Library of Libraries

Expedite Your Antibody Discovery with Twist's Library of Libraries

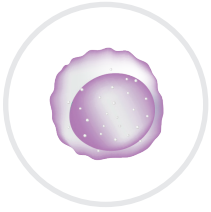
Twist Biopharma has leveraged Twist Bioscience's precise and massively parallel DNA synthesis technology to create the *Library of Libraries*, an unprecedented collection of synthetic antibody libraries that harnesses innovative structural and developability features to cover a wide range of antibody drug targets. Where discovery companies typically offer a single library, our experienced antibody discovery and engineering team has designed and constructed over 15 synthetic libraries to enable discovery of high-affinity drug-like antibodies, often without the need for affinity maturation. Each library contains up to 10^{10} antibodies in proven and highly developable human antibody frameworks across Fab, scFv, and VHH scaffolds.

The *Library of Libraries* is rapidly expanding and offers highly diverse library choices, such as our VHH Library Series and Hyperimmune Library Series, as well as libraries specifically targeting hard-to-drug target classes like GPCRs, ion channels, and carbohydrates. Twist captures and rescues full library diversities to produce robust phage display libraries, which in many cases already include qualified candidates. After biopanning, leads from these libraries can be reformatted as monoclonal antibodies (such as IgG antibodies), combined into multispecific antibodies, or incorporated into chimeric antigen receptors (CARs) for CAR-T cell therapy. The libraries can be licensed individually, together, or as a fully inclusive set. The *Library of Libraries* also forms the basis for Twist's antibody discovery services and partnerships.

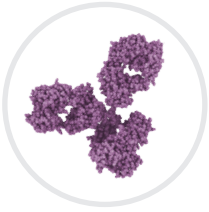
With a large set of libraries to choose from, we have the perfect solution to meet your ever-evolving discovery needs.

GPCR Library Series

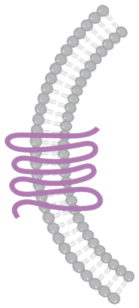
VHH Library Series



Hyperimmune Library Series



scFv Library Series



GPCR Library Series

Twist offers distinct GPCR libraries based on known GPCR binding motifs and GPCR antibodies. This library series enables discovery of novel drug-like antibodies against this hard-to-drug target class.

GPCR 2.0 scFv ($1x10^{10}$ diversity)
GPCR 2.0 scFv is a fully human antibody library that leverages over 150,000 GPCR-binding motifs to direct antibodies to GPCR targets. This high variation library incorporates rules of the human repertoire.

GPCR 3.0 scFv ($1x10^{10}$ diversity)
The GPCR 3.0 scFv library is modeled on 61 GPCR antibody sequences that target 22 different GPCR proteins. This library incorporates 2 heavy chain frameworks and 2 light chain frameworks.

VHH hShuffle GPCR ($1x10^{10}$ diversity)
The VHH hShuffle GPCR library shuffles GPCR-binding motifs in CDR3 from the GPCR 2.0 scFv library with sequences from a naïve llama repertoire (CDR1 and CDR2 regions) in the context of a partially humanized VHH framework.

VHH Library Series

This VHH libary series combines synthetic and naïve approaches to maximize diversity for antibody discovery. These single chain domain libraries are ideal for the creation of bispecific and multispecific antibodies.

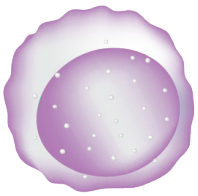
VHH Ratio ($1x10^{10}$ diversity)
The VHH Ratio library models the natural VHH repertoire with 2,391 synthetic CDR sequences analyzed for position-specific variation. The library introduces controlled CDR diversity to produce amino acid ratios randomized at different positions.

VHH Shuffle ($3.2x10^{9}$ diversity)
The VHH Shuffle library shuffles thousands of natural, individually sequenced llama CDR sequences within the context of a llama consensus framework.

VHH hShuffle ($3.2x10^{9}$ diversity)
The VHH hShuffle library shuffles thousands of natural llama CDR sequences within the context of a partially humanized VHH framework that incorporates 1,600 unique CDR3s. This framework confers lowered immunogenicity for therapeutic development.

VHH hShuffle Hyperimmune ($1x10^{10}$ diversity)
VHH hShuffle Hyperimmune is a hybrid library that shuffles llama CDR1 and CDR2 sequences with human CDR3 sequences. Building on the VHH hShuffle library, this library increases CDR3 diversity with over 2.5 million unique human CDR3s.

VHH hShuffle GPCR ($1x10^{10}$ diversity)
See GPCR Library Series.



Hyperimmune Library Series

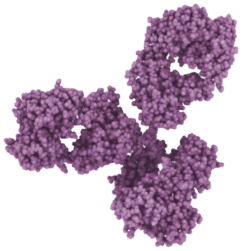
This hyperimmune library series features libraries created using nearly 2.5 million HCDR3s from human naïve and memory B-cell receptor sequences from human donors. These libraries simulate the human antibody repertoire, providing optimal diversity for antibody discovery against any target.

Hyperimmune Fab ($1x10^{10}$ diversity)
The Hyperimmune Fab library offers diversity in both heavy and light chains.

Hyperimmune scFv ($1x10^{10}$ diversity)
The Hyperimmune scFv library offers single-chain binders that are smaller than their Fab counterparts with the same diversity.

Hyperimmune Common Light Chain Fab ($1x10^{10}$ diversity)
The Hyperimmune Common Light Fab library combines the heavy chain diversity from the Hyperimmune Fab library with a fixed trastuzumab light chain, making it useful for generating bispecifics.

VHH hShuffle Hyperimmune ($1x10^{10}$ diversity)
See VHH Library Series.



scFv Library Series

Twist provides cutting-edge scFv libraries for general and target-class specific discovery. Built on structural information, these unique libraries mimic B cell receptor hypermutation, offer ultralong HCDR3s, and more.

AI Hypermutated scFv ($1x10^{9}$ diversity)
The AI Hypermutated scFv Library unleashes the power of artificial intelligence to augment the design of a synthetic antibody library. A neural network mimics B cell receptor recombination and hypermutation and produces antibodies with developability in mind.

Ancestral scFv ($1x10^{9}$ diversity)
The Ancestral scFv Library is a synthetic antibody library developed using trends observed in a curated, yet broad, set of 22,426 therapeutic and diagnostic antibodies. By capturing the diversity observed in examined antibody sequences and mimicking the human antibody repertoire, this library offers higher quality sequences than naïve libraries to help you identify better hits against any target.

Carbohydrate scFv ($2x10^{9}$ diversity)
To address the difficult-to-drug nature of carbohydrates, this library shuffles unique CDRs from 130 existing carbohydrate antibodies across the CDR1 and CDR2 regions. The CDR3 regions derive their diversity from 52 structures of antibodies in complex with carbohydrate antigens and are biased towards incorporating residues that make up the carbohydrate-antigen interface.

Ion Channel scFv ($1x10^{9}$ diversity)
The Ion Channel scFv library integrates loop sequences from natural peptide toxins that target ion channels. This allows the library to target these classically difficult-to-drug proteins without cytotoxicity concerns. This library is available in two formats: one with paired cysteines (Cys+ Library) and one without paired cysteines (Cys- Library).

Minotaur scFv ($>10^{9}$ diversity)
This scFv library inserts ultralong bovine HCDR3s into a human antibody framework. The unique bovine HCDR3s provide access to hard-to-target epitopes, such as those found in pores and channels. This library includes two sublibraries: Sublibrary 1 with cysteines in HCDR3 only and Sublibrary 2 with cysteines in HCDR3 and other regions (HCDR2 and framework).

Structural scFv ($4x10^{10}$ diversity)
This general-use scFv library incorporates CDR sequences from 3,700 antibodies with known crystal structures. By starting with structurally resolved antibodies, this library generates leads that are “well behaved” and therefore have more potential to be developable as therapeutics.

LIBRARY	FORMAT	FRAMEWORKS	TYPE
GPCR 2.0 scFv	scFv	VH1-69, VH3-30, VK1-39, VL1-51, VL2-14, VK3-15	Target-class specific
GPCR 3.0 scFv	scFv	VH3-23, VH1-69, VL2-28, VL1-51	Target-class specific
VHH hShuffle GPCR	VHH	Humanized DP-47-like VHH	Naïve, general discovery
VHH Ratio	VHH	Consensus llama	Naïve, general discovery
VHH Shuffle	VHH	Consensus llama	Naïve, general discovery
VHH hShuffle	VHH	Humanized DP-47-like VHH	Naïve, general discovery
VHH hShuffle Hyperimmune	VHH	Humanized DP-47-like VHH	Naïve, general discovery
Hyperimmune Fab	Fab	VH3-23/VK1-39	Naïve, general discovery
Hyperimmune scFv	scFv	VH3-23/VK1-39	Naïve, general discovery
Hyperimmune Common Light Chain Fab	Fab	VH3-23, fixed trastuzumab light chain	Naïve, general discovery
AI Hypermutated scFv	scFv	VH3-23/VK1-39, VH3-23/VK3-20, VH1-69/VK1-39, VH1-69/VK3-20	Naïve, general discovery
Ancestral scFv	scFv	VH3-23/VK1-39	Naïve, general discovery
Carbohydrate scFv	scFv	VH3-23/VK4-1	Target-class specific
Ion Channel scFv	scFv	VH1-69, VH3-30, VK1-39, VL1-51, VL2-14, VK3-15	Target-class specific
Minotaur scFv	scFv	VH3-23/VK1-39	Naïve, general discovery
Structural scFv	scFv	VH3-23/VK1-39	Naïve, general discovery

Note: A final quote with detailed costs will be generated for specific projects following partnership discussions.

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Please contact us directly for more information about customizing your campaign at **biopharma@twistbioscience.com**