Société d'Encouragement pour l'industrie nationale FONDÉE EN 1801

ABG Association Bernard Gregory

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# Un monde à risques de pandémies : vers quelle biorévolution industrielle ?

## Cycle : Pour le Développement des Sciences et de l'Innovation (PDSI) au service des Transitions

Jeudi 11 mai à l'Hôtel de l'Industrie

Société d'Encouragement pour l'industrie nationale FONDÉE EN 1801

# Conférence PDSI

11 mai 2023

## Un monde à risques de pandémies : vers quelle biorévolution industrielle ?

**Patrick Berche**

Microbiologiste et professeur émérite de l'université Paris Cité

**Chiraz Khayat**

Directrice et chef de produit instrumentation pour la synthèse de l'ADN chez DNA Script.

Modérateur : **Patrice Debré**, Vice-Président de l'AFAS, Professeur émérite d'immunologie à Sorbonne Université, membre titulaire de l'Académie nationale de médecine

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# Conférence PDSI

11 mai 2023

## Chiraz Khayat

Directrice et chef de produit instrumentation pour la synthèse de l'ADN chez DNA Script.

# Content

SECTION 01

# About DNA Script

DNA Script is empowering researchers through EDS: Enzymatic DNA Synthesis technology to make biology programable and accelerate the bio revolution

# DNA Script is innovating DNA-Write

"THERE MUST BE A BETTER WAY THAN WAITING FOR DNA FROM 40-YEAR-OLD CHEMISTRY"

Engineers with experience in synthetic biology found DNA Script

Xavier Godron (CTO)
Thomas Ybert (CEO)
& Sylvain Gariel (COO)


Paris Headquarters

US Headquarters South San Francisco

## 2014

**>200** EMPLOYEES

**>20M** NUCLEOTIDES PRINTED

**$315M** CAPITAL RAISED

## 2021

CATALIO CAPITAL MANAGEMENT
BAILLIE GIFFORD
T.RowePrice
Fidelity INVESTMENTS
COATUE
FARALLON
illumina VENTURES
CASDIN CAPITAL
Agilent
COLUMBIA THREADNEEDLE INVESTMENTS
ARROWMARK PARTNERS
DANAHER

# DNA Script is innovating DNA-Write

FOUNDERS' VISION ORIGINATES FROM THEIR EXPERIENCE IN SYNTHETIC BIOLOGY

## South san francisco, ca

**PRODUCT DEVELOPMENT**
System engineering and software development

**COMMERCIAL OPERATIONS**
Sales, marketing and customer support

**CORPORATE**
HR, Finance, IT, Legal and support operations


**RESEARCH & DEVELOPMENT**
Enzymatic synthesis technology development
Feasibility studies for product development

**MANUFACTURING OPERATIONS**
Key reagent manufacturing and testing
Kits production

**CORPORATE**
HR, Finance, IT, Legal and support operations

DNA Script is empowering researchers through EDS: Enzymatic DNA Synthesis technology to make biology programable and accelerate the bio revolution

# Distributed EDS represents a paradigm shift

SYNTAX ALLOWS YOU TO ITERATE YOUR WORKFLOW FASTER & TO GET BACK IN CONTROL

## Current paradigm = Centralized Chemical DNA Synthesis

Customer request → Order your oligos from service providers → Wait for shipping (can be weeks) → Customer delivery

TAT ~ weeks

*Your workflow is dependent on DNA sequences reception that can be delayed and/or unsecured*

## Current paradigm = In-house CDS

Customer request → Complex pre- & post-synthesis processes → Customer delivery

TAT ~ days

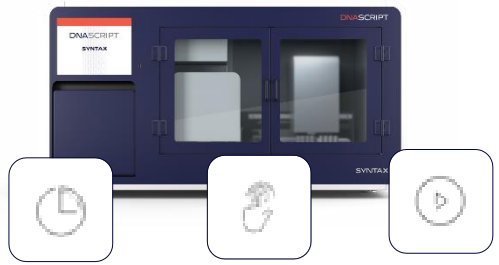
*Obtaining your desired oligos via in-house CDS reduces cycle time but request the presence of highly trained expertise and extensive waste management on site*

## Future paradigm = Distributed EDS

Customer request → End-to-end Enzymatic DNA printer → Directly accessible within your biology lab → Customer delivery

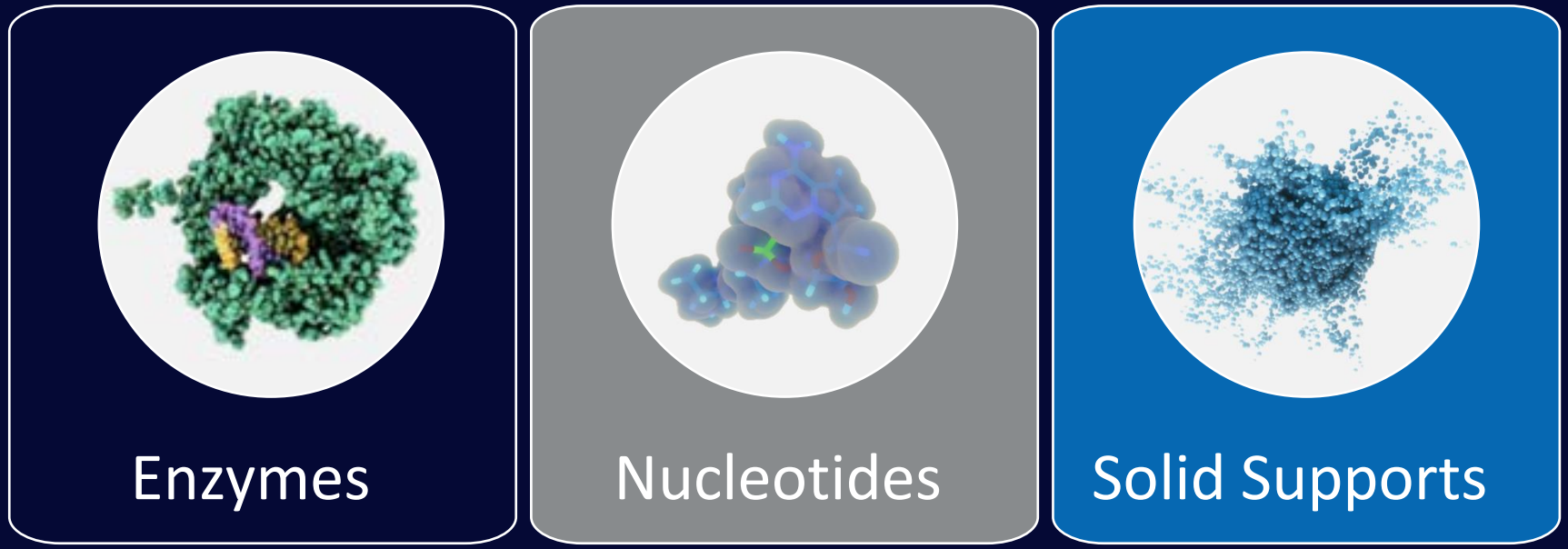
TAT ~ hours

*Printing autonomously your DNA fragments with benchtop distributed EDS allows for fast access to ready-to-use oligos suitable for any molecular biology lab*

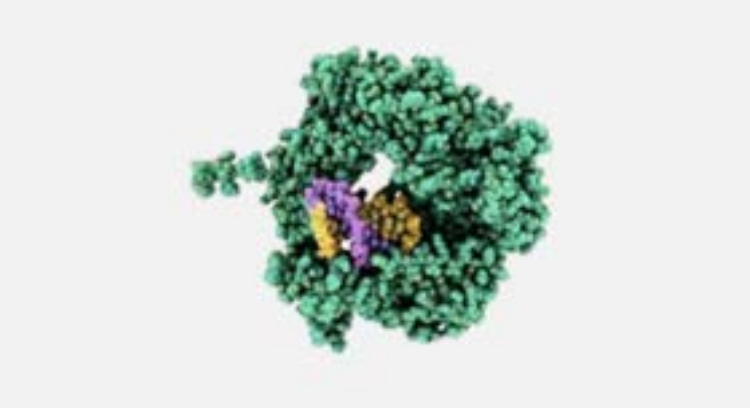


SAME DAY RESULTS | FLEXIBLE | PLUG-N-PLAY

# Enzymatic DNA Synthesis Principle



# 3 Pillars of Enzymatic Synthesis

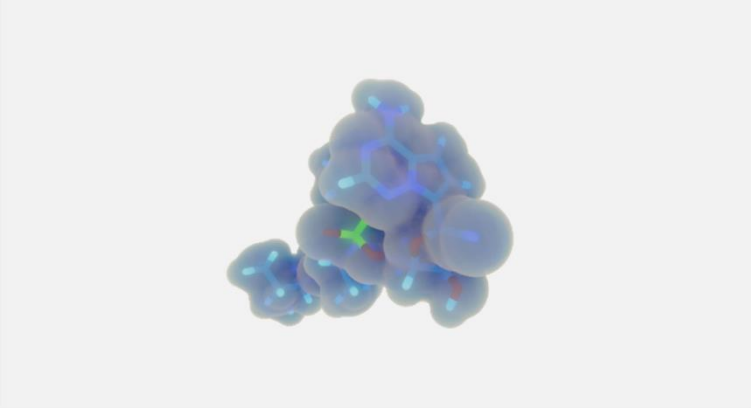


## Enzymes

Terminal Deoxynucleotidyl Transferase (TdT)

TdT has unique ability to create genomic material de novo

Highly-engineered to rapidly and selectively add our reversibly-terminated nucleotides with high fidelity and high coupling efficiency



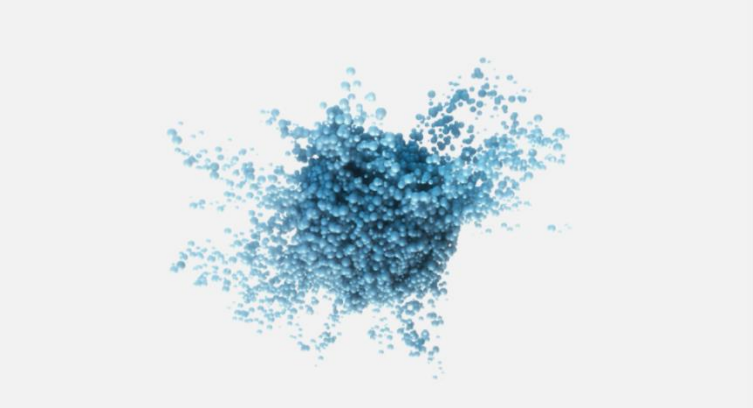
## Nucleotides

Reversibly Terminated Nucleotides

Prevents extension but can be removed to continue synthesis

Permits TdT to use modified bases

Leaves no "scars“ – yields "natural" (native) DNA



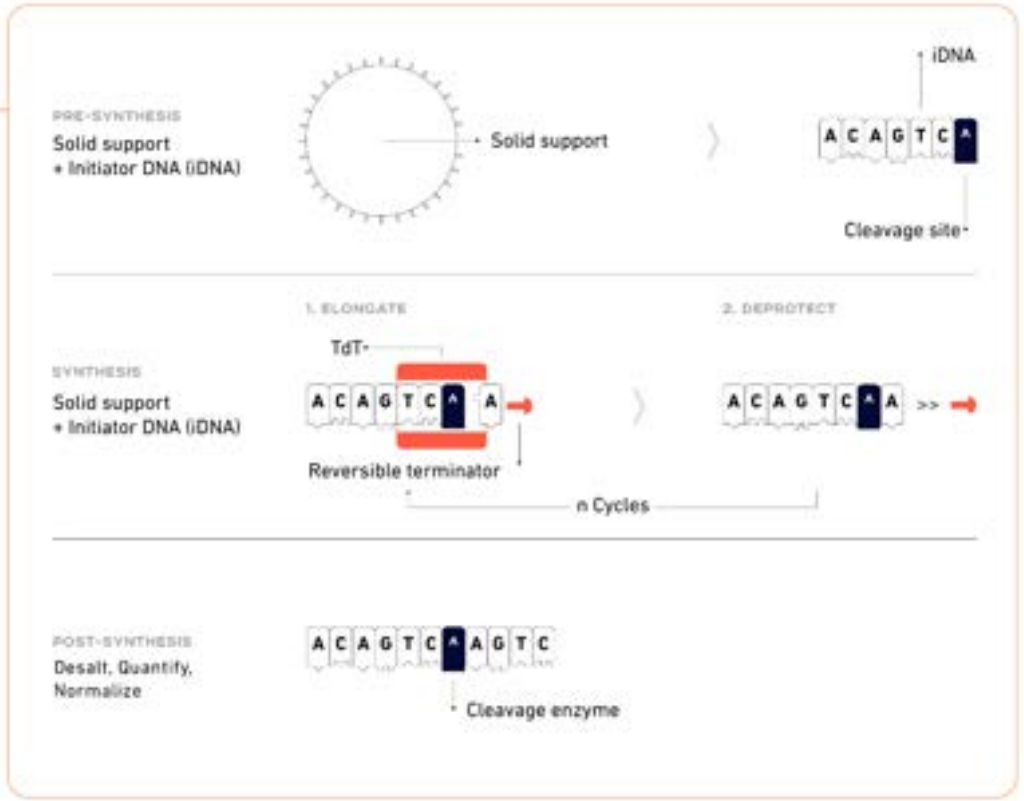
## Solid Supports

Solid support controls synthesis scale

Covalently coated with "initiator DNA" (iDNA)

# Enzymatic DNA Synthesis (EDS)

TWO-STEP ENZYMATIC CYCLE
IS FAST AND EFFICIENT




**PRE-SYNTHESIS**

Solid Support +
Initiator DNA (iDNA)

**2-STEP SYNTHESIS**

Elongation +
Deprotection

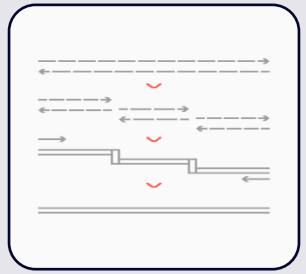
**POST-SYNTHESIS**

Desalt, Quantify,
Normalize

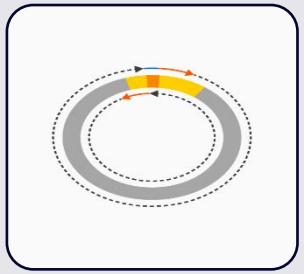
*Enzymatic DNA Synthesis*

# Applications enabled today

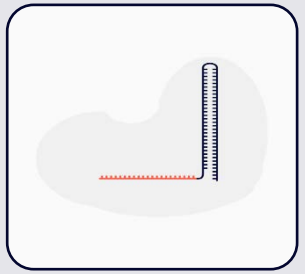
Real Time
qPCR, PCR



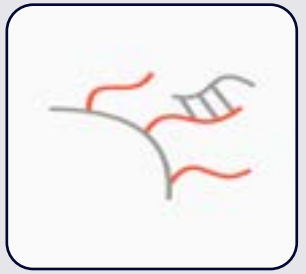
Gene Assembly



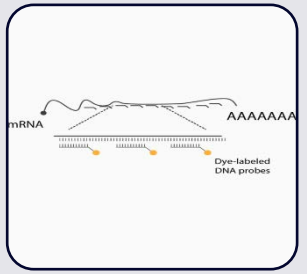
Protein
engineering



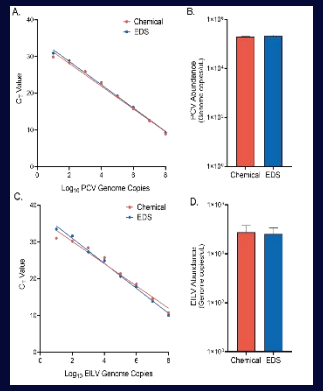
CRISPR
Gene Editing

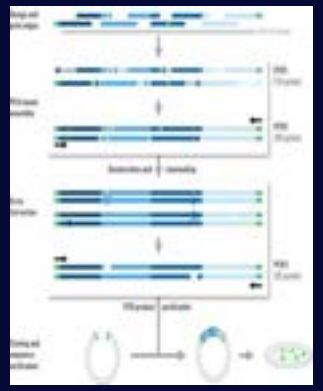


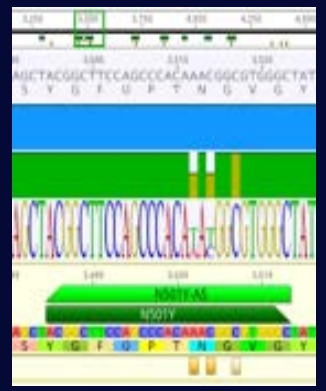
NGS Target
Enrichment

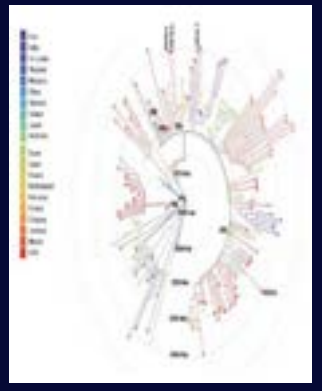


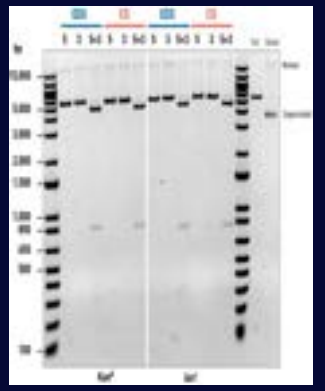

smFISH/FISH

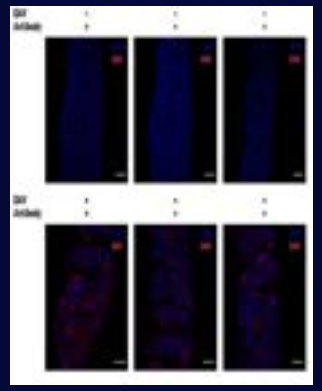












SECTION 04

# SYNTAX Platform:
# The World's first Enzymatic DNA Synthesis printer

# SYNTAX STX-200 Platform

A SINGLE INTEGRATED SOLUTION FOR OLIGO SYNTHESIS

## SOFTWARE

SYNTAX System Software

Console Software

## SYSTEM


Barcode reader

Vacuum cabinet

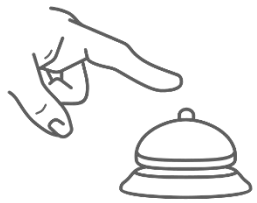
## KITS

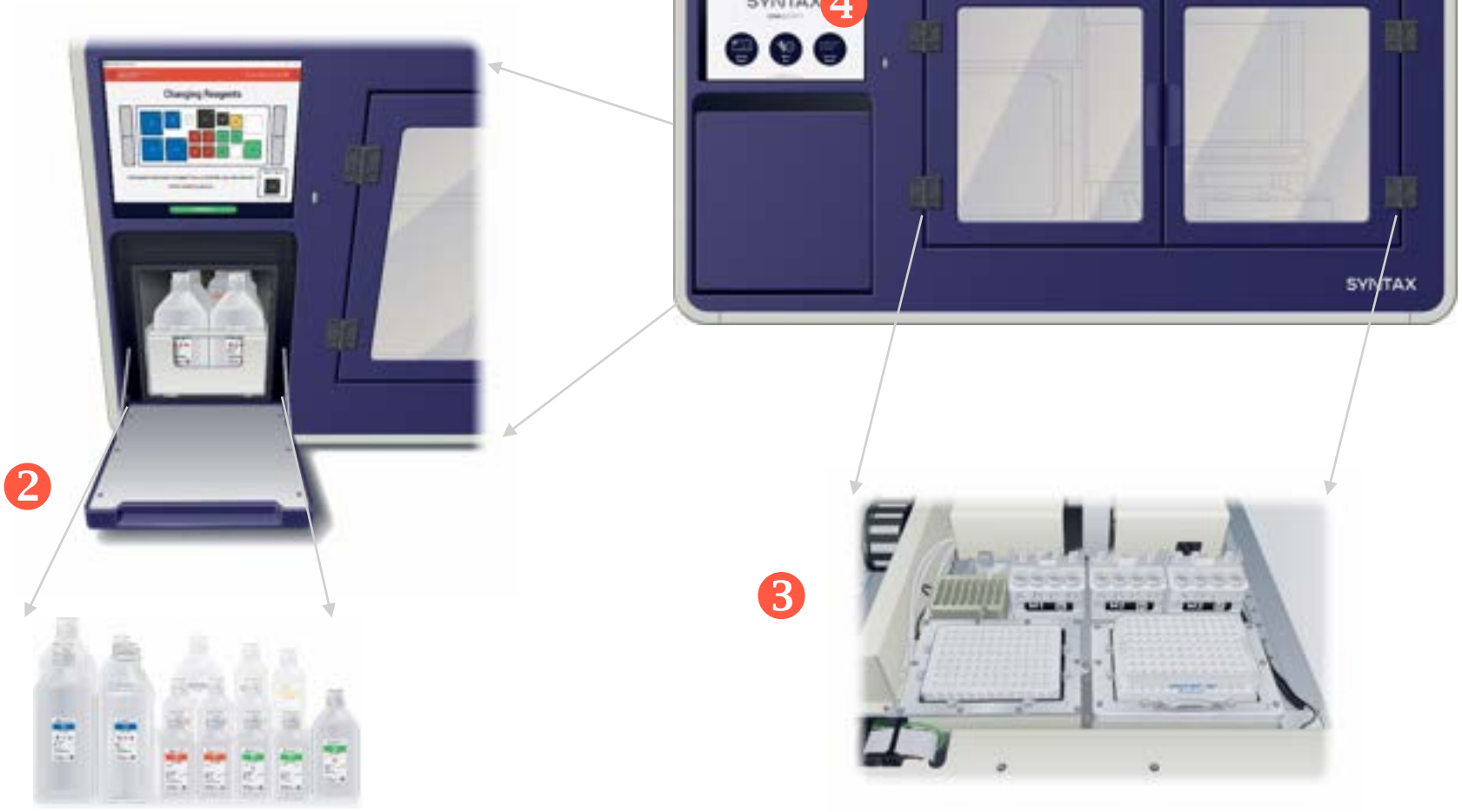
# PLUG-N-PLAY

❶ Load sequences → ❷ Load Reagents → ❸ Load microplates → ❹ Push button → get your oligos

15 - 30 min

- 96 oligos
- 20 mers
- 6h






# SYNTAX System

## Enzymatic DNA Synthesis Printer


STX–200 model now available

## FULLY INTEGRATED & AUTOMATED
## DESIGNED FOR DNA ON DEMAND

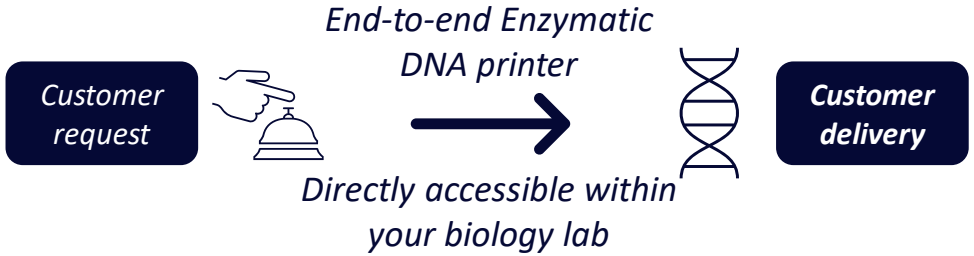
| | |
|---|---|
| | Synthesize, in parallel, any number of oligo - up to 96 or 384 |
| | Print oligos modified with fluorophores, quenchers, or biotin |
| | <15-min Hands-on Time<br>6-hr 20-mers \| 23,5-hr 120mers |
| | 15-120 nt oligo synthesis<br>+ customizable iDNA of 1-45 nt |
| G A T C | Scarless natural A, T, C and G |
| | Fully Automated:<br>Sequences in - oligos out |

DNASCRIPT

SECTION 05

# Example of COVID CRISIs in 2020

# COVID Crisis in **2020**


## Urgency at the Worldwide level


- Populations
- Governments
- Companies
- Biotechs & Pharmas

- Understand the phenomenon
- Activate task force
- Evaluate which resources, technologies & knowledge can be **rapidly** deployed
- Order **Oligos** for future vaccines

# The race for vaccine development

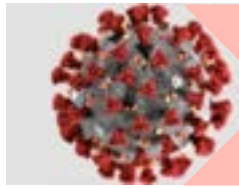
## DNA SYNTHESIS IS USED IN ALL STEPS OF THE EPIDEMIC RESPONSE

- Metagenomics
- Amplicon enrichment

- Monitor mutations
- Amplicon enrichment
- Sanger confirmation

- LAMP
- qPCR
- CRISPR diag

- Antibody development
- RNA and DNA vaccines



IDENTIFICATION → MONITORING → DIAGNOSTICS DEVELOPMENT → VACCINE DEVELOPMENT

The Jackson Laboratory

Two top US Labs asked for ARTIC primers ASAP!!

In both cases, we were able to deliver before commercial players

Institut Pasteur

NEW ENGLAND BioLabs Inc.

Sent LAMP oligos to multiple labs to develop new assays

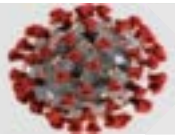
We received several requests from different groups for LAMP assay development. We sent oligos to 2 of them and managed to deliver before anyone else

moderna™ messenger therapeutics

DNA synthesis (genes) are needed for development and production

# Mutation monitoring

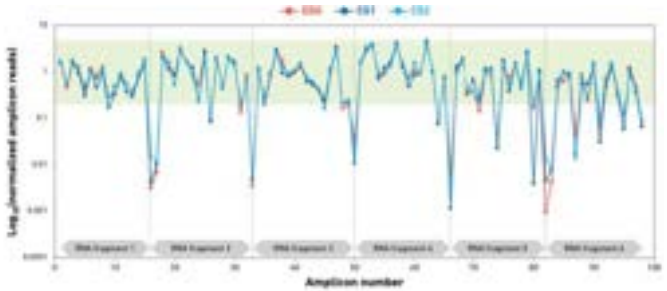
TOOK 3 MONTHS TO HAVE A GOOD WAY TO SEQUENCE SARS-COV-2



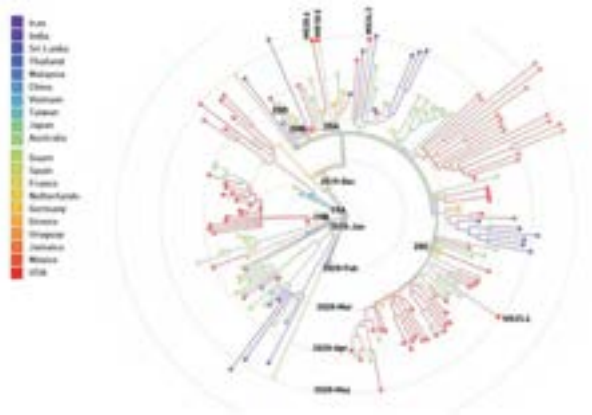
IDENTIFICATION | MONITORING | DIAGNOSTICS DEVELOPMENT | VACCINE DEVELOPMENT

You need to synthesize DNA to sequence DNA.
196 primers needed to sequence SARS-CoV-2

- Performance of our DNA strictly similar to the competition

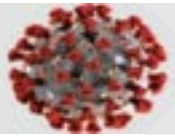


- Used our DNA to sequence 5 patients and identify mutations and virus evolution



# Mutation monitoring

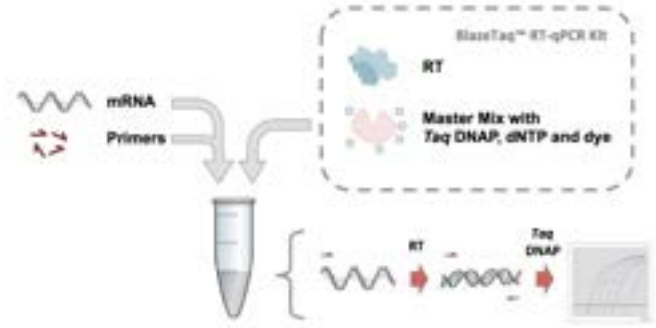
1 MONTH TO ORDER PCR DNA DELAYED TEST DEVELOPMENT IN 2020

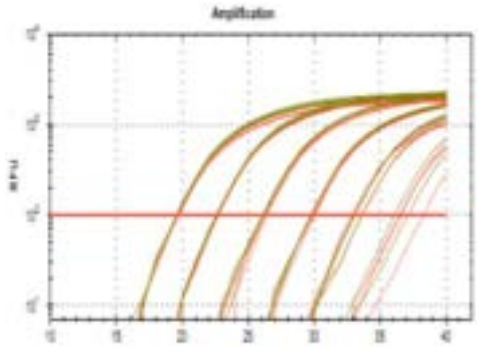


IDENTIFICATION | MONITORING | DIAGNOSTICS DEVELOPMENT | VACCINE DEVELOPMENT

You need to synthesize DNA to sequence DNA. 196 primers needed to sequence SARS-CoV-2

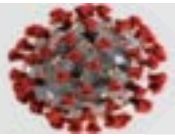
- Primers generated in the shortest possible time



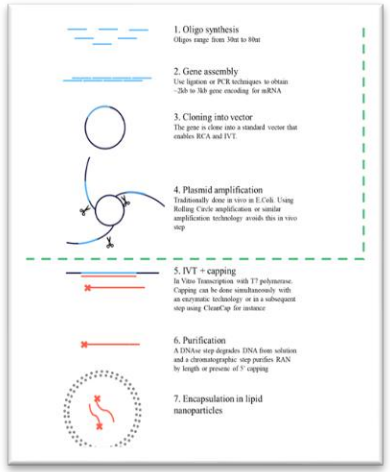
# Mutation monitoring

SYNTAX CAN ACCELERATE VACCINE DEVELOPMENT



IDENTIFICATION > MONITORING > DIAGNOSTICS DEVELOPMENT > VACCINE DEVELOPMENT

Be able to produce 500 doses of mRNA vaccine in 48h from a digital sequence in a truck

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DARPA

# Thank you

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DNASCRIPT

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# Un monde à risques de pandémies : vers quelle biorévolution industrielle ?

## MERCI POUR VOTRE PARTICIPATION !

**Cycle : Pour le Développement des Sciences et de l'Innovation (PDSI) au service des Transitions**

Jeudi 11 mai à l'Hôtel de l'Industrie