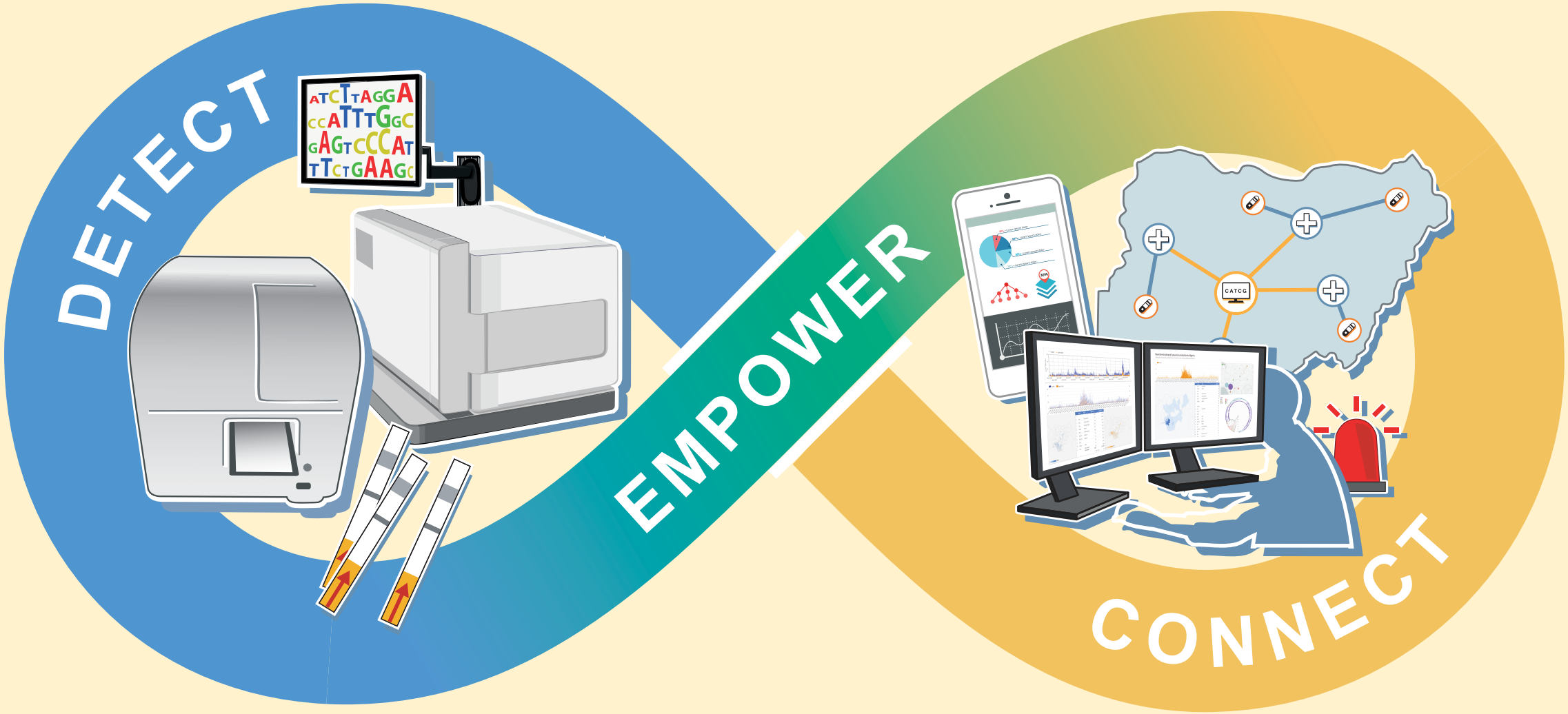


Sentinel – Pandemic response in the genomic and information age

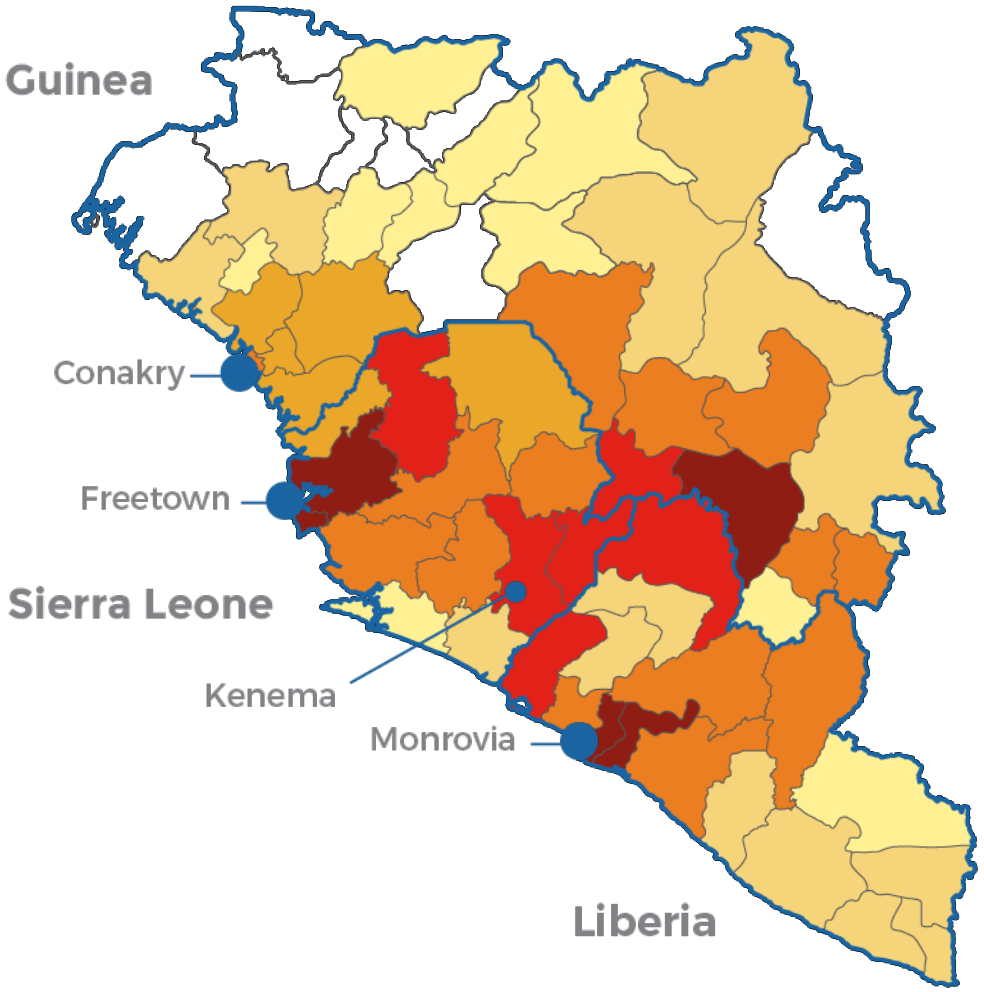
Conflict of Interest

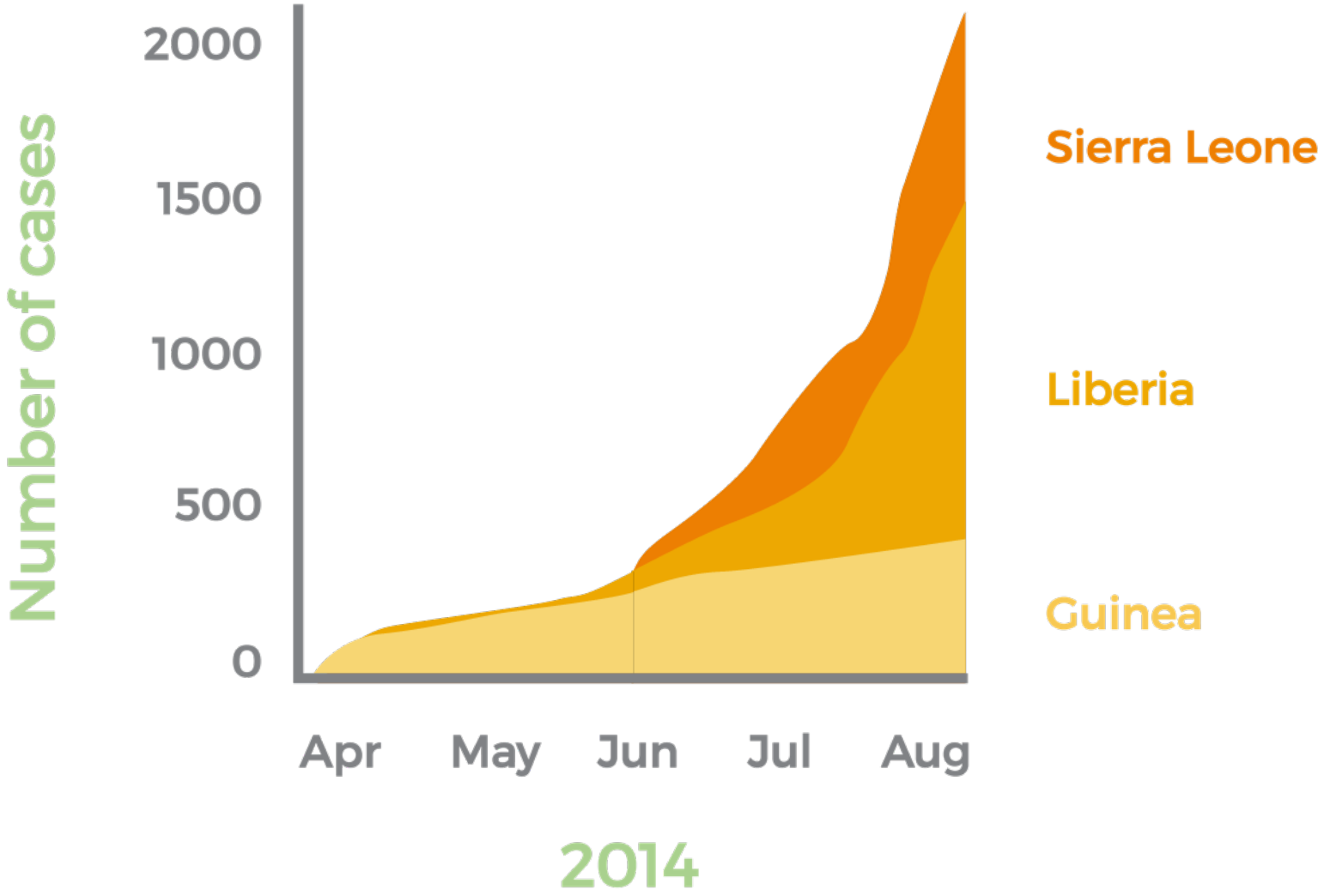
- Co-founder, consultant, and shareholder in Sherlock Biosciences
- Board member and shareholder of Danaher Corporation (Cepheid, IDT)

MARCH 2014

"The Ebola virus has been identified as the cause of an outbreak of haemorrhagic fever now believed to have killed nearly 60 people in southern Guinea, government officials say."

BBC News
Sat 22 Mar 2014


Guinea
Conakry
Freetown
Sierra Leone
Kenema
Monrovia
Liberia


Number of cases
2000
1500
1000
500
0
Apr
May
Jun
Jul
Aug
2014
Sierra Leone
Liberia
Guinea

BIOHAZARD
CLOSED

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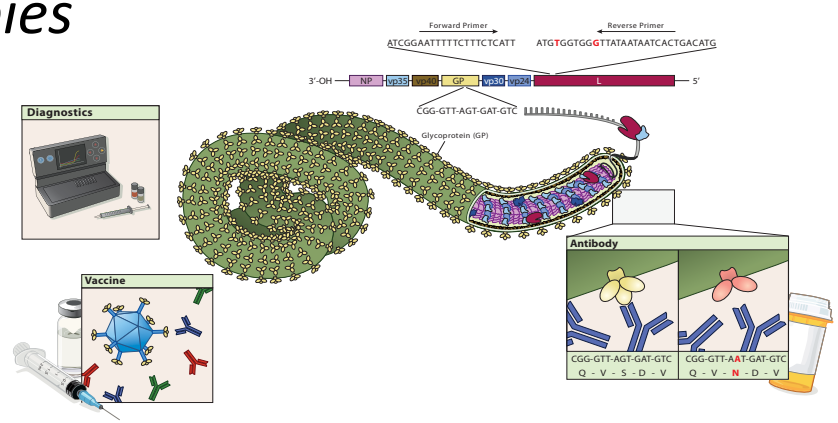
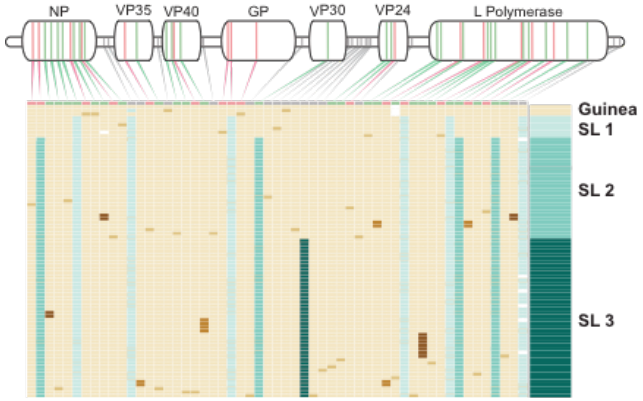
Genomics Can Provide Powerful Information in Real-Time

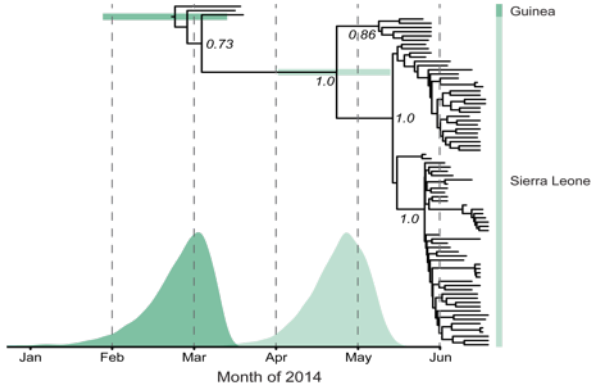
Informing diagnostics, vaccines, and therapies



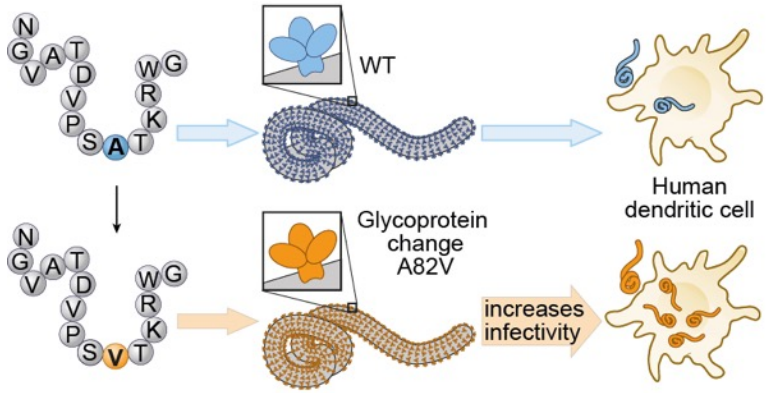
Identifying variation across the genome



Tracking and characterizing outbreak transmission



Getting to functional mutations

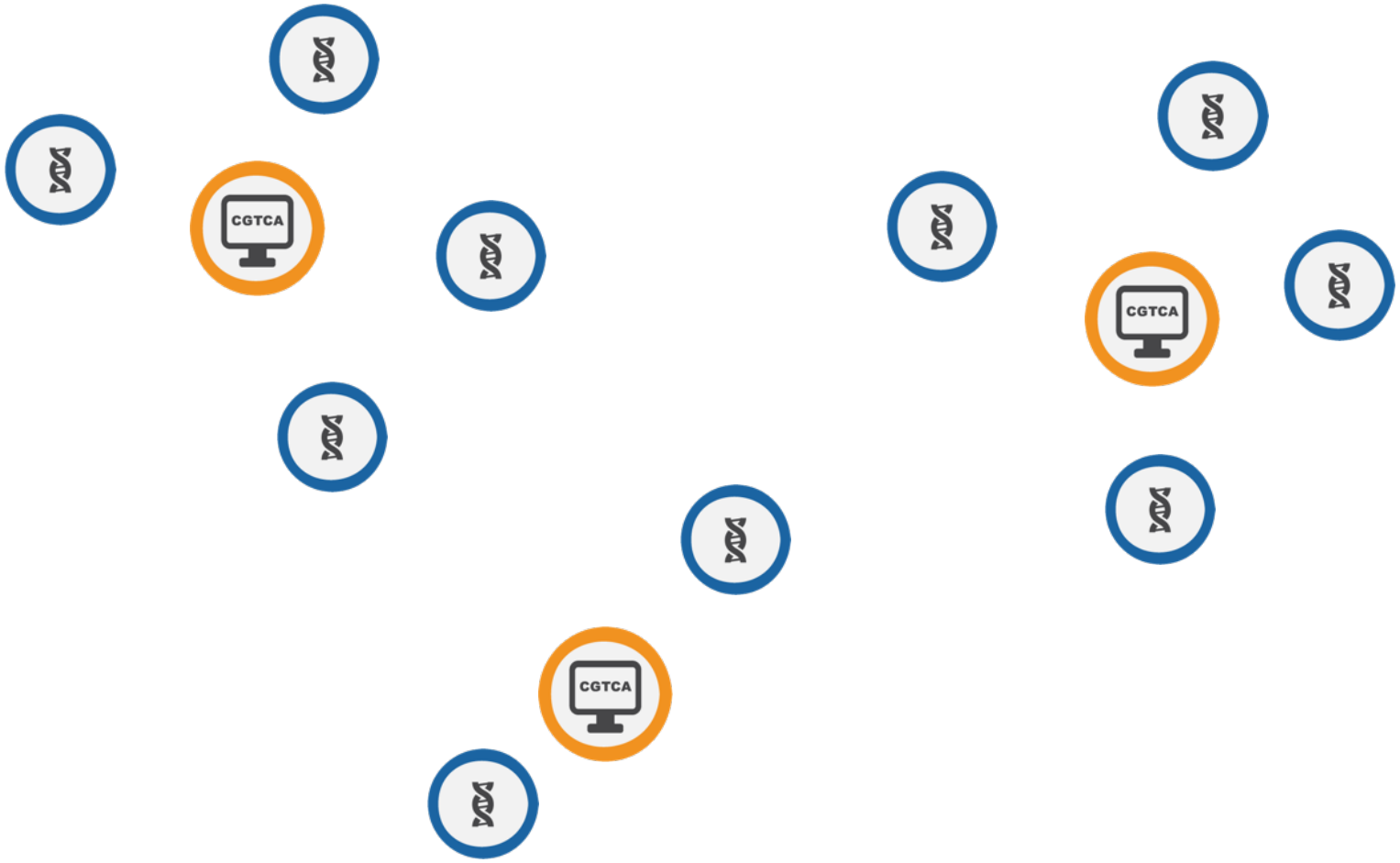


Gire et al. *Science* 2014, Park et al. *Cell* 2015, Diehl et al. *Cell* 2016

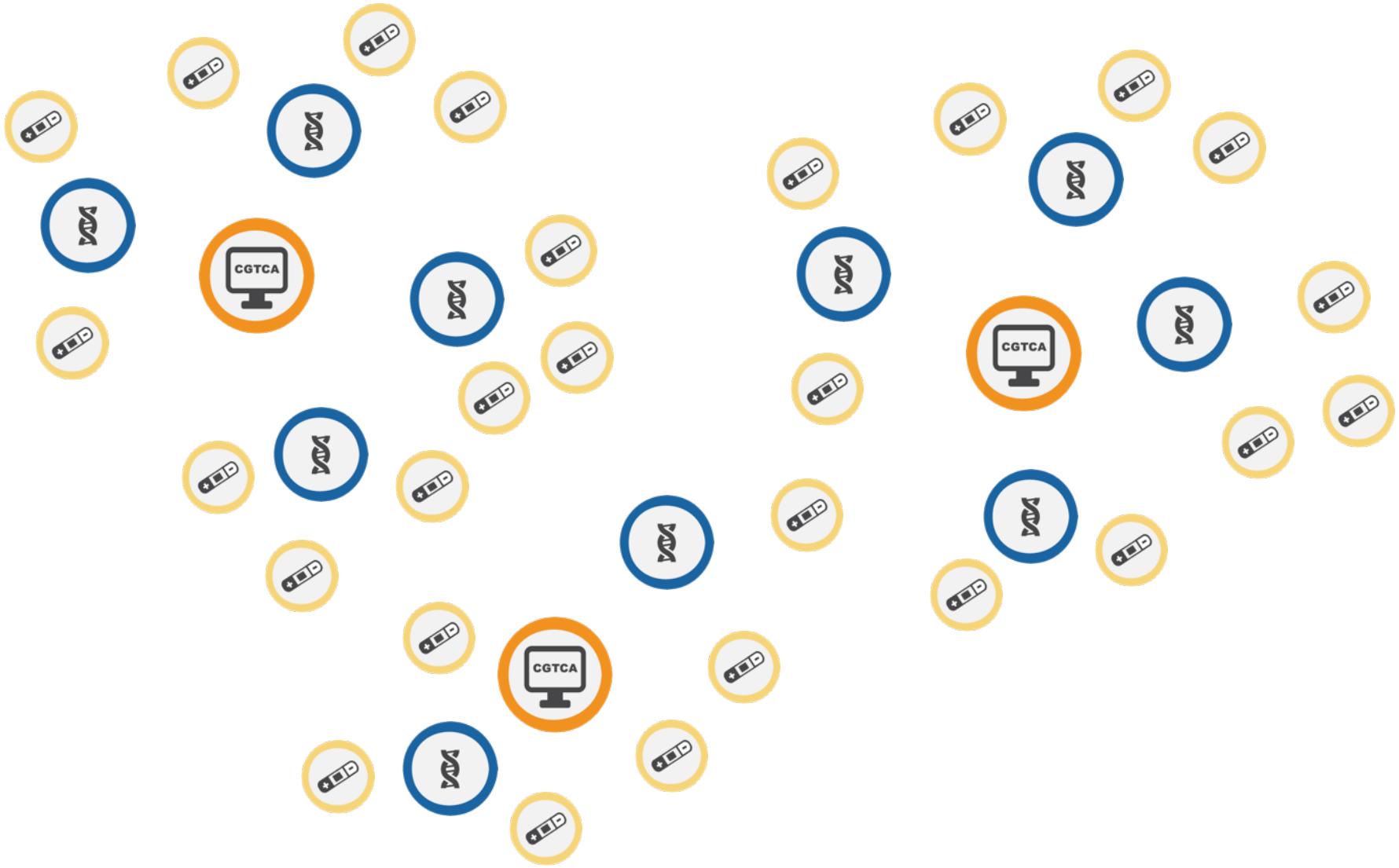
BAefiteare

EBOLA SOMETIME LIVES IN ANIMALS LIKE MONKEY
AND BAT
YOU EAT THEM YOU MAY GET
EBOLA

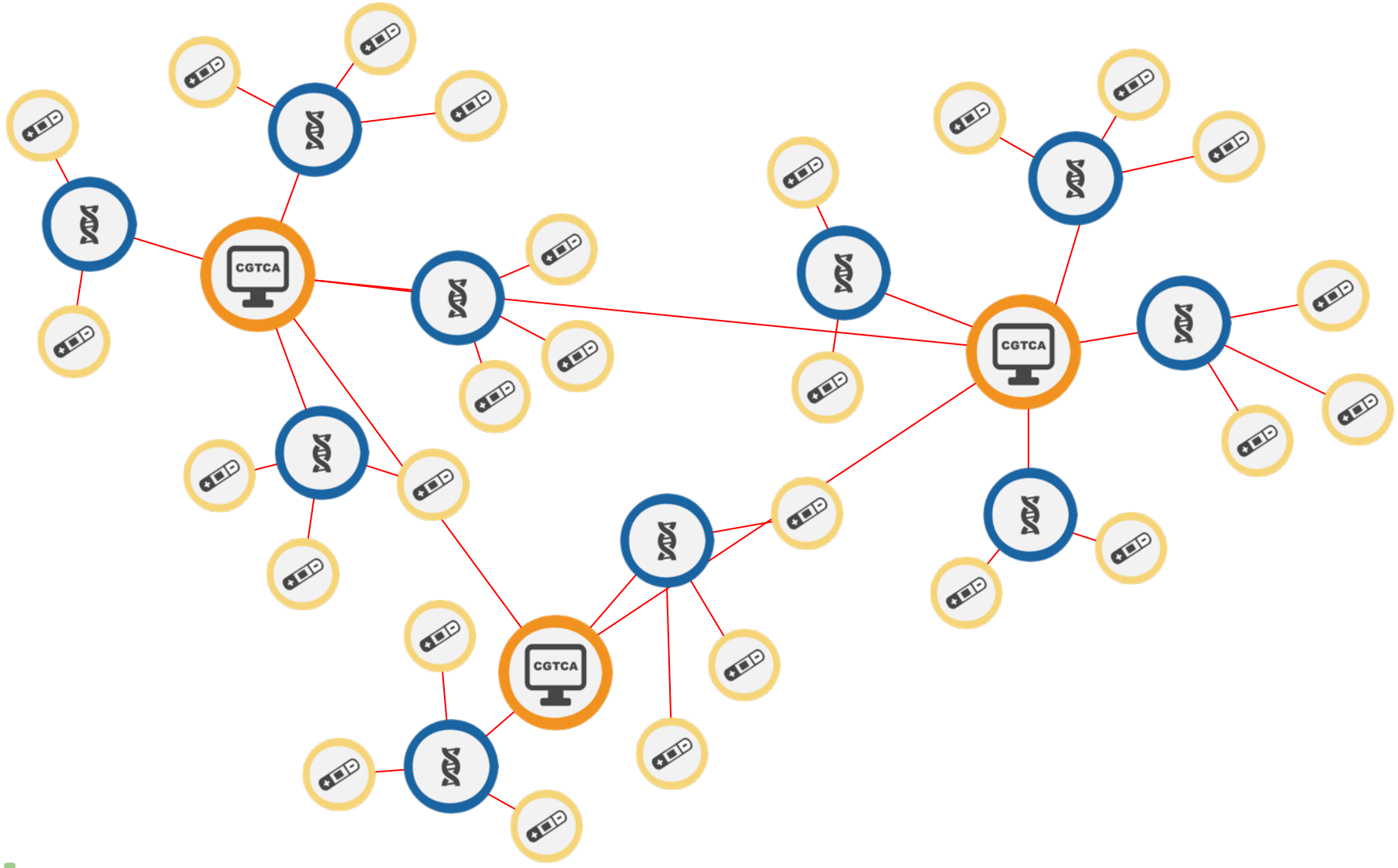
Detect



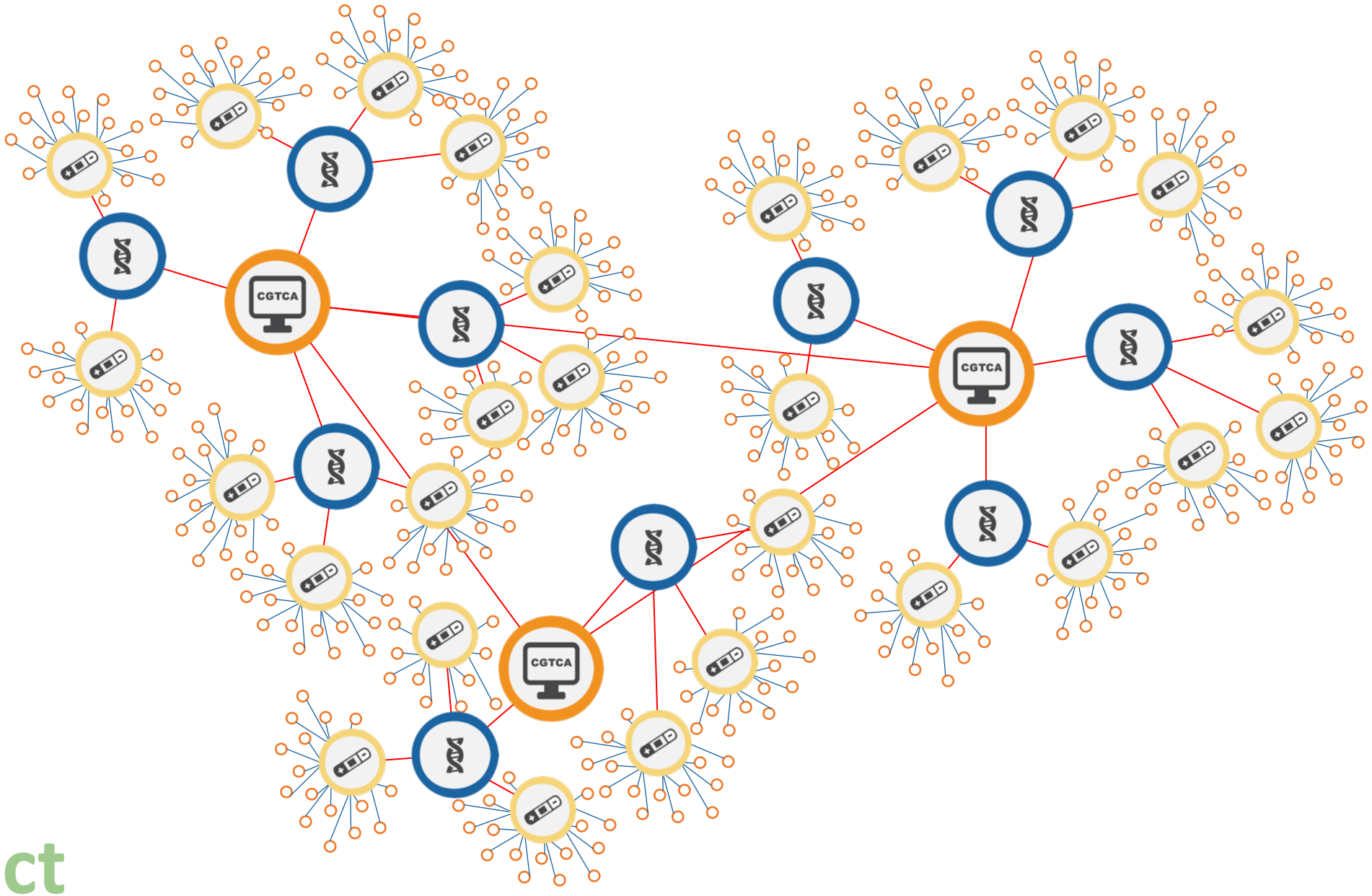
Detect



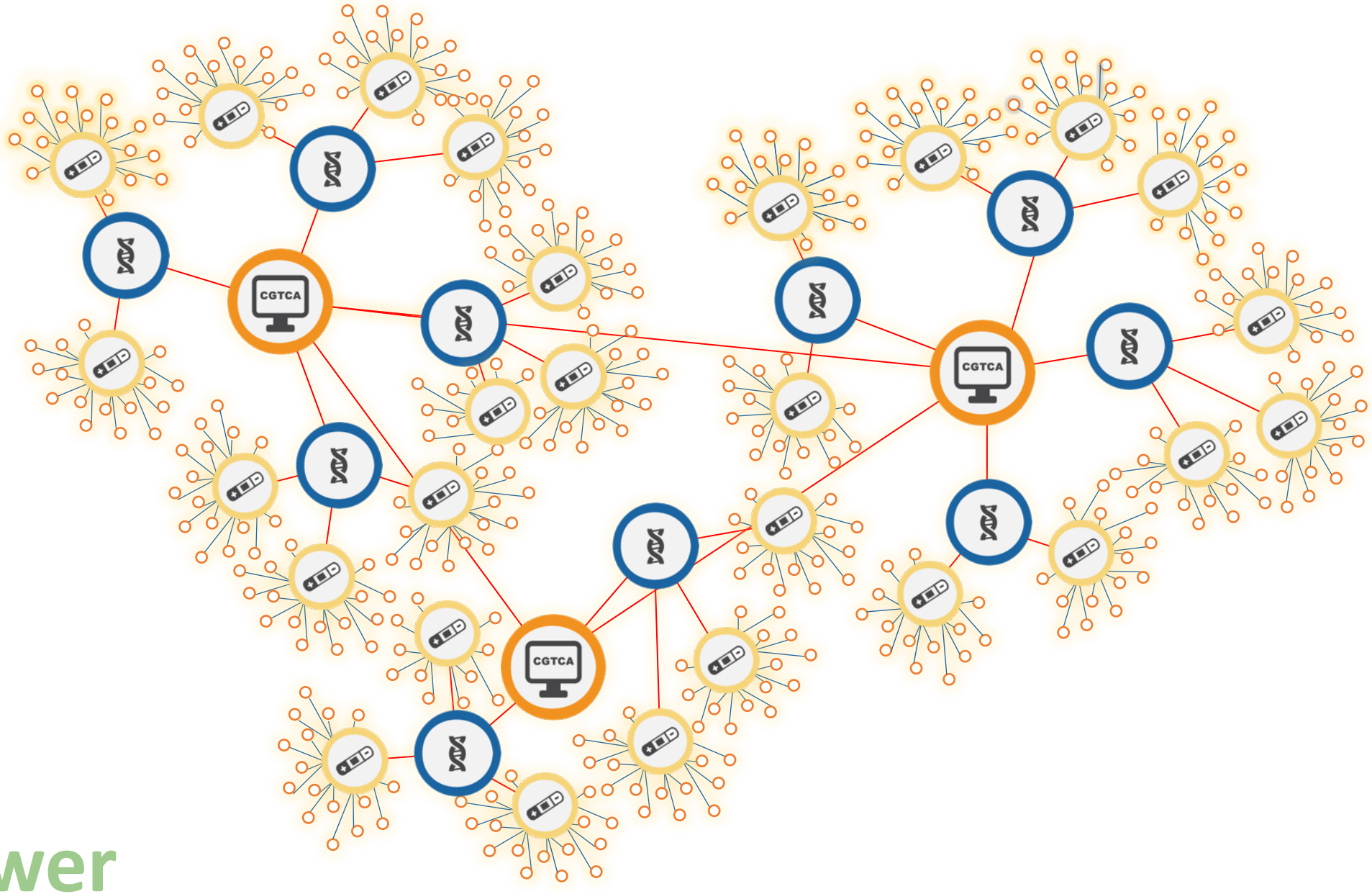
Detect



Connect

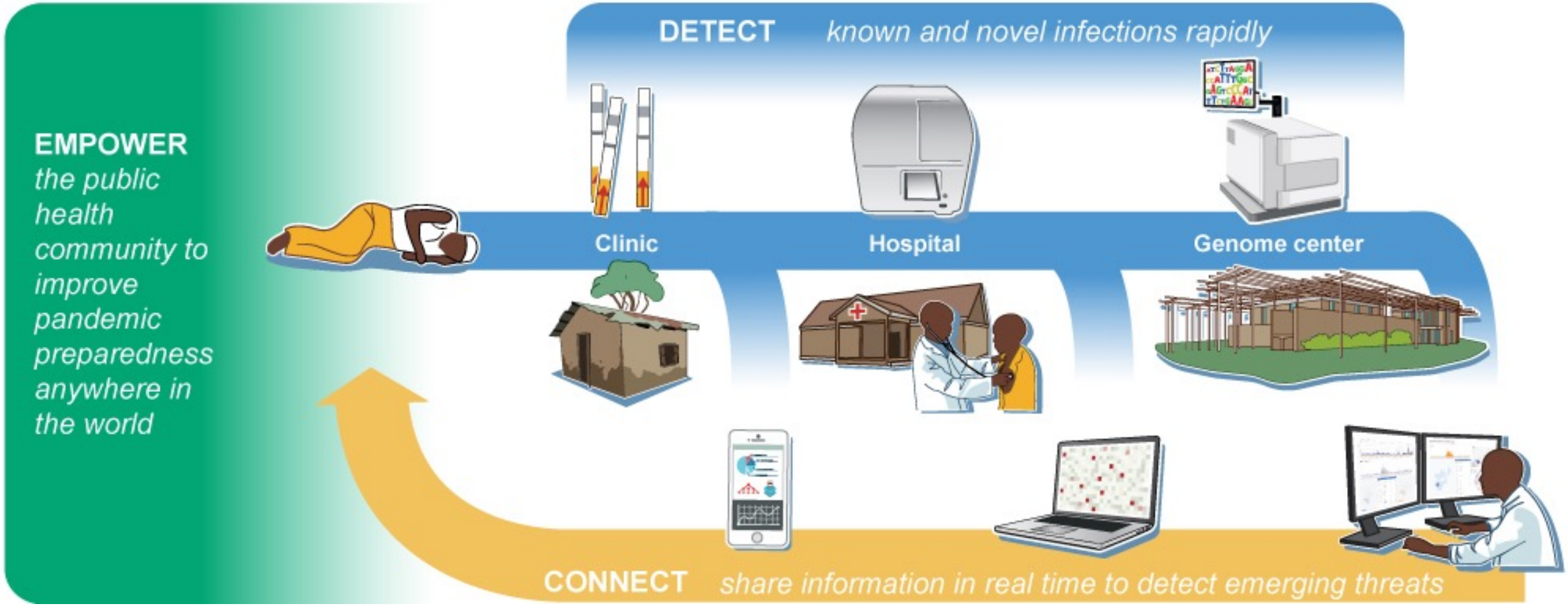


Connect



Empower

Sentinel


EMPOWER
the public health community to improve pandemic preparedness anywhere in the world
DETECT
known and novel infections rapidly
Clinic
Hospital
Genome center
CONNECT
share information in real time to detect emerging threats

Detect

GGTGGAAAGTTGTTGGGCGGTATAGAGTTTGATGTGACTCACAAAGGATGGCCTATTGCATAGACTG
AAAACTAATGACTTTGCCCCTGCATGGTCAATGACAGGAACCTATTTCCCATTTA ATCCGA
ATTCCACATTGAATCACCGCTGTGGGCACTGAGAGTCATCCTTGCTGCAGGGA GTTA
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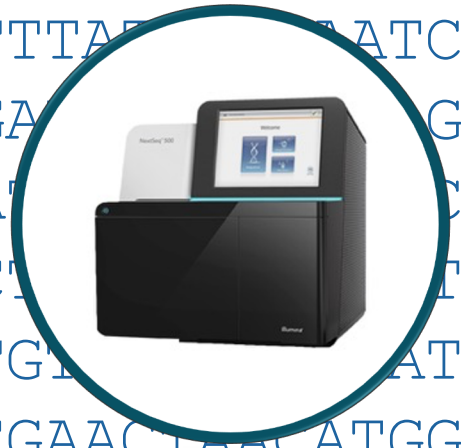
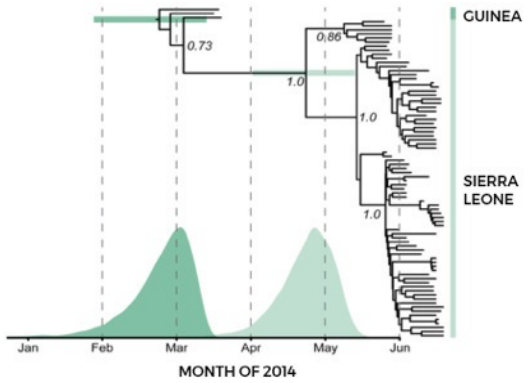
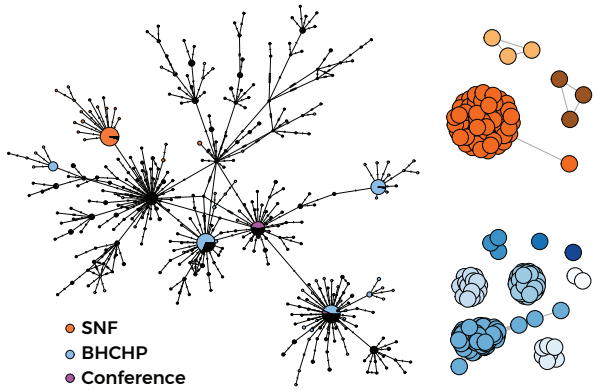


Detect: Genomics informs public health response

Transmission Patterns

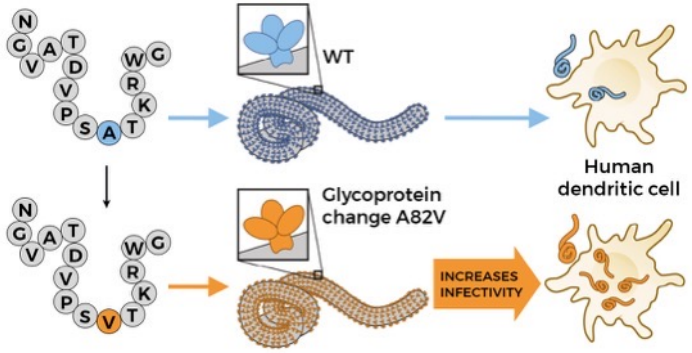


Ebola was spreading human to human

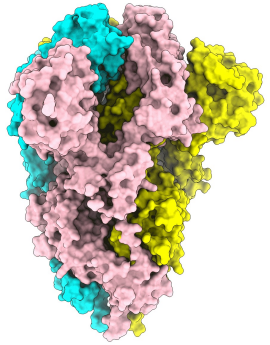


COVID driven by superspreader events

Novel Mutations

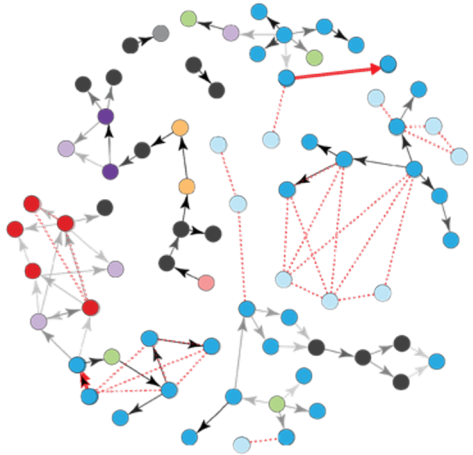


Ebola mutations increased infectivity



COVID's D614G mutation does as well

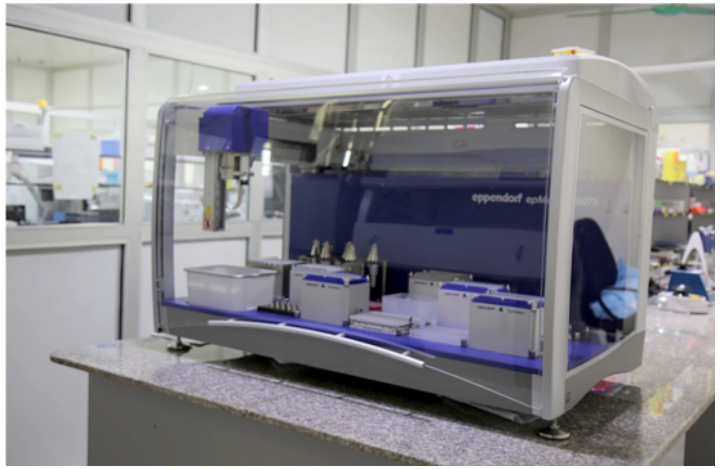
Contract Tracing



Traditional epi is accurate but underpowered

Gire et al. *Science* 2014, Lemieux et al. *Science* 2020, Diehl et al. *Cell* 2016, Yurkovetskiy et al. *Cell* 2020, Wohl et al. *PLoS Biology* 2020

ACEGID has become a national diagnostic center

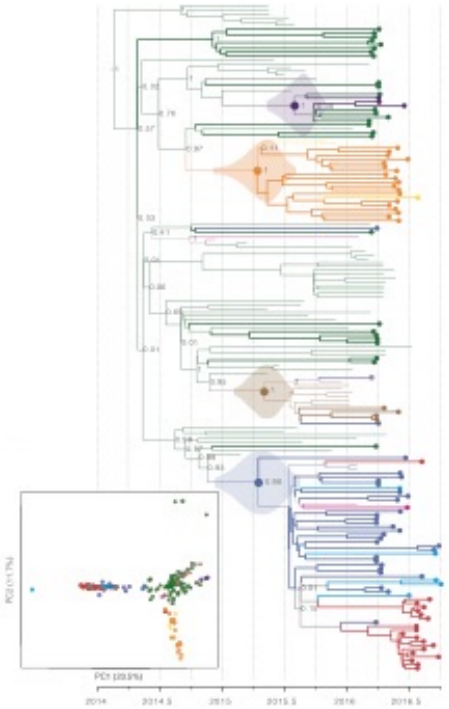


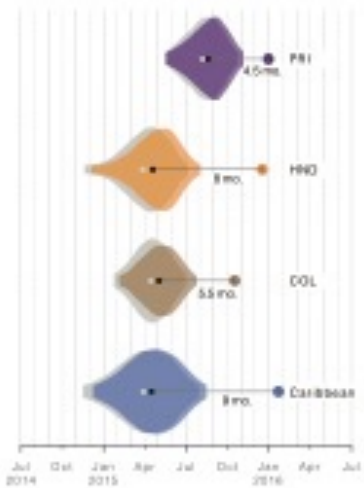
- Established diagnostics in early February in Nigeria, Sierra Leone and Senegal
- Running 1k diagnostics a week
- Serving 30 million people in Nigeria

ACEGID
African Centre of Excellence for Genomics of Infectious Disease
Redeemer's University, Nigeria

Zika – deployable diagnostics

Virus circulating months before first detection



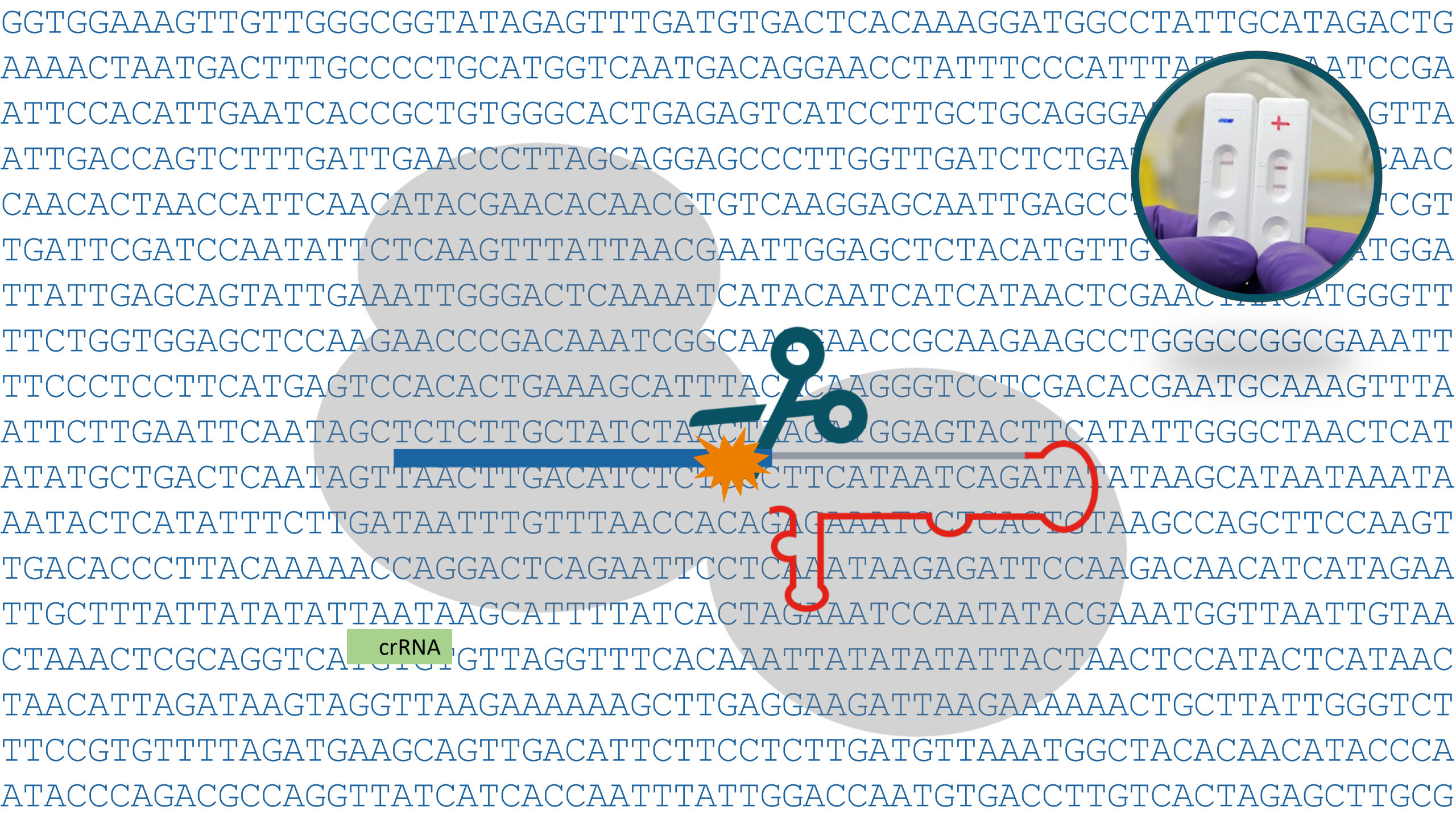


The New York Times

Pregnant Women Anxious as Florida's Zika Test Results Take Weeks

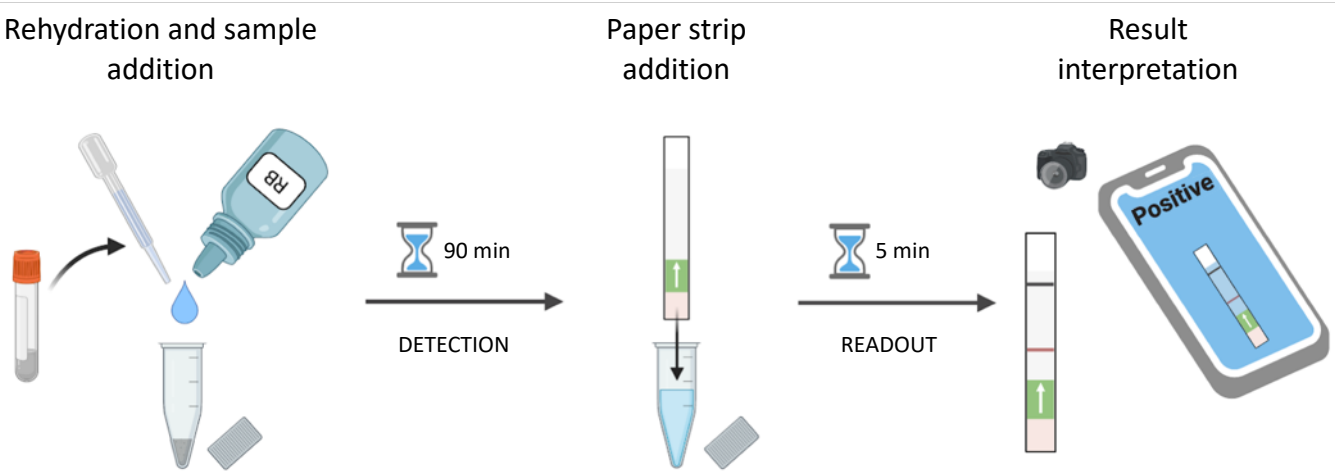
By LIZETTE ALVAREZ SEPT. 12, 2016

Metsky et al. *Nature* 2017, Myhrvold et al. *Science* 2018

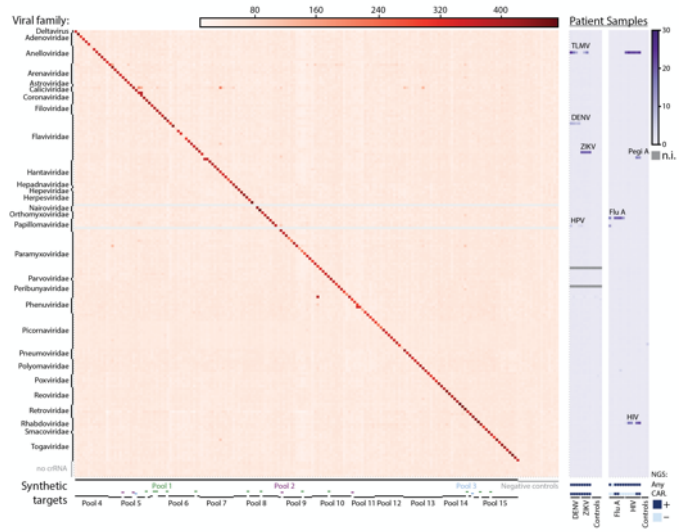

crRNA

DETECT: with new technologies

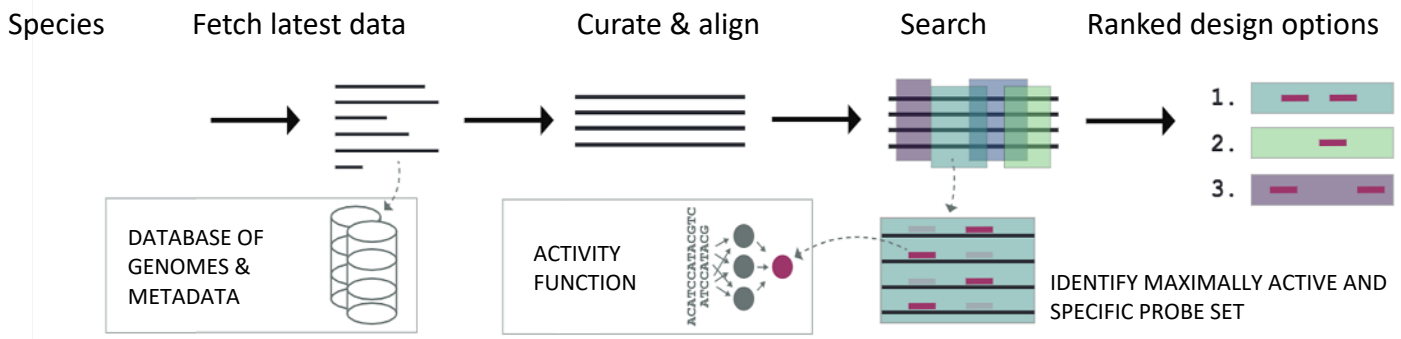
Point-of-Care



Massive Throughput

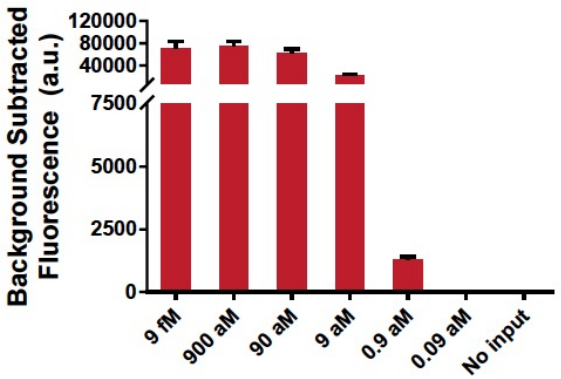


Rapid Deep Learning-Based Design



CRISPR-Cas13 can achieve these goals

Highly sensitive assay



Fully field deployable

Urine

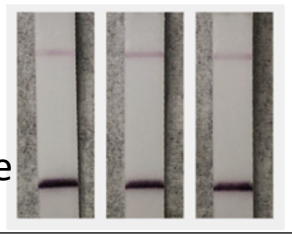
Saliva

Dengue Patient

Healthy

Test line

Control line

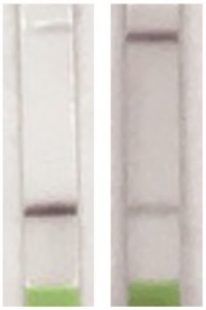


Distinguishes subtypes and variants

patient genotype: WT

Test line

Control line



Rapid assay development

Day 1:
Design crRNAs & RPA primers

Days 2-5:
crRNAs, primer, target synthesis

Day 6:
lab testing

Gootenberg et al. *Science* 2017; Myhrvold, Freije et al. *Science* 2018

DETECT: with new technologies

MENU **nature** Subscribe Search

NEWS · 19 FEBRUARY 2019

Faster, better, cheaper: the rise of CRISPR in disease detection

Powerful gene-editing tool could help to diagnose illnesses such as Lassa fever early and rein in the spread of infection.

Amy Maxmen

AMY MAXMEN

A researcher in Nigeria uses a CRISPR diagnostic test to look for Lassa virus in a blood sample.

EPIDEMIOLOGY

CRISPR tools help to detect illnesses

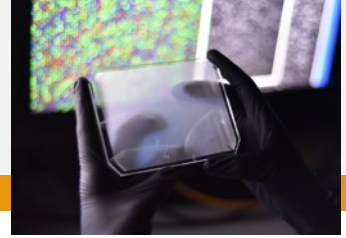
Researchers turn to powerful gene-editing method to diagnose diseases and curb the spread of infections.

Incubation Time	Sensitivity	Specificity
30 mins	90%	94%
1 hour	94.7%	97%
2 hours	98%	98%

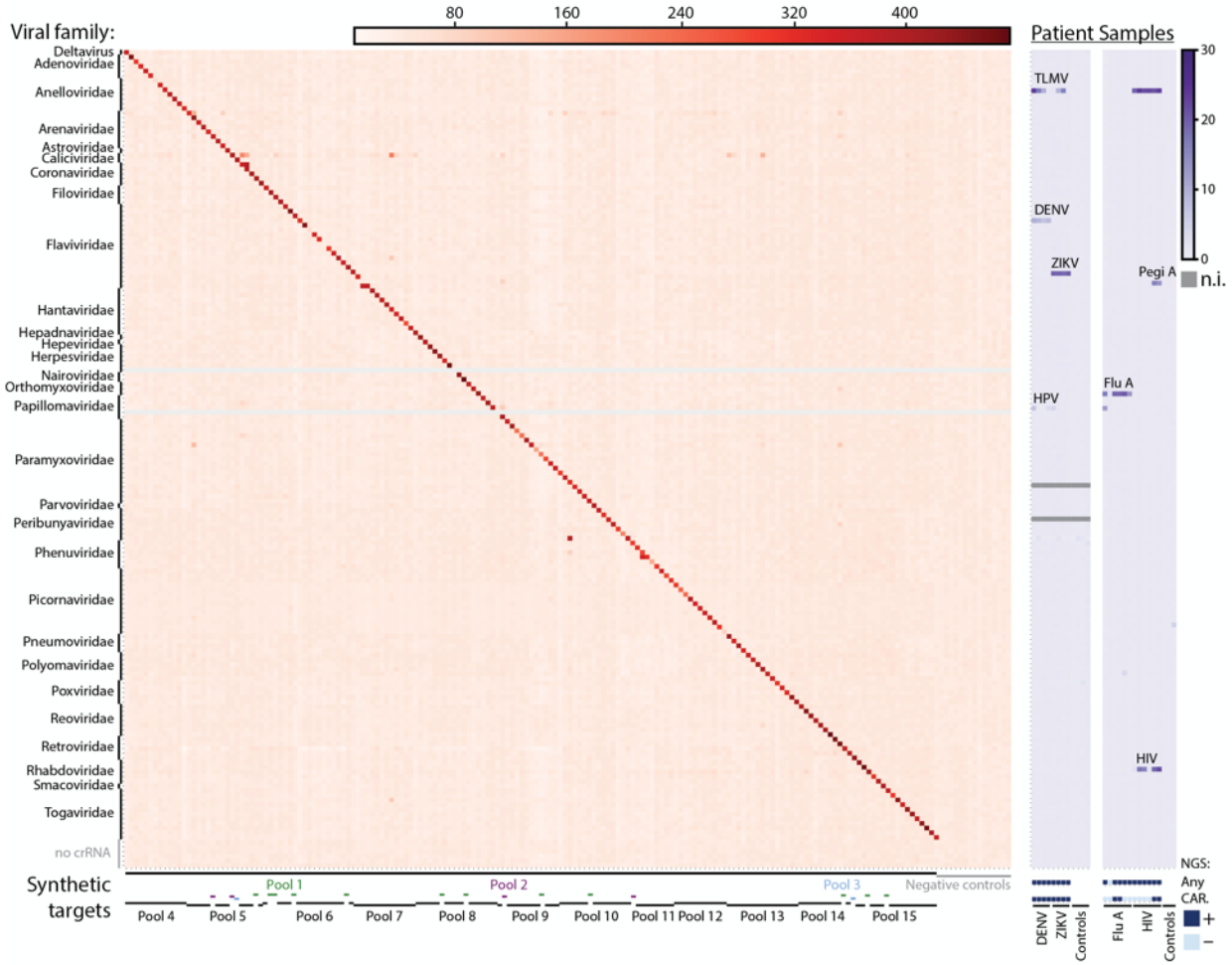
Note: samples tested have qPCR Ct <30

ACEGID
African Centre of Excellence for Genomics of Infectious Disease
Redeemer's University, Nigeria

CARMEN – High Throughput Diagnostics

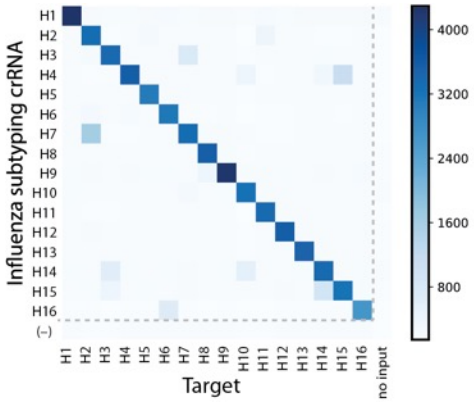


Distinguishes human associated viruses

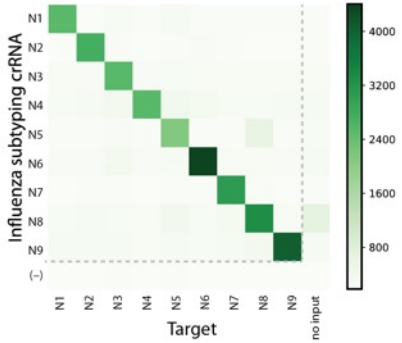


Distinguishes subtypes and variants

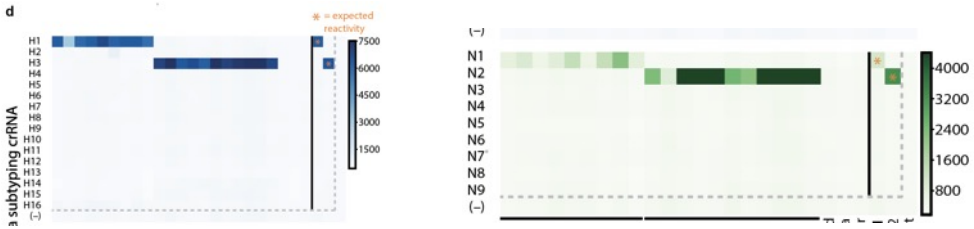
H1-H16



N1-N9

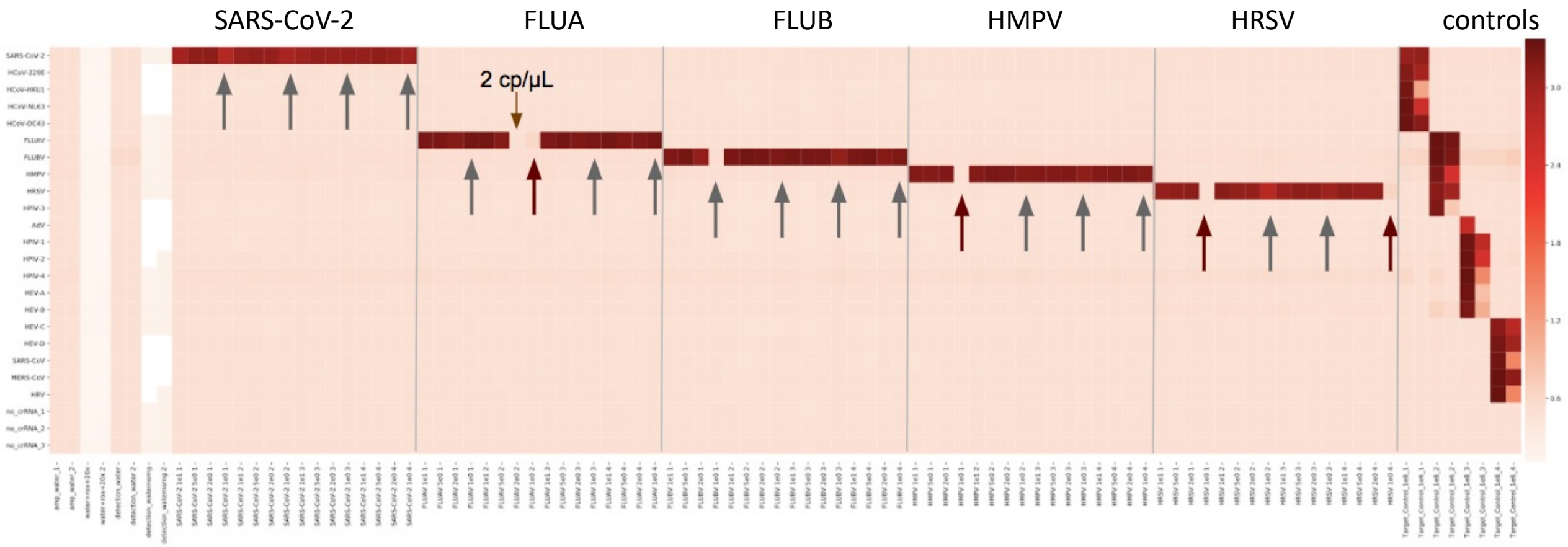


Works well on clinical samples



Ackerman, Myhrvold, *Nature* 2020

CRISPR-Cas13 can be run on Fluidigm



Synthetic targets ranging from 10 cp/µL to 1 cp/µL

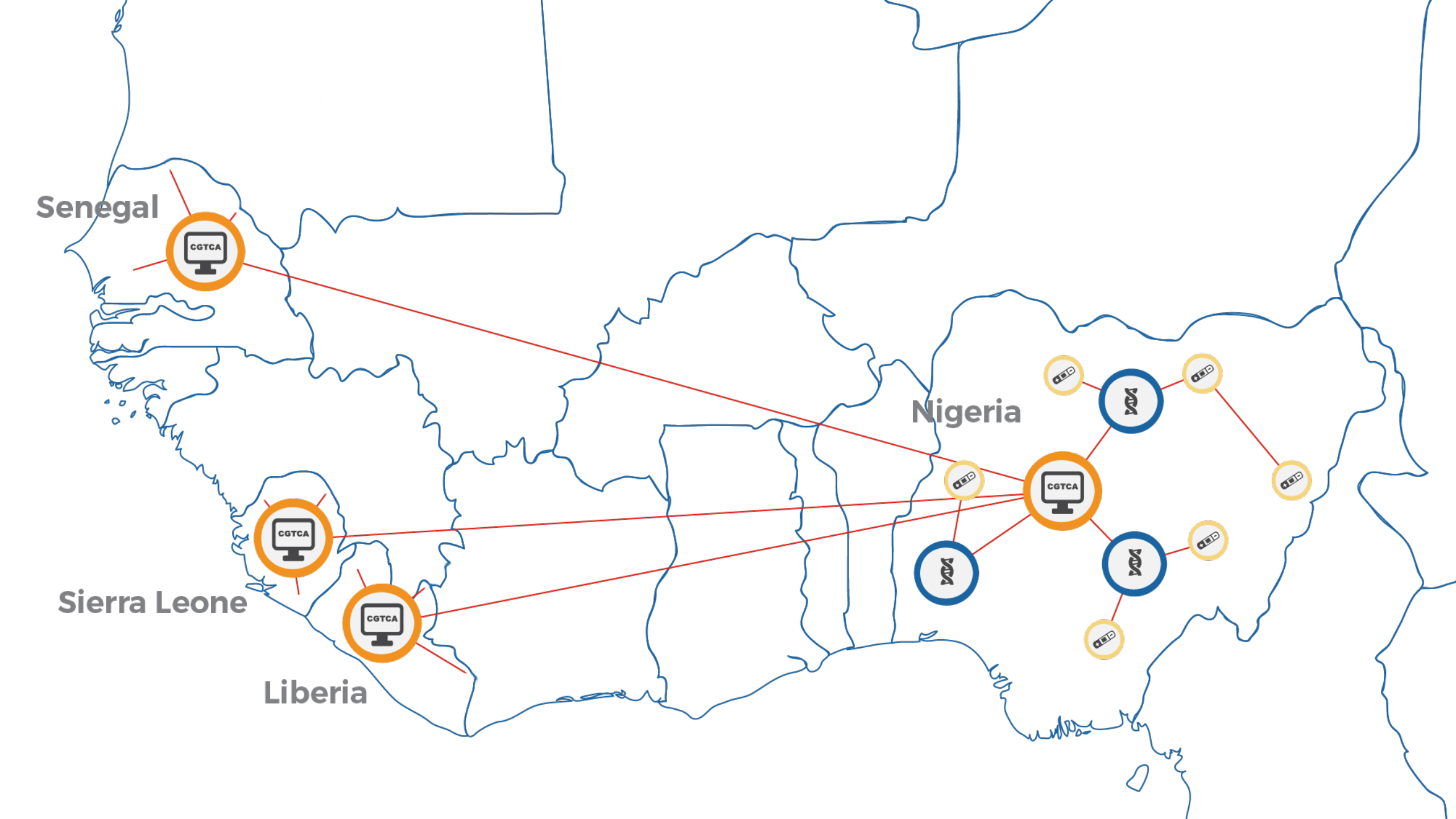
1 cp/µl detected

1 cp/µl not detected

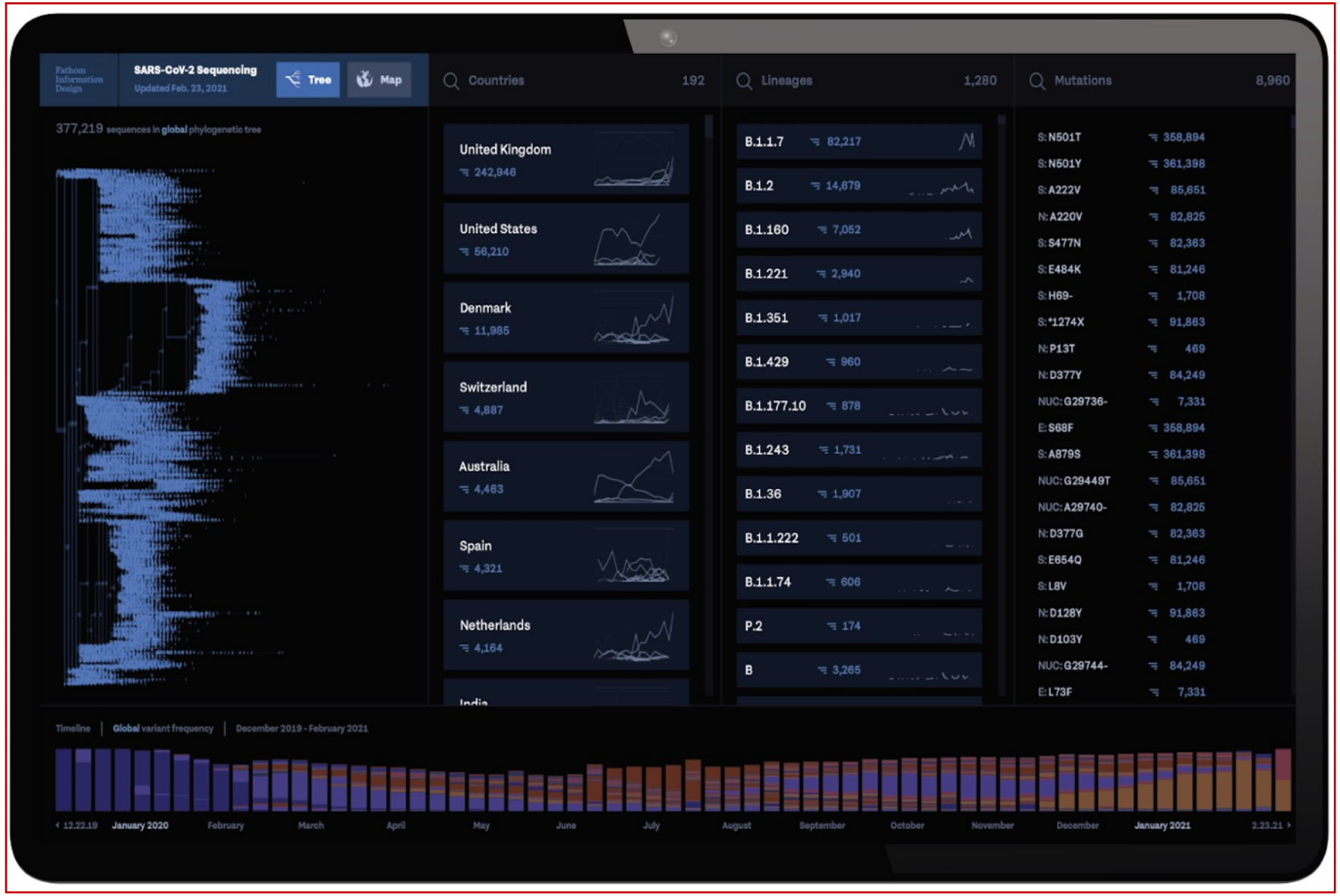
LOD around 1 - 5 copies/µL

Connect

CONNECT: frontline workers with actionable information


Senegal
CGTCA
Nigeria
CGTCA
Sierra Leone
CGTCA
Liberia
CGTCA

Creating global views of all genomics datasets



Fathom Information Design & Broad Institute

Fathom Information Design

Global sequencing

SARS-CoV-2 • Feb. 23, 2021

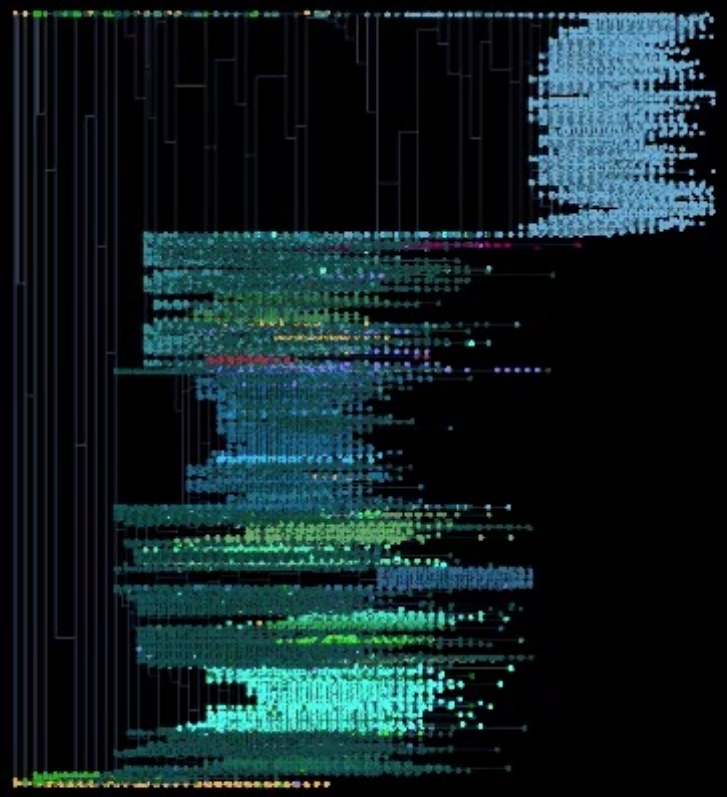
Countries 172

Lineages 1,246

Mutations 61,302

544,234 sequences

902,640 additional cases without sequences



UK	327,826
USA	214,625
Denmark	50,525
Germany	38,751
Canada	23,510
Switzerland	21,873

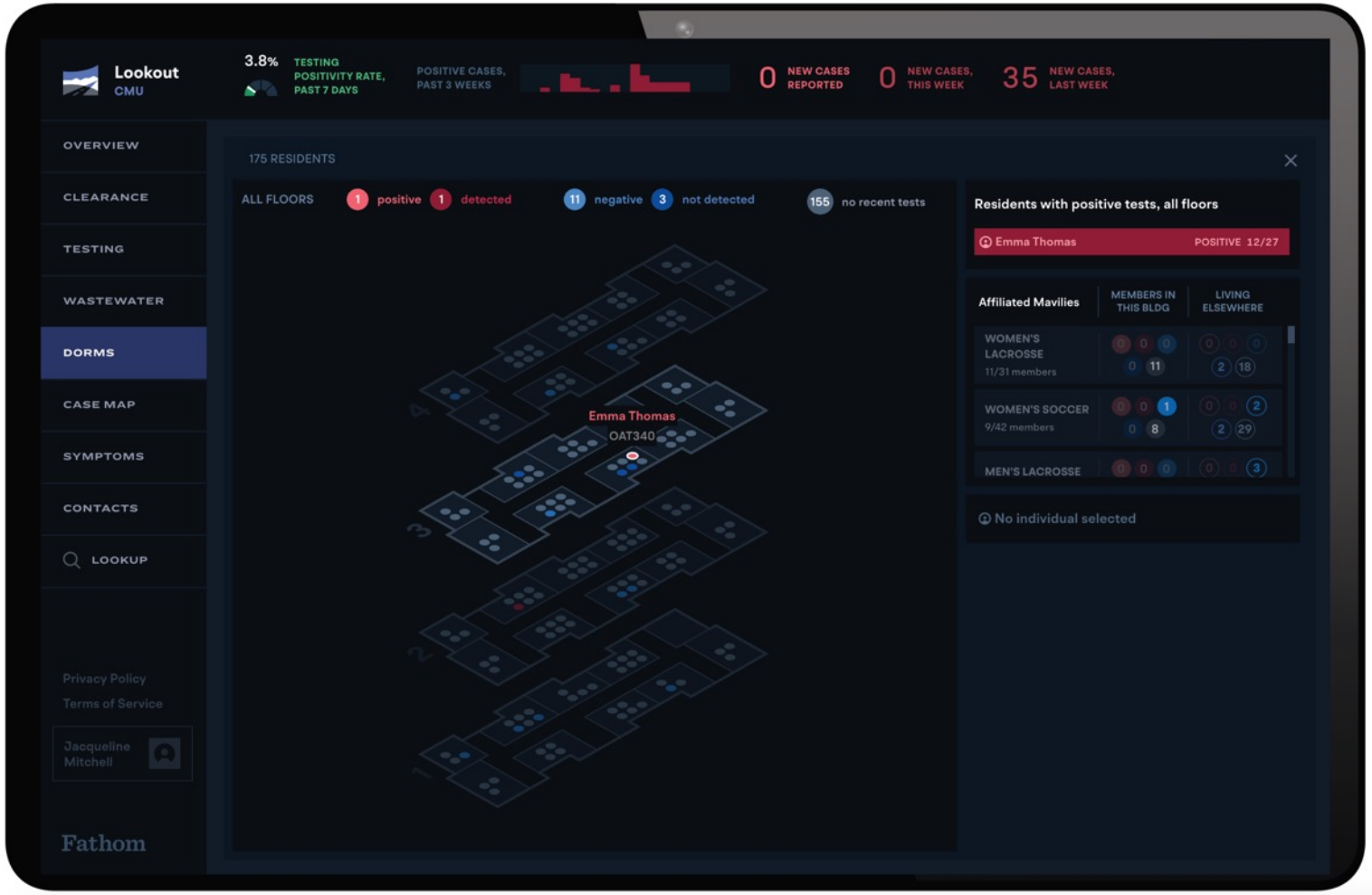
B.1.1.7	231,769
B.1	68,339
B.1.177	62,818
B.1.2	59,311
B.1.1	38,815
B.1.160	17,699
D.2	12,713
B.1.429	12,622
B.1.177.21	10,473
B.1.221	10,406
B.1.258	10,235
B.1.1.214	8,655

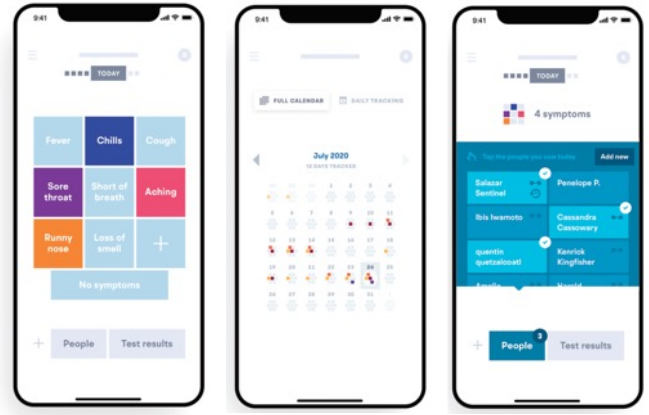
S:D614G	866,076
S:N501Y	237,663
S:A570D	231,117
S:L452R	21,037
S:E484K	13,895
S:A701V	9,872
S:K417N	5,801
S:D253G	5,032
S:A67V	1,913
S:F888L	934

Timeline

Mar. April May June July August September October November December Jan. 2021 Feb. Mar.

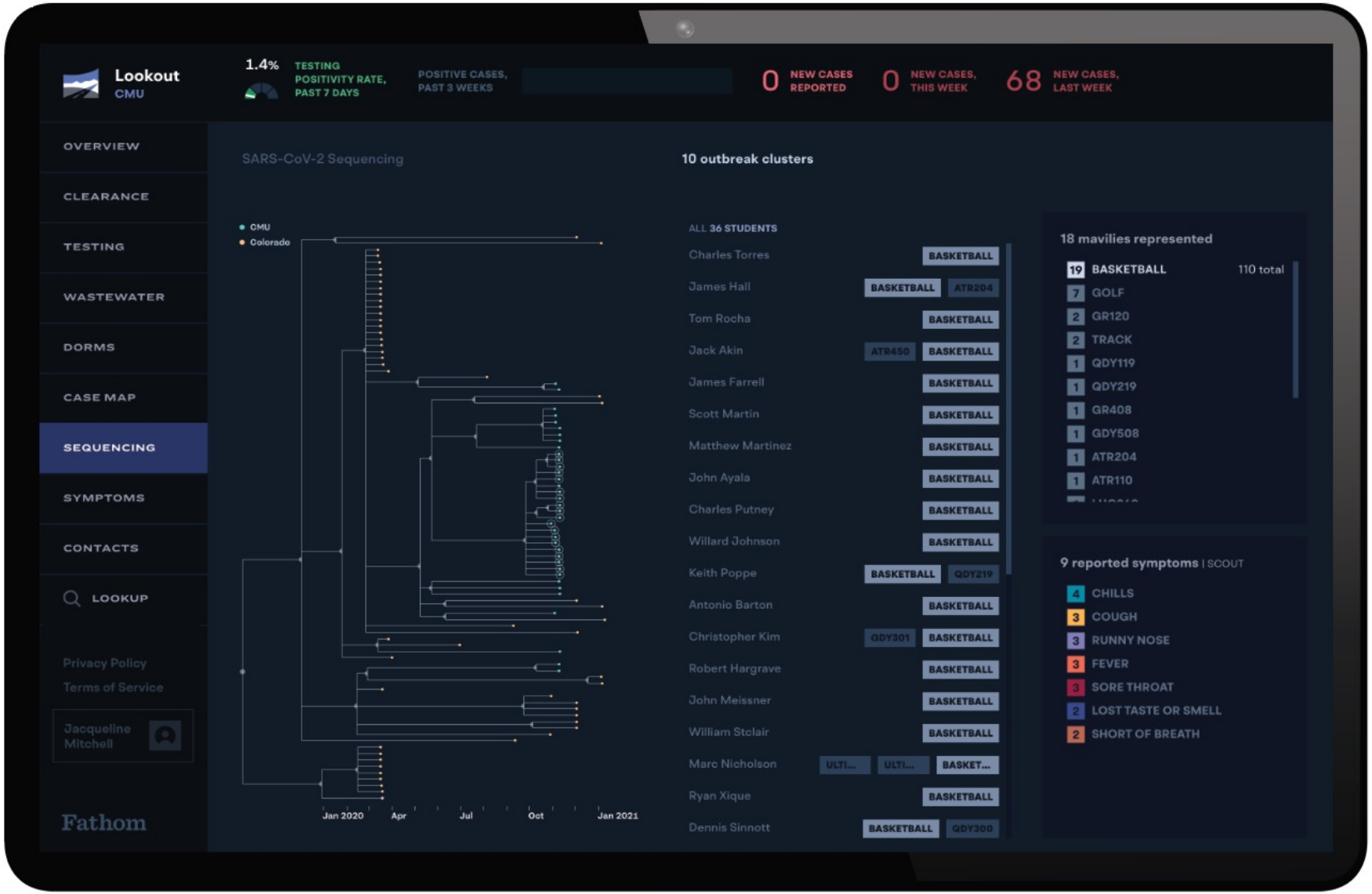
Enhancing public health investigations





Fathom Information Design & Broad Institute (data based on real work at CMU, but anonymized)

Combining genomic and epi data



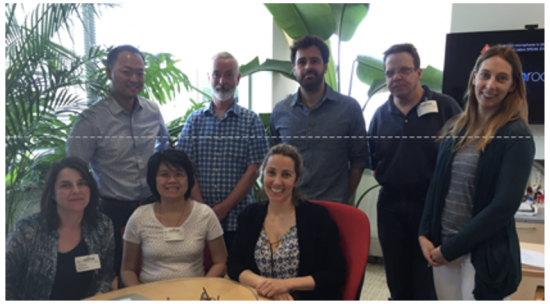
Fathom Information Design & Broad Institute (data based on real work at CMU, but anonymized)

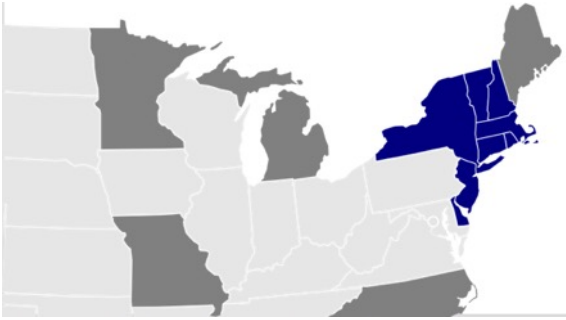
Empower

All outbreaks - importance of empowering every actor

ACEGID
AFRICAN CENTRE OF EXCELLENCE FOR GENOMICS OF INFECTIOUS DISEASES

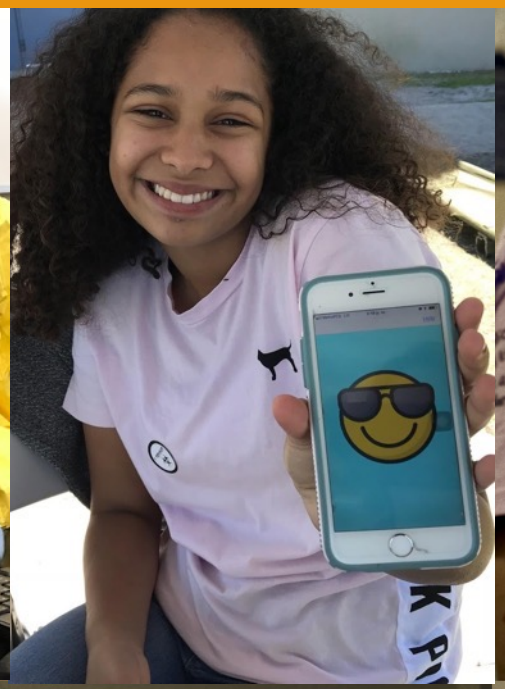
CDC





EMPOWER: every actor in the system

Operation Outbreak



OO mobile app

Asymptomatic

$P_{sick} = 0.6$

$P_{v.sick} = 0.4$

Sick

Very sick

$P_{sick \to rec} = 0.6$

$P_{sick \to dead} = 0.5$

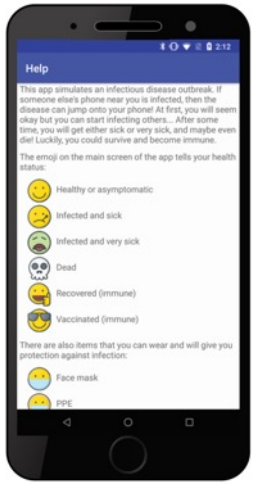
$P_{v.sick \to rec} = 0.1$

$P_{v.sick \to dead} = 0.9$

Recovered

Dead

Can test interventions



Mask

Vaccine

OO Data

Visualize **ground truth** data, including "patient zero" and all transmission events.

Track **super-spreader** events.

Monitor **infection patterns**.

Assign, in real-time, **physical distancing** scorecards to individuals and institutions.

Colubri *et al.*, *Cell* 2020

OPERATION OUTBREAK

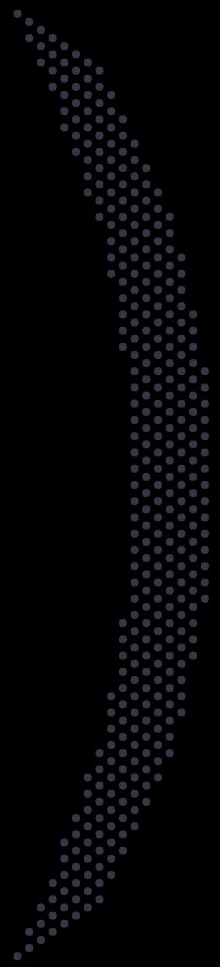
358 PARTICIPANTS

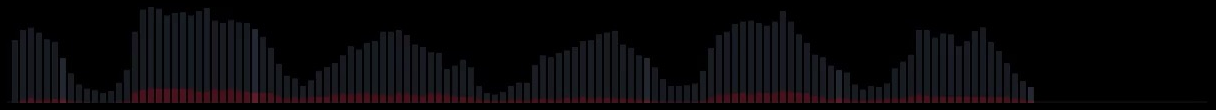
0
INFECTED

0
RECOVERED

0
VACCINATED

0
DECEASED





8:00 pm

Thursday, October 29

Fathom

OO Curriculum

Chapter topics include:

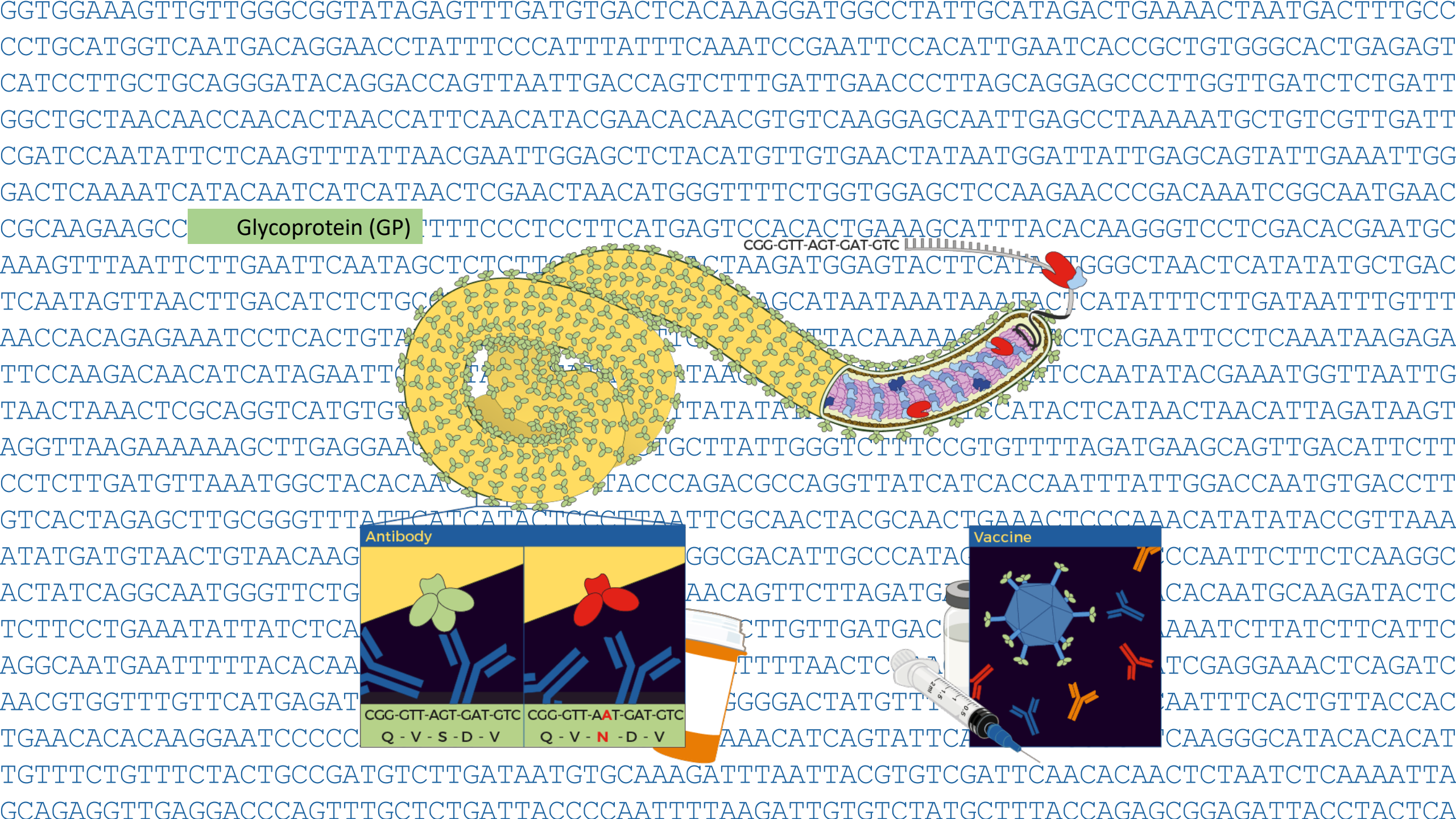
- *Epidemiology*
- *Biology of microbes*
- *Emerging pathogens*
- *Genomics and Evolution*
- *Molecular diagnostics*
- *Our immune defenses*
- *Vaccines*
- *Prevention and control*
- *Social Drivers of Disease*
- *Public health policy*
- *Mathematical modeling*

Course Video Series

(in production)

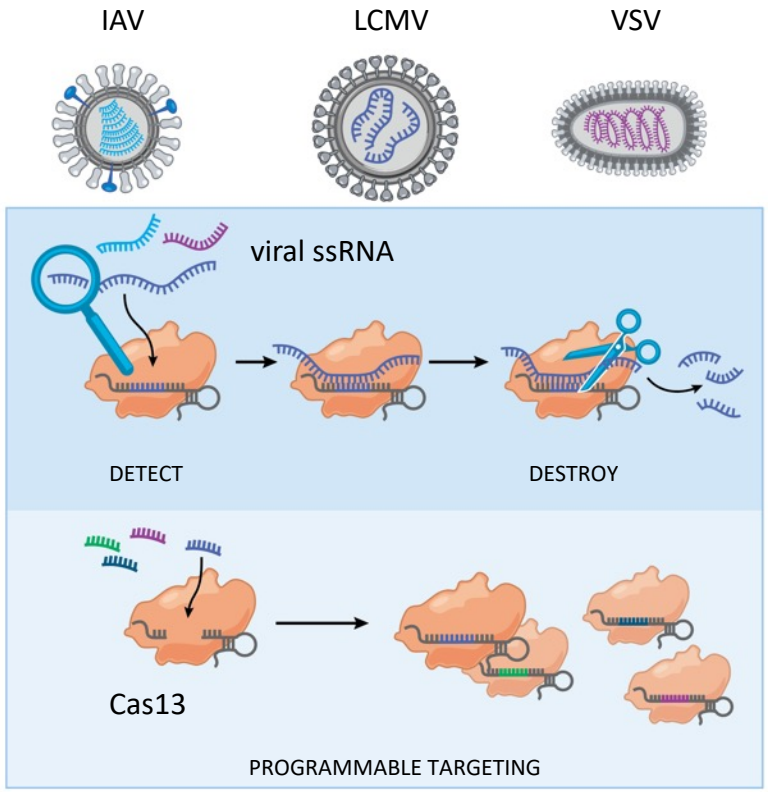
CRASH COURSE

Overcome

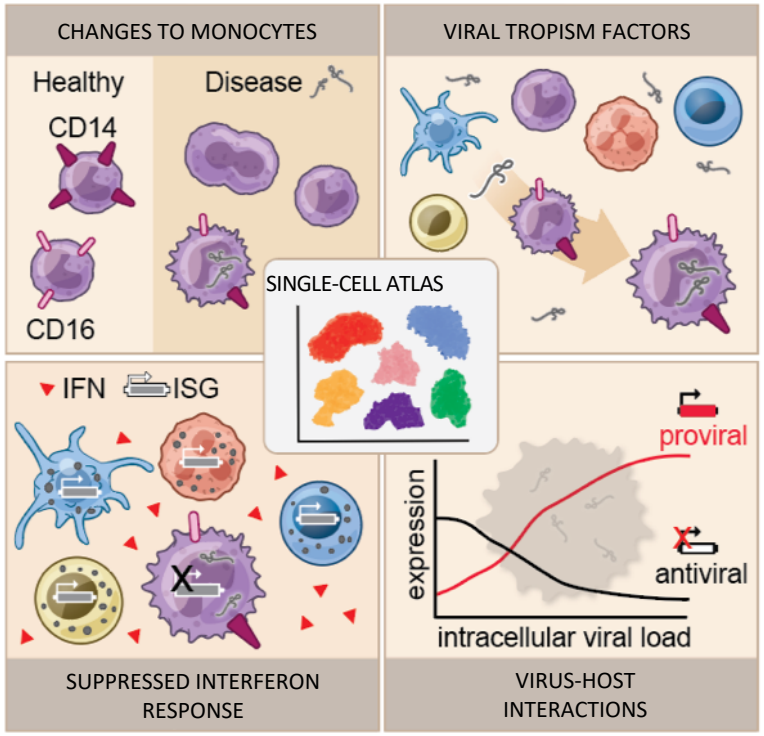

Glycoprotein (GP)
CGG-GTT-AGT-GAT-GTC
Antibody
CGG-GTT-AGT-GAT-GTC
Q - V - S - D - V
CGG-GTT-AAT-GAT-GTC
Q - V - N - D - V
Vaccine

OVERCOME: through therapies and vaccines

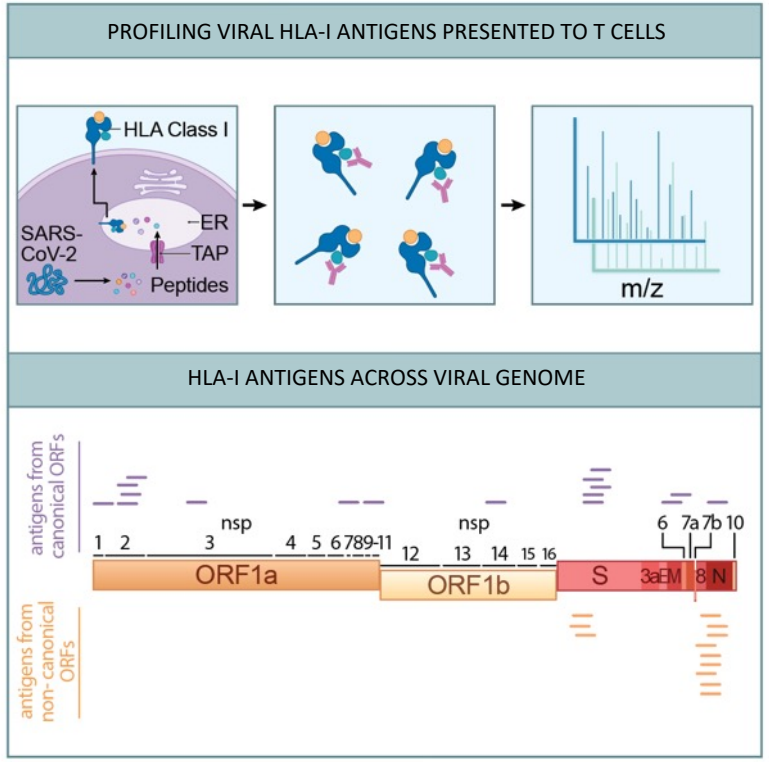
CRISPR Antivirals



Host Response at Single Cell Resolution



Viral Antigen Presentation



Freije et al. *Molecular Cell* 2019, Kotliar et al. *Cell* 2020, Weingarten-Gabbay et al. *Cell* in press

REDEEMER'S UNIVERSITY

Thanks to So Many Amazing Partners

NATIONAL INSTITUTES OF HEALTH

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DEPARTMENT OF DEFENSE · UNITED STATES OF AMERICA

FDA

THE AUDACIOUS PROJECT

THE WORLD BANK

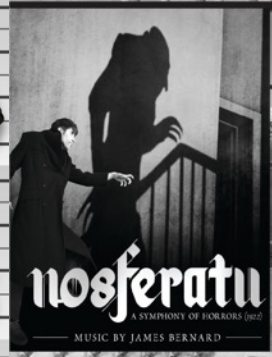
UNITED STATES AGENCY INTERNATIONAL DEVELOPMENT · USAID

BILL & MELINDA GATES foundation

H3

the David & Lucile Packard FOUNDATION

BURROUGHS WELLCOME FUND



As we enter the 2020s,
we reflect with pride on our collective accomplishments over the last century while we work toward a better future, one marked by excellence, inclusion, and respect. Wishing you a wonderful holiday season and prosperous New Year.

SEVERELY INFECTED
By Science
CLOSER TO BE INFECTED

ACEGID
African Centre of Excellence
for Genomics of Infectious Dise