



Brand New:

**Novel Approaches Toward
identification and Characterization
of an Old Pathogen**



**The future of decentralized
diagnostics at the point of need**

June 12, 2023



Our mission

Revolutionize the field of disease diagnostics by harnessing the power of **CRISPR** technology.

Our **innovative platform** enables direct measurement and quantification of active disease elements, providing healthcare providers with critical information for treatment monitoring and optimizing drug efficacy.

CRISPR AS A SUPERIOR DIAGNOSTIC APPROACH TO TB

At the conclusion of this session, the participant will be able to:

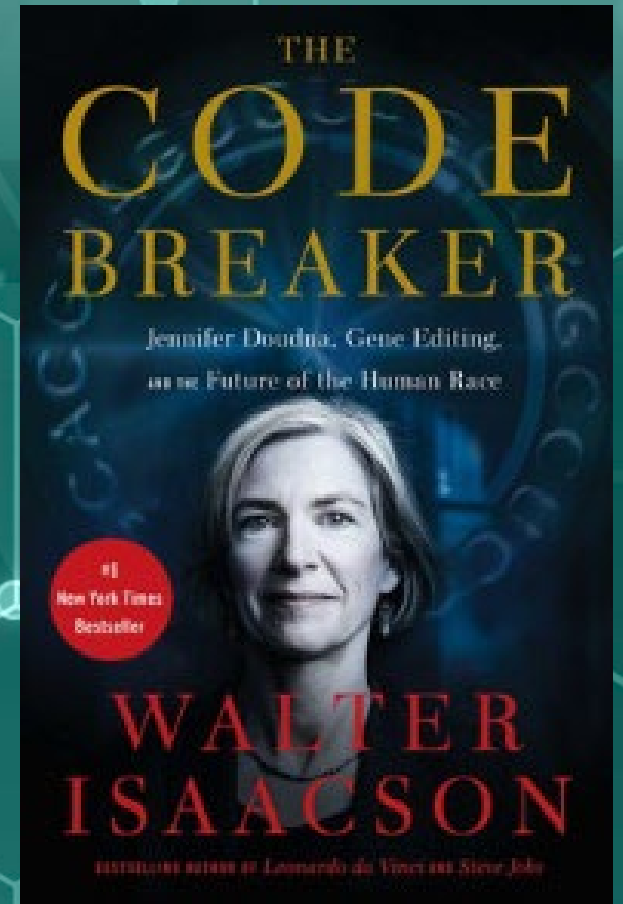
- Demonstrate an introductory knowledge of CRISPR and its uses in molecular diagnosis, especially in regard to TB
- Explain the advantages of blood-based testing utilizing CRISPR over other testing methods for diagnosing TB
- Explain the advantages of blood-based testing utilizing CRISPR over other testing methods for the laboratorian

WHAT IS CRISPR?

CRISPR, short for clustered regularly interspaced short palindromic repeats, is a microbial “immune system” that bacteria use to prevent infection by certain viruses.

The CRISPR system gives prokaryotes the ability to recognize precise genetic sequences that match certain invaders and target these sequences for destruction using specialized enzymes.

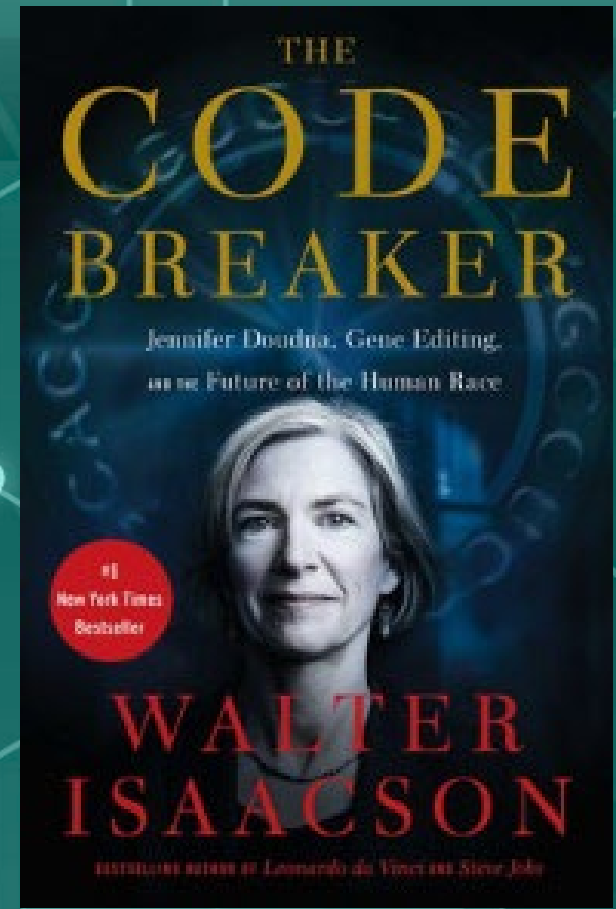
CRISPR can be used as a gene-editing technique and the Nobel Prize in Chemistry was awarded in 2020 to Drs. Emmanuelle Charpentier and Jennifer Doudna for their work in this field.



WHAT IS CRISPR?

CRISPR has been discussed largely as a way of recognizing and then editing individual genes, but there are other uses for this technique.

What about recognizing the genetic sequence of interest and releasing an identifying marker?



USE OF CRISPR in DIAGNOSTICS

When a specific sequence of DNA or RNA is present, a CRISPR enzyme is activated and, much like a pair of scissors, starts cutting nearby genetic material, releasing a fluorescent signal that indicates a positive result.

In May 2020, Sherlock Biosciences (Cambridge MA) received Emergency Use Authorization (EUA) from the U.S. Food and Drug Administration (FDA) for its Sherlock™ CRISPR SARS-CoV-2 kit, the first FDA authorized use of CRISPR technology.

Mechanisms of CRISPR-PCR molecular assay for TB in blood to provide rapid quantitative results

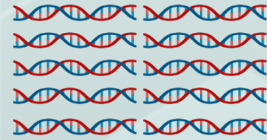
cfDNA isolation
Up to 96 samples



e.g. Thermo Scientific™
KingFisher™ Flex



Applied Biosystems
QuantStudio™ 5



Target DNA for
detection

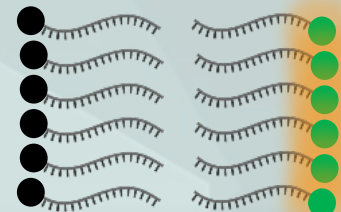
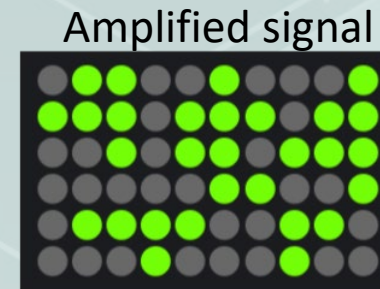
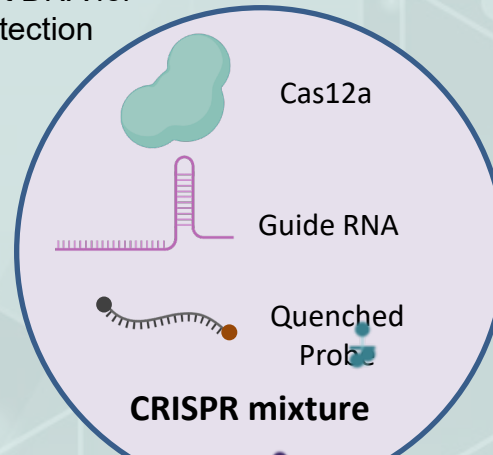
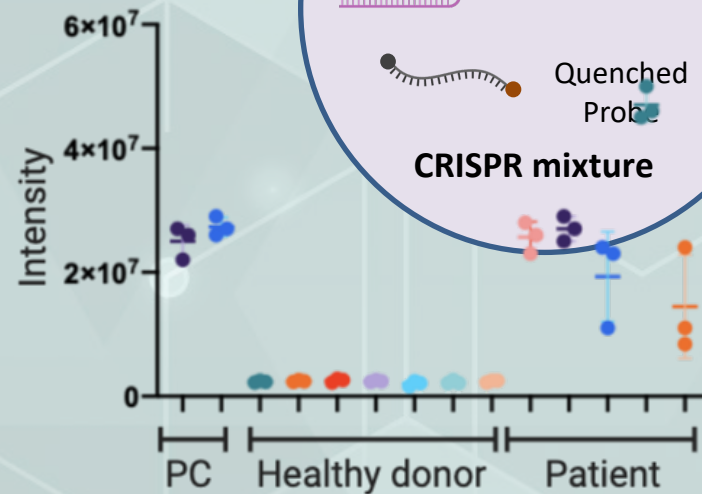


Target DNA



Activated
Cas12a

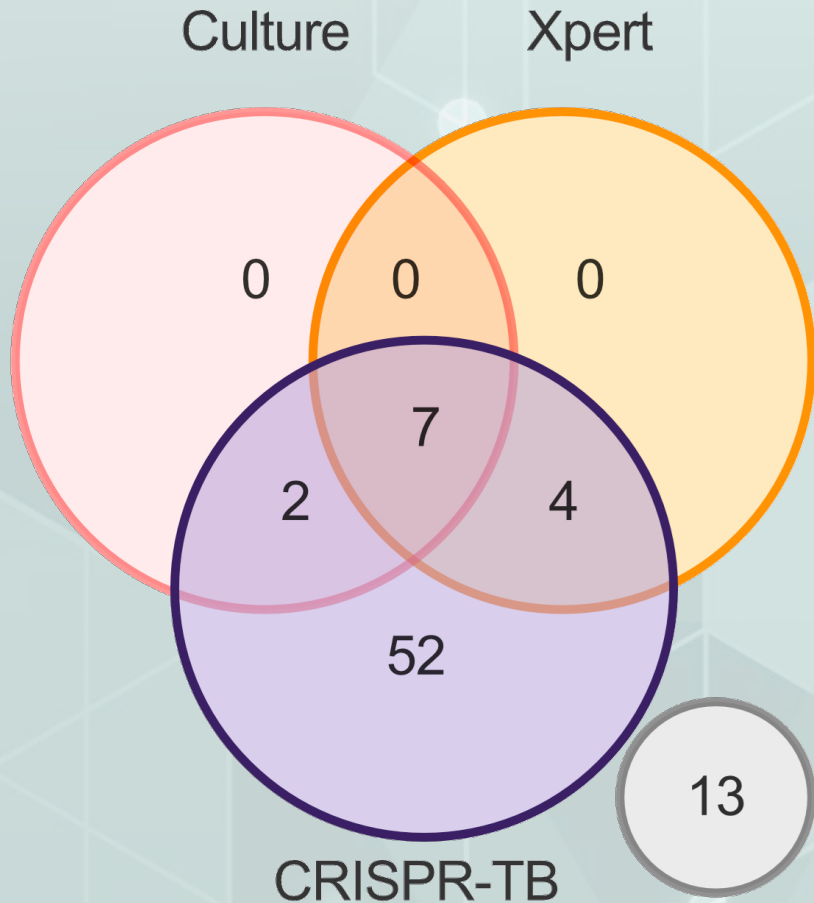
- Our CRISPR detection**
- ✓ Two amplification steps to achieve ultra-sensitive detection
 - ✓ High degree of specificity
 - ✓ High-throughput platform integration
 - ✓ Designed for large scale screening



Explain the advantages of blood-based testing utilizing CRISPR over other testing methods for TB

	CRISPR-TB	Culture	GeneXpert	IGRA	Smear	Skin TST
Test to Result	30 minutes	~4-6 weeks	2 hours	~24 hours	~4-6 weeks	✗
Direct	✓	✓	✓	✗	✓	✗
Sample Size	Small	✗	✗	✗	✓	✗
Active vs Dormant	✓	✗	✓	✗	Moderate	✗
HIV Co-infected	✓	✗	Moderate/ Low	✗	✗	✗
Sensitivity / Specificity	High/ High	Moderate/ High	Moderate/ High	High/ High	Low/ High	Moderate/ Low

Clinical study results



Confirmed & Unconfirmed TB
(N=78)

Kenyan CLHIV cohort:

- CRISPR-TB detected all (13 [100%] of 13, CI 7-100) confirmed tuberculosis cases
- CRISPR-TB detected 85% (39 [85%] of 46, CI 71-94) of unconfirmed tuberculosis cases diagnosed by non-microbiological clinical findings.

Explain the advantages of blood-based testing utilizing CRISPR over other testing methods for the laboratorian

Simplicity of operation

- 96-well plate for high-throughput results
- CRISPR reagent preloaded into wells
- Easy blood sample preparation
- Standard PCR processing
- Amplified fluorescent readout for results

Explain the advantages of blood-based testing utilizing CRISPR over other testing methods for the laboratorian

Simplicity of operation

Less hands-on time

- 15 minutes of sample preparation and loading

Quick turnaround time

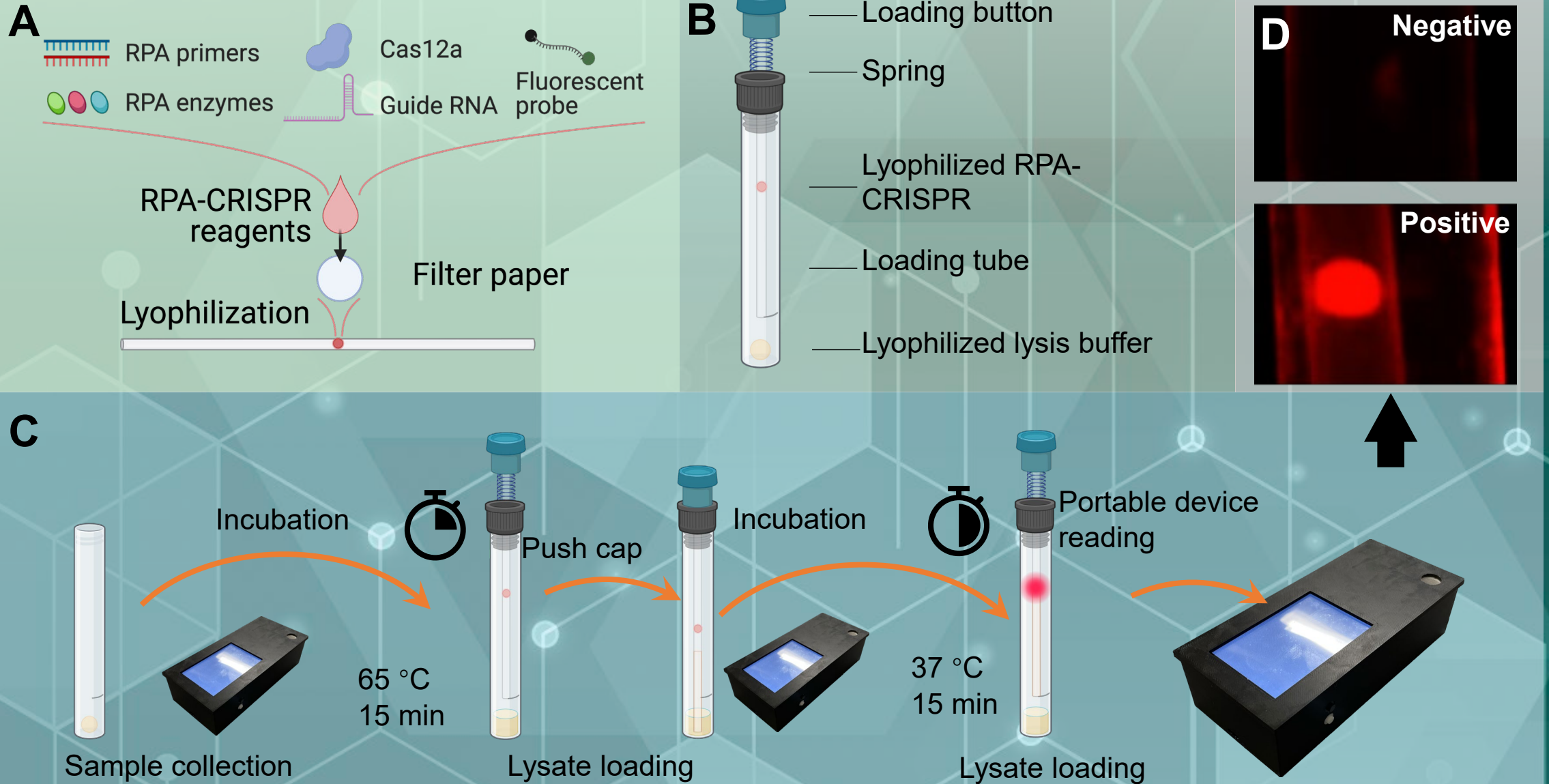
- 30 minutes to results

Clear results

- Amplified fluorescent readout for results



Point-of-care for TB: Lab-in-Tube CRISPR



Our vision is creating
**world-changing diagnostic
platforms that transform
the lives of people
impacted by infectious
diseases.**



IntelliGenome

We are the future in IVD



Explain the advantages of blood-based testing utilizing CRISPR over other testing methods for TB

Mantoux tuberculin skin test (TST)

Pros	Cons
Moderately invasive	Wide range of scoring
Works in all age groups	Requires trained analysis
Well understood	False positives (BCG, NTM ...)
Detects pulmonary & extrapulmonary TB	False negatives (very recent TB infection)
	48-72 hour window to in-person result
	Ineffective in patients co-infected with HIV

Explain the advantages of blood-based testing utilizing CRISPR over other testing methods for TB

● Acid-fast bacilli (AFB or smear) testing

Pros	Cons
Rapid: 1 to 2 days to lab result	Sputum based
Can provide quantitative data	Requires confirmation with culture
	Cannot distinguish active from latent TB
	Multiple specimens needed per patient
	Detects pulmonary TB only
	Ineffective in patients co-infected with HIV

Explain the advantages of blood-based testing utilizing CRISPR over other testing methods for TB

Interferon-gamma release assays (IGRAs)

Pros	Cons
Blood based	Cannot distinguish active from latent TB
High degree of specificity and sensitivity	Only provides + or - : no quantitative data
Rapid: 1 to 2 days to lab result	False negatives (very recent TB infection)
False positives are rare	Sample management is critical
	Unreliable in children, the immunocompromised & patients co-infected with HIV

Explain the advantages of blood-based testing utilizing CRISPR over other testing methods for TB

Gene XPert

Pros	Cons
Rapid: 1 day to lab result	Requires significant infrastructure
Highly sensitive	Expensive
Can detect TB in patients co-infected with HIV	Maintenance required at least annually

Explain the advantages of blood-based testing utilizing CRISPR over other testing methods for TB

CRISPR-TB

Pros	Cons
Blood based	Not yet commercially available
High degree of specificity and sensitivity	Requires significant infrastructure
Rapid: <1 day to lab result	
Can detect TB in patients co-infected with HIV	
Inexpensive	