Just – Evotec Biologics

AI-Derived Antibody Discovery - Humanoids for Global Good

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Just – Evotec Biologics is a technology design company

Our mission

Design and apply innovative technologies to dramatically expand global access to biotherapeutics

Deeply Experienced Team

Integrated Technology Platform

Strategic Partnerships

Unique and integrated: Utilizing the power of machine learning and analytics in drug development

J.DESIGN™ Technology Platform

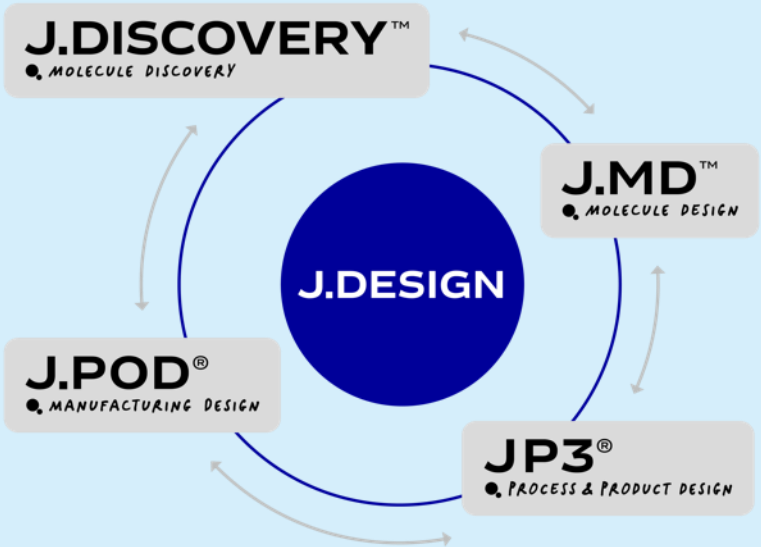
A common dataset supports integrated, continuous learning

High quality molecules

Speed to proof of concept

Robust, efficient manufacturing

Superior Molecule Discovery



Sequence optimized for developability

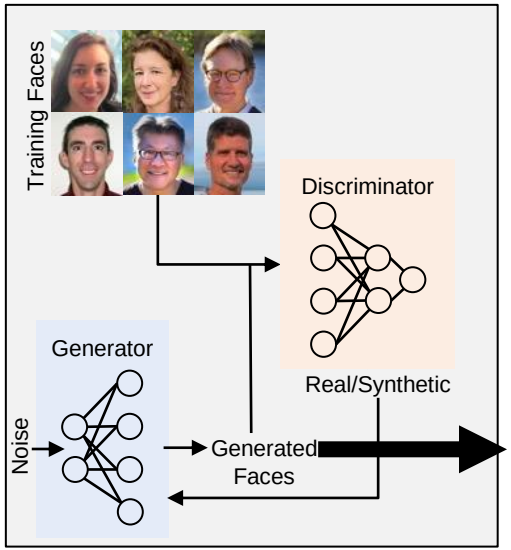
Clinical and Commercial Manufacturing

Cell line, process and formulation development

J.HAL℠ utilizes Generative Adversarial Networks (GAN) to create synthetic realistic outcomes

GAN generators output results trained to fool a trained discriminator

- Using human faces as an example:
- Lightly train a Discriminator neural network on real human faces
- A generator begins generating images that sometimes fools the discriminator, and slowly learns to better fool the discriminator
- Continue training the discriminator with real human faces, forcing the generator to improve
- Eventually the generator can fool both discriminator and humans



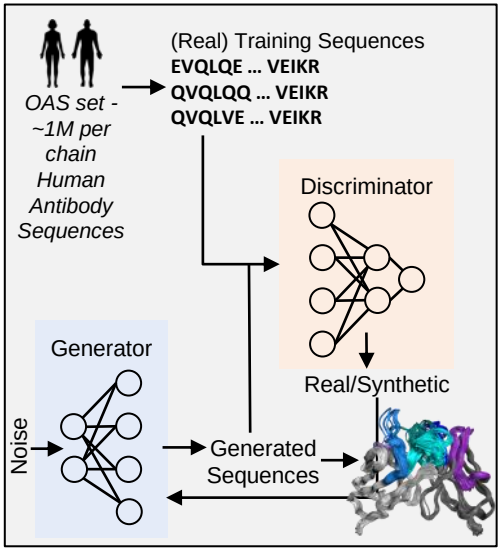
Real or Synthetic?

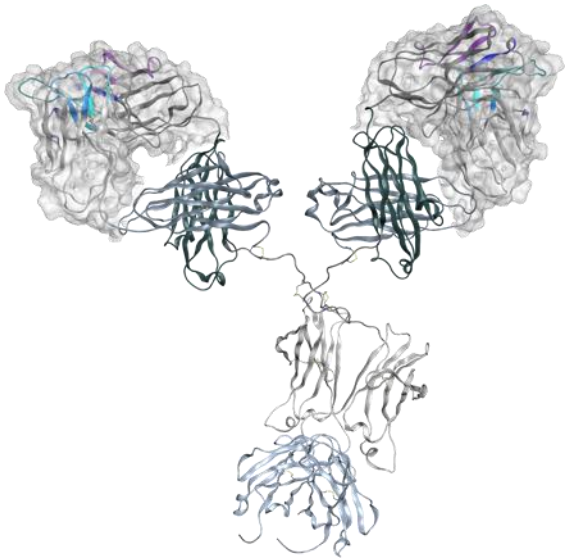
https://thispersondoesnotexist.com/

J.HAL℠ technology is a GAN application for antibody sequences

Trained on **real** mature human antibody sequences

- Large, human-derived antibody sequence training set extracted from OAS
- Abacus™ is used to clean, analyze, classify, and place sequences into structure positions
- GAN training models are germline specific
- Ability to generate synthetic humanoid large, diverse, combinatorial germline pairings for library creation
- **GAN-generated antibodies represent B-cell response – including full SHM**
- Preprint available at bioRxiv (*https://www.biorxiv.org/content/10.1101/2020.04.12.024844v2*)
  (Search bioRxiv for “Amimeur”)



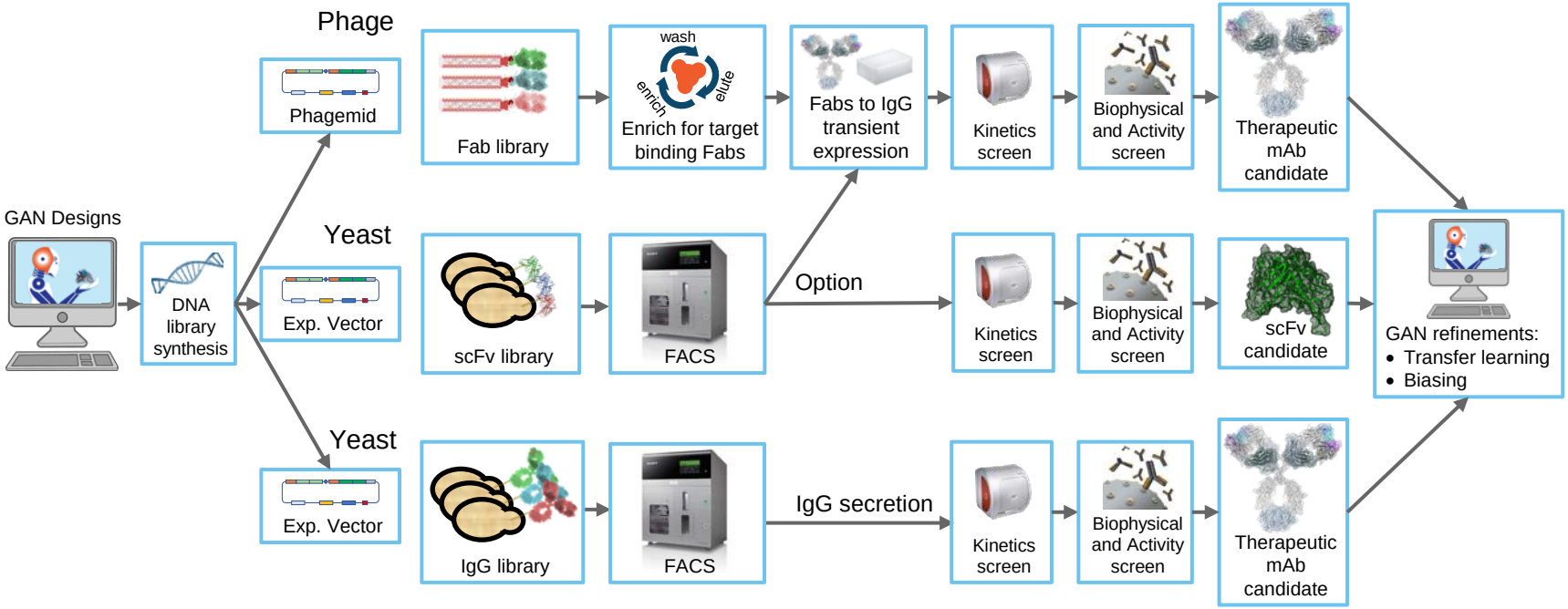


Real or Synthetic?

OAS paper: Kovaltsuk, A., Leem, J. et al (2018). J. Immunol. 201. 2502-2509

Antibody display library screening workflows

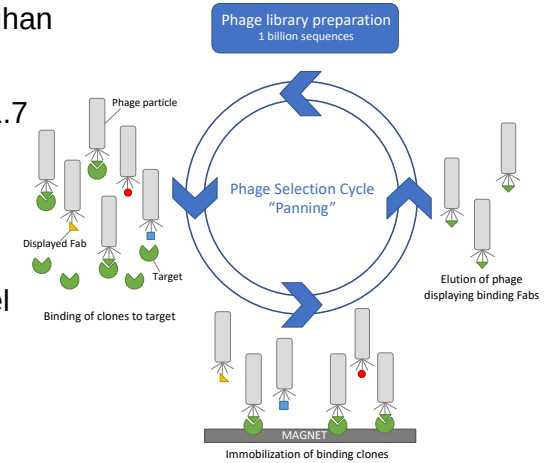
DNA sequencing is performed at most steps for panel identification

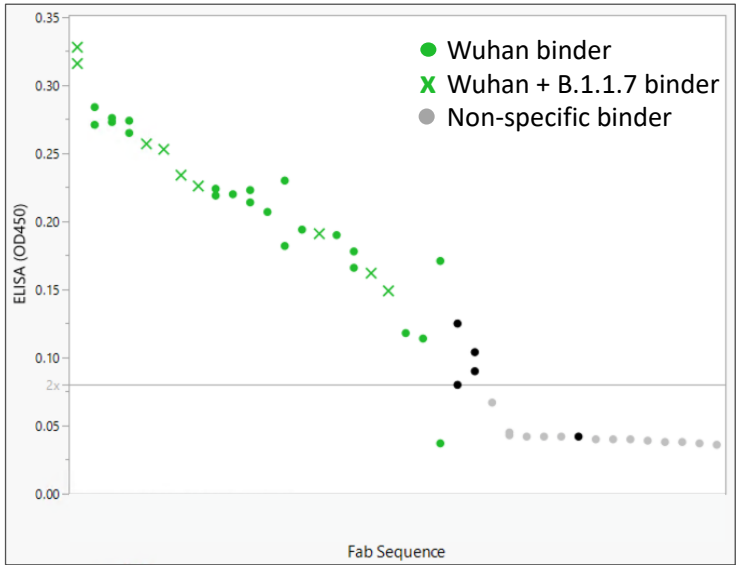


Screening the initial J.HAL library against SARS-CoV-2 RBD resulted in several panning hits

These Wuhan RBD hits cross react with UK variant

- 3 rounds of panning performed
- 176 clones sequenced – 35 were unique
- 22 were positive to SARS-CoV-2 Wuhan RBD in phage ELISA (“hits”)
- 8 hits also bound SARS-CoV-2 B.1.1.7 Spike variant
- Further hits are being extracted
- Leads being tested for binding and activity against broader antigen panel

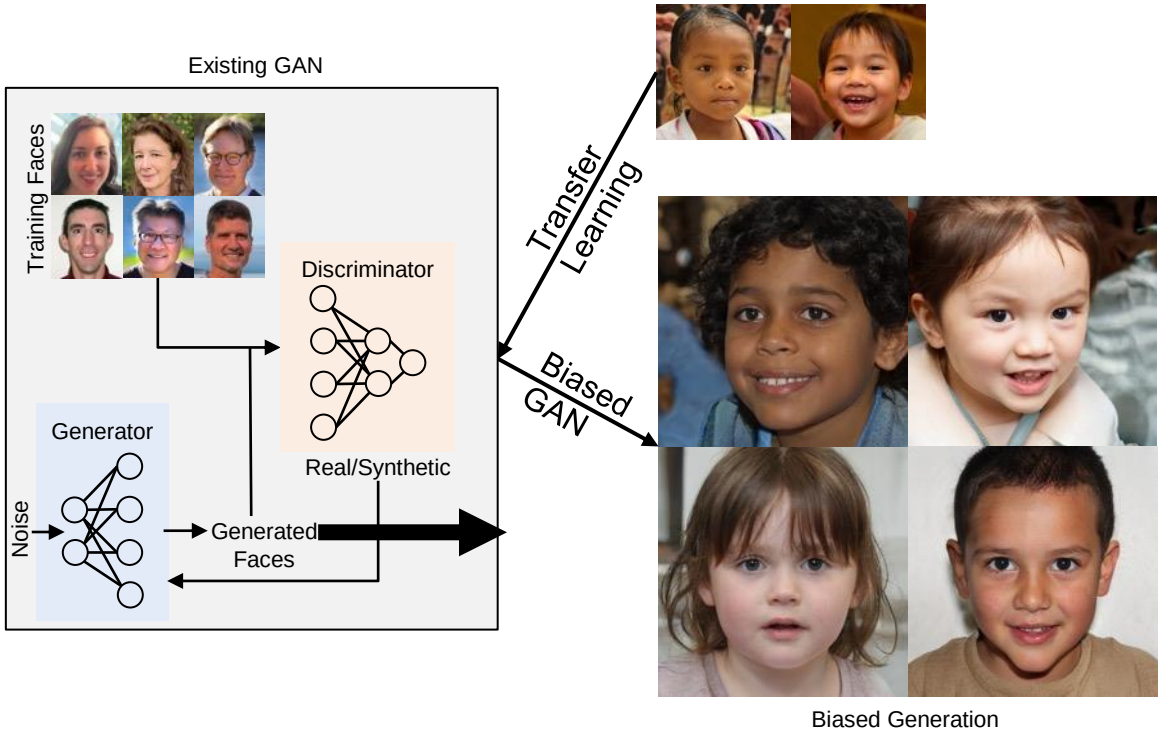




J.HAL℠ utilizes Transfer Learning to bias the output to desired properties

GAN generators may then output focused and purposeful results based on broader training sets

- Use an existing trained GAN
- Supply faces with desired property
- The GAN learns this new property
- The output of the GAN is shifted, or biased, toward the new property



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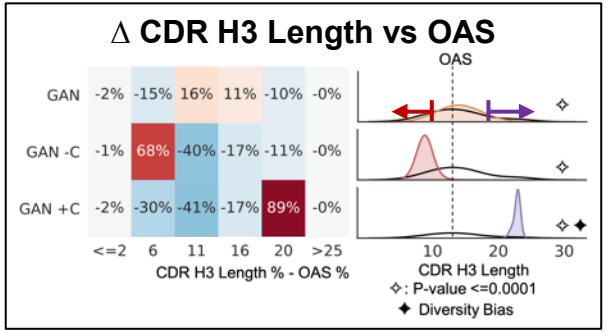
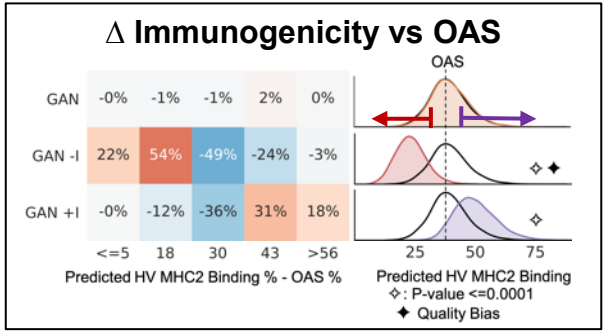
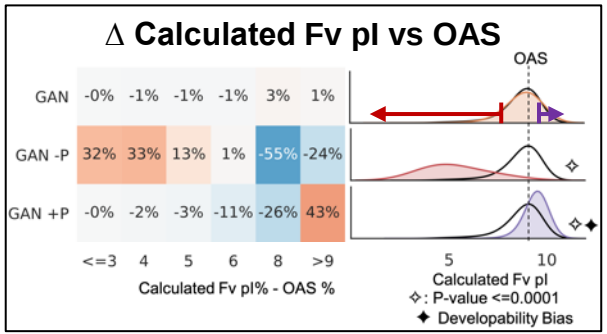
GANs control design through transfer learning

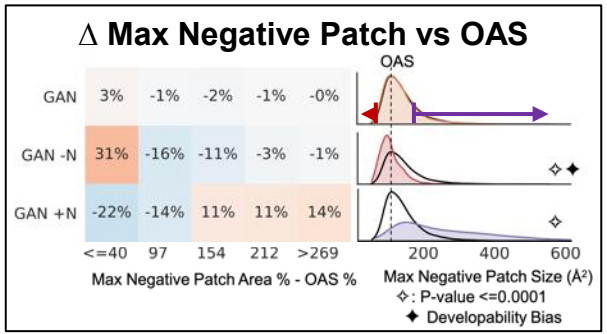
This allows us to shift the generator for desired properties

- Properties are transfer learned by further training the existing GAN with sequences which exhibit the desired property
- The mechanism of the property could be known or unknown
- A **known mechanism** could be CDR length, charge, pI, predicted immunogenicity, etc.
- An **unknown mechanism** could be temperature or pH stability, long pharmacokinetics, etc.
- J.HAL℠ under continuous development and growth







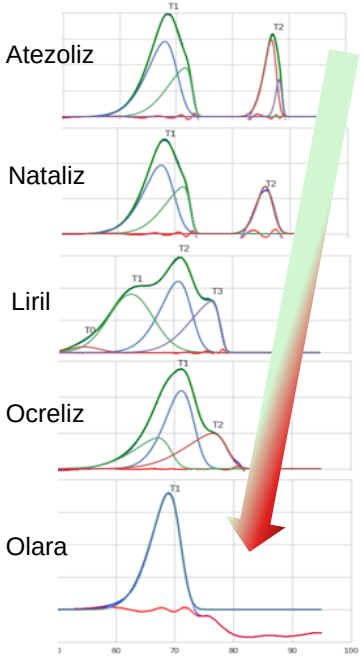


Ultra High Throughput Method Development – Christine Siska

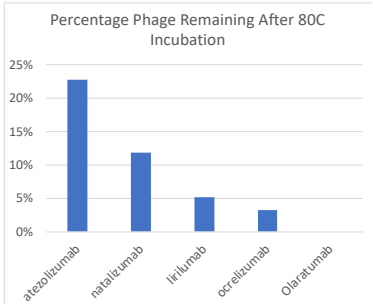
Biasing the library for favorable biophysical characteristics

- Using model proteins, determine **stress** conditions that distinguish between favorable and unfavorable molecules displayed on phage or yeast
- Develop a **capture** and purification mechanism that will bin displays based on resistance to stress conditions
- Next gen **sequencing** will be utilized to link library genotype to phenotype of each bin
- Data can be used for machine learning to guide GAN to generate more manufacturable mAbs
- Begin with heat denaturation in phage display

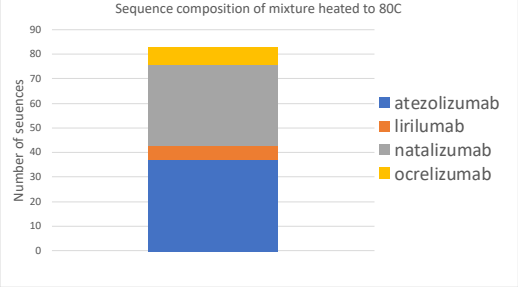
Model Proteins with decreasing thermal stability



Anti-Fab capture mechanism isolates folded Fabs after stress



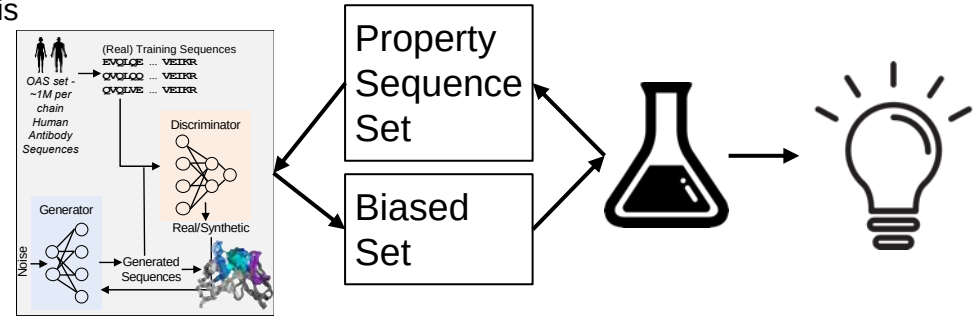
Fab sequences that are resistant to thermal denaturation are enriched in a mixture

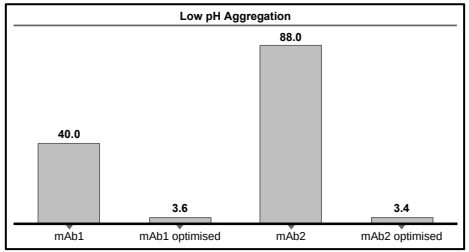


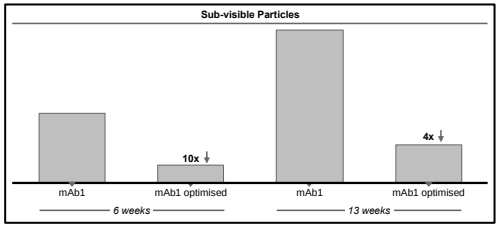
Purposeful hypothesis-driven GAN biasing is a tremendous tool for the exploration of antibody development and *in vivo* behavior

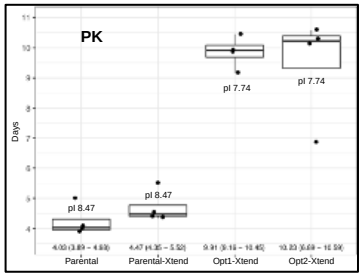
The results lend themselves to the elucidation of first principles causes

- Sequences with observed properties may be used to bias the GAN to generate a larger, diverse set of sequences which is biased toward or away from that property
- Applications could include variable domain impact on
  - Conformational stability
  - Colloidal stability
  - Host cell protein interactions
  - Blood-brain barrier passage
  - Pharmacokinetics, including target-mediated effects, intracellular trafficking, in-serum stability
  - Effector function
  - Glycosylation
  - Tissue sequestering
  - PTMs
  - …









Questions?

- How are you building sequence sets with associated data to transfer learn?
- How are you pursuing some of the more difficult properties such as PK?
- Do your current library antibodies display improved properties?
- Can we give you massive amounts of cleaned data to help your transfer learning efforts?
- Could the GAN technology be applied to other biologics formats?
- Can you use the GAN methodology to improve existing antibodies?
- Can I come work with you at Just – Evotec Biologics?
- How can we collaborate?
- Can we start a discovery project with you?

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