

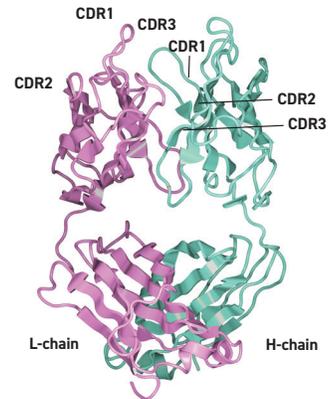
Twist Antibody Optimization Platform

Quickly generate high-diversity, high-quality molecules inspired by human and non-human repertoires

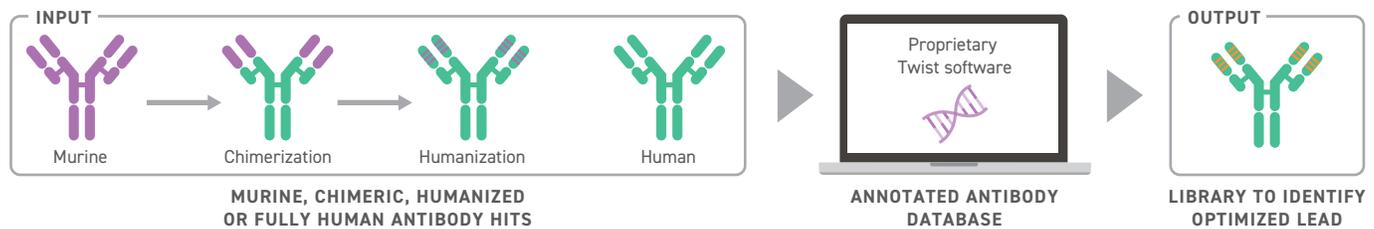
Why TAO?

Using a wide sequence space of tens of millions of natural human antibody sequences, Twist creates an optimization library that precisely matches the human repertoire.

- Liabilities are removed, e.g. isomerization, cleavage, deamidation, glycosylation sites, liability dipeptide motifs
- Rational sampling from desired sequence space
- Workflows available for non-human species (e.g. felis or canis)
- Accurate representation: motif sequences explicitly encoded in oligos
- With our silicon-based DNA writing platform, have confidence that accurate, clone-perfect sequences are made when producing antibodies for screening

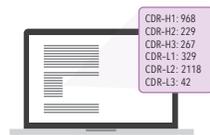


How it works: canonical humanization workflow shown

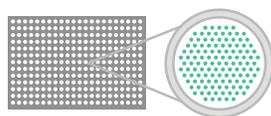


4 MONTHS

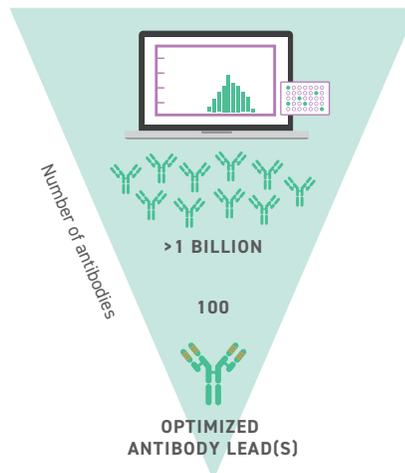
STEP 1
In Silico sequence assessment



STEP 2
Order oligo pool sequences for library generation

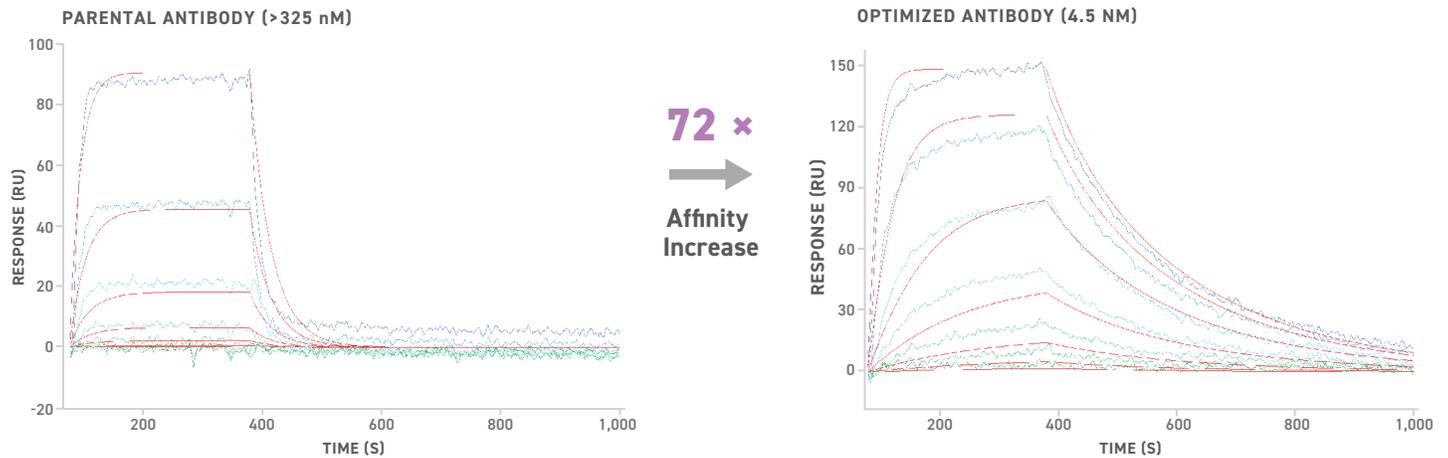


STEP 3
Twist Biopharma creates library



- 1 Construct phage library
- 2 Cell- or bead-based selection
- 3 NGS and Sanger clone sequencing
- 4 Reformating to IgG, DNA scale-up, and expression
- 5 High-throughput antibody purification
- 6 High-throughput analytical characterization and developability

Using Twist Antibody Optimization, PD-1 Inhibitors Have Higher Affinity and Potency



Multiple Optimized Leads Block the PD-1/PD-L1 Interaction

CLONE	SPR KD (nM)	IC50 (nM)	BMAX (RU)
PD1_TA01	4.5	0.434	693
PD1_TA015	7.3	0.562	634
PD1_TA091	9.2	0.868	664
PD1_TA02	9.8	0.848	661
PD1_TA07	10.5	0.896	642
PD1_TA075	11.2	0.418	614
Nivolumab	14.5	1.345	628
PD1_TA060	16.5	1.614	776
PD1_TA08	78.1	1.968	436
PD1_TA058	96.7	3,384	446
PD1_TA080	125	2.129	450
Parental	325	4.122	449

- After Twist Antibody Optimization:
 - Binding affinity went up 72×
 - Function increased by 9.5×
 - **Six antibodies identified with higher binding affinity and function than nivolumab**

Addition of anti-PD1 antibody blocks the PD-1/PD-L1 interaction, releases inhibitory signal and results in TCR activation and NFAT-RE-mediated luminescence (RU).

