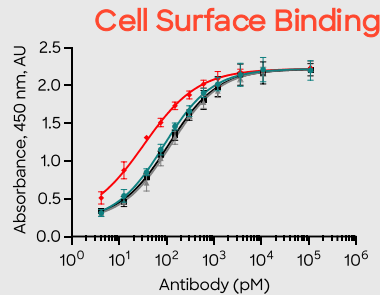
Variant #	HCDR3 sequence	Potency		AC-SINS (nm shift)	HIC (Relative RT)	Polyspecificity		FcRn chromatography (RT, min)
		Cell binding (EC50, pM)	ADCC (EC50, pM)			Insulin (score)	DNA (score)	
1	TRYFFNGWYYFDV	87.4	53.8	2.4	1.21	0.517	0.175	28.13
2	ARYYYGFYYFDY	33.2	14.6	3.1	1.11	0.176	0.127	26.98
3	ARWGNYYYYMDY	122.2	77.9	9.1	1.27	0.205	0.132	29.79
4	ANDIYIQGYDLNR	105.7	58.7	1.8	1.14	0.168	0.101	27.35
5	ARYYGYYGGYYFDY	107.4	46.5	2.4	1.09	0.250	0.122	27.31
6	ARWGGDFYAMDY	78.1	34.8	0.4	1.05	0.187	0.122	26.74
7	ARWYGYGGYYFDY	87.1	57.7	4.4	1.16	0.175	0.133	29.56
8	ARYGYAPGFYYMDV	103.4	62.8	3.1	1.14	0.187	0.126	27.50
9	TRWGGYYFDY	104.8	50.2	9.1	1.21	0.200	0.121	29.10
10	APYGPYWGCV	99.8	50.1	-0.9	1.16	0.138	0.125	28.06
11	ARYYYDYYYFDY	128.1	48.8	5.1	1.56	0.170	0.124	27.61
Trast	SRWGGDFYAMDY	110.7	57.0	0.4	1.01	0.195	0.121	26.74

Green: increased potency; Red: developability flag

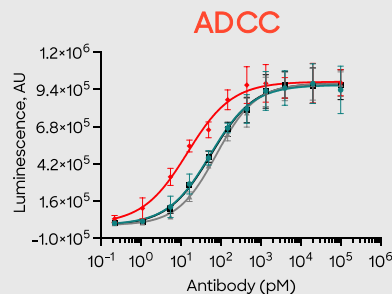
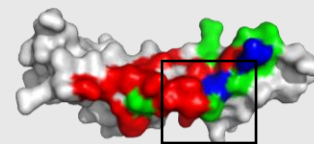
Epitope mapping using HT-SPR and the Carterra LSA Platform reveals a functionally superior variant



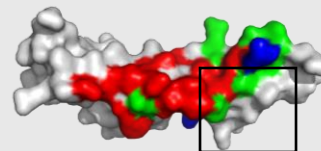
Epitope maps of high affinity AI-designs compared to trastuzumab



Trastuzumab WT



Candidate #2 (most potent)



Epitope hotspot controls potency

Epitope mapping reveals molecular determinants of improved cellular function

Designing and validating novel antibodies using zero-shot generative AI



JAN 2023- UPDATED JAN 2024

Functional *wet-lab validation* of novel antibodies designed using *zero-shot* generative AI - demonstrating the potential to go from target to therapeutic antibody at a click of a button

(Shanehsazzadeh et al. 2024)



DEC 2023

in vitro validated antibody design against multiple therapeutic antigens using generative inverse folding model

(Shanehsazzadeh et al. 2023)



AUG 2022

Used artificial intelligence to *simultaneously optimize* multiple parameters important to drug discovery and development

(Bachas et al. 2022)

Absci's work is enabled by interdisciplinary talent and resources



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***In vitro* validated antibody design against multiple therapeutic antigens using generative inverse folding**

Amir Shanehsazzadeh, Julian Alverio, George Kasun, Simon Levine, Jibrán A. Khan, Chelsea Chung, Nicolas Diaz, Breanna K. Luton, Ysis Tarter, Cailen McCloskey, Katherine B. Bateman, Hayley Carter, Dalton Chapman, Rebecca Consbruck, Alec Jaeger, Christa Kohnert, Gaelin Kopec-Belliveau, John M. Sutton, Zheyuan Guo, Gustavo Canales, Kai Ejan, Emily Marsh, Alyssa Ruelos, Rylee Ripley, Brooke Stoddard, Rodante Caguat, Kyra Chapman, Matthew Saunders, Jared Sharp, Douglas Ganini da Silva, Audree Feltner, Jake Ripley, Megan E. Bryant, Danni Castillo, Joshua Meier, Christian M. Stegmann, Katherine Moran, Christine Lemke, Shaheed Abdulhaqq, Lillian R. Klug, Sharrol Bachas, Absci Corporation

Unlocking *de novo* antibody design with generative artificial intelligence

Amir Shanehsazzadeh, Matt McPartlon, George Kasun, Andrea K. Steiger, John M. Sutton, Edriss Yassine, Cailen McCloskey, Robel Haile, Richard Shuai, Julian Alverio, Goran Rakocevic, Simon Levine, Jovan Cejovic, Jahir M. Gutierrez, Alex Morehead, Oleksii Dubrovskiy, Chelsea Chung, Breanna K. Luton, Nicolas Diaz, Christa Kohnert, Rebecca Consbruck, Hayley Carter, Chase LaCombe, Itti Bist, Phetsamay Vilaychack, Zahra Anderson, Lichen Xiu, Paul Bringas, Kimberly Alarcon, Bailey Knight, Macey Radach, Katherine Bateman, Gaelin Kopec-Belliveau, Dalton Chapman, Joshua Bennett, Abigail B. Ventura, Gustavo M. Canales, Muttappa Gowda, Kerianne A. Jackson, Rodante Caguat, Amber Brown, Douglas Ganini da Silva, Zheyuan Guo, Shaheed Abdulhaqq, Lillian R. Klug, Miles Gander, Engin Yapici, Joshua Meier, Sharrol Bachas

absci®



This **revolution** is
only just beginning.