Twist AI Hypermutated scFv Library

Elevate your antibody development capabilities with AI-guided library design

The Twist AI Hypermutated scFv Library unleashes the power of artificial intelligence to augment the design of a synthetic antibody library with fully human antibody sequences. A neural network mimics B cell receptor recombination and hypermutation, producing antibodies with developability in mind.

KEY BENEFITS

Produce scFv antibodies optimized for development

- Proven, highly manufacturable framework
  - Built on multiple antibody backbones
  - Optimized for functionality
- Fully human antibody sequences
- 1 x 10^9 diversity

Unlock unique yet natural antibody repertoires with AI

- Design algorithm trained on millions of antibody sequences
- AI mimics natural B cell receptor development
- Capture the diversity produced by rearrangement and hypermutation

Synthetic library advantage

- Avoid immunization
- Focus on effective sequence space
- Screen multiple targets simultaneously
- Engineer and optimize antibodies with ease

APPLICATIONS

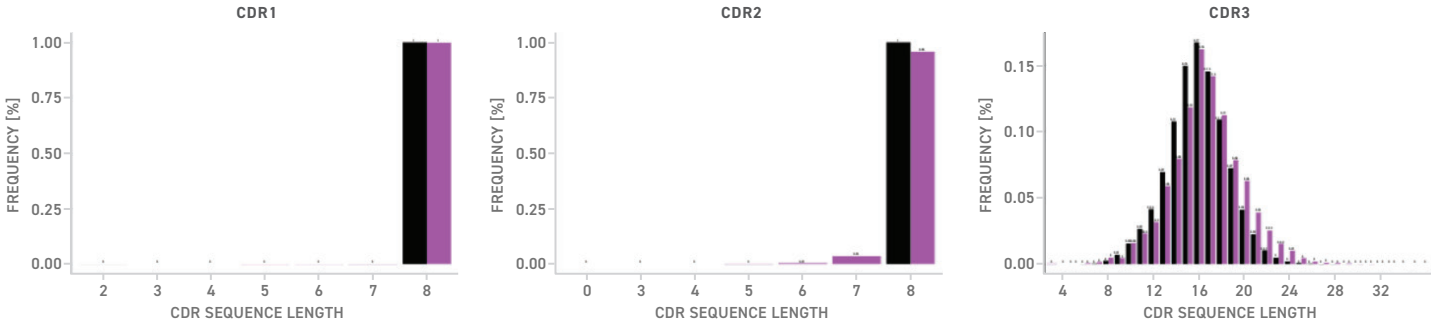
Therapeutic antibody discovery and development for any indication

Library Specifications

Designed using deep learning, the Twist AI Hypermutated scFv Library provides a versatile platform for antibody discovery. The neural network used to design the library mined millions of antibody sequences to generate diverse antibody repertoires in a process that resembles natural B cell receptor hypermutation and recombination. The library limits diversity in complementarity-determining regions 1 (CDR1) and 2 (CDR2) while maximizing that of CDR3. Four combinations of heavy chains and light chains (VH3-23/VK1-39, VH3-23/VK3-20, VH1-69/ VK1-39, and VH1-69/VK3-20) each incorporate 200 linked HCDR1-HCDR2 sequences with 100,000 HCDR3s, and 100 linked LCDR1-LCDR2 sequences with 10,000 LCDR3s. Combinatorial assembly results in a fully human scFv library with 400,000 HCDR3s, 40,000 LCDR3s, and a diversity of 1 x 10^9.

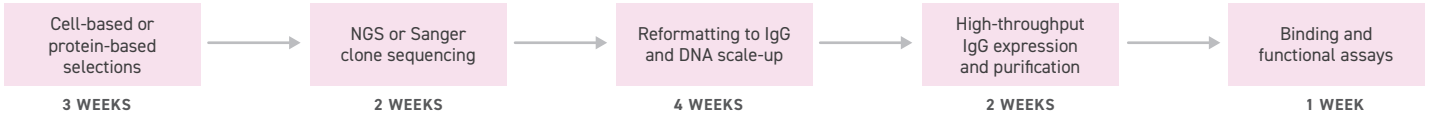
CDR Length Diversity Matches Human Repertoire Distribution

The sequences in the AI Hypermutated scFv library are computationally derived using a carefully selected subset of a full database of naturally occurring human antibodies. For CDR1, CDR2, and CDR3 of IGHV3-23, the length distributions of the selected antibody sequences (purple) closely mimic the natural human antibody repertoire (black).



Library Panning & Screening

Go from panning to functional assays in 10–12 weeks. The process starts with phage screening the diverse Twist AI Hypermutated scFv Library against target antigens and ends with reformatting candidate antibody fragments to full-length IgG.

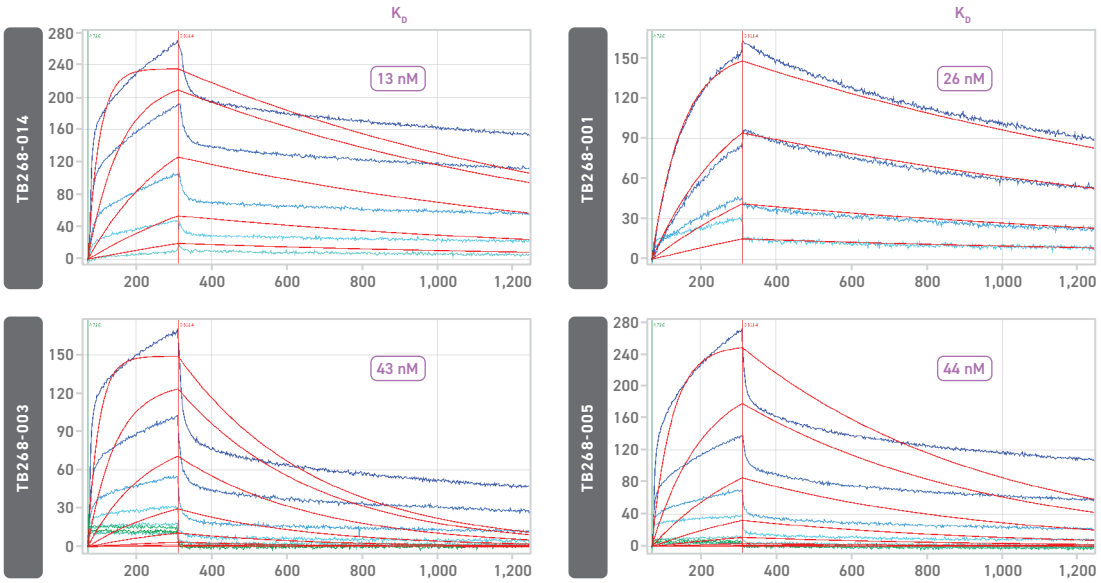


Proof of Concept Data

The Twist AI Hypermutated scFv Library was successfully panned against SARS-CoV-2 Spike Protein S1, a key protein on the surface of the coronavirus, to identify unique clones with desirable properties. Affinity was determined via surface plasmon resonance and activity was demonstrated in competition assays.

Kinetics with Directly Coupled Anti-S1 Antibodies

The AI Hypermutated scFv Library effectively uncovers SARS-CoV-2 S1 antibody leads with high binding affinities.



Potent Inhibition of VERO E6 Cells by FACS

A panel of anti-S1 antibodies from the AI Hypermutated scFv library shows inhibition of S1 binding to ACE2-expressing VERO E6 cells. A flow cytometry plot for representative clone TB268-14 illustrates a shift in the transfectant population compared to the parental population.

SAMPLE	MEDIAN RL1-H OF SINGLETS	COMPETITION FACTOR
Anti S1 control	1347	5.12
TB268-014	1907.5	3.61
TB268-008	3212	2.15
TB268-004	3378.5	2.04
TB268-012	3509	1.96
TB268-007	3571.5	1.93
TB268-002	3703	1.86
TB268-005	3790	1.82
TB268-009	3851	1.79
TB268-001	4898	1.41
TB268-010	5077	1.36
TB268-011	5225	1.32
TB268-016	6386	1.08
TB268-013	6926	1.00
TB268-006	6965	0.99
TB268-017	7395	0.93
TB268-015	7401	0.93
TB268-003	7807	0.88