TWIST BIOSCIENCE

#WEMAKEDNA
TWISTBIOSCIENCE.COM

Variant Libraries

COMBINATORIAL | SOLD | SITE SATURATION

UNCOVER MORE WITH TWIST

DRUG DISCOVERY.
ANTIBODY AND ENZYME ENGINEERING.
PROTEIN ENGINEERING AND STABILIZATION.

DIFFERENT APPLICATIONS, EACH WITH THE SAME STARTING POINT. VARIANT LIBRARIES.

Twist's high-quality libraries make it possible for you to explore a diverse range of potential variants and identify every hit, instead of just a few. Our years of molecular biology expertise, and dedication to what we create, ensures that you uncover more of what you want, and only what you want.

To create the libraries you want, we've used Twist's proprietary silicon-based synthesis platform, leveraging massively paralleled oligonucleotide synthesis to print each variant base-by-base enabling precise synthesis of desired variants at user-defined ratios without restriction sites and unwanted motifs that can impact downstream processes. This has allowed us to develop diverse, high-quality libraries that are just what you need to streamline your screening process, identify hits faster, and achieve higher success rates.

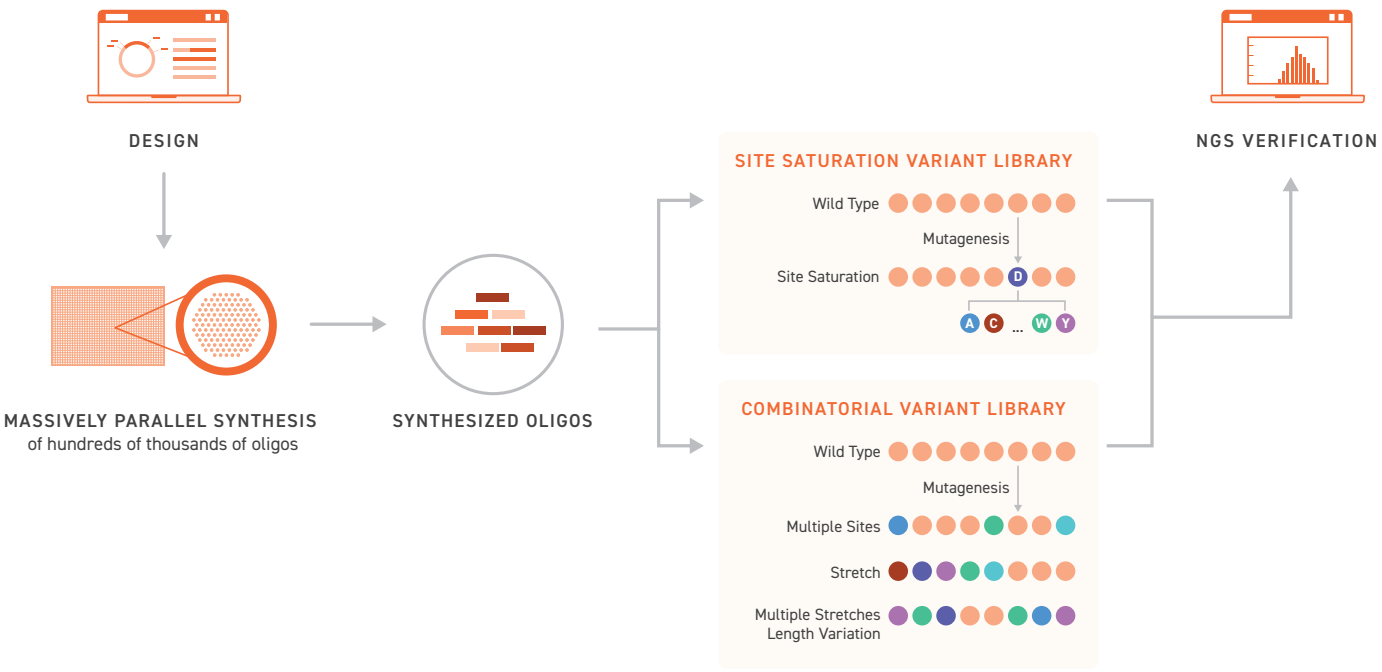
All of the NGS-verified quality control is done in-house, ensuring that both the input and output are high-quality and clean, and that all desired variants are present.

TECHNOLOGY TO DISCOVER MORE

Twist's proprietary oligo synthesis technology offers a unique approach to library creation. The silicon-based synthesis platform generates high-quality oligo pools, which are used to build fully-customized, user-defined variant libraries on a single chip.

Our molecular biology experts use this novel technology to develop Combinatorial Variant and Site Saturation Variant Libraries that outperform those developed with less-precise methods.

With Twist libraries, every variant is designed in-silico and screened prior to synthesis, eliminating unwanted sequence bias, premature stop codons, and undesirable motifs.



"The Library we've asked for was very complex. Based on our analysis, **the library we received was excellent. What we've designed is what we've obtained."**

DR. SANDRINE MOUTEL
MANAGER OF TECHNOLOGY, INSTITUT CURIE
Recombinant Antibody Platform and TAb-IP Platform

LIBRARIES THAT YIELD VIABLE VARIANTS

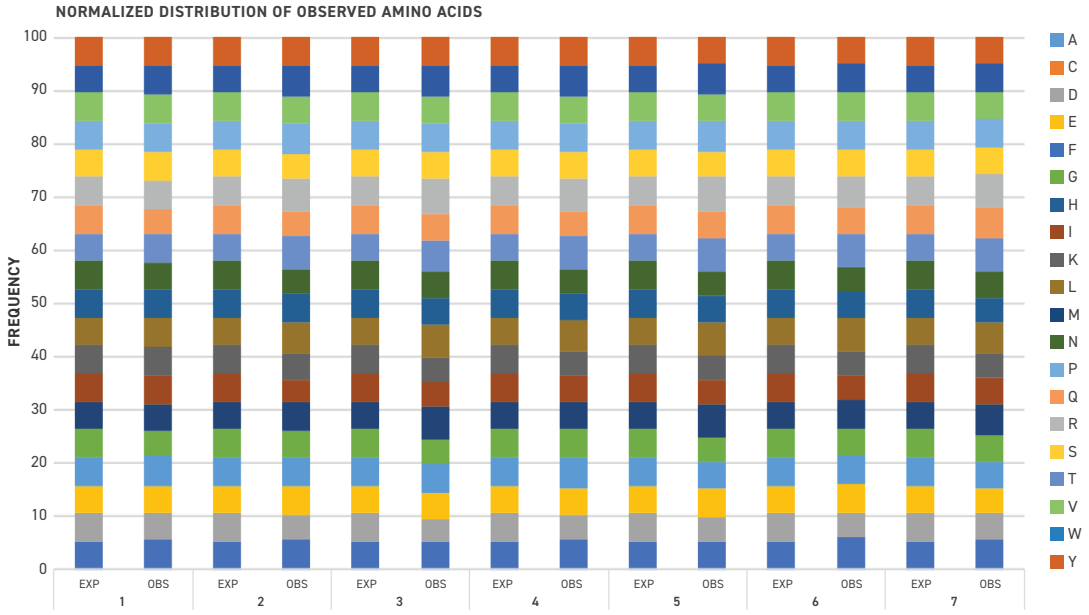
Combinatorial Variant Libraries

Our Combinatorial Variant Libraries are designed to create gene variants that express proteins with better stability, binding affinity, and enzymatic activity. Whether it be antibody humanization libraries or controlled complexity discovery libraries, our variant cassettes can be seamlessly incorporated into single or multiple scaffolds to yield >10^{10} variants.

	DEGENERATE (NNK/NNS)	TRIM/TRIMER CONTROLLED	TWIST COMBINATORIAL VARIANT LIBRARIES
Eliminates sequence bias	No	No	Yes
Number of codons available	32	20	All 64
Prevents undesirable motifs	No	No	Yes
Allows codon optimization	No	No	Yes
Avoids stop codons	No	Yes	Yes

High-Diversity Libraries

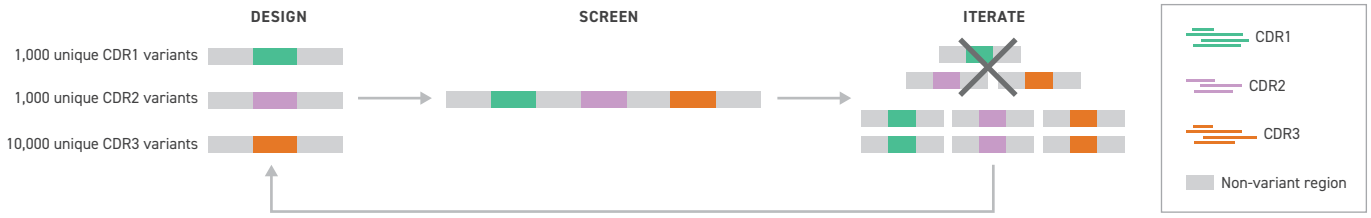
Optimize your antibody and protein-screening experiments using more extensive high-diversity libraries that eliminate sequence bias and undesirable motifs. Study what you want without wasting time on multiple iterations and screening rounds—spend that time exploring a much larger sequence space that contains more hits in areas of interest. And you can rest assured that these libraries are absent of premature polypeptide sequence truncation, as Twist libraries do not contain stop codons.



Example Application: CDR-H3 is largely responsible for the diversity among antibody structures and is critical for antigen binding. High-diversity libraries remove bias often seen with other technologies such as NNK and Trimers. The diversity of this cassette enables a more comprehensive interrogation of gene variant space.

User-Defined CDR Libraries

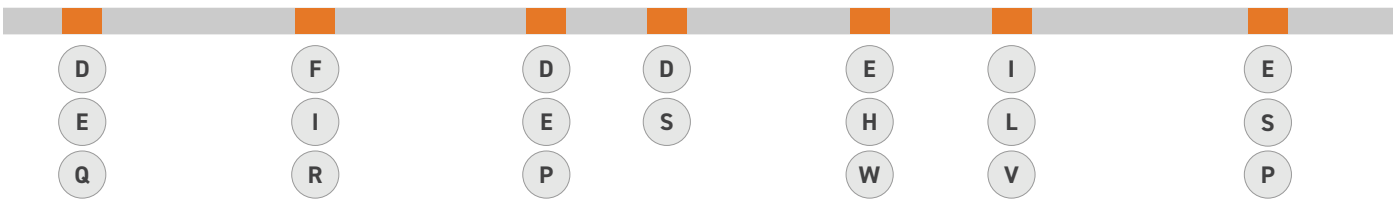
Our Precision Variant Library allows you to choose what unique CDR (complimentary defining regions) sequences you want to be incorporated into the choice of framework(s). Each CDR can be codon-optimized to avoid the creation of unwanted restriction sites. Machine learning has become an integral part of scientific research and has been used as a tool to analyze antibody libraries and identify unique CDR combinations that would yield, for example, higher affinity and specificity. Coupled with Twist's silicon-based synthesis platform, explicit library combinations generated from the analysis can be synthesized and seamlessly incorporated into a fully synthetic library to refine the exploration of the variant space. Since every library is NGS QC'd, negative data can be used to identify mutations that do not yield improved functions, and those can be removed in the next iteration of library design.



SOLD (Spread-Out Low Diversity) Libraries

Twist's SOLD Libraries are a time- and money-saving tool for mapping protein sequences, allowing you to explore the complex relationship between a protein and its environment. It enables targeted exploration of the sequence space encoded by mutating multiple positions simultaneously scattered across the parental sequence to generate a diverse library of proteins.

These high-fidelity libraries are a fast and cost-effective alternative to NNK, trinucleotide mutagenesis (TRIM) technology, error prone PCR, random mutagenesis and DNA Shuffling. Unlike the Combinatorial Variant Libraries (CVLs), SOLD Libraries offer precise incorporation of diversity across the parental sequence without the restriction of variant domains. In addition, SOLD Libraries allow you to explore multiple mutations simultaneously, unlike Site Variant Libraries (SVLs).

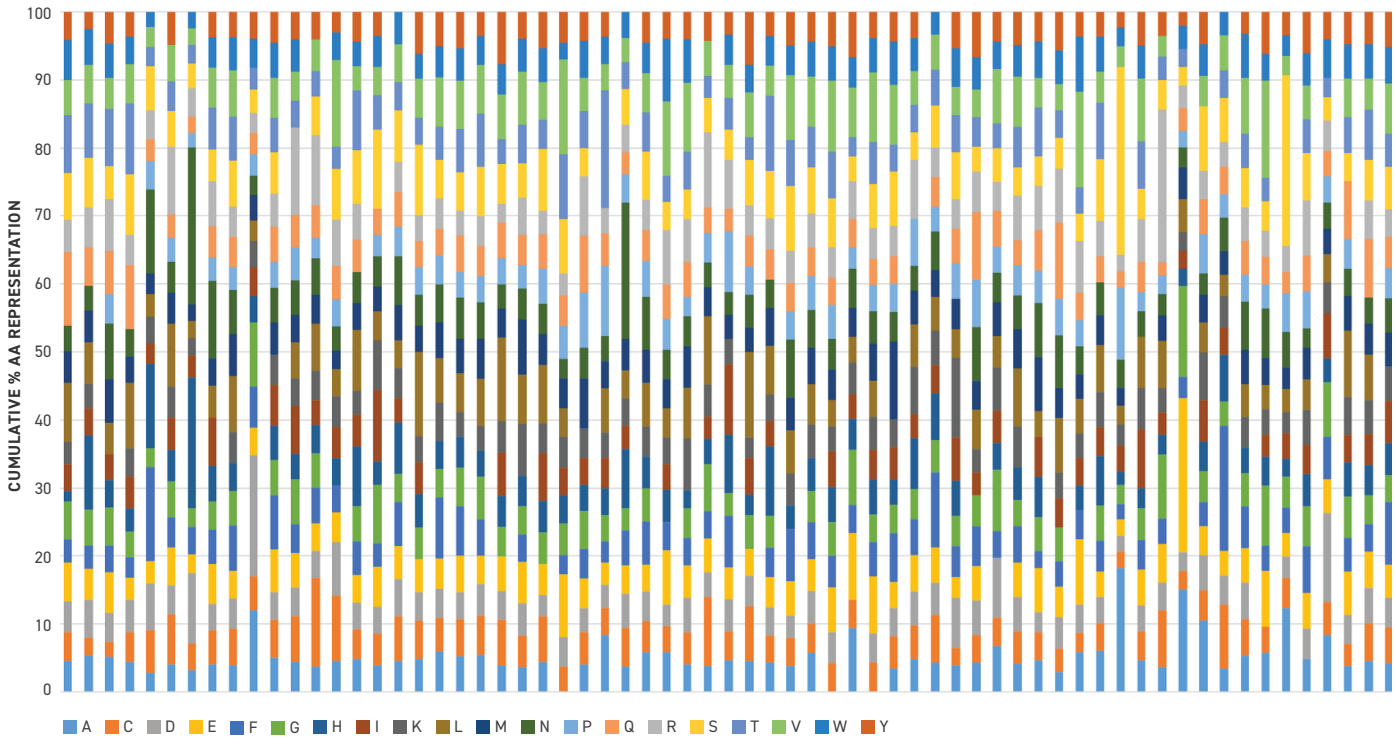


Site Saturation Variant Libraries

Twist's Site Saturation Variant Libraries allow you to investigate the relationship between sequence and protein structure and function. These libraries are capable of generating 99% of desired variants and come in pooled or pooled-per-position options. They enable screening of 1–20 different amino acids (and up to 64 codons) at each position and a comprehensive investigation of sequence variants.

	ERROR PRONE PCR	DEGENERATE (NNK/NNS)	TWIST SITE SATURATION VARIANT LIBRARIES
Eliminates sequence bias	No	No	Yes
Number of codons available	Unknown	32	All 64
Prevents undesirable motifs	No	No	Yes
Allows codon optimization	No	No	Yes
Avoids stop codons	No	Yes	Yes

Site Saturation Variant Libraries enable efficient sampling of a protein's sequence space in screening assays. The figure below is data from a Twist Site Saturation Variant Library with variants at 65 positions (19 variants per position). The bars represent a different amino acid position, with each color indicating the observed variant frequency. All variants are present in the expected ratios.



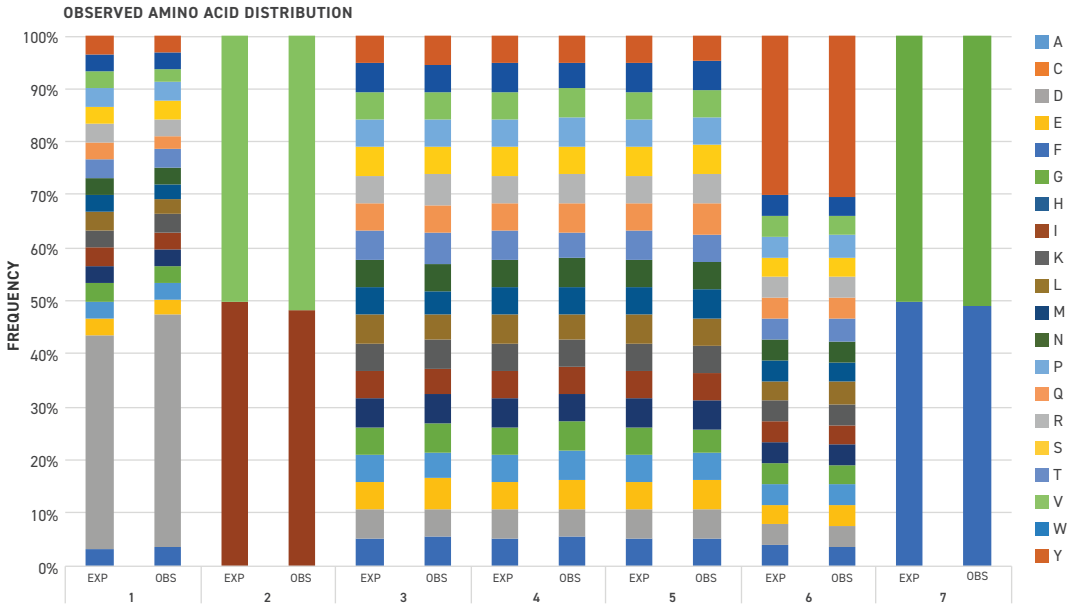
BUILT-IN QUALITY

At Twist, we use our molecular biology expertise to precisely and efficiently construct variant libraries. Our single-base control approach allows us to deliver high-diversity libraries without motifs that could confound your screening process. We deliver fully-customized libraries of unparalleled quality, with desired variants present at user-defined ratios.

Below you'll see a CVL example representative of that quality. Variants in seven sequential amino acid positions were generated, and all have expected variants at the positions shown, with nearly all at the desired ratio:

· At positions 1 and 6, the wild type amino acid was requested at 40% (position 1) and 30% (position 6). The remaining 18 amino acids were all requested to be as low as 3.3%.

· At position 3 to 5, all 19 amino acid residues were requested and observed at 5.3%.



Twist Bioscience's silicon-based platform enables the fabrication of customized libraries at the base-by-base level. The ability to precisely capture the variant diversity enables a comprehensive screen of the variant space while eliminating the risk of missing key variants.

"Working with Twist...was a great experience...[Twist's] support was amazing. We have performed the first validation selections which looks promising..."

DR. AHUVA NISSIM
PROFESSOR IN ANTIBODY AND THERAPEUTIC ENGINEERING,
QUEEN MARY UNIVERSITY OF LONDON

DISCOVER EVERYTHING WITH TWIST HIGH-QUALITY LIBRARIES

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#WeMakeDNA

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