

## Powering the Synthetic Biology and Genomics Revolution

2019



Emily Leproust, PhD CEO

@TwistBioscience #SyntheticDNA





Founded 2013

San Francisco

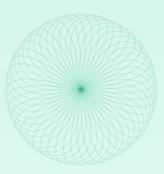
South San Francisco

**Tel Aviv** 

San Diego

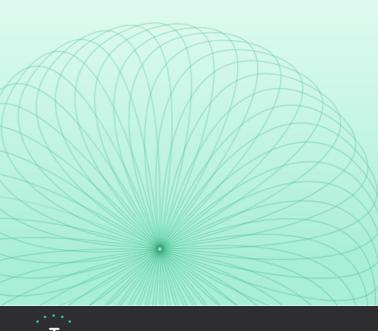
Singapore

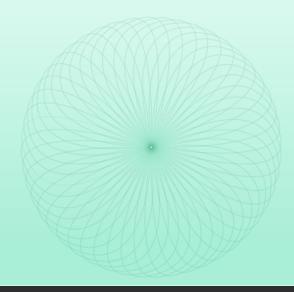


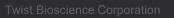




# Synthetic DNA has the potential to solve critical challenges that face humanity

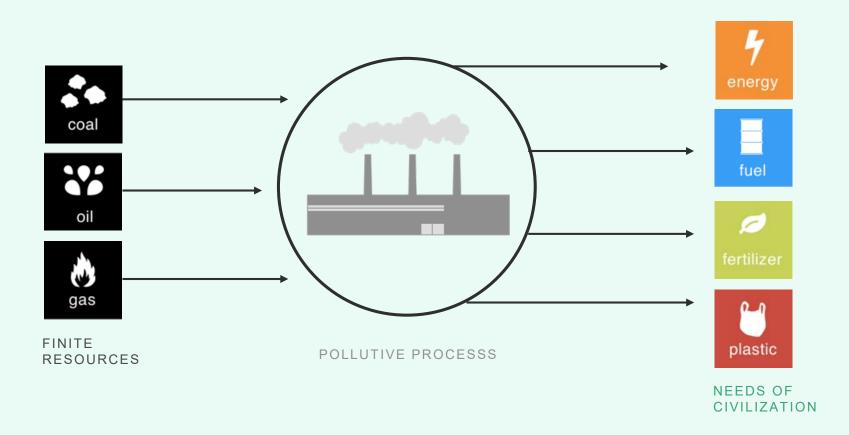






## **Sustainability**

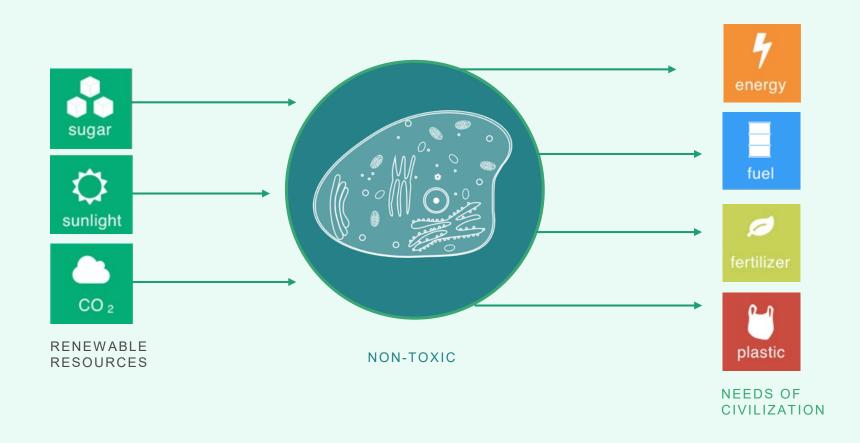




- Our population is rapidly growing but resources are unable to keep up
- Leads to increased industrial production to meet the growing needs of civilization

## **Sustainability**



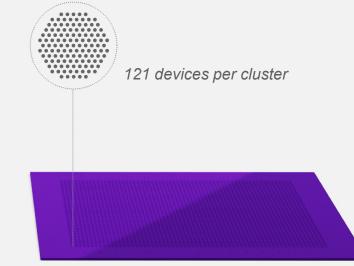


Shifting to renewable resources, leveraging biology as sustainable factories

## Technology fueling growth & expansion into new applications



### **Rewriting DNA with the Power of Silicon**





96 WELL PLATE makes 1 gene TWIST SILICON PLATFORM makes 9,600 gene

Developing Game-Changing Throughput and Cost through Quality and Speed at Scale

## What can Twist do for you?

Precision DNA Synthesis at Scale











Genes

Oligo Pools

Libraries

NGS

Data Storage









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## Why clone? Let Twist Bioscience build genes for you.

Perfect Sequence for 1 or 10,000 Genes, or More



YOUR GENES, YOUR WAY

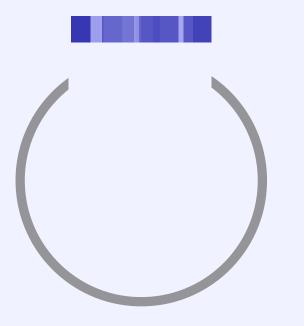




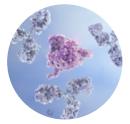


### Synthetic Genes at the core of various pipelines





Your Gene + Your Vector



Antibody-Based Drug Development



Gene Editing: Donor DNA Synthesis



**Pathway Assemblies** 



**Gene Therapy** 



### GENE FRAGMENTS Up to 1.8 kb

7¢/bp

6 to 9 business days

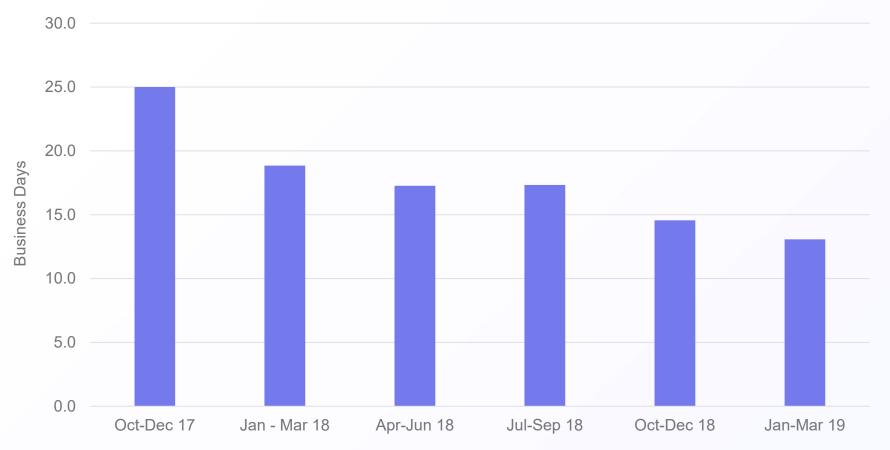
CLONAL GENES Up to 5.0 kb

From 9¢ / bp

11 to 17 business days

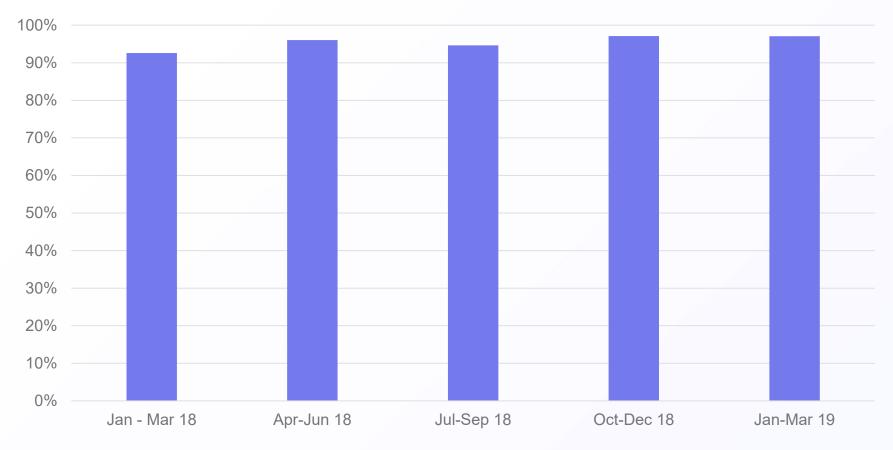


### **TURNAROUND TIME**





### SUCCESS RATE

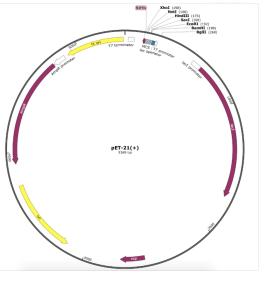




## **Twist Vectors**

A multitude of possibilities in your gene design with our expanded menu of Twist Cloning and Expression Vectors

#### My Vectors Start new order Twist Cloning (8) Twist Expression Vectors (15) RESISTANCE All (15) Ampicilin (12) Kanamycin (3) ORGANISM All (15) Ecoli (4) Mammalian (9) Viral (2) 57 pET-21(+) (5365 bp) Licensing Info 0 B Download T7 RNA polymerase driven transcription vector for expression in E. coli. The vector, which lacks the ribosome binding site and ATG start codon, is designed for protein expression from translation signals carried by the cloned DNA. Vector features: C-terminal His•Tag® sequence lac repressor / lac operator INSERTION POINTS Name Supported sequence length Resistance Copy # Organism BgIII\_Xhol 0.3-5.0 kbp pET-21(+) Ampicilin Medium Ecoli BamHI\_HindIII 0.3-5.0 kbp





In partnership with





## **Oligo Pools**



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## Think big, screen once. Let Twist build for you.

Industry leading error rates and scalability. From 100 to more than 1 million oligos.



PRECISION EDITING OF TARGET LOCI



MAXIMIZED SCREENING EFFICIENCY



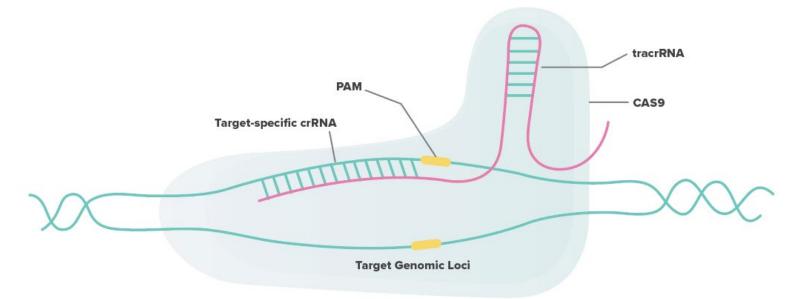
LIBRARY DESIGNS MADE EASY



## **Fueling Genome-Wide Experiments**



#### **CRISPR-CAS9**



### Editing Outcomes

#### **Gene Silencing**

## **NHEJ** (non-homologous end joining)

Gene disruption – repair to native sequence results in frameshifts or mutations

#### **Gene Correction**

#### HDR

(homology-directed repair Co-transfect cells with donor DNA)

#### **DNA Insertion**

Insert promoter, gene tags, and single or multiple genes

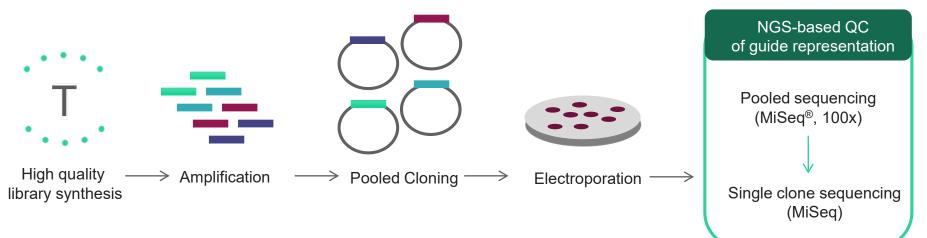
## **Application: Human Epigenetic CRISPR Screen**

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**Objective:** Cancer drug target discovery using CRISPR-Cas9

**Experimental Approach:** Introduce mutations in exons that encode functional domains using CRISPR-Cas9

The Workflow:



6,000 & 18,000 pooled oligos

#### Data from: Oxford Genetics Ltd.

## Highly Efficient Cloning of a 6k & 18k plex CRISPR Library

Frequency Density

1.5

1.0

0.5

0.0

0.0

0.5

1.0

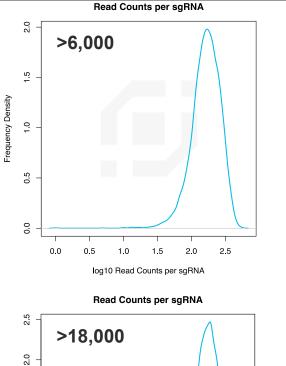
log10 Read Counts per sgRNA

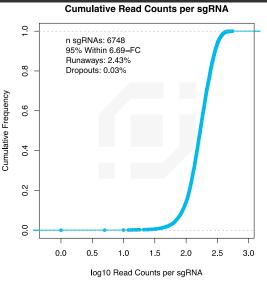
1.5

2.0

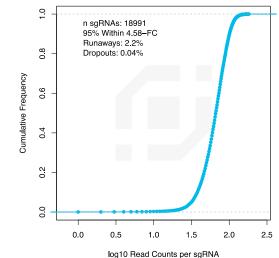
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- Cleaner, uniform smaller and larger pools with little bias
- Uniformity is unparalleled: 95% of bases within 4.58 and 6.67 fold count
- Minimal dropouts







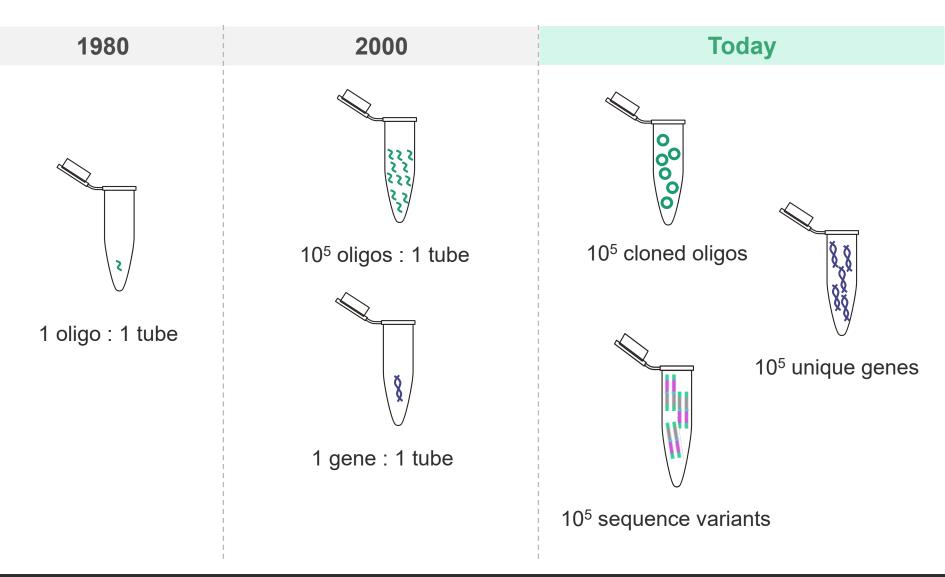




## **Twist Alpha Program**



## **Twist's New Early Access Products**

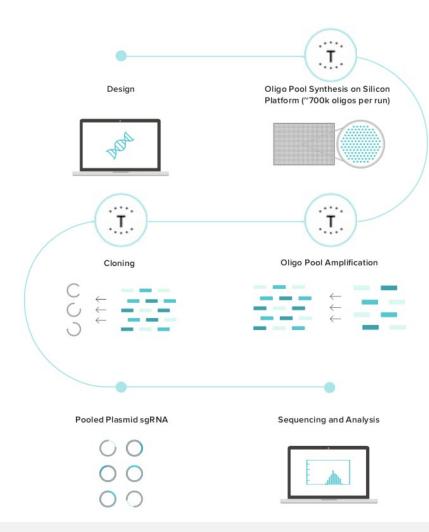


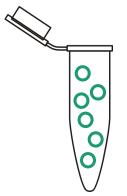


## **Cloned Oligo Pools**



Simplify your experiments. Don't clone - focus on experiments that matter.





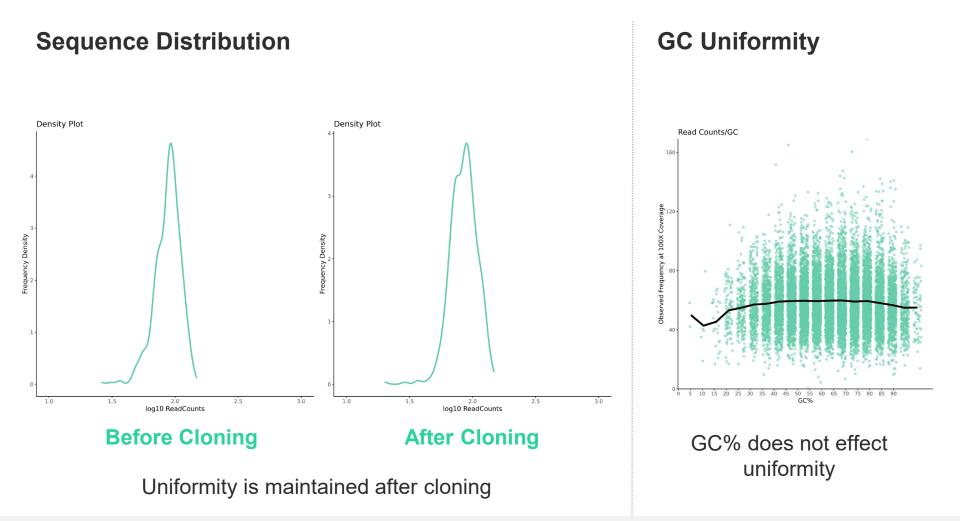
### Cloned oligo pool

10<sup>5</sup> oligos cloned into your vector

## **Cloned Oligo Pools**



Cloned oligo pools maximize experimental efficiency, maintain diversity and ensure uniformity



### Gene Pools





### Do more with synthetic DNA for less

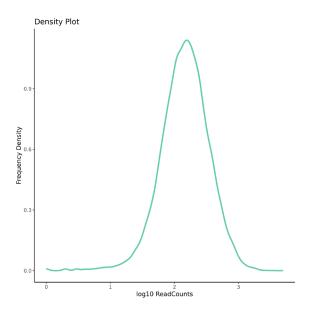


High quality gene pools minimize wasted time and resources in high throughput screens

### **Sequence Distribution**

### Sequence Quality

%Indel Free Sequences of 400bp Gene Pool



Gene Count

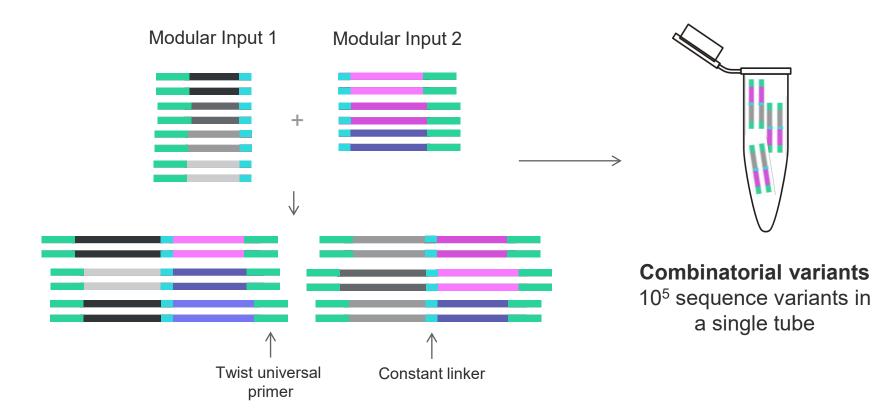
#### . 0.00 0.05 0.10 0.15 0.20 0.25 0.30 0.35 0.40 0.45 0.50 0.55 0.60 0.65 0.70 0.75 0.80 0.85 0.90 0.95 1.00 Indel Free % (bin)

The trend of count of Gene for Indel Free % (bin). The data is filtered on Type, which keeps Pass and Runaway.

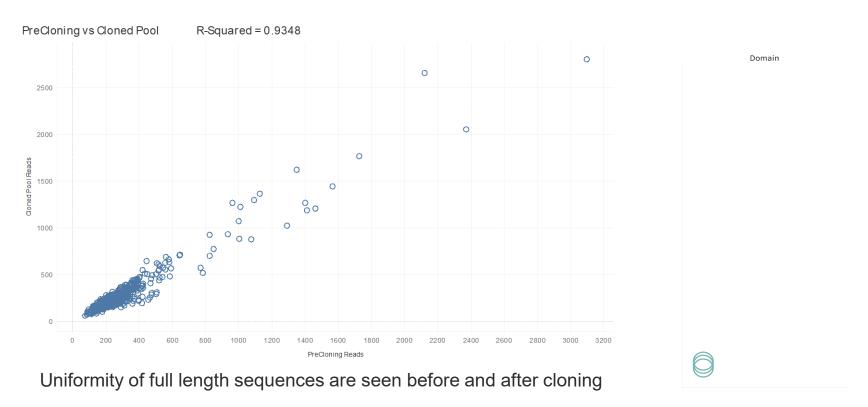
### Maximize screening efficiency

Access every sequence

Save time and money by accessing complete combinatorial sequence diversity



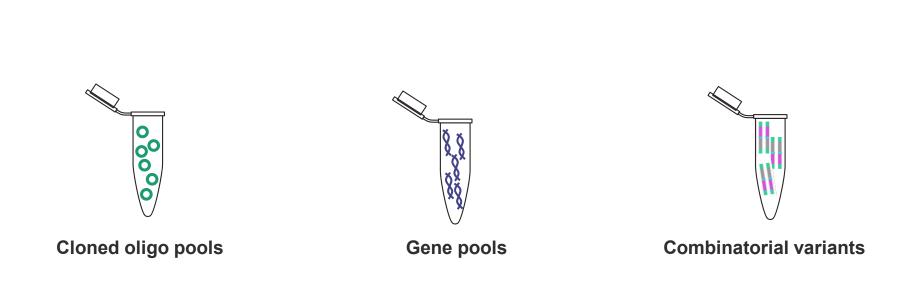
### Combinatorial assembly with 4 input pools and a final diversity of ~150,000 combinations



Uniform variant frequency

Twist's experience in combinatorial DNA assembly results in little bias.





### Comprehensive screening solutions at all scales



## What can Twist do for you?

Precision DNA Synthesis at Scale











Genes

Oligo Pools

Libraries

NGS

Data Storage

Powering the Synthetic Biology & Genomics Revolution



Thank you!

