Hyperimmune Library

Create and explore diverse synthetic fully human antibody libraries for therapeutic development

The Twist Hyperimmune Library synthetically mimics the human *in vivo* antibody repertoire, providing optimal diversity for antibody development against any target. This naïve library is the original design of the Twist Hyperimmune Library series, which also includes the VHH hShuffle Hyperimmune (HI) and Common Light Chain Hyperimmune libraries.

BENEFITS

- Fully human antibody sequences
- Improved diversity
  - Based on NGS sequencing of human naïve B and memory B cell receptors
  - 2.5 million human HCDR3 regions
- Proven, highly manufacturable framework
- Superior binding affinity and specificity

APPLICATIONS

- Targeted drug discovery and development of antibodies suitable for treating antibody-mediated diseases or disorders

Library Specifications

A synthetic phage antibody library was derived from public databases of naïve and memory B-cell receptor sequences from three human donors. More than two million HCDR3 sequences were gathered and constructed with Twist's DNA synthesis capabilities. Duplicates and potential development liability motifs were excluded. HCDR3 sequence diversities were combinatorially assembled and incorporated into the VH3-23 human framework to construct a highly functional antibody Fab library of ~10^{10} size. Finally, a highly diverse kappa VK1-39 light chain library was paired with the VH3-23 heavy chain library to yield a highly diverse fully human Fab phage display library. For the Common light chain hyperimmune library, trastuzumab light chain is cloned in place of this light chain library.

- Humanized VH3-23 framework
- > 2 million human CDR3 sequences
- Highly functional Fab library
- Final library diversity = 1 x 10^{10}
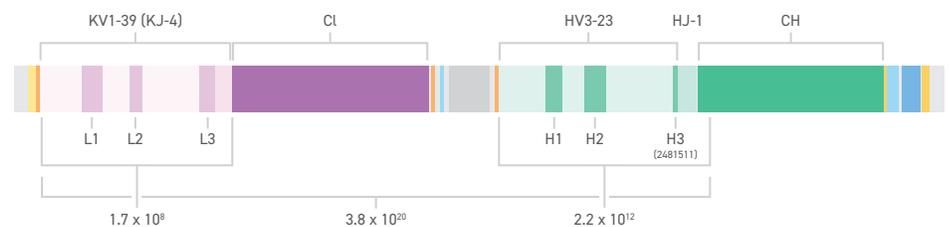
Library Diversity

Next-generation sequencing showed high diversity in CDR length distribution, particularly within the Twist optimized CDRH3 region that usually confers most binding activity and specificity to target proteins.
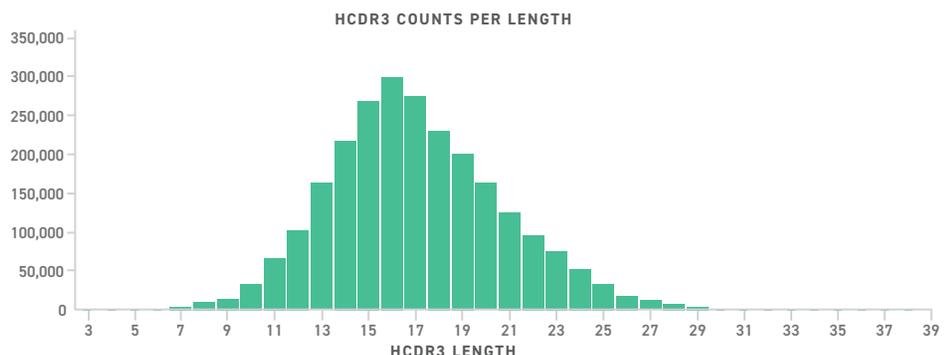
Proof of Concept Data

Twist's Hyperimmune Library was panned against the SARS-CoV-2 S1 Spike antigen. A large number of unique clones including TB182-3, -4, and -7, were identified possessing a range of binding affinities. Their activities were demonstrated in competition and functional studies.

Library Panning and Screening: Panning to Functional Assays Using Full-Length IgG

This diverse Hyperimmune Library is screened against target antigens. Functional antibodies can be obtained in 8+ weeks.

HYPERIMMUNE LIBRARY FAB PHAGE LIBRARY
(LIBRARY DIVERSITY: 1×10^{10})

HIGH AFFINITY AND POTENCY TARGET SPECIFIC IgG

Cell-based or protein-based selections	NGS or sanger clone sequencing	Reformatting to IgG and DNA scale-up	High-throughput IgG expression and purification	Binding and functional assays
2 WEEKS	1 WEEK	3 WEEKS	1 WEEK	1 WEEK
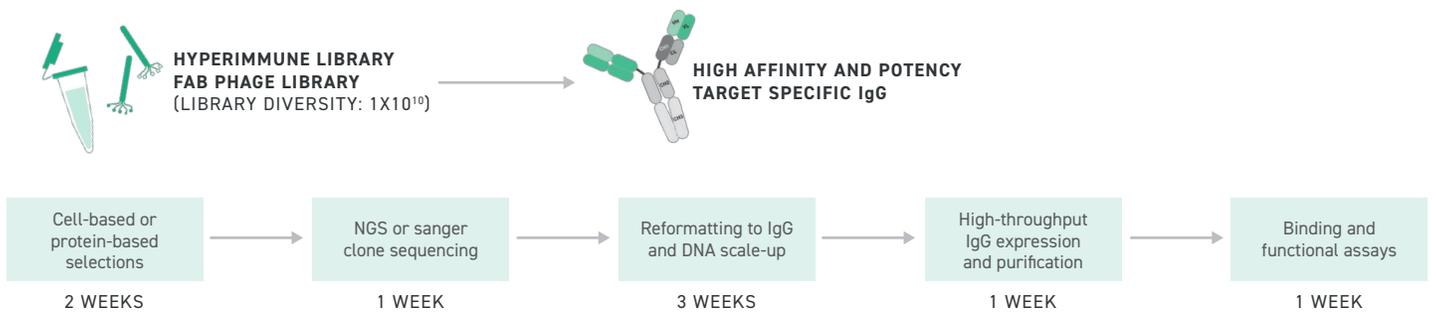
Anti-S1 mAbs Kinetics, SARS-CoV-2 (Top Leads): Direct Coupled Antibodies

Twist's Hyperimmune Library has been effective at uncovering SARS-CoV-2 S1 Protein virus leads as well as broad CD3e discovery effort.
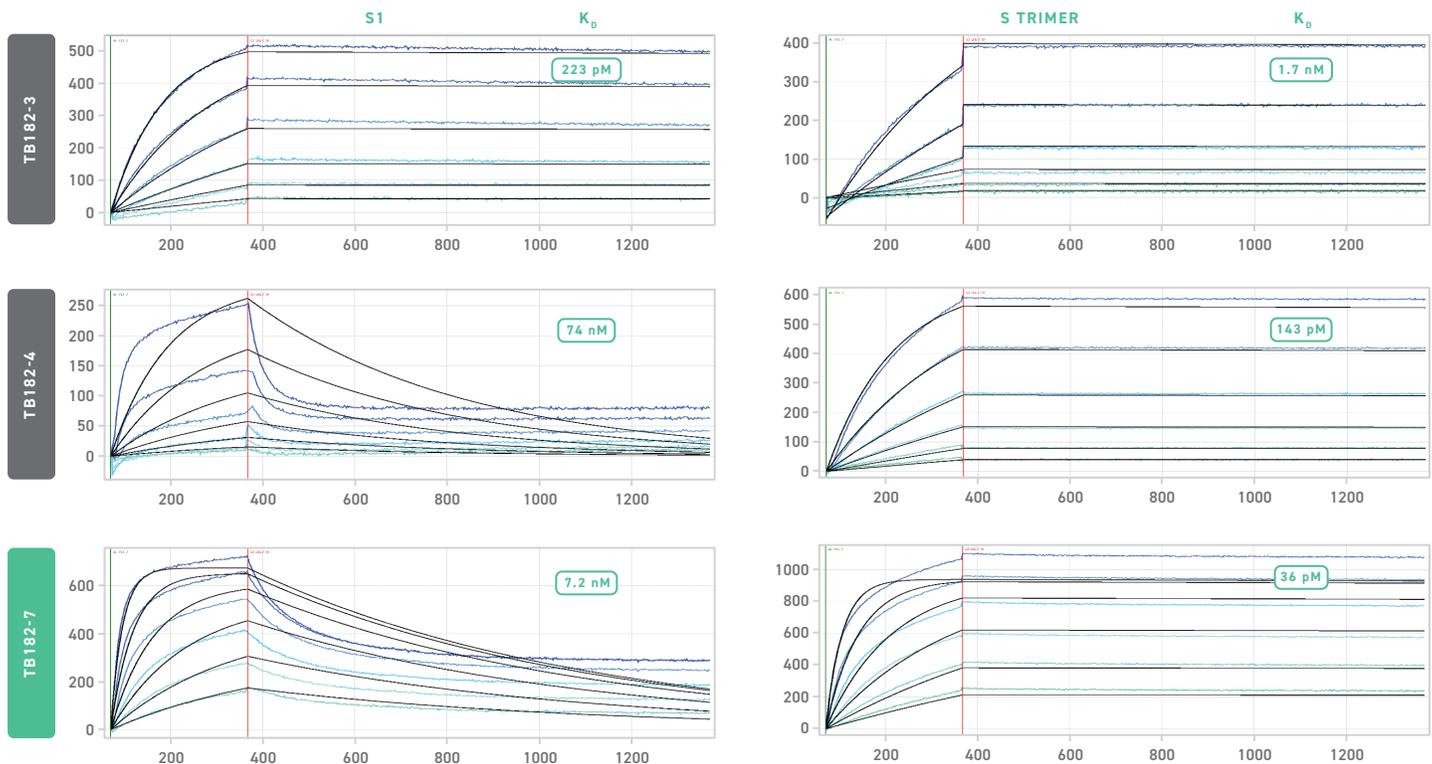
S1 RBD: VERO E6 Inhibition by FACS

TB182-3 and TB-182-4 Show Potent Inhibition of S1 Binding to ACE2-expressing VERO E6 cells.

ACRO ANTI-S1 + ABCAM CR3022
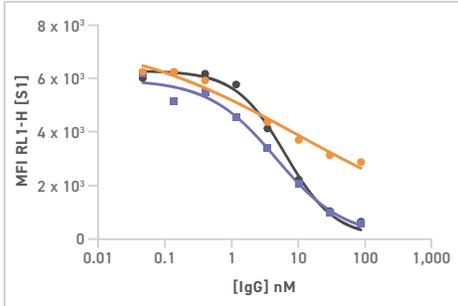
TB182-3 + TB182-4
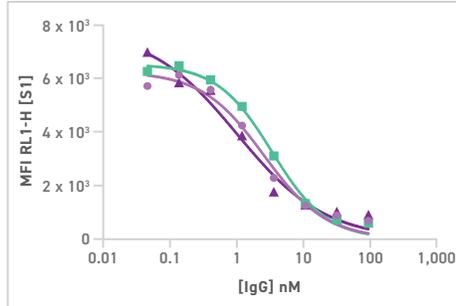
**COMPETITION ASSAY:**
TB182-3, TB182-4, Acro anti-S1, Abcam CR3022
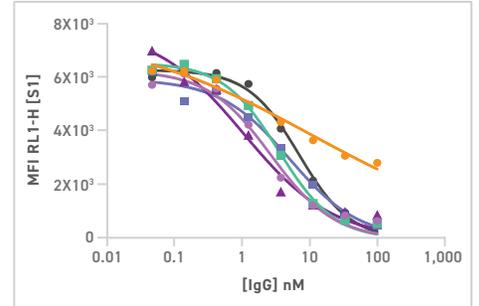
ANTIBODY	Abcam + Acro	Acro	Abcam	TB182-3 + TB182-4	TB182-3	TB182-4
EC$_{50}$ [nM]	5.036	6.918	11.11	2.627	3.417	1.043

ALL LEADS
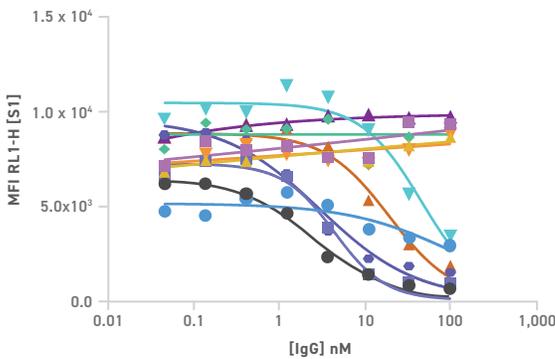
ANTIBODY	IC50 (nM)
Acro Neutralizing Ab	2.7
TB181-03	NC
TB181-04	NC
TB181-08	NC
TB181-13	NC
TB181-63	106.6
TB182-03	4.4
TB182-04	3.0
TB182-06	46.3
TB182-07	NC
TB182-13	19.5

Anti-ACE2 Antibody

SARS-CoV-2 Virus

Infection

Epithelial Cell

Anti-S1 Protein Antibody
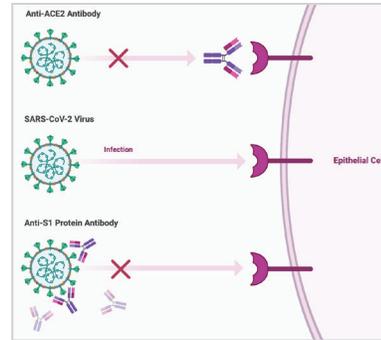
Learn more about other products in Twist's Hyperimmune Library Series:

· VHH Single-Domain Antibody Libraries
· Common Light Chain Hyperimmune Library