Combinatorial Variant Libraries

Twist's massively parallel silicon-based DNA synthesis platform produces highly uniform and accurate oligos, with 90% of oligos represented within <2.5x of the mean, along with an industry-leading low error rate of 1:2,000 nt. Combined with our well established molecular biology expertise, it enables the fabrication of highly diverse gene mutant libraries with excellent variant representation and highly specific user-defined composition with no unwanted bias or motifs. Twist library technology enables a comprehensive interrogation of the variant sequence space.

SPECIFICATIONS

- Product Format: Linear double-stranded DNA, NGS-verified
- Delivery and Yield: All variants pooled in a single tube, up to 1 µg (depending on length of fragment)
- Scale up: Option to scale up library to 50 µg
- Cloning: Library can be cloned into custom vector delivered at 50 µg plasmid DNA, with an option for scale up
- Additional options: Glycerol stock upon request, phage library upon request and option to add in Sanger QC

KEY BENEFITS

High Diversity Precision

- Multiple variant domains in single or multiple scaffolds
- Precise control over codon usage (all 64 codons), amino acid distribution, and length variation

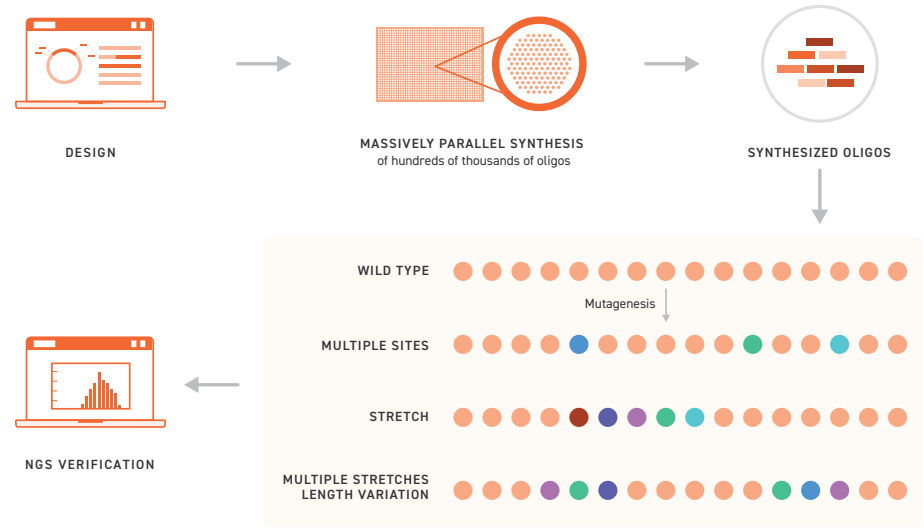
Verified Quality

- Rigorous quality control, including NGS verification of modified regions
- Sequence variant ratios documented

Flexibility

- Design all sequences, single or multiple domains and combinations—single, pairwise, or triple variants
- Modular synthesis system enables iteration of future libraries

Precision Library Generation Fueled by Silicon-Based DNA Synthesis Platform



Massively parallel oligonucleotide synthesis, combined with molecular biology expertise and high-throughput automation approaches, generates extremely precise combinatorial libraries for use in antibody and protein engineering screens.

	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

Comparison of Combinatorial Variant Library generation methods.

Rationally Sculpted Cloned Libraries

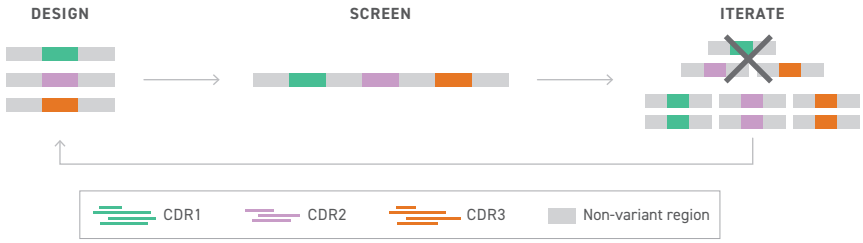
Our platform enables uniform synthesis of highly complex oligonucleotides which minimizes potential bias in the downstream workflow. Our team of scientists have developed a strategy to maintain that uniformity throughout library fabrication and cloning. Taken together, our approach to synthesis, fabrication, and cloning helps to avoid steps that have been commonly shown to introduce bias, which can lead to some variants showing up disproportionately in screens/assays.

By maintaining the starting uniformity and minimizing the dropouts as well as under-represented variants, our cloned libraries are able to maintain a high level of diversity which helps reduce screening time and effort.

ORF-AA POSITION	POSITION 1			POSITION 2			POSITION 3			POSITION 4		
	Expected	Linear	Cloned	Expected	Linear	Cloned	Expected	Linear	Cloned	Expected	Linear	Cloned
A	5%	5%	5%	5%	5%	5%	5%	4%	4%	5%	5%	5%
C	5%	5%	5%	5%	5%	5%	5%	6%	6%	5%	5%	5%
D	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%
E	5%	5%	5%	5%	5%	5%	5%	6%	6%	5%	6%	6%
F	5%	5%	5%	5%	5%	5%	5%	4%	4%	5%	4%	4%
G	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	6%	6%
H	5%	6%	6%	5%	5%	5%	5%	5%	5%	5%	4%	4%
I	5%	5%	5%	5%	5%	5%	5%	5%	4%	5%	4%	4%
K	5%	5%	5%	5%	5%	5%	5%	6%	6%	5%	6%	6%
L	5%	6%	6%	5%	5%	5%	5%	5%	5%	5%	5%	5%
M	5%	5%	5%	5%	5%	5%	5%	6%	6%	5%	5%	6%
N	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	4%	4%
P	5%	5%	5%	5%	5%	5%	5%	4%	4%	5%	4%	4%
Q	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	6%	6%
R	5%	5%	5%	5%	5%	5%	5%	7%	7%	5%	6%	6%
S	5%	5%	5%	5%	5%	5%	5%	3%	2%	5%	5%	5%
T	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%
V	5%	5%	5%	5%	5%	5%	5%	4%	4%	5%	6%	6%
W	5%	5%	5%	5%	5%	5%	5%	6%	6%	5%	6%	6%
Y	5%	4%	4%	5%	5%	5%	5%	5%	5%	5%	4%	4%

Modular, Multi-Use Libraries

Another area where the Twist library fabrication technology excels is in the construction and archiving of cassettes or modules of diversity and constant regions. A selection of complex libraries is fabricated by assembling several specific cassettes with different design and diversity. Much like Lego blocks, Twist can provide its library users with a variety of interchangeable building blocks that can be assembled in different ways to create similar, but different, structures. This benefits antibody developers and protein engineers by providing the ability to iteratively alter and evolve library designs on an ongoing, as needed basis.



We Deliver Precisely What You Design

- Precisely controlled single, pairwise, and triple combinatorial variation.
- Multi-variant domains in single or multiple scaffolds.
- Accurate ratio control of amino acid distribution and length variation within domains.
- All possible binary substitutions within domains for effective humanization.
- Avoid or minimize unwanted sequence motifs and restriction sites.
- Every library is NGS-verified so you know exactly which variants are being screened. This enables you to use the negative data from the screen to make informative decisions on next iteration of your library design.

DOC-001057 REV 2.2