

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(as
say="SPR")

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Corporate Presentation March 2023

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What if the next transformative drug was not disc wered. but created at a click of a button?

The Problem – Current Need For Generative AI The drug discovery paradigm is ripe for disruption



Long iterative process resulting in drug candidates with suboptimal attributes



Why Hasn't Generative AI Transformed Biologic Drug Discovery?

Unlocking the potential of generative AI in biology requires scalable biological data



Biotech Industry Inflection Point

Absci is solving the problem of scalable biological data enabling true generative AI for biologics drug discovery



import de_novo_model model = de_novo_model.load_latest() antigen = model.load_pdb("7olz.pdb", antibodies = model.predict(antigen, N=300000) from absci_library import codon_optimizer library timizer.reverse_translate(library) library.to_csv("covid-antibody-") library.to_wet_lab(assay="ACE")

Instead sf finding the needle in the haystack, Absci is creating the needle.

Incuba

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The Solution

Absci is leading the way with our Integrated Drug Creation™ platform

DATA TO TRAIN

Proprietary wet-lab assays capable of generating billions of protein-protein interactions a week for ML training

WET LAB TO VALIDATE

Scalable wet-lab infrastructure capable of validating 2.8 million unique Al-generated designs a week



AI TO CREATE

Generative AI engine to create new antibodies and next-gen biologics Absci is the Leader in Generative AI Drug Creation for Biologics

Cycles completed within weeks



Absci's rapid cycle times allow for:



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

Absci is the first to 2005: 20 approved, 11.2% of drugs entering clinical trials approved 2008: 24 approved, 9.2% 2009: 26 approved, 7.8% 2010: 21 approve 2013: 27 approved, 5.2% 2014: 41 approved, 6.7% 2015: 45 approved design and validate new antib@dies with zeroshot generative Al

Absci's End-to-End Platform Solution

The leading full-stack AI platform for biologics drug creation



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de novo Drug Creation in silico

De novo drug creation with 'zero-shot' generative Al



- <u>Zero-Shot</u>: Model has never seen an antibody that binds to the target or homologs
- Binders were identified straight out of the model – no lead optimization was performed
- Demonstrated across four therapeutic targets: HER2, VEGF-A, COVID omicron, undisclosed target

Case Study: de novo Discovery in silico

Unlocking *de novo* antibody design with generative Al

Unlocking *de novo* antibody design with generative artificial intelligence

Amir Shanehsazzadeh^{*}, Sharrol Bachas^{*}, George Kasun, John M. Sutton, Andrea K. Steiger, Richard Shuai, Christa Kohnert, Alex Morehead, Amber Brown, Chelsea Chung, Breanna Luton, Nicolas Diaz, Matt McParthon, Balley Knight, Macey Radach, Katherine Bateman, David A. Spencer, Jovan Cejovic, Gaelin Kopec-Belliveau, Robel Haile, Edriss Yassine, Cailen McCloskey, Monica Natividad, Dalton Chapman, Luka Stojanovic, Rodante Caguiat, Shaheed Abdulhaoq, Zheyuan Guo, Katherine Moran, Lillian R. Klug, Miles Gander, Joshua Meier²⁰

Absci Corporation, New York (NY) and Vancouver (WA), USA

Abstract

Generative artificial intelligence (AI) has the potential to greatly increase the speed, quality and controllability of antibody design. Traditional de novo antibody discovery requires time and resource intensive screening of large immune or synthetic libraries. These methods also offer little control over the output sequences, which can result in lead candidates with sub-optimal binding and poor developability attributes. Several groups have introduced models for generative antibody design with promising in silico evidence [1-10], however, no such method has demonstrated de novo antibody design with experimental validation. Here we use generative deep learning models to de novo design antibodies against three distinct targets in a zero-shot fashion where all designs are the result of a single round of model generations with no follow-up optimization. In particular, we screen over 400,000 antibody variants designed for binding to human epidermal growth factor receptor 2 (HER2) [11] using our high-throughput wet lab capabilities. From these screens, we further characterize 421 binders biophysically using surface plasmon resonance (SPR), finding three that bind tighter than the therapeutic antibody trastuzumab [12]. The binders are highly diverse and have low sequence identity to known antibodies. Additionally, these binders score highly on our previously introduced Naturalness metric [13], indicating that they are likely to possess desirable developability profiles and low immunogenecity. We open source the binders to HER2 and report the measured binding affinities. These results unlock a path to accelerated drug creation for novel therapeutic targets using generative AI combined with high throughput experimentation.





Case Study: de novo Discovery in silico

Al model generated highly diverse and effective binders from massive search space



AI-Designed & Wet Lab Validated HER2 Binders

- Hundreds of binders created
- Ability to generate binders near to and far from trastuzumab
- Binding affinity maintained even when mutating >90% of the CDR3 region
- All binders to HER2 and HER2 homologs removed from the training dataset

Case Study: de novo Discovery in silico

AI model is broadly applicable and enables higher potential therapeutics

Better therapeutics, faster

- Successfully designed antibody variants with higher Naturalness score
- The Naturalness score is associated with developability metrics such as immunogenicity

Model is validated and broadly applicable

 Successfully demonstrated across four therapeutic targets: HER2, VEGF-A, COVID omicron, undisclosed target

Rapid progress towards fully *in sili*co drug creation



AI Driven Lead Optimization

Multiparametric AI lead-optimization can enable higher potential therapeutics and increased PoS



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Case study: AI-Driven Lead Optimization

Multiparametric AI lead-optimization for increased success rates & higher potential therapeutics



Case study: AI-Driven Lead Optimization

Multiparametric AI lead-optimization validated in the wet-lab



Case study: AI-Driven Lead Optimization 85% of Top 100 "natural" Trastuzumab variants exhibit higher-affinity than wild-type



- AI predicts the affinity of unseen variants from libraries generated using diverse mutational strategies and combinatorial sequence space
- AI models make predictions with actionable performance using <0.1% of the combinatorial sequence space as training set
- Naturalness is associated with developability metrics and expression titer
- Enables one-shot multiparametric lead optimization accelerating time to clinic

Novel Target Discovery

The leading AI platform for AI-enabled biologics drug creation



Leveraging exceptional immune responses to identify new postential cancer specific targets and therapeutics

Antibodies selected in tertiary lymphoid structures bind to cancer cells and are associated with favorable clinical outcomes



Tertiary Lymphoid Structures (TLS) are centers of immune activity (B-cell proliferation and antibody production) that develop in chronically inflamed tissues such as tumors.

Meylan, Maxime, et al. "Tertiary lymphoid structures generate and propagate anti-tumor antibody-producing plasma cells in renal cell cancer." Immunity 55.3 (2022): 527-541. CORPORATE PRESENTATION MARCH 2023 | ABSCI CORPORATION 2023 ALL RIGHTS RESERVED



- The presence of TLS is associated with longer progression-free survival and better response to immune checkpoint inhibitors.
- Rapidly growing evidence illustrates correlation between TLSderived antibodies in the tumor microenvironment and positive clinical outcomes.
- TLS-derived antibodies have been shown to be associated with apoptosis of cancer cells in patients.

Our integrated workflow identifies the antigens targeted by exceptional immune responses



Absci's workflow identifies antigens targeted by exceptional immune responses



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antigens, cytokine receptors, checkpoint inhibitors and other targets

Absci's End-to-End Platform Solution

The leading AI platform for AI-enabled biologics drug creation



Bionic[™] protein technology: Non-standard amino acid (nsAA) incorporation

Absci is advancing a high-yielding SoluPro[™] platform that enables **selective site-specific nsAA** incorporation into difficult-to-produce biologics

Bionic[™] protein technology enables:

- Rapid assessment of payload location
- Precise control over payload location
- Uniform and homogenous Drug-Antibody-Ratio (DAR) for ADCs
- Attachment of diverse chemical moieties for novel applications

EXPRESSION OF MAB IN BIONIC SOLUPRO[™] CELL LINE (ADC PRECURSOR)



SoluPro[™] & Bionic SoluPro[™] – Specialized *E. coli* cell lines



SoluPro[™] & Bionic SoluPro[™]

Patented *E.* coli cell lines bioengineered for production of mammalian proteins and site-specific incorporation of non-standard amino acids

Semi-oxidized cytoplasm

Engineered redox environment to achieve scalable, soluble protein production



Precise expression control

SoluPro[™] cell lines achieve precise control over induction through genetic engineering of metabolic pathways and proprietary plasmid designs



Bionic SoluPro[™] cell lines for nsAA incorporation

A SoluPro[™] cell line optimized for high-efficiency incorporation of non-standard amino acids

Case Study: Trastuzumab nsAA incorporation

Bionic SoluPro[™] enables nsAA incorporation in different frameworks (mAb and Fab)



Value Creation for Patients and Partners - TODAY

Unlocking new and differentiated value drivers

Higher Potential Biologics with Increased PoS

Multidimensional optimization in parallel creates higher quality biologics with an increased Probability of Success



Reducing Time & Increasing Competitiveness

Drug creation process significantly shortened reducing research costs and increasing competitiveness



Novel biology: Multivalent biologics & conditional biologics

Preclinical development: Cross-species binding to improve success rates & speed



Broadening Intellectual Property Space

AI-driven drug creation generates valuable IP



Better Biologics Faster

Accelerating time to clinic while increasing PoS



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Business Model

Creating Compounding Value for Shareholders



*Illustrative of Discovery Partnership; assuming successful commercialization. Regulatory milestone captured in clinical development, and single digit royalty rates

Well positioned to revolutionize Al drug creation



Partnerships

Technology validated through industry-leading partnerships



BioSpace **"Merck leans into AI with \$610M in biobucks for Absci drug discovery pact"**

"At Merck we are continually evaluating new ways to build, expand, and refine our biologics capabilities. Absci's platform offers a compelling opportunity to design new biologic candidates and explore the expression of complex proteins."*

Dr. Fiona Marshall

Former SVP, Head of Discovery, Preclinical and Translational Medicine

EQRx

"EQRx and Absci Announce Partnership to Discover and Develop Next-Generation Protein-Based Drugs"

"Absci's technology platform enables rapid discovery and production of well-differentiated protein-based drugs that are elusive to other discovery approaches. We are excited to work with Absci..."

Dr. Carlos Garcia-Echeverria Chief of Rx Creation

Trailblazing Management Team

The right leadership team to accomplish the Impossible





SEAN MCCLAIN Founder & CEO Director

ANDREAS BUSCH, PHD **Chief Innovation Officer**

GREG SCHIFFMAN, CPA **Chief Financial Officer**







SARAH KORMAN, PHD, JD

JACK GOLD **Chief Marketing Officer**

KARIN WIERINCK Chief People Officer

PENELOPE Chief Morale Officer

Senior leadership bring experience from industry leaders including:



Chief Legal Officer

Backed by a board of industry, platform, and scientific innovators

Board of Directors



IVANA MAGOVCEVIC-ZACH JONASSON, PHD LIEBISCH, PHD, JD Managing Partner, CEO & President, Viail Neuroscience PVP Board Chairperson



KAREN MCGINNIS, CPA Former CAO, Illumina

AMRIT NAGPAL Managing Director, Redmile Group



JOSEPH SIROSH, PHD Vice President, Alexa Shopping, Amazon

HARVARD NEURO HARVARD

DAN RABINOVITSJ VP Connectivity. Meta







VICTOR GREIFF, PHD Associate Professor. University of Oslo

TIM LU, MD Co-Founder and CEO. Senti Biosciences

HUBERT TRUEBEL, MD, PHD Head of Development, CMO, AiCuris











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This revolution is only just beginning.