# Twist Structural scFv Library

Leverage insights from crystallized antibody structures
in your drug discovery efforts

The Twist Structural scFv Library harnesses sequences from every antibody crystal structure in a worldwide protein structure database. By building on the knowledge of antibody structure-function relationships, this synthetic antibody library provides a platform for generating a wide range of antibodies for therapeutic indications.

## KEY BENEFITS

**Produce optimized scFv antibodies**
- Proven, highly manufacturable framework
  - Manufacturing liabilities removed
  - Low immunogenicity
- Fully human antibody sequences
- $4 \times 10^{10}$ diversity

**Harness crystallized antibody structures**
- Binding sites informed by 3,700 crystal structures
- Structural information confers:
  - Superior binding affinity
  - Enhanced specificity
  - Increased structural diversity

**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

The Twist Structural scFv Library is a synthetic antibody library that incorporates the CDR sequences from 3,700 antibodies with known crystal structures in a protein structure database.



To improve manufacturability, liabilities such as unpaired C- and N-glycosylation, deamination, and hydrolysis sites are eliminated. The heavy chain (VH) library shuffles 148 unique CDR1s, 151 unique CDR2s, and 564 unique CDR3s into the human IGHV3-23 framework. The light chain (VL) library shuffles 134 unique CDR1s, 158 unique CDR2s, and 278 unique CDR3s into the human IGKV1-39 framework. When combined, the VH and VL libraries yield a fully human scFv library with a diversity of $4 \times 10^{10}$.
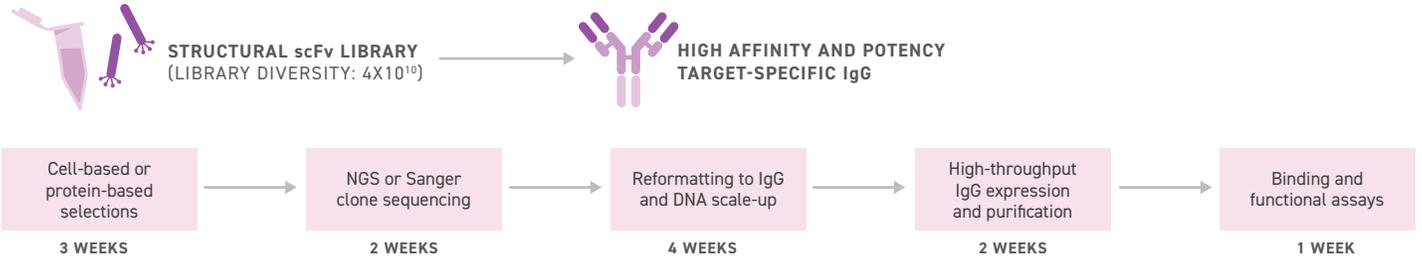
**HEAVY CHAIN DESIGN (IGHV3-23 framework):**



| | CDR1 | CDR2 | CDR3 | |
| N | 148 unique CDR1s | 151 unique CDR2s | 564 unique CDR3s | C |

**LIGHT CHAIN DESIGN (IGHV1-39 framework):**



| | CDR1 | CDR2 | CDR3 | |
| N | 134 unique CDR1s | 158 unique CDR2s | 278 unique CDR3s | C |

# Library Panning & Screening

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

**STRUCTURAL scFv LIBRARY**
(LIBRARY DIVERSITY: 4X10$^{10}$)

**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 |
|---|---|---|---|---|
| **3 WEEKS** | **2 WEEKS** | **4 WEEKS** | **2 WEEKS** | **1 WEEK** |

# Proof of Concept Data

The Twist Structural scFv Library was successfully panned against CD3, an important cell surface target in immunology, to identify unique clones, such as TB138-6, with desirable properties.

**Cross-reactive with cynomolgus CD3**
Titration ELISA shows the cross-reactivity of TB138-6 with human and cynomolgus monkey CD3.
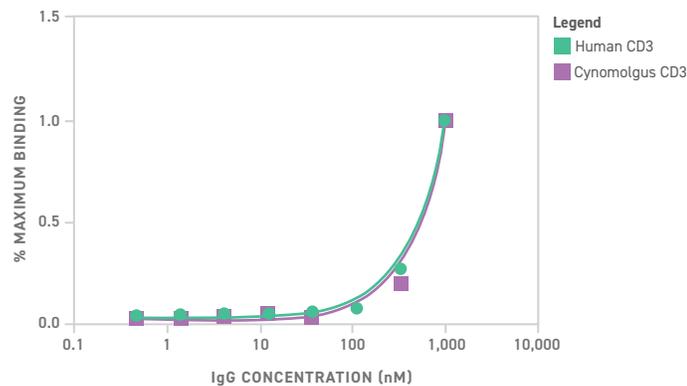
**Binds cell surface CD3 on human CD8+ T-cells**
Flow titration demonstrates that TB138-6 binds CD3+ cells (CD8+ T-cell) and not CD3- cells (CHO-GLP1R).



Legend
- Human CD3
- Cynomolgus CD3



Legend
- CD8+ T-cell
- CHO-GLP1R