

# INTRODUCTION TO INTEGRATED DNA TECHNOLOGIES

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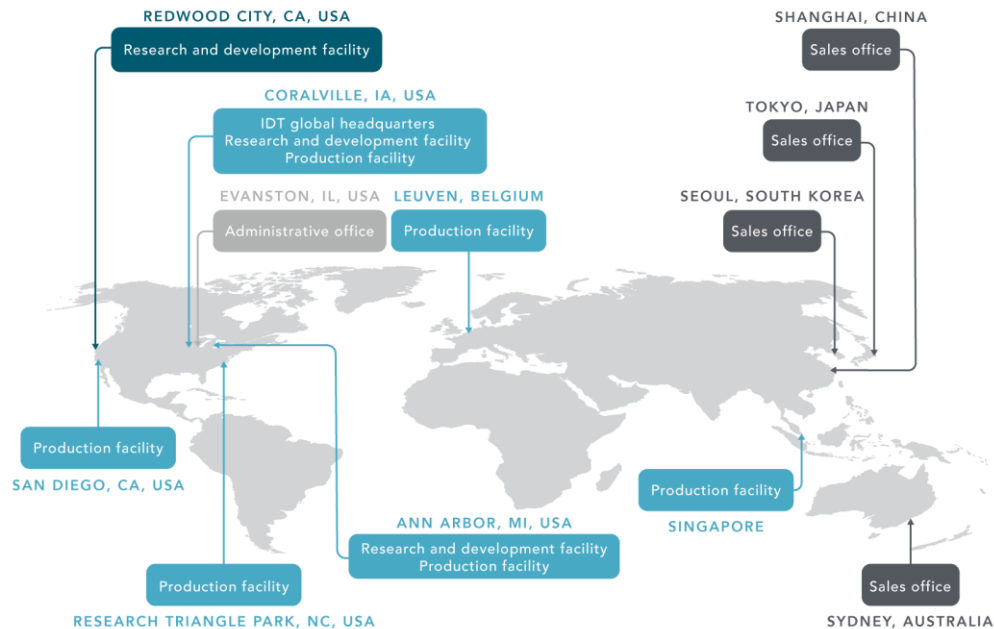


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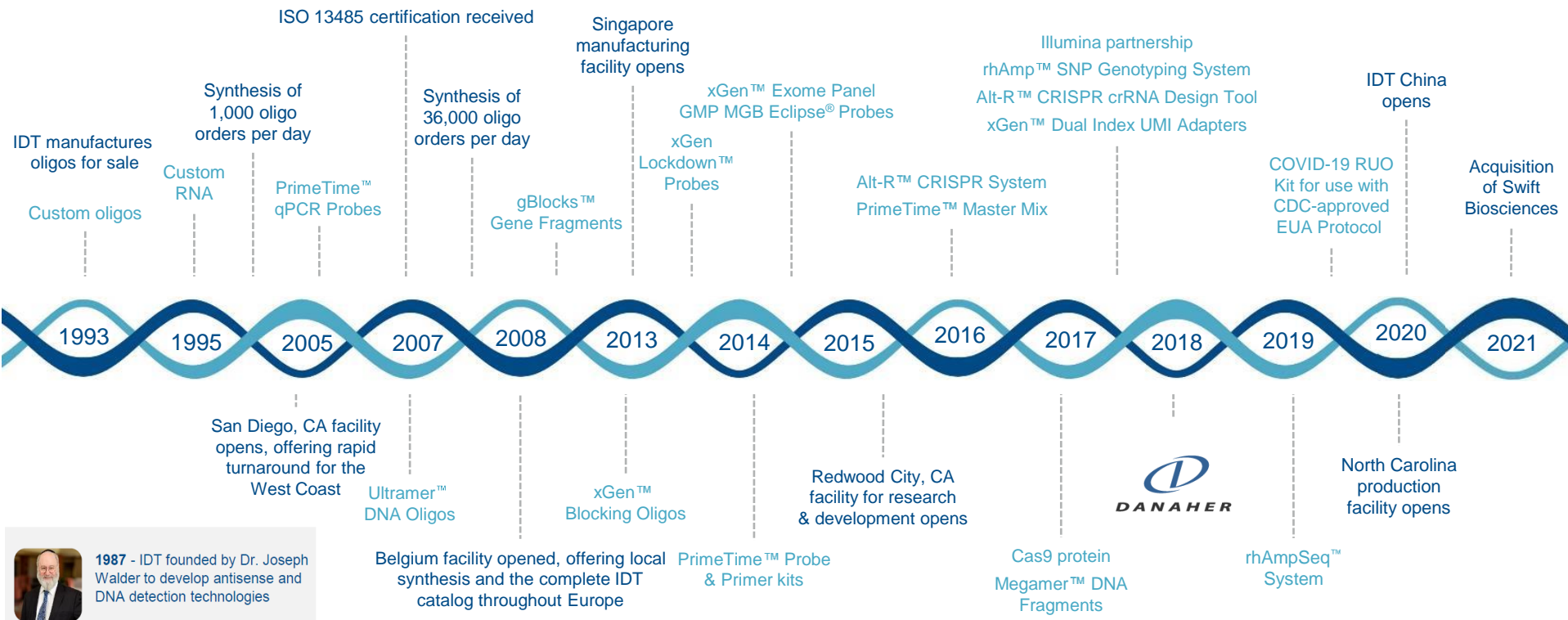
# A global leader in DNA and RNA synthesis

Serving academic researchers, biotech, and pharma customers around the world

- >4,200 orders per day
- >100,000 oligonucleotides produced per day
- >1,400 genes and gene fragments produced per day
- >135 million bases of DNA per month
- “Courier zones” near plants to deliver oligos to customers faster than FedEx



# Advanced oligo capabilities enable product evolution



- PRODUCT LAUNCHES
- KEY COMPANY EVENTS

For research use only. Not for use in diagnostics or therapeutics.

# Danaher 2022

A global purpose-driven science and technology leader

## LIFE SCIENCES



## DIAGNOSTICS



## ENVIRONMENTAL and APPLIED SOLUTIONS

### Water quality



### Product ID





# IDT's commitment to sustainability

## Our environmental policy

- Integrated DNA Technologies, Inc. is committed to minimizing the environmental impacts of its manufacturing and research operations and its products and services, and to continuously improving its environmental management programs.

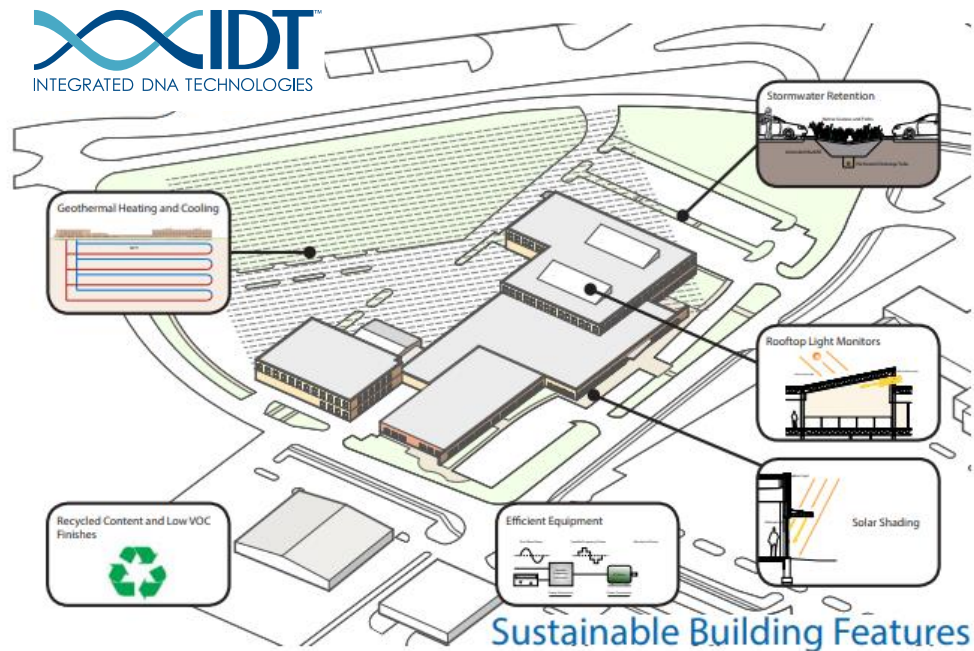
## Elimination of hazardous waste streams

- IDT received the Greenovation Award in 2017, 2018, 2019, 2020, and 2021. The awarded recognizes outstanding efforts in sustainability, reuse, green remediation, and alternative and renewable energy utilization.
- Beneficial Reuse: Since 2016, IDT HQ has participated in a beneficial reuse partnership; it allowed for the recycling of >773,000 lbs. of material in 2018.



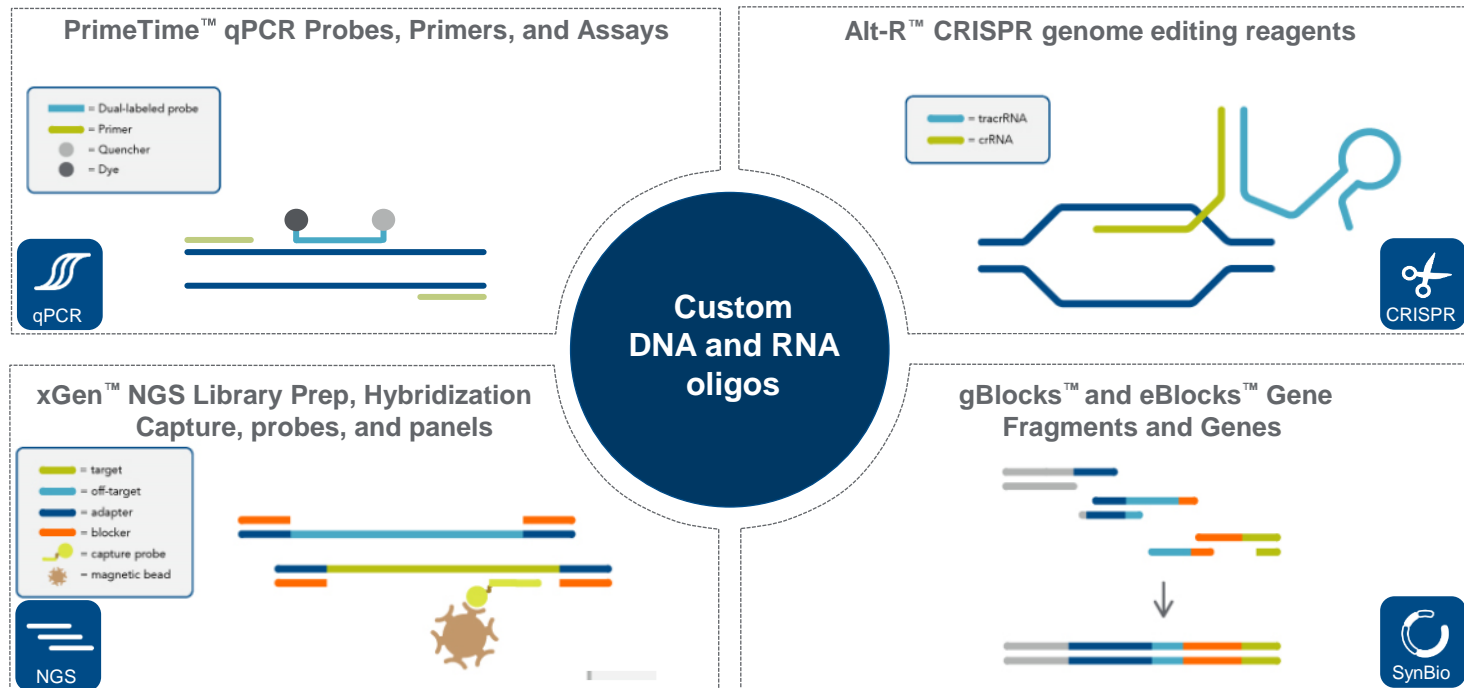
# IDT headquarters' sustainable building features

- Geothermal heating and cooling
- Recycled building materials
- Energy-efficient equipment
- Stormwater bioswales
- Rooftop light monitors
- Solar shading



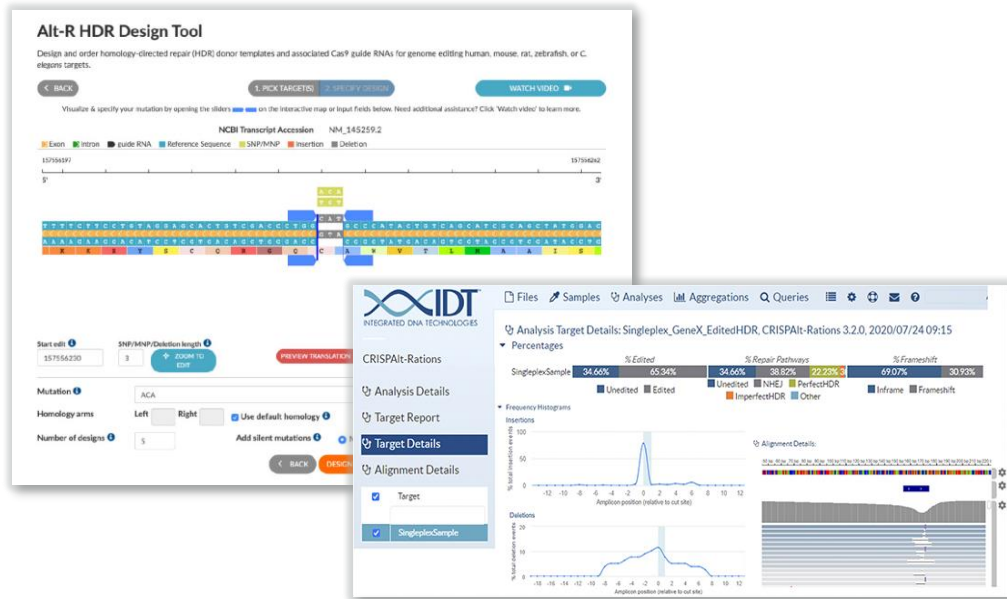
# Innovative genomics solutions

Leveraging expertise in DNA synthesis



# End-to-end solutions

Complete workflows with reagents, enzymes, and bioinformatics tools



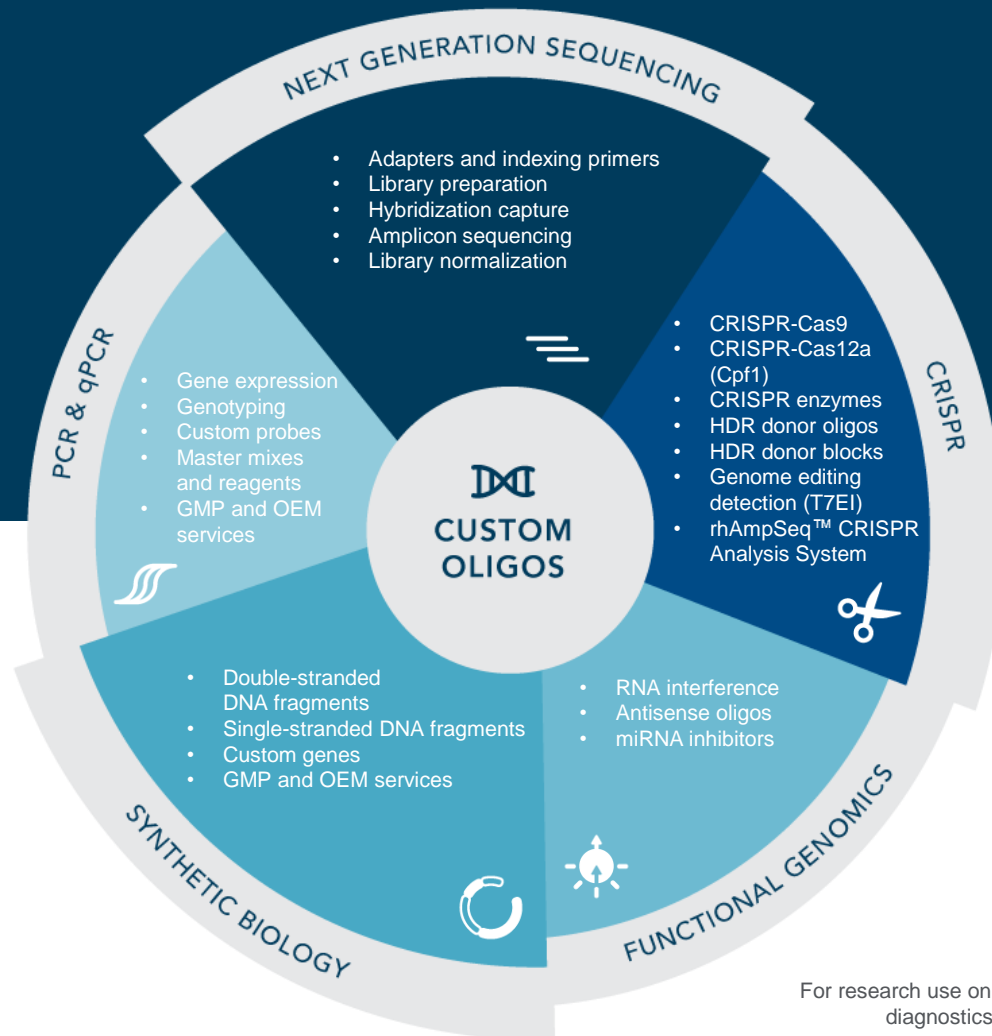
Product lines that include relevant enzymes and reagents:

-  qPCR and PCR
-  CRISPR
-  NGS

Design and analysis tools support your research beyond the bench



# IDT HAS EVOLVED— FOR YOU



# IDT'S PRODUCT LINES

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# Custom oligos



Custom  
oligos

Custom DNA and RNA oligos  
RUO-to-GMP solutions



PCR

PCR  
qPCR  
digital PCR

# Oligo and PCR solutions



## Custom oligos

### Custom oligos

- Custom DNA oligos
- Custom RNA oligos
- oPools™ Oligo Pools
- Large-scale synthesis
- SameDay oligos
- Affinity Plus™ DNA and RNA oligos
- Inventoried oligos
- Oligo modifications



## Gene expression

### PrimeTime™ qPCR Primer and Probe Assays

- Predesigned or custom assays

### PrimeTime™ gene expression Master Mix

- Optimized for probe-based qPCR

### Custom qPCR probes

- Made to your specifications

### SARS-CoV-2 qPCR panels

- Primers and probes made to your specifications in purity and scale



## Genotyping

### rhAmp™ SNP Genotyping System

- Easy, out-of-the-box solution

### Affinity Plus™ qPCR Probes

- Locked nucleic acids for probe stability

### PrimeTime™ LNA qPCR Probes

- Locked 5' nucleic acid for improved detection

### MGB Eclipse Probes

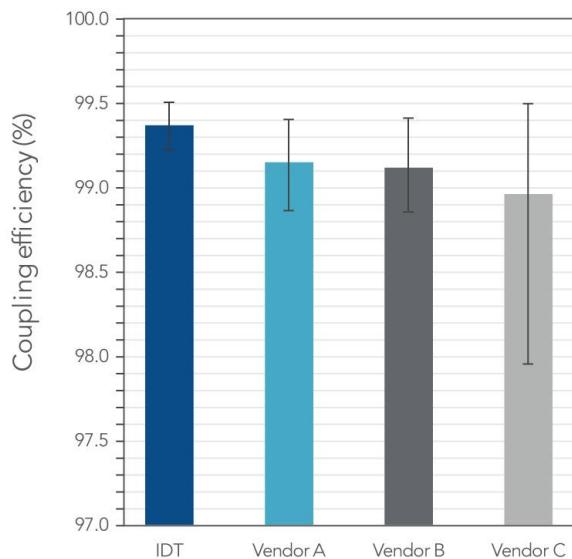
- Dual-labeled 5' nuclease probes

### PACE SNP Genotyping Assays

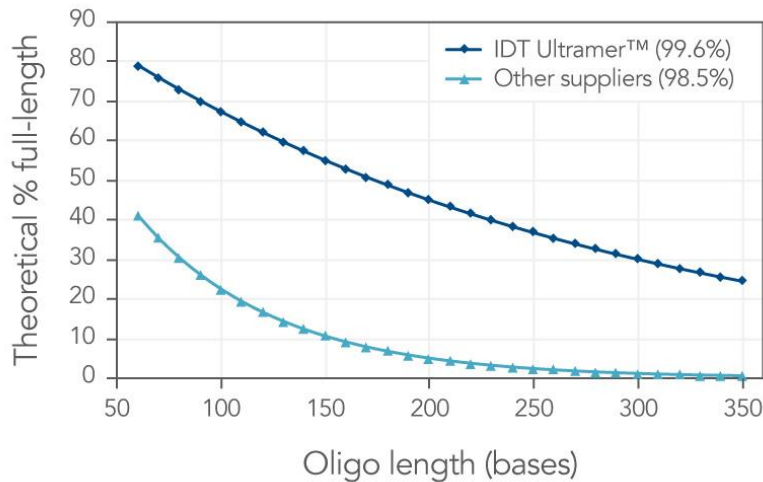
- A reliable, cost-effective approach for SNP and indel detection

# Oligo synthesis expertise

IDT's high coupling efficiency results in more full-length product



30–45 nt oligos



Longer oligos, up to 200 nt

Our proprietary oligo manufacturing process enables a 99.4–99.6% coupling efficiency

# Synthetic biology solutions and services

## Single-stranded DNA



Ultramer™ Oligos



Megamer™ Fragments



oPools™ Oligo Pools

## Linear double-stranded DNA



gBlocks™ and  
gBlocks™ HiFi  
Gene Fragments



eBlocks™ Gene  
Fragments

## Custom gene synthesis



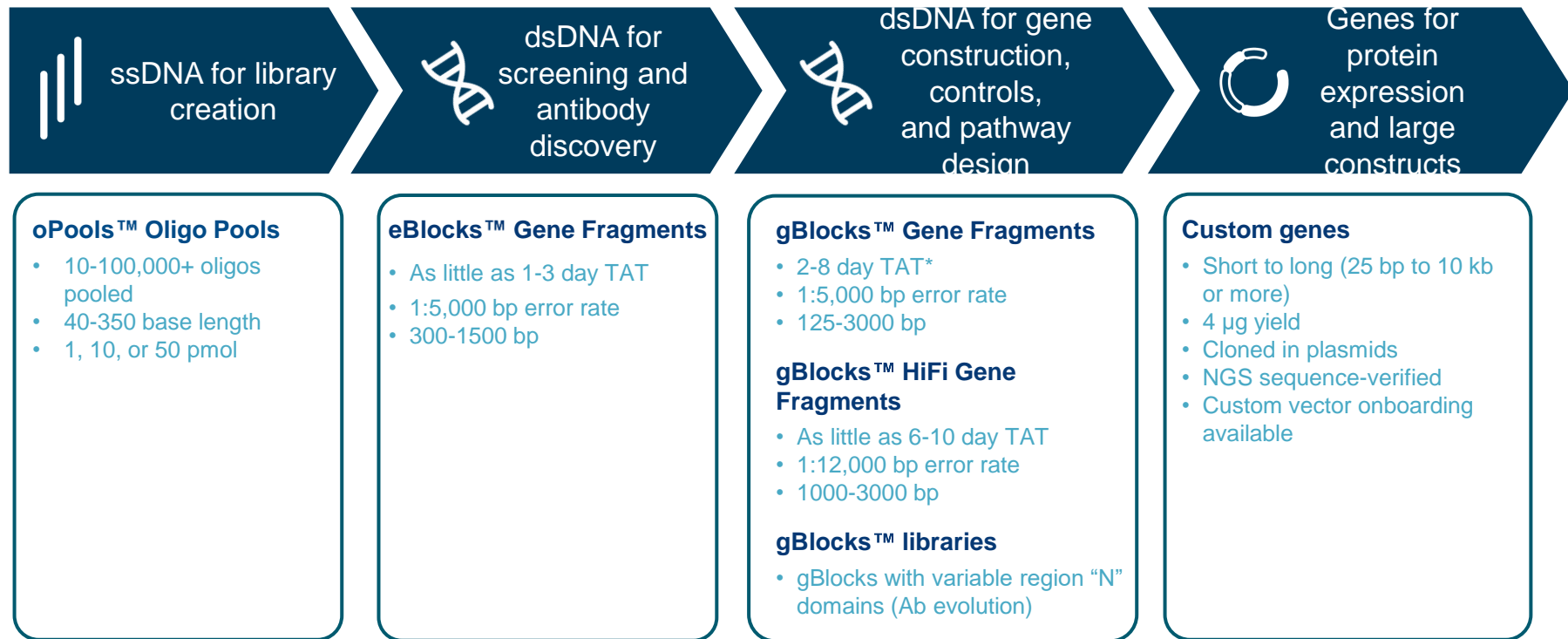
Double-stranded DNA  
in a cloning vector

## Custom projects



Project-based solutions

# Synthetic biology portfolio and applications



\* This estimated shipping time is for tubes only. Plates estimated ship date is 10-15 business days.

# Higher-fidelity DNA fragments

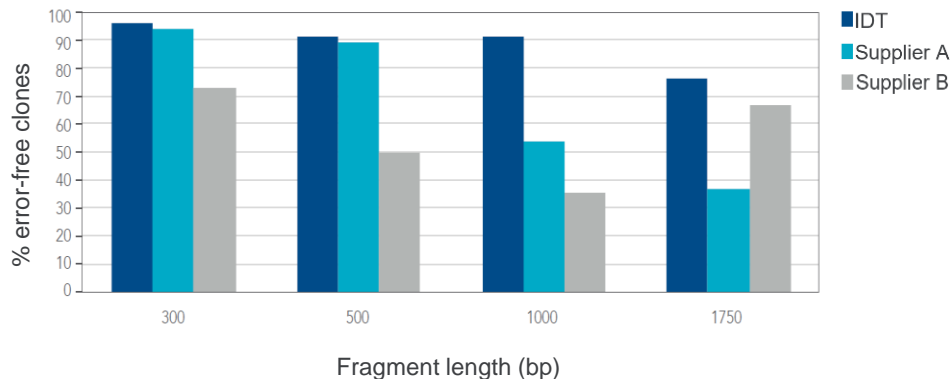
Streamline cloning workflows by screening fewer colonies

synthetic biology

white paper

## Effects of sequence fidelity on cloning efficiency

How DNA synthesis and sequence error correction processes at IDT positively impact fidelity and screening efforts compared to alternative suppliers



dsDNA fragments between 300-1750 bp were cloned into a pUC-based vector, screened, and NGS sequence verified. N = 24 colonies per supplier per sequence.



# CRISPR and Functional Genomics solutions



CRISPR

Enzymes, gRNAs, donor templates, enhancers, and design and analysis tools



Functional  
genomics

Antisense oligos (ASOs), RNA interference (Dicer substrate siRNAs, MicroRNA inhibitors)

# Alt-R™ CRISPR System



Design



Knock-out  
(KO)  
reagents



Knock-in  
(HDR)  
reagents



Analysis

## Alt-R™ Cas9 gRNA Design Tool

- Predesigned guides
- Custom designs
- Design checking

## Alt-R™ Cas9 HDR Design Tool

- Friendly UI
- Empirically defined design rules
- Integration with Cas9 gRNA designs

## rhAmpSeq™ Design Tool

## Alt-R™ gRNAs

- Cas9 crRNA:tracrRNA
- Fluorescently labeled tracrRNAs
- Cas9 sgRNA
- Cas12a crRNA
- Custom ordering for any gRNA (i.e., pegRNA, Cas13)–36 to 150+ bases

## Alt-R™ CRISPR proteins

- WT Cas9
- HiFi Cas9
- Cas9 nickases, dCas9
- *A.s.* Cas12a *Ultra*
- *L.b.* Cas12a *Ultra*
- Fluorescently labeled Cas9

## Alt-R™ Electroporation Enhancers

## Alt-R™ HDR Donor Oligos

- Up to 200 nt
- Modified ssODNs

## Alt-R™ HDR Donor Blocks

- Modified to reduce blunt integration
- Up to 3000 nt
- Sequence-verified by NGS

## Alt-R™ HDR Enhancers

- v2 small molecule
- New enhancers coming!

## Megamer™ Fragments

- ssDNA 200-2000 bases
- Alternative for specific cell types where dsDNA may be cytotoxic

## Genome Editing Detection Kit

- T7EI assay

## rhAmpSeq™ CRISPR Analysis System

- Multiplexed amplicon NGS sequencing (singleplex on-target, multiple off-target)
- Cloud-hosted interface for customer analysis of NGS CRISPR editing data (CRISPRAltRation platform)



*IDT scientists are authors on 30 CRISPR-related publications and are involved in numerous partnerships to advance the field of genome editing.*

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# IDT's CRISPR R&D program facilitates a complete workflow solution

## ARTICLE

<https://doi.org/10.1038/s41467-021-24017-8>

OPEN



## AsCas12a ultra nuclease facilitates the rapid generation of therapeutic cell medicines

Liyang Zhang<sup>1,4</sup>, John A. Zuris<sup>2,4</sup>, Ramya Viswanathan<sup>2</sup>, Bernice Thommandru<sup>1,4</sup>, H. Tomas Rube<sup>3,4</sup>, Steve E. Gle Sarah F. Beaudoin<sup>1</sup>, Swarali Lele<sup>2</sup>, Sean N. Scott<sup>2</sup>, Kevi Mollie S. Schubert<sup>1</sup>, Gavin L. Kurgan<sup>1</sup>, Matthew S. M. Richard A. Morgan<sup>2</sup>, Mark A. Behlke<sup>1ES</sup> & Christophe

Though AsCas12a fills a crucial gap in the currently poor editing efficiency, restricting its overall variant, "AsCas12a Ultra", that increased editing examined in HSPCs, iPSCs, T cells, and NK cells high on-target specificity thereby mitigating the risk for complex therapeutic genome editing applications. Three clinically relevant genes in T cells at >90 knock-in efficiencies of up to 60%. We demonstrate cells, which afforded enhanced anti-tumor NK cell generation of allogeneic cell-based therapies in CRISPR nuclease with significant advantages in edited cell medicines.

NATURE COMMUNICATIONS | (2021)12:3908 | <https://doi.org/10.1038>



## ARTICLES

<https://doi.org/10.1038/s41591-018-0137-0>

nature  
medicine

## A high-fidelity Cas9 mutant delivered as a ribonucleoprotein complex enables efficient gene editing in human hematopoietic stem and progenitor cells

Christopher A. Vakulskas<sup>1,7</sup>, Daniel P. Dever<sup>2,7</sup>, Garrett R. Rettig<sup>1</sup>, Rolf Turk<sup>1</sup>, Ashley M. Jacobson<sup>1</sup>, Michael A. Collingwood<sup>1</sup>, Nicole M. Bode<sup>1</sup>, Matthew S. McNeill<sup>1</sup>, Shuqi Yan<sup>1</sup>, Joab Camarena<sup>2</sup>, Ciaran M. Lee<sup>3</sup>, So Hyun Park<sup>3</sup>, Volker Wiebking<sup>2</sup>, Rasmus O. Bak<sup>4,5</sup>, Natalia Gomez-Ospina<sup>2</sup>, Mara Pavel-Dinu<sup>2</sup>, Wenchao Sun<sup>6</sup>, Gang Bao<sup>3</sup>, Matthew H. Porteus<sup>2\*</sup> and Mark A. Behlke<sup>1\*</sup>

Translation of the CRISPR-Cas9 system to human therapeutics holds high promise. However, specificity remains a concern especially when modifying stem cell populations. We show that existing rationally engineered Cas9 high-fidelity variants have reduced on-target activity when using the therapeutically relevant ribonucleoprotein (RNP) delivery method. Therefore, we devised an unbiased bacterial screen to isolate variants that retain activity in the RNP format. Introduction of a single point mutation, p.R691A, in Cas9 (high-fidelity (HiFi) Cas9) retained the high on-target activity of Cas9 while reducing off-target editing. HiFi Cas9 induces robust AAV6-mediated gene targeting at five therapeutically relevant loci (HBB, IL2RG, CCR5, HEXB, and TRAC) in human CD34<sup>+</sup> hematopoietic stem and progenitor cells (HSPCs) as well as primary T cells. We also show that HiFi Cas9 mediates high-level correction of the sickle cell disease (SCD)-causing p.E6V mutation in HSPCs derived from patients with SCD. We anticipate that HiFi Cas9 will have wide utility for both basic science and therapeutic genome-editing applications.

NATURE MEDICINE | VOL 24 | AUGUST 2018 | 1216-1224 | [www.nature.com/naturemedicine](http://www.nature.com/naturemedicine)

**IDT**  
INTEGRATED DNA TECHNOLOGIES

# xGen™ NGS—made with comprehensive solutions



Whole genome  
sequencing



Targeted, whole  
exome sequencing



Methyl sequencing



RNA sequencing

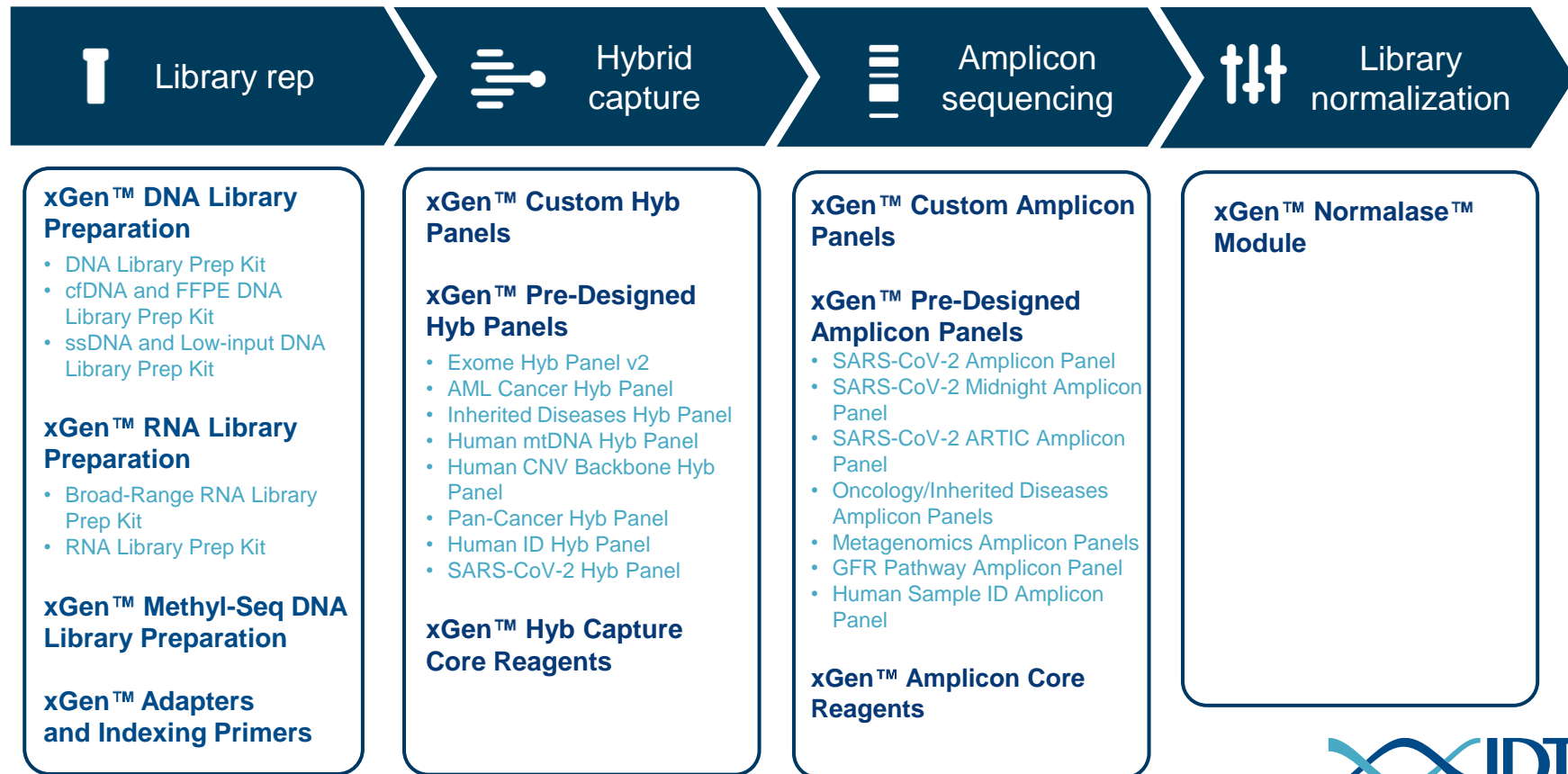


Normalase™  
Technology



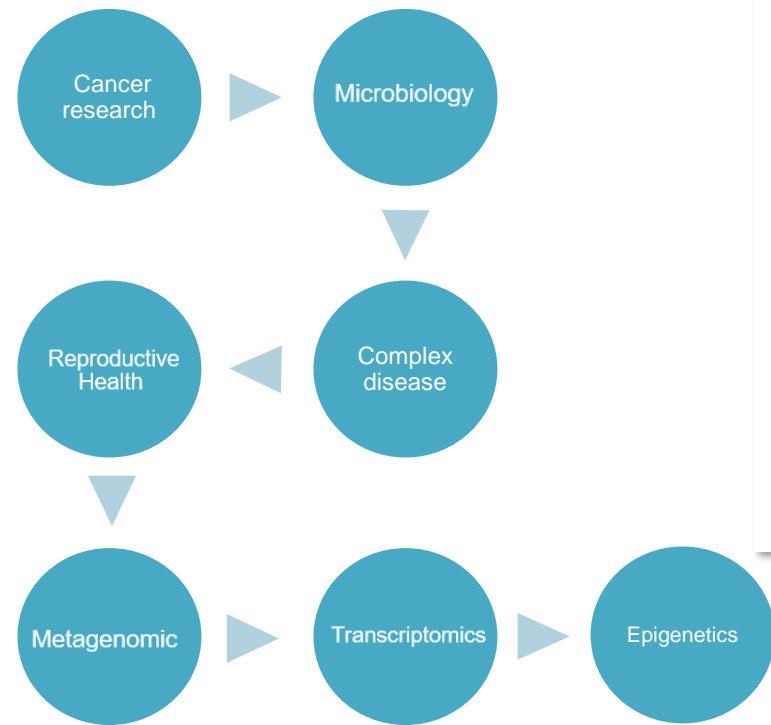
OEM services

# xGen™ NGS—made for research flexibility



# Workflow flexibility for many different applications

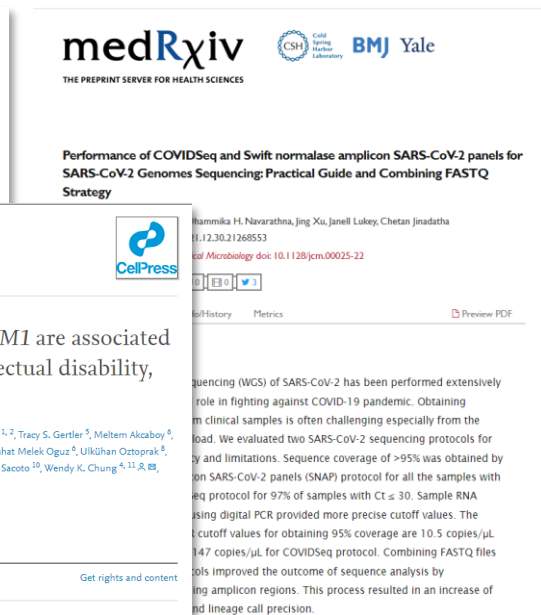
More than 500+ published studies use IDT's xGen™ NGS products



Oncology research



Viral research



Exome research



# IDT's design & analysis tools



## Oligo design and handling

- OligoAnalyzer™ Tool
- UNAFold Tool
- Resuspension calculator
- Dilution Calculator



## qPCR assays and genotyping

- PrimerQuest™ Tool
- Realtime PCR Tool
- Predesigned qPCR Assays
- PrimeTime™ Multiplex Dye Selection
- rhAmp™ Genotyping Design Tool



## CRISPR genome editing

- Alt-R™ Predesigned and Custom Cas9 crRNA Selection Tools
- CRISPR-Cas9 Design Checker
- Alt-R™ HDR Design Tool
- rhAmpSeq™ CRISPR Analysis Tool



## NGS tools

- Library Concentration Conversion Calculator
- Target Capture Probe Design and Ordering Tool
- Custom Adapter Configurator Tool
- xGen™ NGS Solutions Builder Tool (NEW!)



## Genes and gene fragments

- Codon Optimization Tool
- gBlocks™ Gene Fragments Entry Tool



## Gene regulation and RNAi

- Predesigned DsiRNA Selection Tool
- RNAi Design Tool



The background of the slide is a blue-tinted photograph of a multi-channel pipette with several tips positioned over a microplate. The pipette is in the upper half of the frame, and the microplate is in the lower half. The text is overlaid on the upper portion of the image.

# IDT B2B: 21 CFR 820 GMP COMPLIANT AND ISO 13485:2016 CERTIFIED

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# Strategic Services: We offer key GMP components to help build your assays

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## Our track record:

- >90,000 GMP oligonucleotides synthesized per year, largely as components of molecular assays
- 2 sites (Coralville, Leuven) with dedicated GMP production capabilities
- >500 diagnostic and biotechnology organizations served
- >1,000 molecular assays or OEM products commercialized using IDT components

GMP refers to products manufactured under ISO 13485: 2016 QMS. Purchaser is solely responsible for all decisions regarding the use of these products and any associated regulatory or legal obligations for their legal marketing.



QUALITY



FLEXIBILITY



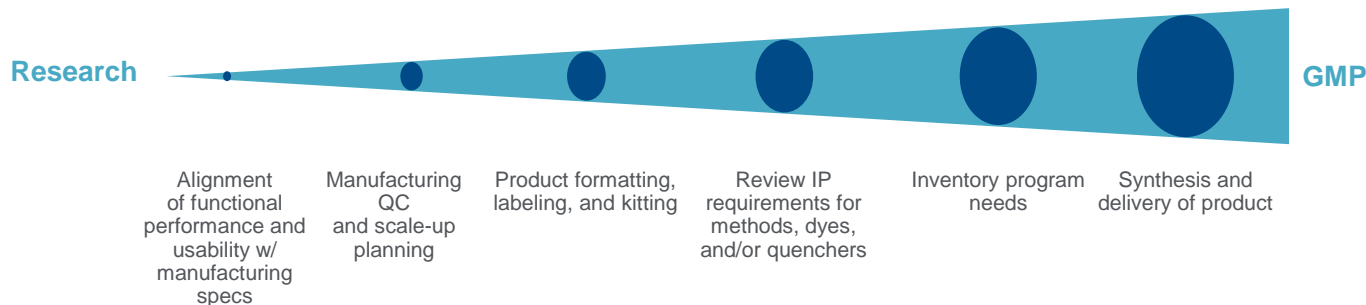
SPEED



PERSONALIZED SUPPORT

# Why choose IDT to transition from research to GMP?

- Dedicated strategic account manager to help align on specs, timelines, pricing, supply agreements, inventory programs, and more
- Years of technical expertise and experience in oligo design, synthesis, manufacturing, and end-use application
- Lot-to-lot consistency
- Picomole to multi-gram single-lot scalability
- Your product, your way (plates and tubes, custom formulations/spec sheets, your packaging)



GMP refers to products manufactured under ISO 13485: 2016 QMS. Purchaser is solely responsible for all decisions regarding the use of these products and any associated regulatory or legal obligations for their legal marketing.

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# Support and education

## Take advantage of IDT's extensive resources

- Expert customer service available 24/7
- Regular webinars and presentations from our R&D team
- Educational resources on the web, including
  - [FAQs](#)
  - [DECODED online newsletter](#)
  - [IDT community blog](#)
  - [IDT publications](#)
  - [Past webinars and video tutorials](#)

### Questions?

### Contact us:

#### USA and Canada

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Coralville



Leuven



San Diego



Singapore



# THANK YOU



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