Surveillance Advances Progrès dans le domaine de la surveillance

Genomics for Public Health Surveillance

La génomique pour renforcer la surveillance de la santé publique

Speakers

Dr. Jennifer Gardy Bill & Melinda Gates Foundation

Dr. Linda Hoang

British Columbia Centre for Disease Control



National Collaborating Centre for Infectious Diseases

Centre de collaboration nationale des maladies infectieuses



Public Health Age Agency of Canada pub

Agence de la santé publique du Canada



Land Acknowledgment: NCCID

The National Collaborating Centre for Infectious Diseases is hosted by the University of Manitoba. Both the University of Manitoba and I are situated on Treaty 1 Territory, the original lands of the Anishinaabe, Cree, Oji-Cree, Dakota, and Dene peoples, and homeland of the Métis Nation. I am thankful for these lands that I live and work upon as a descendant of settlers with European ancestry and with inherited responsibilities for the lands' protection.

As an organization, NCCID recognizes the systemic inequities and treaties that have been implemented as part of the process of colonization intended to benefit some while harming others. We are committed to working with our partners towards reconciliation and we strive to honour the lands and their original caretakers in our work.

Housekeeping

- Seminar recording and presentation slides will be available shortly after the seminar at the NCCID website: <u>https://nccid.ca/</u>
- If you have technical problems with Zoom, please email us at nccid@umanitoba.ca
- The chat box for participants has been disabled for this session. We will use the chat box to share additional information.
- Please use the Q&A tab to submit your questions for our speakers. ulletYou can "like" other people's questions to push them up in priority

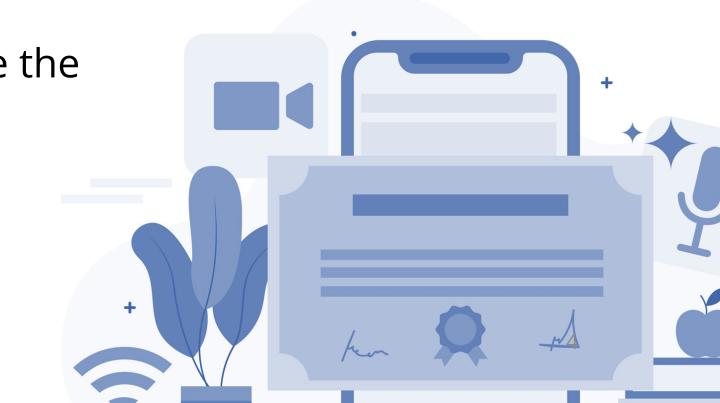


Accreditation

Surveillance Advances is a self-approved group learning activity (Section 1) as defined by the Maintenance of Certification Program of the **Royal College of Physicians and Surgeons of Canada**.

The seminar series is also approved by the Council of Professional Experience for professional development hours for members of the **Canadian Institute of Public Health Inspectors**.

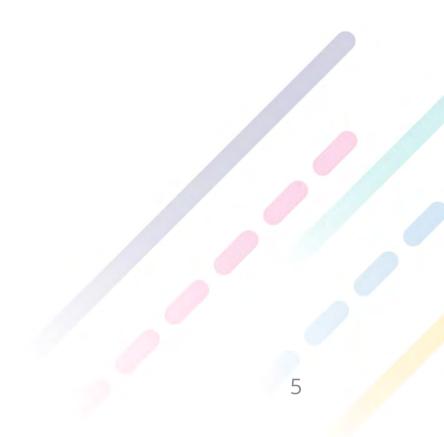
If you would like a letter of participation, please complete the survey which will be shared after the seminar.



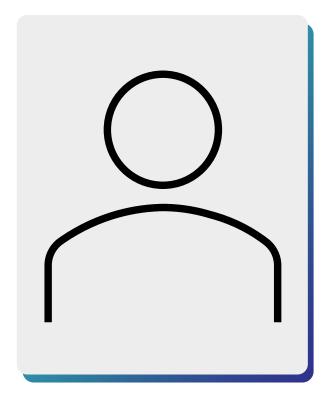
Land Acknowledgment: PHAC

I would like to take this time to acknowledge the land that I live and work on is the traditional territory of the Wendat, the Anishnaabeg, Haudenosaunee, Métis, and the Mississaugas of the Credit First Nation.

It is home to many First Nations, Métis, and Inuit peoples. I am grateful for the opportunity to share their home.



Today's speakers



Dr. Jennifer Gardy

PhD, Bioinformatics

Deputy Director, Surveillance, Data, and Epidemiology (Malaria), Bill & Melinda Gates Foundation

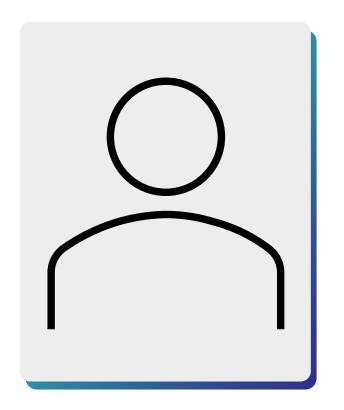


Dr. Linda Hoang MD, MSc, DTM&H, FRCPC

Medical Director, British Columbia Centre for Disease Control



Today's speakers



Dr. Jennifer Gardy PhD, **Bioinformatics**

- Deputy Director, Surveillance, Data, and Epidemiology (Malaria), Bill & Melinda \bullet **Gates Foundation**
- Leadership team and recent Interim Director, Institute for Disease Modeling ۲ (IDM), Bill & Melinda Gates Foundation
- Canada Research Chair in Public Health Genomics, British Columbia Centre for • Disease Control and the University of British Columbia's School of Population and Public Health
- 2018 One of BC's Most Influential Women in STEM by BC Business Magazine ulletand one of the Government of Canada's 20 Women of Impact in STEM
- 2021 Elected to the National Academy of Medicine (pathogen genomic epidemiology)
- Award-winning science communicator (The Nature of Things, Daily Planet, \bullet children's science books)

Today's speakers



Dr. Linda Hoang MD, MSc, DTM&H, FRCPC

- Medical Microbiologist, Clinical Professor, and Medicator Director, British Columbia Centre for Disease Control (BCCDC) Public Health Laboratory (PHL)
 - Pathogen genomics program for COVID-19 pandemic response measures
- Recent Medical Co-Director, Provincial Infection Control Network (PICNet), BC
 - Carbapenamase producing organism (CPO) surveillance program
- Passionate about operationalization of pathogen genomics methods to provide a standardized tool informing infection prevention and public health responses in BC and Canada

Strengthening Genomic Surveillance for Malaria Across sub-Saharan Africa

Jennifer Gardy

PhD Deputy Director, Surveillance, Data, & Epidemiology Bill & Melinda Gates Foundation



Conflicts of interest

None to declare



Learning Objectives

- Describe the role genomics can play in surveillance, strategic planning, and commodity procurement in malaria-endemic countries
- Understand the Bill & Melinda Gates
 Foundation's strategic priorities for malaria genomic surveillance
- Articulate some of the challenges associated with establishing genomic surveillance capacity in sub-Saharan Africa



Polling Question

How many SARS CoV-2 genomes have African labs sequenced and shared globally?

- A. <1,000
- **B. 1,000-10,000**
- C. 10,000-50,000
- D. 50,000-100,000
- E. >100,000



Malaria genomic surveillance (parasites & vectors) can inform country planning & resource procurement/allocation

Assay	Microscopy 🛒	PCR	Serology 🎢	Am Sec
Description	 Manual visual examination of blood smears using a microscope 	 Molecular laboratory assay used to amplify and detect parasite DNA 	 Protein-based laboratory assay used to detect anti- malaria antibodies 	• Ta pa in
Data Generated	 Presence of malaria parasite 	 Presence of malaria parasite Emergence of resistance 	 Past exposure to malaria parasite Population-level 	• Re su ge

Malaria genomics addresses multiple use cases

Resistance

- Detect/track antimalarial drug resistance
- Detect/track pfhrp2/3 gene deletions
- Detect/track insecticide resistance
- Monitor changes over time in antimalarial and insecticide resistance

Transmission:

- Identify local transmission
- Distinguish local from imported cases

surveillance

- Identify outbreaks
- Quantify transmission intensity and changes over time
- Determine connectivity of parasite populations



argeted sequencing of the parasite or vector genome n specific genetic regions

esistance in known, usceptible regions of the enome

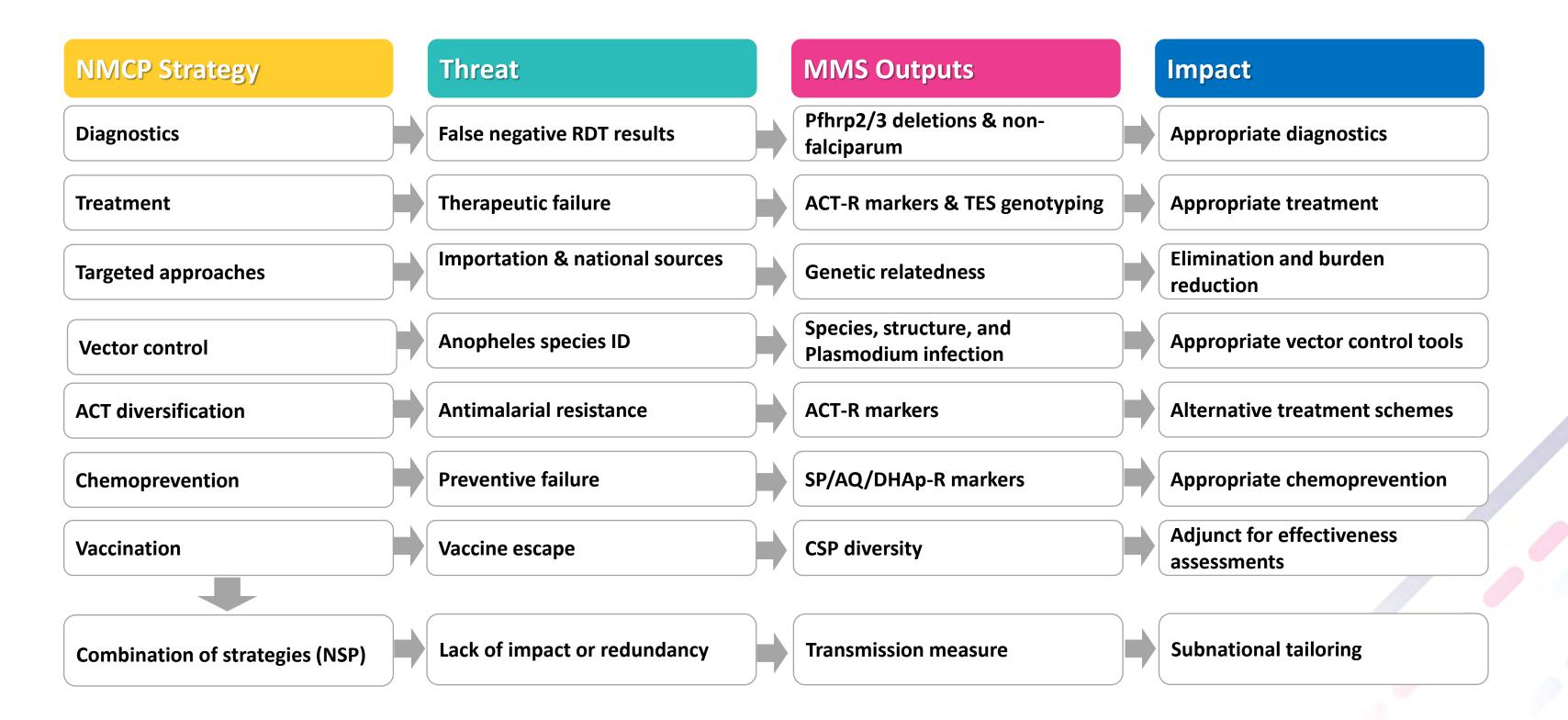
- Whole Genome Sequencing
- Broad sequencing of the parasite or vector genome to identify novel markers
- Novel drug resistance markers and population genetics structures

Population dynamics:

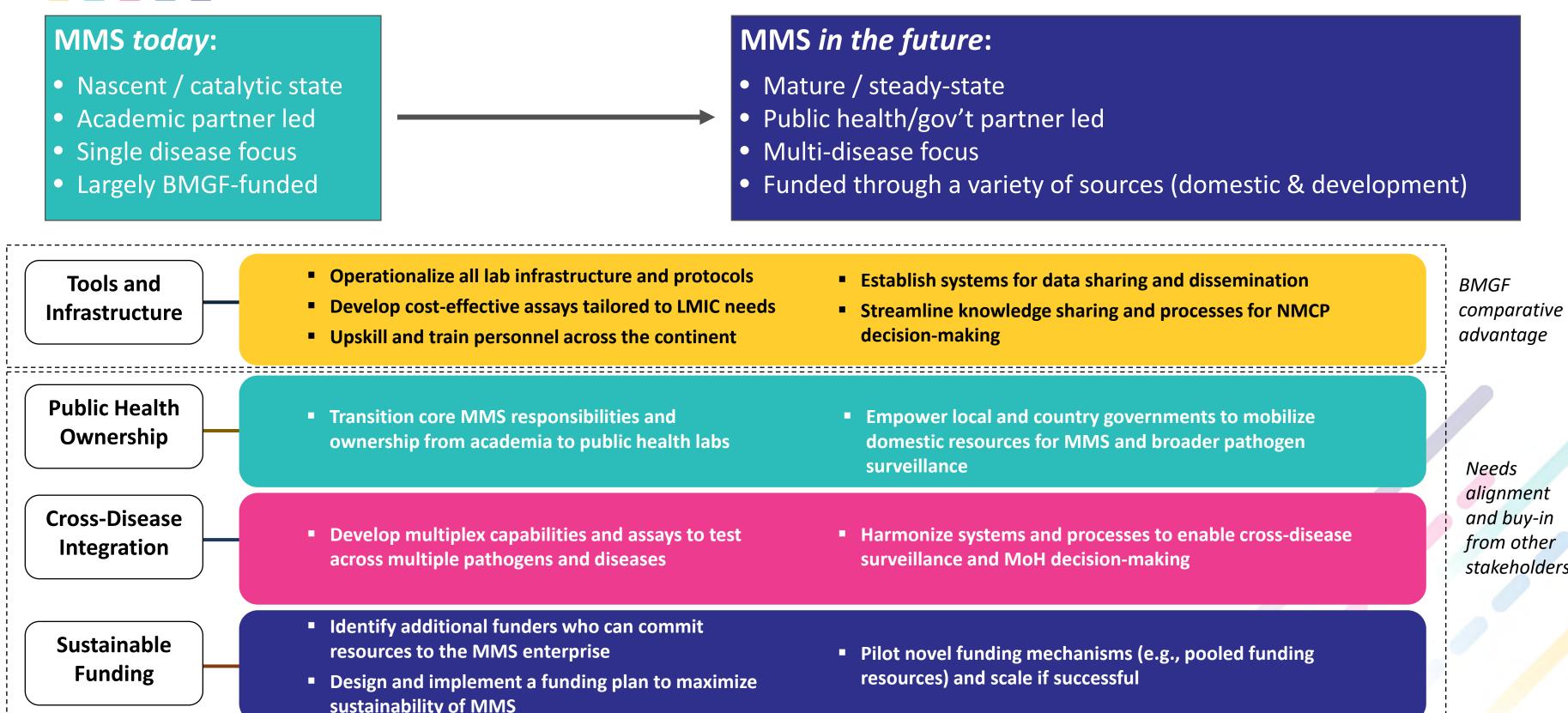
 Monitor parasite populations and
changes over time

- Monitor vector populations and changes over time, including A. stephensi and gene drive releases
 - Survey for variation in vaccine, monoclonal Ab, and gene drive target sites

Malaria genomic surveillance (parasites & vectors) can inform country planning & resource procurement/allocation



Getting to an ideal future state requires investment across multiple thematic areas



Genomics In the Time of COVID Public Health Laboratory BC Centre for Disease Control

Linda M. N. Hoang, MSc, MD, DTM&H, FRCPC

Medical Director BCCDC Public Health Laboratory BC Centre for Disease Control Provincial Health Services Authority

Clinical Professor Department of Pathology and Laboratory Medicine Faculty of Medicine **The University of British Columbia**





BC Centre for Disease Control

Provincial Health Services Authority

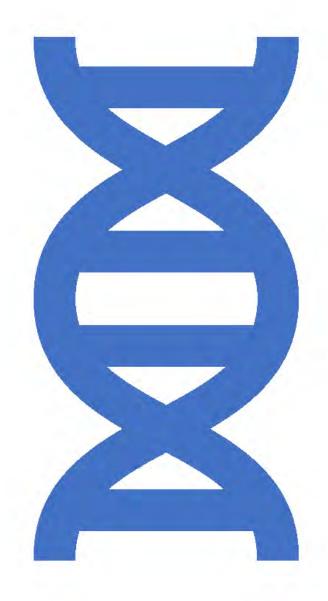
Inherent Rights of Indigenous Peoples



- First Nations territories stretch to every inch of this province, and across Canada
- Inherent rights, rooted in connection to lands and waters, have never been ceded or surrendered.
- Inherent rights are upheld in international, national and provincial law.
- Long-standing Indigenous laws and systems are integrally tied to the lands and waters of these territories.
- Generations of Indigenous rights holders who are First Nations, Métis, and Inuit from elsewhere in "Canada" also call these lands and waters home.

We gratefully acknowledge that we live and work on the traditional unceded territory of the Coast Salish Peoples, including the Squamish, Musqueam and Tsleil-Waututh First Nations 2

Objectives



- Describe advances in microbiology tools for surveillance, an important core function of a public health laboratory
- Outline the key applications of pathogen genomics for patient care and public health response
- Describe the development of a pathogen genomics program at the BC Centre for Disease Control
- Outline features of a genomics infrastructure, to inform patient care, public health and One Health

Subtyping and Fingerprinting

Information:

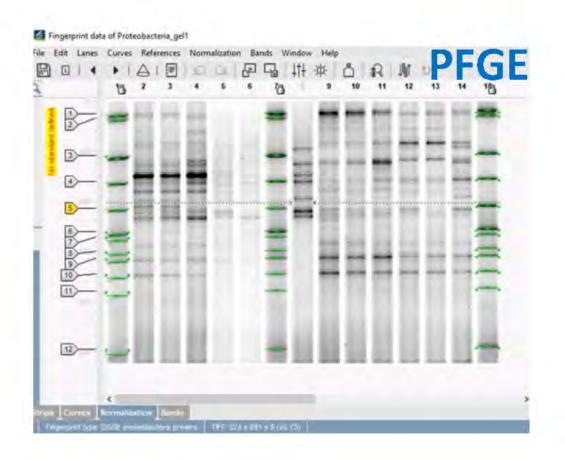
- Strain typing
- Cluster identification
- Virulence characterization
- Strain evolution
- Resistance profiling

E.g. Common tools

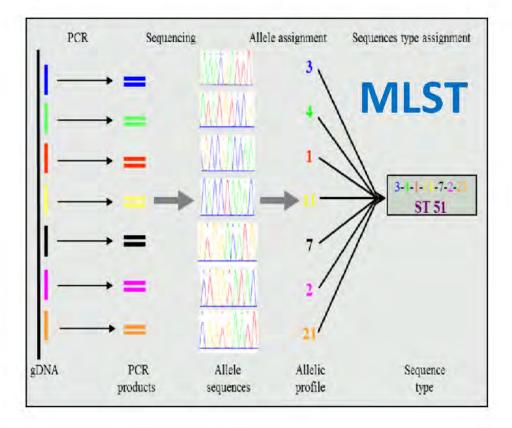


Limitations:

- Can be subjective
- Low sample throughput
- Slow turn around time, serial testing
- Poorly discriminative



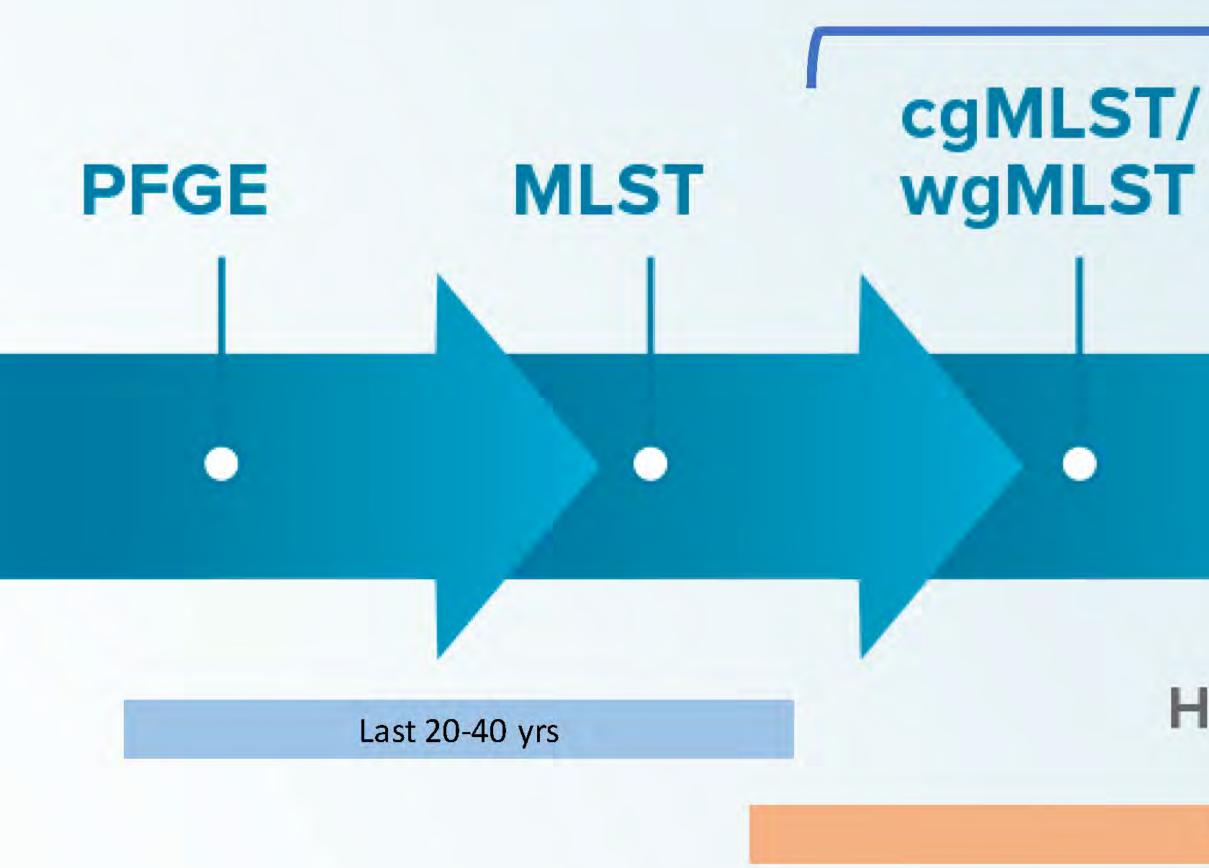




Whole Genome Sequencing

SNP

ANALYSIS



HIGH RESOLUTION

Last 10 yrs



Advances in genomics over the past 10 yrs allows direct access to entire genetic makeup of microbes

 Technical advances Cost reduction • Turn-around time Computational capacity • Mechanism for linking meta-data Information is clear and actionable Available accreditation standards

One Method --> Many potential types of information



Input: DNA/RNA

NGS

Bioinformatics

Output: Information From Sequence Data

Comparative Genomics

Identification High resolution straintyping Cluster identification Molecular evolution Genotypic characterization Virulence, Antimicrobial resistance Functional annotation Diagnostic dev/validation Minor populations, quasispecies Host/pathogen expression

Metagenomics

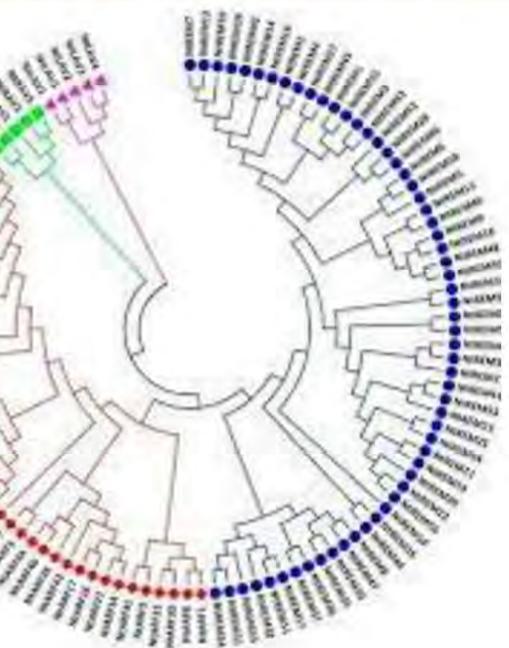
Pathogen identification/discovery Culture-independent diagnostics Microbial ecology/diversity

Many results from a single dataset. Faster and cheaper than serial tests.

Genomics superpower is in its database!!!

- Standardized and quality assured sequences
- Curated, robust
- Unbiased representation
 - o Time
 - o Person
 - \circ Place
- Improves discriminatory power
- Confidence in results
- Needs regular maintenance for circulating strains

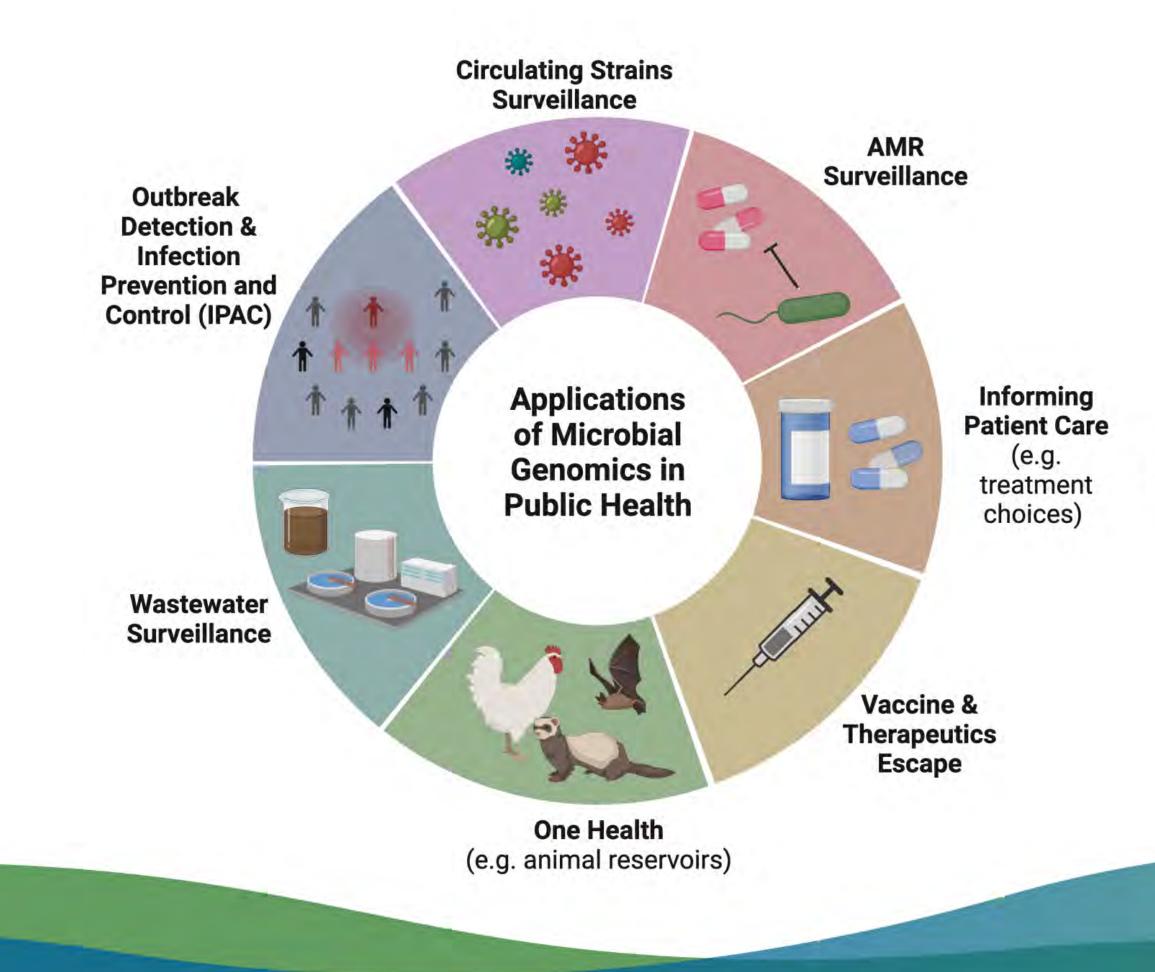




"Pathogen genomics is one of the most powerful tool we have against infectious diseases and environmental hazards"

Professor Susan Hopkins Chief Medical Advisor, UK Health Security Agency







Genomics Program Informs Public Health & Patient Care



Early Genomics Adoption at BCCDC Public Health Lab

External/grant funded (CIHR, Genome BC, Genome Canada, NML, etc)

- PulseNet Canada Foodborne Bacterial Pathogen Surveillance
- Carbapenemase Producing Organisms Genomics Surveillance
- Tuberculosis
- Avian Influenza



en Surveillance ics Surveillance

Pre-pandemic (2019) State of Genomics at BCCDC

	Pathogen	Wet Lab	Bioinformatics	Reporting/ Data Viz
	SARS-CoV-2			
1	Human influenza A			
RESPIRATORY	Hummy influenza B			
	RSV			
	78			
WASTEWATER	SARS-CoV-2			_
60	СРО			
	Shigella			
AMR	ТВ			\bigcirc
HCAI*	Various Dacteria			
~~~	Salmonella			
ENTERIC	E. coli			
LITENO	Listeria			
antina.	Hispattile 2			
$\odot$	N. gonorrhaene	1		
STBBI	Syphills	1		
	Avian influenza			
	Massi			
ENERGING	H. Influenzae b			
EMERGING THREATS	Enteroviruses			
	Group A Strep			
PARASITES	Leistmania			
METAGENOMICS	Variims Bacteria			

**Resources:** 

perational

Develop

rioritized

- •
- Operationalized as part of PulseNet •
- CPO genomics, PICNet provincial ۰ surveillance
- No dedicated scientific staff (PhD)

Throughput:

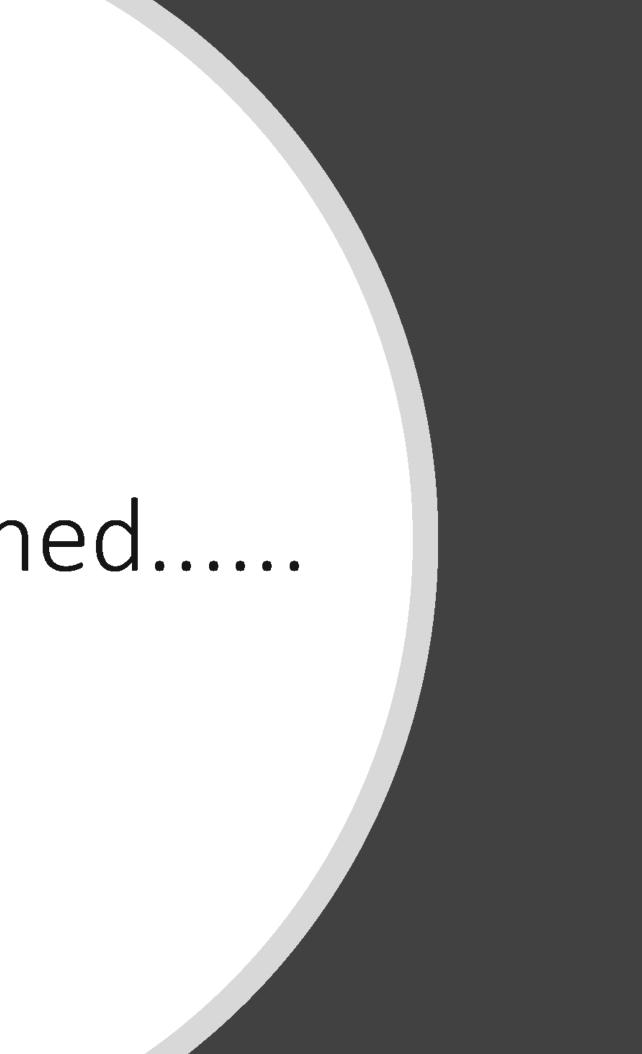
- Up to 3-4 weeks to generate a WGS result months to generate an outbreak report Up to 24 samples per week
- •

*Healthcare-associated infections (e.g. MRSA, C. difficile, Pseudomonas, Serratia)



## Shoe-string resources

# COVID-19 happened.....



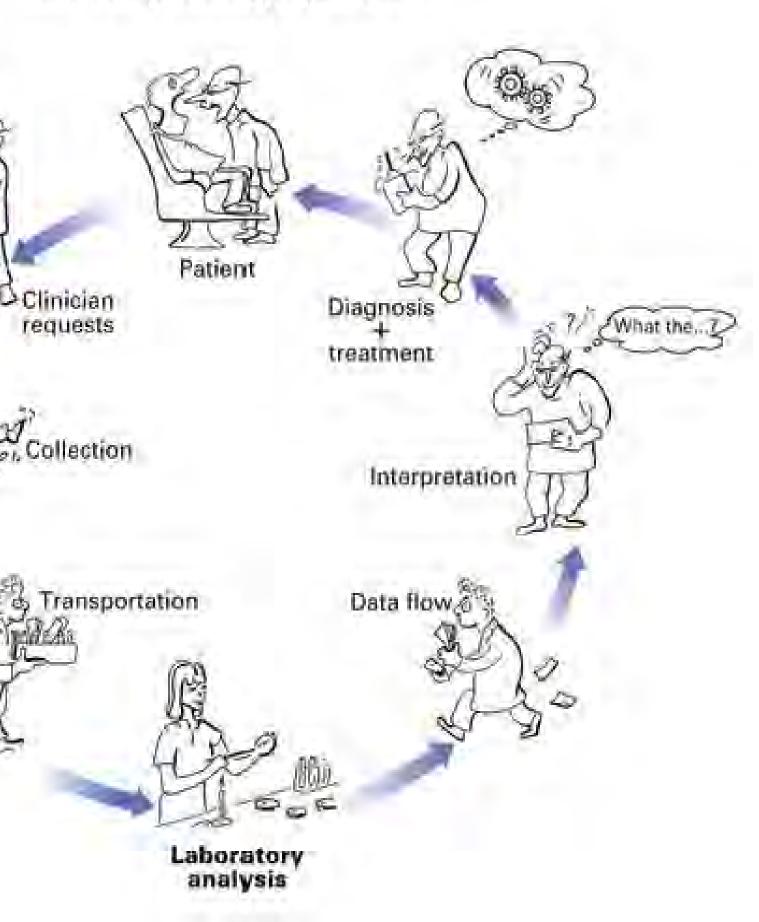
To stand up a SARS-CoV2 genomics testing program:

Need high volume sequencing capacity

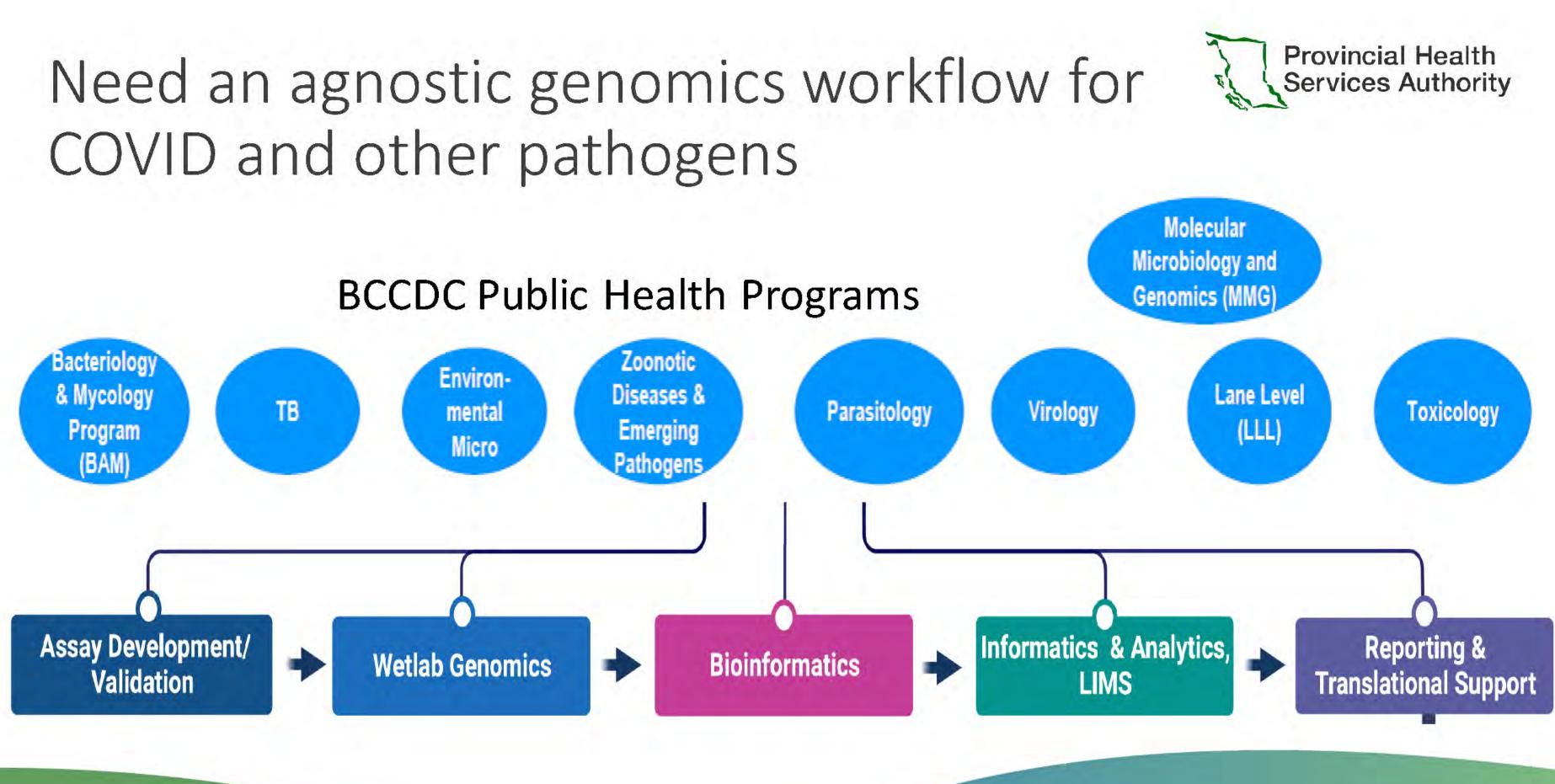
Need process improvement and automation

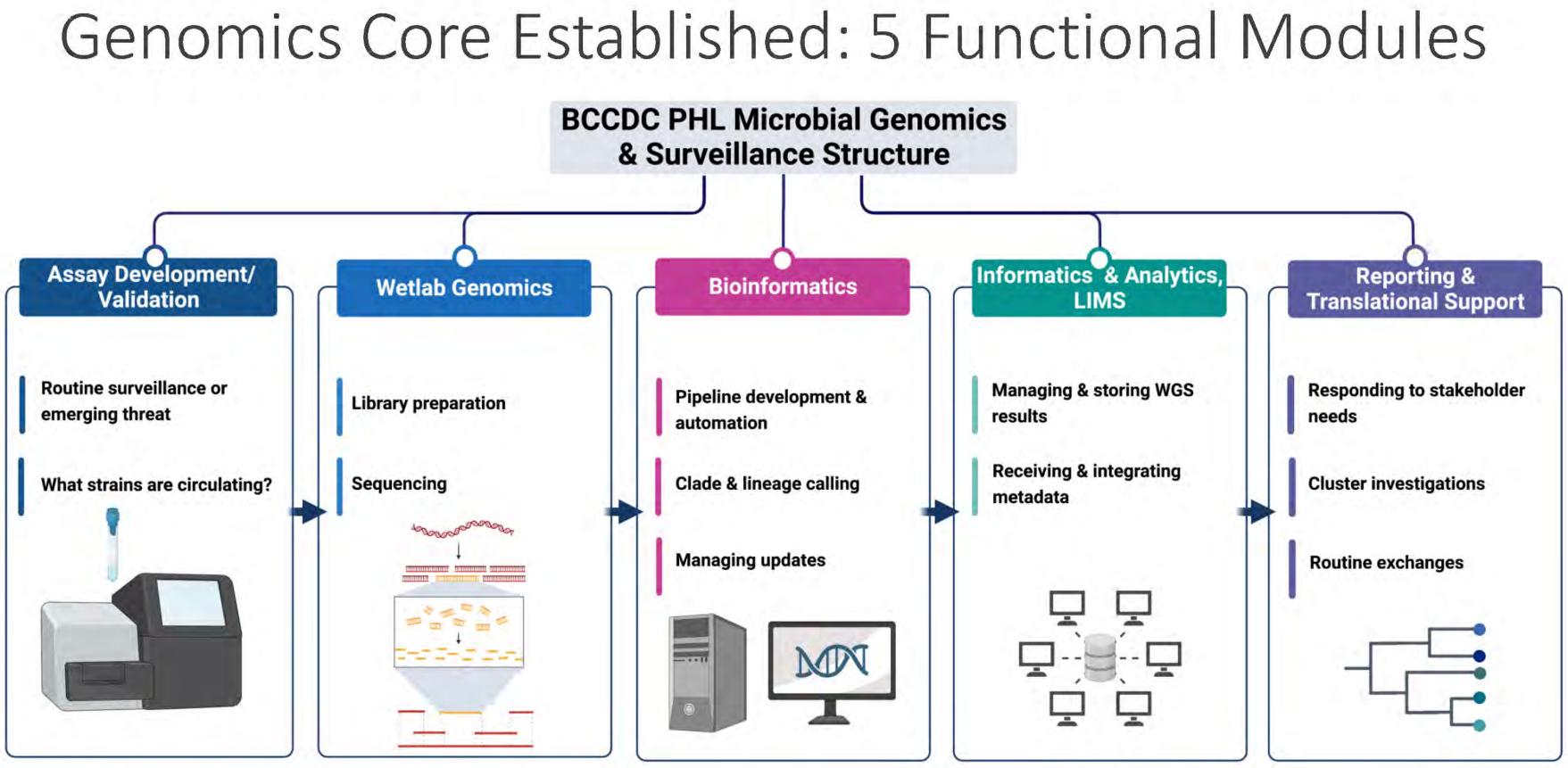
Affects all stages from patient sample to interpreted results The Laboratory Cycle-begins and ends with the patient/population

Plafection ungal culture Virus culture



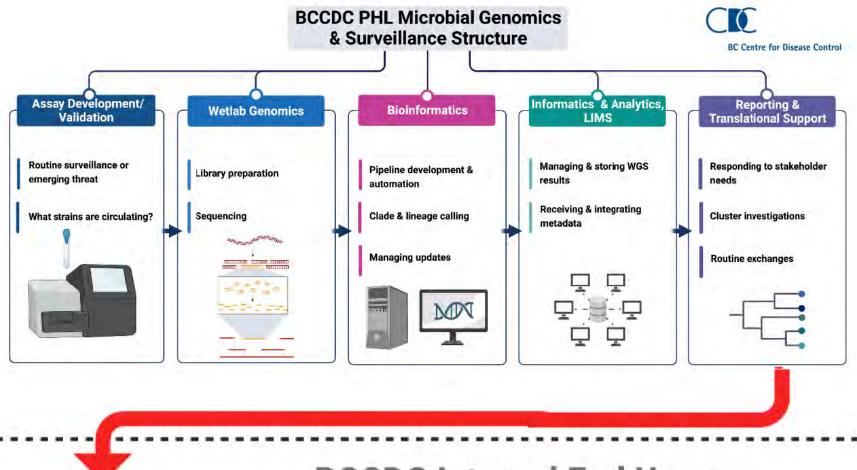


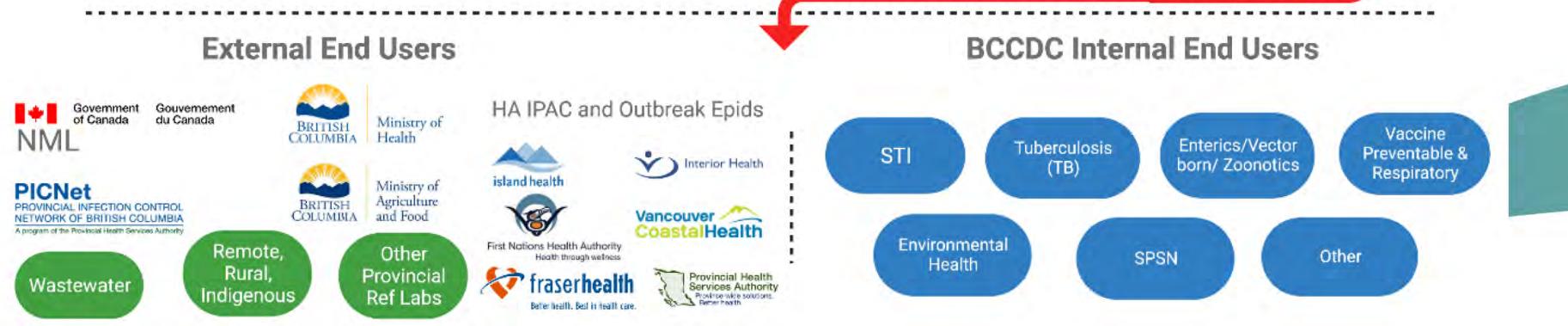




# Modular work flow

- Organism agnostic
- Easy to pivot
- Respond to priority pathogens
- Centralize skillsets and expertise
- Integrated
- Meets needs of end users







I Clinical Microbiology | Research Article | 5 February 2024

# Rapid, high-throughput, cost-effective whole-genome sequencing of SARS-CoV-2 using a condensed library preparation of the Illumina DNA Prep kit

Authors: Rebecca Hickman, Jason Nguyen, Tracy D. Lee, John R. Tyson, Robert Azana, Frankie Tsang, Linda Hoang, Natalie A. Prystajecky 💿 🔛 | AUTHORS INFO & AFFILIATIONS

BCCDC Method minimizes cost, hands-on time, and complexity while maintaining high-quality and robust sequence data.

1 tech in 1 x 8 hr shift -1 x 96 well plate --> 576 library prep -600-800% improvement in throughput



### f 🎔 in 🗳

# BCCDC COVID-19 Genomics Surveillance

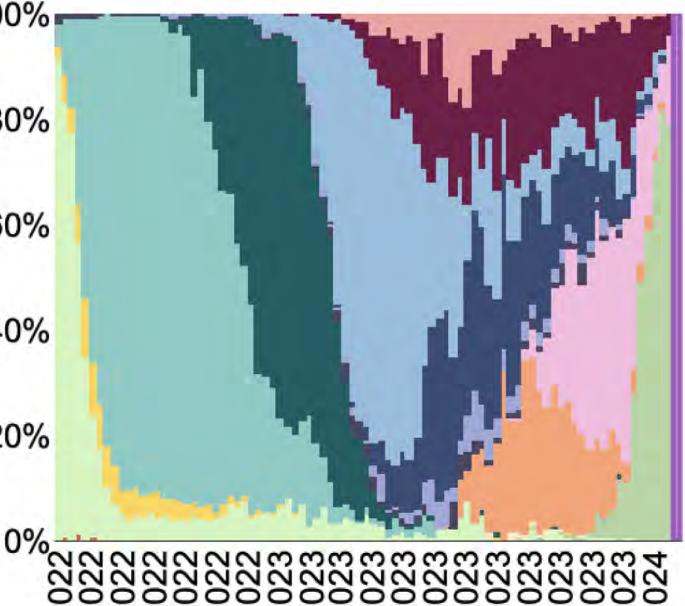
<ul> <li>COVID-19 genomics knowledge contributes to the understanding of the changing nature of circulating COVID-19 variants.</li> </ul>	100
<ul> <li>Data system integration a legacy for BCCDC/PHSA/BC</li> </ul>	80
<ul> <li>BCCDC Public Health Lab (PHL)</li> <li>BCCDC Data and Analytics Services (DAS)</li> </ul>	oe 60
Public Health Reporting Data Warehouse (PHRDW)Data, Analytics, Evaluation and Reporting (DARE)	onbag
Public health Lab Operations Data ViEwer and Reporter (PLOVER)	
https://bccdc.shinyapps.io/genomic_surveillance/	



Jan

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BC n= 41420



-ineages

## Genomics clusters – going beyond samples to provide insights into local outbreaks

Scitchmana et al BMC Germanics (2022) 23:710 https://doi.org/10.1186/s12864-022-08936-4

**BMC Genomics** 

Open Acces

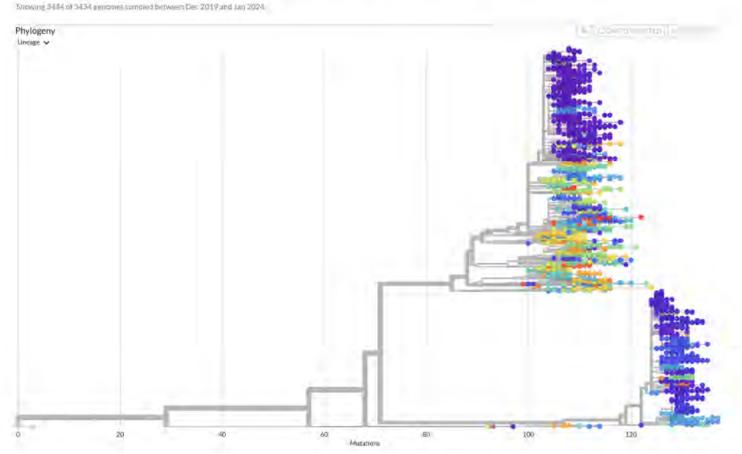
### RESEARCH

### Cov2clusters: genomic clustering of SARS-CoV-2 sequences

Benjamin Sobkowiak^{1*}, Kimia Kamelian², James E. A. Zlosnik¹, John Tyson¹, Anders Gonçalves da Silva^{*}, Linda M. N. Hoang¹³, Natalie Prystajecky¹³ and Caroline Colin⁷

### Nextstrain build for SARS-CoV-2 - Displaying Illumina Run-1-2824 Tree (September-January)

Data updated 2024-01-29



### Problem: .

- phylogenetic tree.
- 0
- 0
- 0

### Solution: .

- Cov2Clusters tool built.
- $\bigcirc$ 
  - for over 2 years.

• We needed an automated way of detecting samples that cluster with each other on a

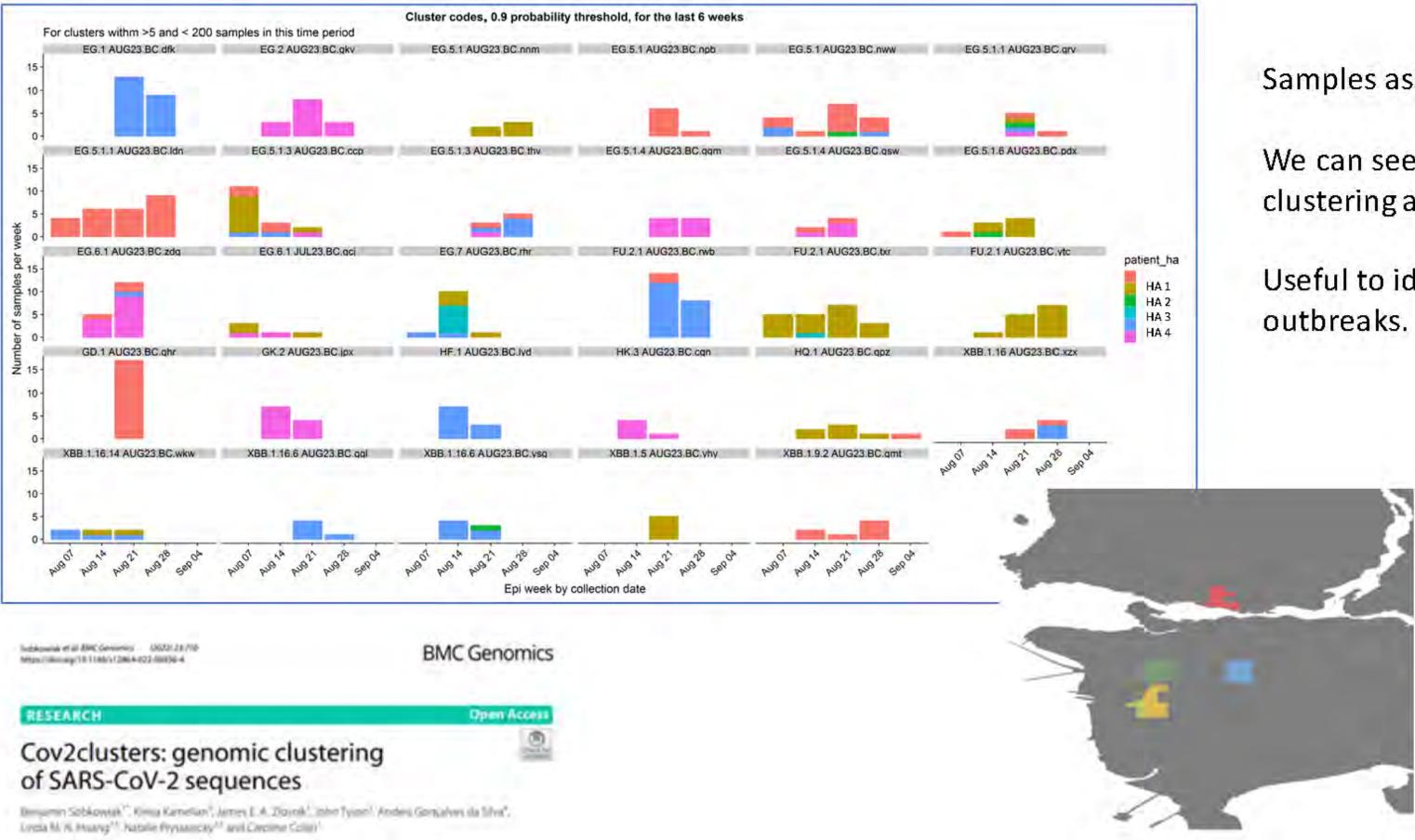
Tools existed that met academic needs (typically a single tree for publication)

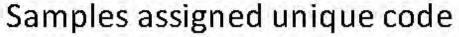
None suitable for public health needs because the cluster code changes as soon as new samples were added (new tree built).

Additionally, phylogenetics is very challenging!

We run on ever tree we build and has been stable

### Genomics clusters – going beyond samples to provide insights into local outbreaks





We can see geographic clustering around outbreaks

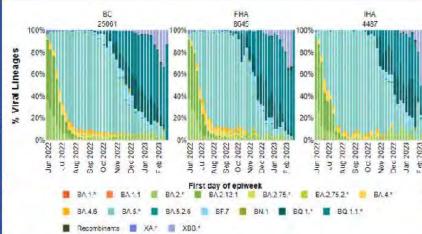
Useful to identify unknown

Lineage - Cluster(nxtstr 0.9) EG.1 - AUG23.BC.dfk

- EG.1.7 JUL23.BC.zrb
- FU.2.1 AUG23.BC.rwb
- XBB.1.5.44 JUL23.BC.jfp

NA NA

## **BCCDC PHL Surveillance Services for End-Users**



#### Surveillance **Dashboards**

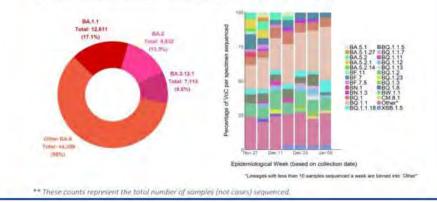
#### **Genomic Surveillance**

Whole genome sequencing (Illumina only) was performed on 185,737 specimens up t week 2 (January 08 - January 14) in BC. Figure 4 above illustrates BC's whole genome sequencing strategy of COVID cases.

The VOCs represent a cumulative 85.5% of all the variants that were detected in the p since the start of the pandemic (see WGS frequency of lineages table on BCCDC websit Delta (n = 57,837) and Omicron (n = 73,915) variants account for largest proportion of the VOCs. Omicron includes B.1.1.529, the parent lineage, and BA sub-lineages (Figure 5 and appendix Table).

#### Figure 5. Distribution of Omicron**

Panel A: three most prevalent lineages cumulatively; Panel B: sublineages in the past 6 weeks



#### Public Health Laboratory Mar 29, 2021 D-Smith, HA BCEDC Public Health Laborator COVID-19 Whole Genome See 5-CoV-2 (COVID-18 virus) ed (6/7). 4 cases at funter insertionation beings to 1 distinct second VIJ Unwageds) H.1.2 them 11 Name 1, MRI Col/ 2 assertio diversity in a



Cluster 1	-100 (BA.1.2,	Clade 1)-	-6
Chatter 1.0	00 (BA 1 32.1,	Outient	-8

road by the BCCDC PHE. This tre

flean Linda Hoang MSc. MD, DTM&H, FRCP

Surveillance Reports



#### **Cluster/Outbreak** Reports







"Genome sequencing is a powerful tool in Canada's public health response to COVID-19, allowing decision makers to respond rapidly to new outbreaks and variants of concern."

Sr. Stephen Lucas, Deputy Minister of Health Canada (April 2021)



Genomes passed QC: 205,586 Sequences in GISAID: 179,458

**Outbreaks Investigated:** ~1000

**VOC Sequenced.** 

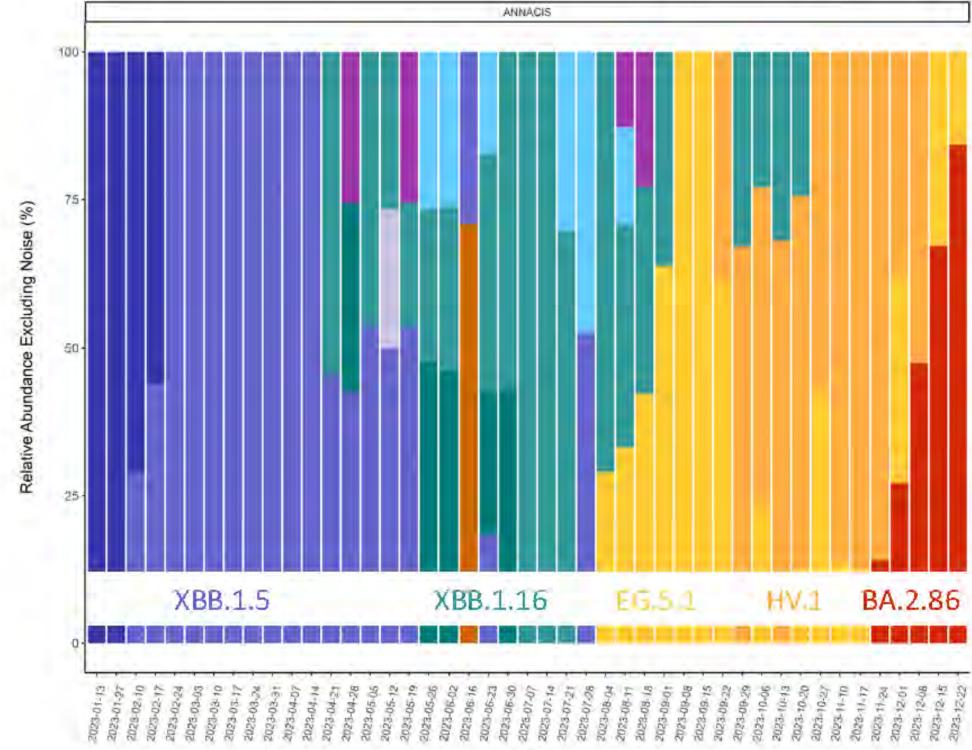


Alpha: 15,034 Gamma: 11,918 Delta: 58,557 **Omicron**: 93,928



# COVID-19 Sequencing on Illumina (Aug 2020 – present)

## Transitioning COVID-19 Sequencing Know-How to Wastewater Sequencing of SARS-CoV-2



Date



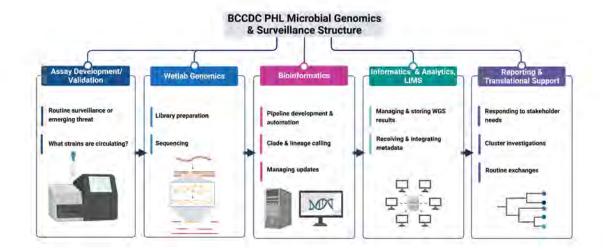
## Other recent applications

## **Mpox: COVID genomics experience applied**

- **Developed detection assay**
- Genomic mutational tracking for •
  - o epidemiological introductions,
  - outbreak investigations 0
  - monitoring for vaccine effectiveness drift

### TB antibiotic resistance testing now routine

- Faster detection of resistance for early appropriate treatment • (TB takes weeks/months to grow)
- Supports TB elimination goal •



## **Current State of Genomics Capacity**

Operational

	Pathogen	Wet Lab	Bioinformatics	Reporting/ Data Viz
RESPIRATORY	SARS-CoV-2			
	Human influenza A			
	Human influenza B			
	RSV			
	ТВ			
WASTEWATER	SARS-CoV-2			
AMR	CPO			
	Shigella			
	ТВ			
HCAI*	Various bacteria			
ENTERIC	Salmonella			
	E. coli			
	Listeria			
STBBI	Hepatitis C			
	N. gonorrhoeae	$\bigcirc$		
	Syphilis			
EMERGING THREATS	Avian influenza			
	Мрох			
	H. influenzae b			
	Enteroviruses			
	Group A Strep			
PARASITES	Leishmania			
METAGENOMICS	Various bacteria			

*Healthcare-associated infections (e.g. MRSA, C. difficile, Pseudomonas, Serratia)

- Staff additions
- Senior scientists: support genomics
- Bioinformaticians: PHL + NML resources
- Technical staff (COVID Contingency funding)
- Capital additions: liquid handlers, 2 highthroughput sequencers
- 3-7 days to generate a WGS result 1 week to generate an outbreak report
- activity

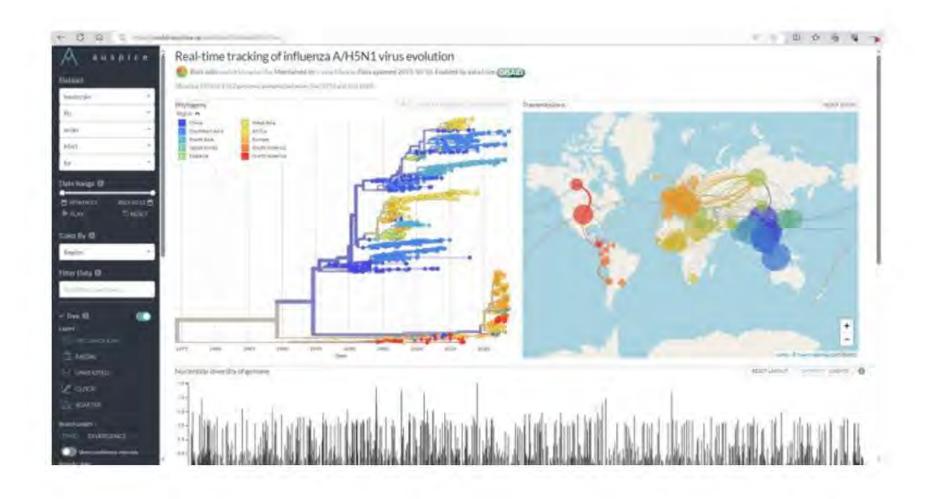




• ~4K samples per week during peak COVID

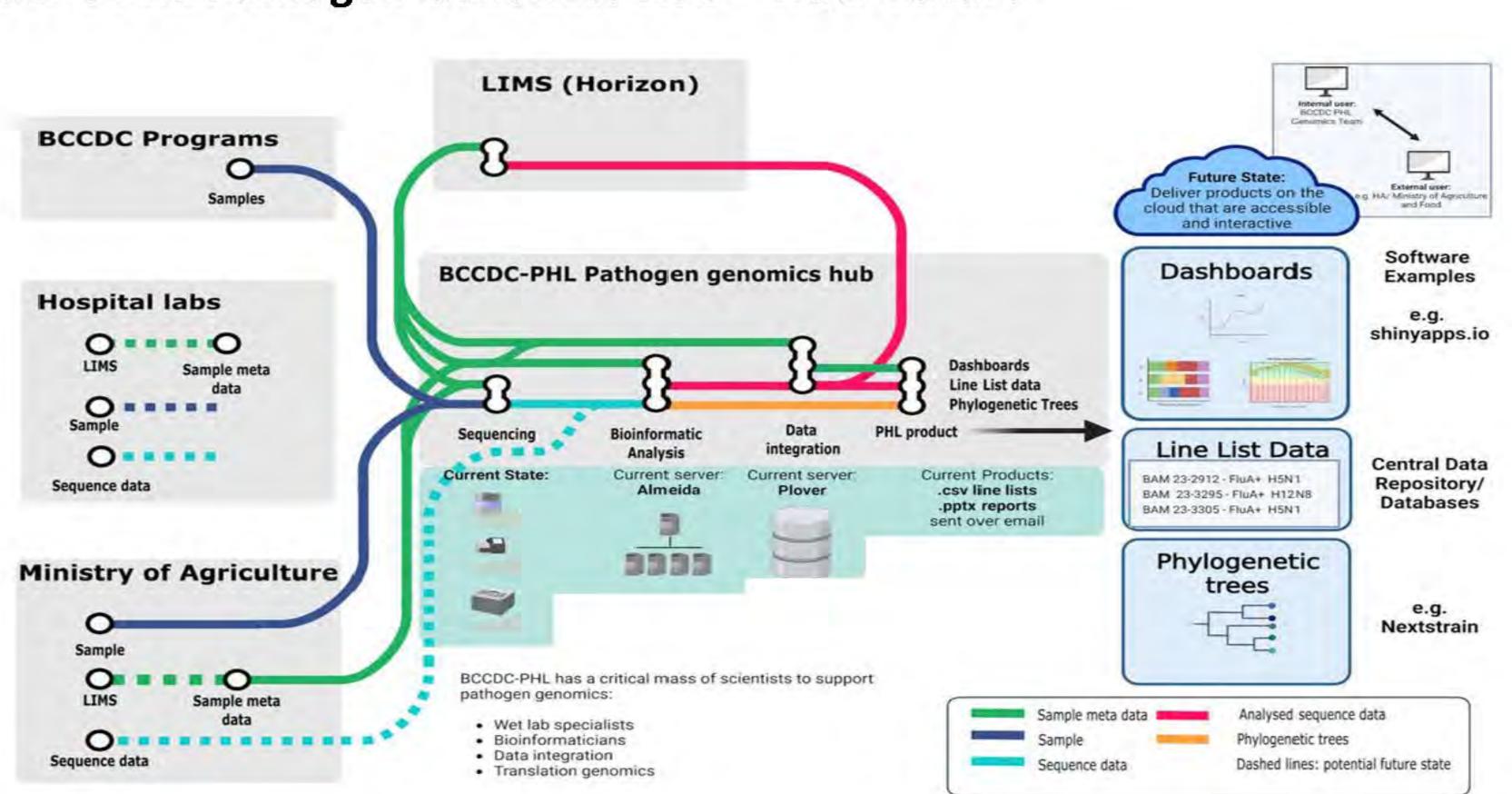
# One Health Proof-of-Concept

- BCCDC PHL sequencing highly pathogenic avian influenza for Animal Health Centre (Ministry of Agriculture and Forestry)
- Results are in PDF or in Powerpoint format, not user friendly
- --> provide genomics dashboard, and software access to AHC via PHSA Cloud
- --> automate reports and dashboards

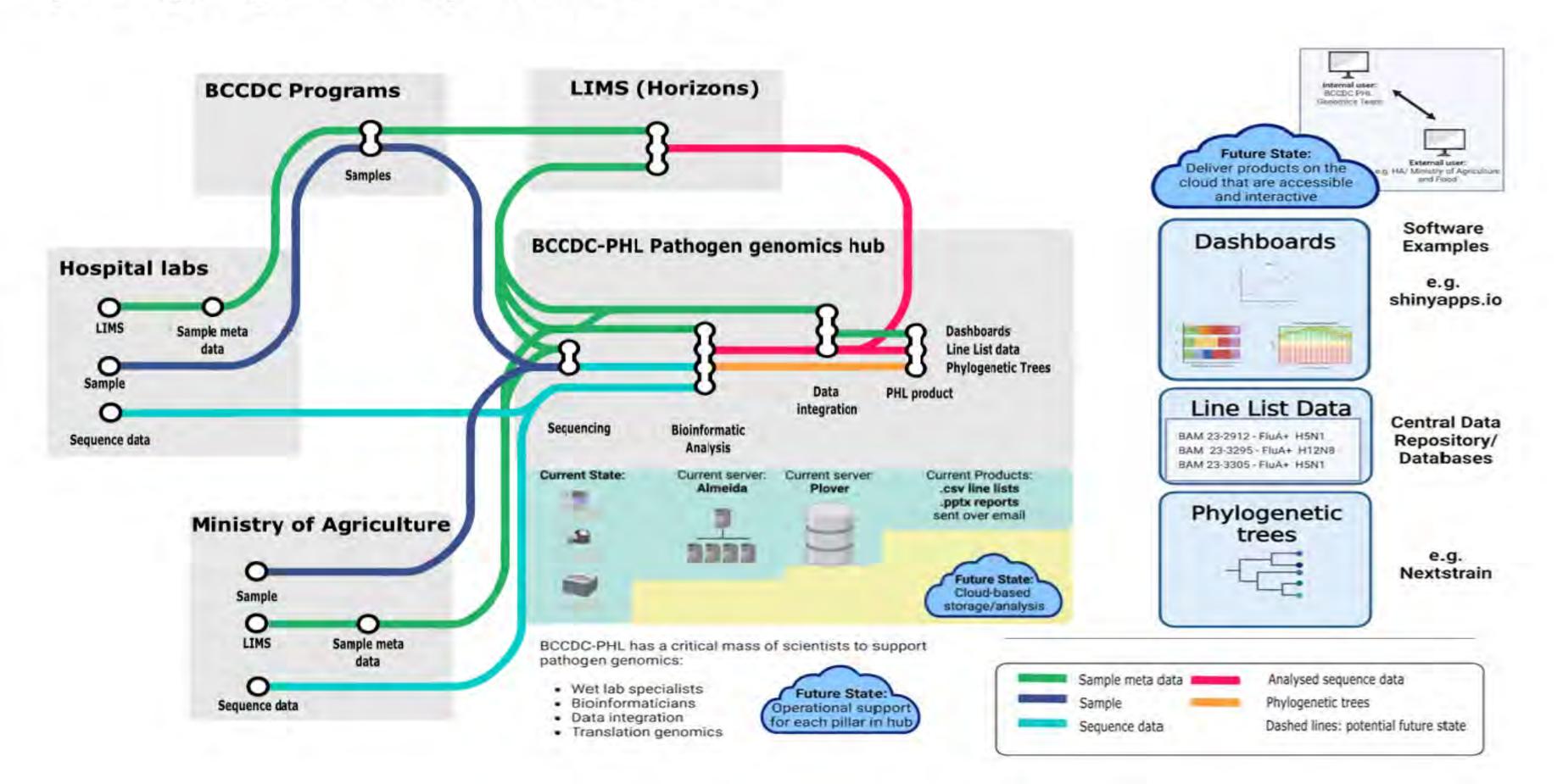




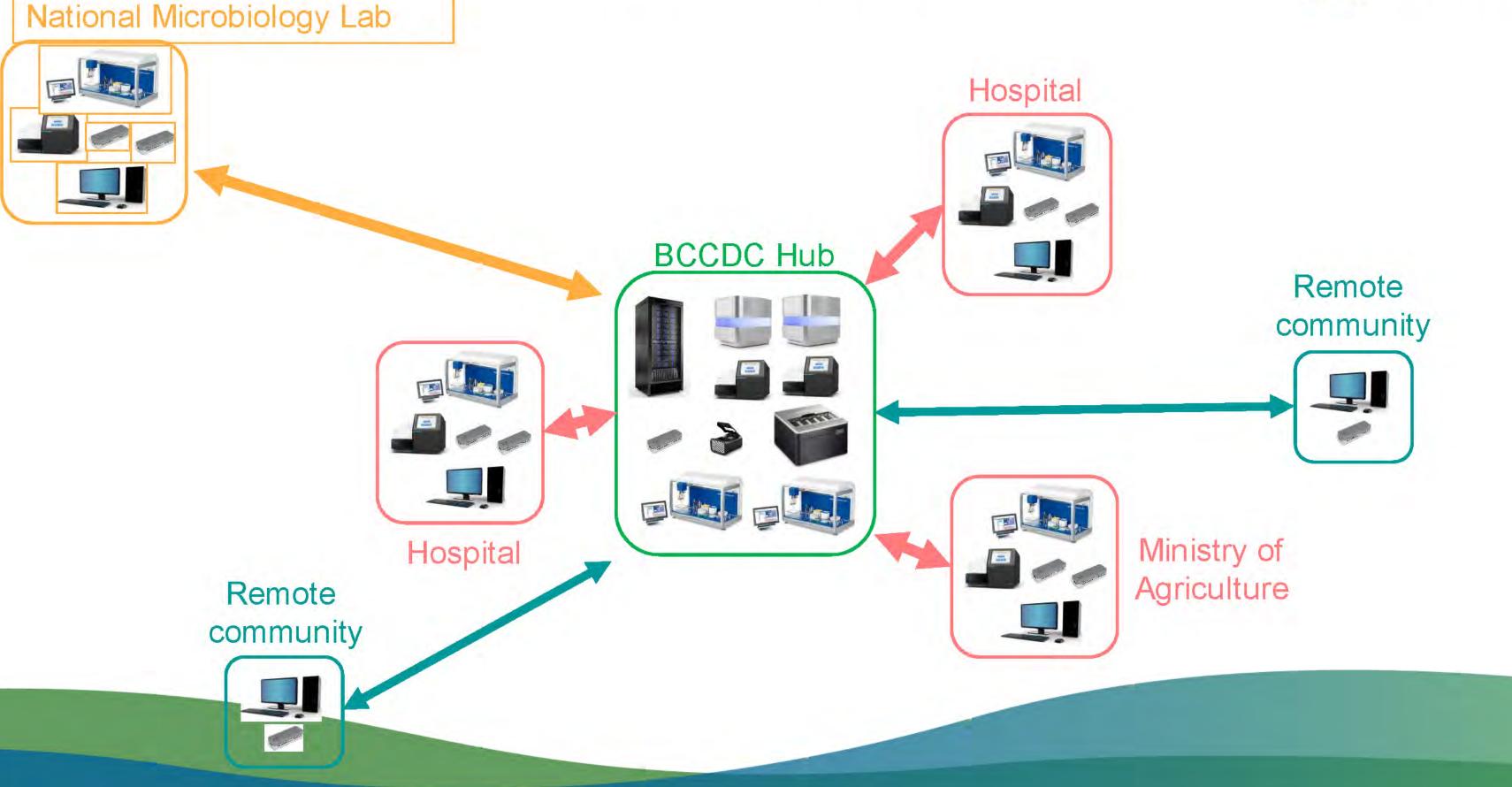
### **BCCDC PHL Pathogen Genomics Hub – Near Future**



# BCCDC PHL Pathogen Genomics Hub: Future State, an integrated pathogen genomics platform for BC



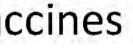
## **Genomics Hub and Spoke Model**



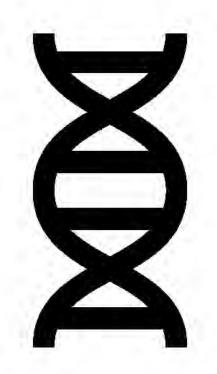


## Role of Pathogen Genomics in BC

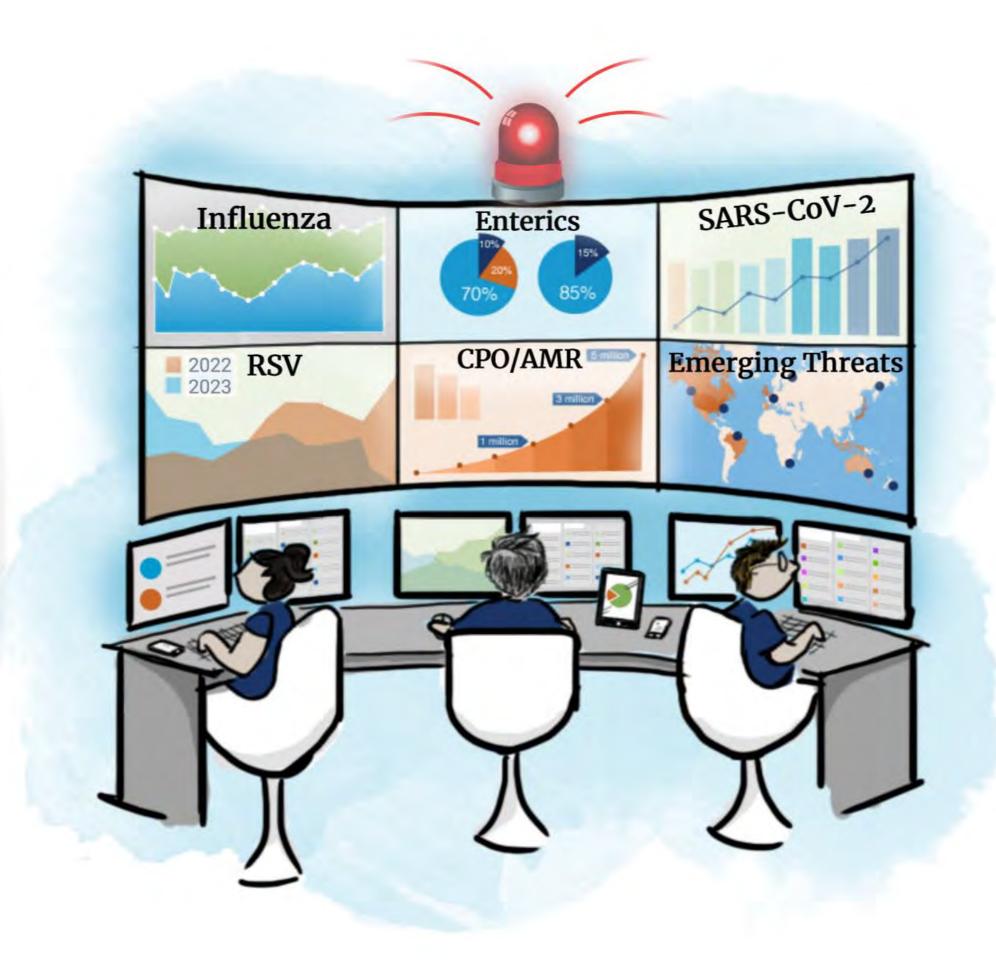
- Drive improvement in diagnostics, therapeutics and vaccines •
- Inform clinical, public health, policy decision making
  - Based on provincial/national/international databases
  - o Core "brain trust"
  - Innovation capacity
  - Response ready
- Build cost-effective, integrated capacity and services
- Equitable access to advanced genomics tools across RHAs
- Optimize connectivity
- One Health







## The vision: Provincial hub-spoke microbial genomics <u>infrastructure</u> and <u>tools</u> to support patient care, public health and One Health



## Acknowledgements

#### **BCCDC Public Health Lab**

#### **BCCDC Public Health Lab, Medical Staff**

•Dr. Natalie Prystajecky, Dr. Agatha Jassem, Dr. Muhammad Morshed, Dr. Adriana Adriano Dr. Inna Sekirov, Dr. Jennifer Grant, Dr. Catherine Hogan, Dr. Mel Krajden

#### BCCDC Public Health Lab, Genomics Senior Scientists

- •Dr. James Zlosnik (Bioinformatics)
- •Dr. John Tyson (Wetlab)
- •Dr. Shannon Russell (Translational Genomics)
- Dr. Chris Fjell (Data Informatics)

#### **BCCDC Public Health Lab/NML Bioinformaticians**

- Dan Fornika
- Sherrie Wang
- Jessica Caleta
- Tara Newman
- Adriana CarbreraDelgado
- •John Palmer

## KhunKhun

Informatics

team

Virus Isolation

Mycobacteriology

Hon and team

**oFrankie** Tsang

- oKevin Yang(NML LLTO)
- Outbreak coordinator oYin Chang

#### **BCCDC Data and Analytics Services**

•Dr. Hind Sbihi Yayuk Joffres And team!!!!

**Provincial Health** 

Services AutorARE/PANDA

#### **BCCDC Public Health Lab, Programs**

 Molecular and Microbial Genomics (MMG) oFrankie Tsang, Tracy Lee, Kathleen Kolehmainen, Cindy Zheng and

Bacteriology and Mycology

oJanet Fung, Rob Azana, Loretta Janz, Corinne Ng, Anthea Lam, Ben

AND SO MANY OTHERS!!!

oMabel Rodrigues, Trevor Hird, Danielle Jorgensen, Rupinder

oKelvin Lam, King Choi, Harris Kim, Omid Ghahramani

# THANK YOU!





## **Discussion Period**

### Any questions?

Please use the **Q&A tab** to submit your questions for our speaker. You can "**like**" other people's questions to push them up in priority.



## **Closing Remarks**



### **Thank You!**

Join us on Tuesday, June 25, 2024 (1:00-2:00pm ET) for the next seminar!

Please complete our **survey** that will be shared shortly after the seminar. Scan the QR code.

Seminar recording and presentation slides will be posted on <u>https://nccid.ca/</u> within two weeks.

Visit <u>https://nccid.ca/surveillance-advances-seminar-</u> <u>series/</u> for more information about the Surveillance Advances seminar series.

