Twist Hyperimmune Library Series

Explore diverse synthetic fully human antibody libraries for therapeutic development

The Twist Hyperimmune Library Series synthetically mimics the human *in vivo* antibody repertoire, providing optimal diversity for antibody development against any target. This naïve library series includes the Hyperimmune Fab, Hyperimmune scFv, Hyperimmune Common Light Chain Fab, and VHH hShuffle Hyperimmune libraries.

KEY BENEFITS

Optimal Diversity

- 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

Precisely Designed

- Superior binding affinity and specificity
- Highly functional Fab or scFv library
- Humanized VH3-23 framework
- Final library diversity = 1 x 10^{10}

Synthetic Library Advantage

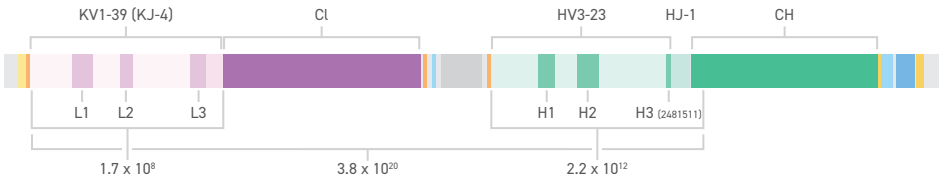
- Avoid immunization
- Focus on effective sequence space
- Screen multiple targets simultaneously
- Engineer and optimize antibodies with ease

APPLICATIONS

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

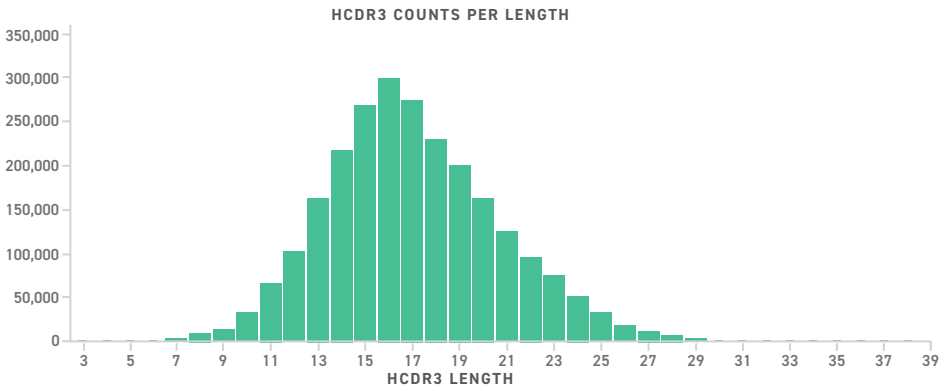
Library Specifications

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 humanized VH3-23 framework to construct the heavy chain library, which was then paired with a highly diverse kappa VK1-39 light chain library. This combination yields a highly functional antibody library of ~10^{10} size. Originally offered as a Fab library, the library is now also available in the more compact scFv format. 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 the VK1-39 light chain library.



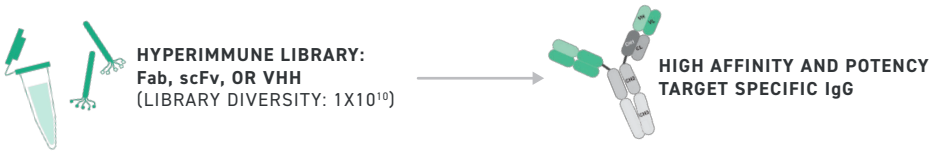
Library Diversity

Next-generation sequencing showed high diversity in CDR length distribution, particularly within the Twist optimized HCDR3 region that usually confers most binding activity and specificity to target proteins.



Library Panning & Screening

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



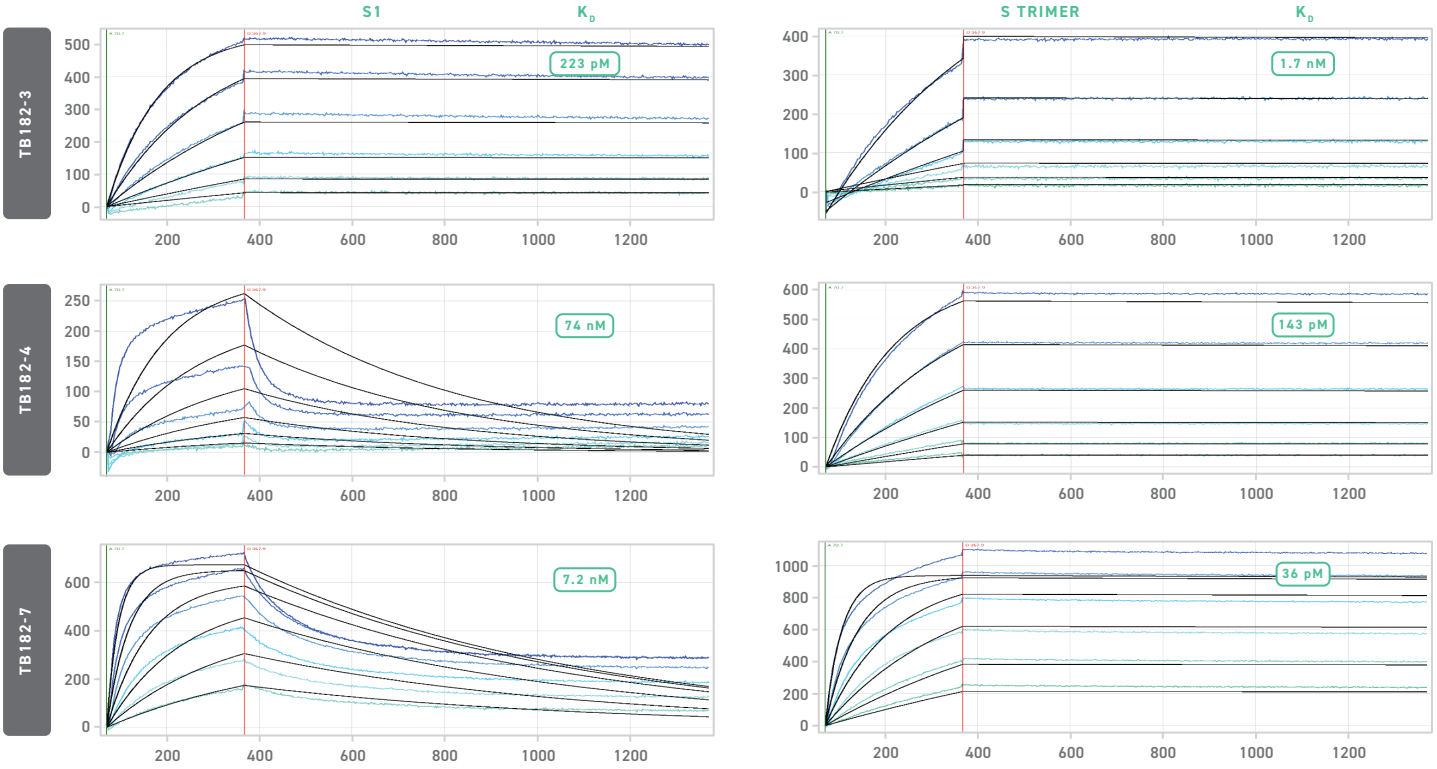
Cell-based or protein-based selections	NGS or Sanger clone sequencing	Reformatting to IgG and DNA scale-up	High-throughput IgG expression and purification	Binding and functional assays
3 WEEKS	2 WEEKS	4 WEEKS	2 WEEKS	1 WEEK

Proof of Concept Data

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

Anti-S1 mAbs Kinetics: Directly Coupled Antibodies

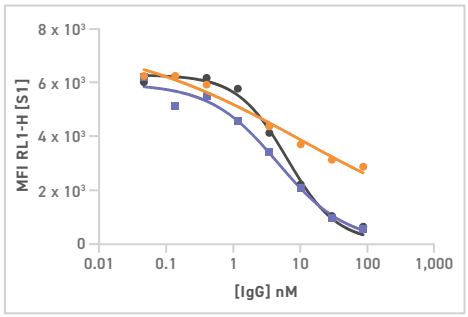
Kinetics with directly coupled anti-S1 antibodies via surface plasmon resonance identifies antibodies like TB182-3, TB182-4, and TB182-7 with high binding affinity for S1 and S trimer.



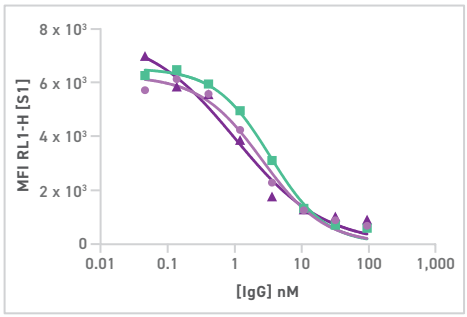
S1 RBD: VERO E6 Inhibition by FACS

TB182-3 and TB-182-4 show potent inhibition of S1 binding to ACE2-expressing VERO E6 cells.

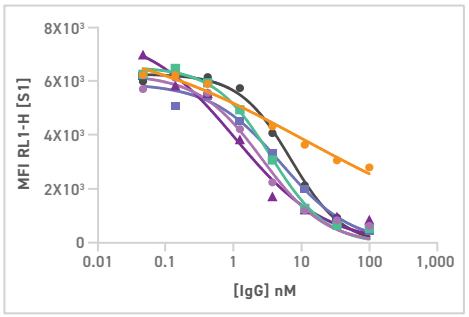
ACRO ANTI-S1 + ABCAM CR3022



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