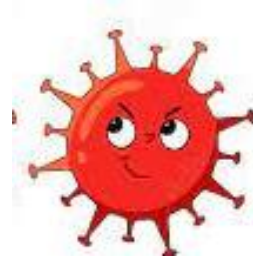
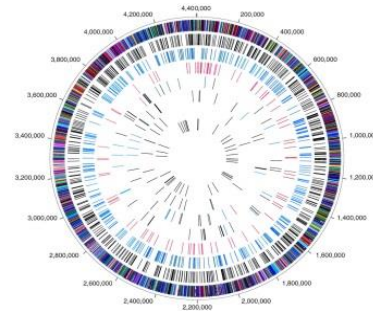
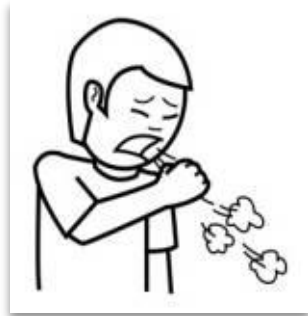


Infection Control Strategies: Innovative strategies for infection control in hospitals.



Darío García de Viedma

Hospital General Universitario Gregorio Marañón, Madrid, Spain



ciberes
Centro de Investigación Biomédica en Red
Enfermedades Respiratorias

Human - Centric Indoor Climate for Healthcare Facilities (HumanIC)
HORIZON-MSCA-2022-DN-01

Warsaw February 27th 2024

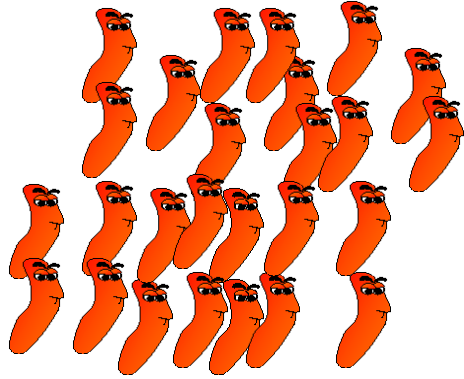


Infection Control Strategies: Innovative strategies for infection control in hospitals.

or

How to Use Genomic Epidemiology to
understand transmission dynamics and
orientate interventions

Genomic epidemiology



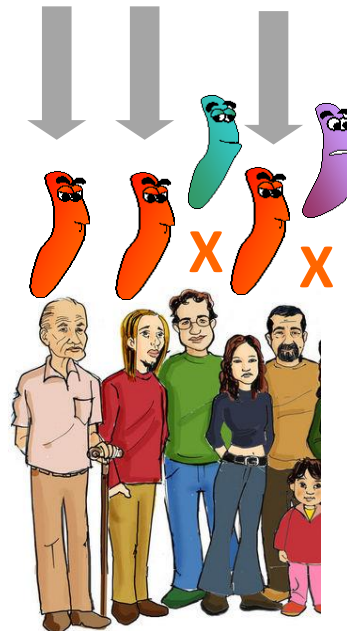
Bacteria X (Pseudomonas aeruginosa)



Different
STRAINS

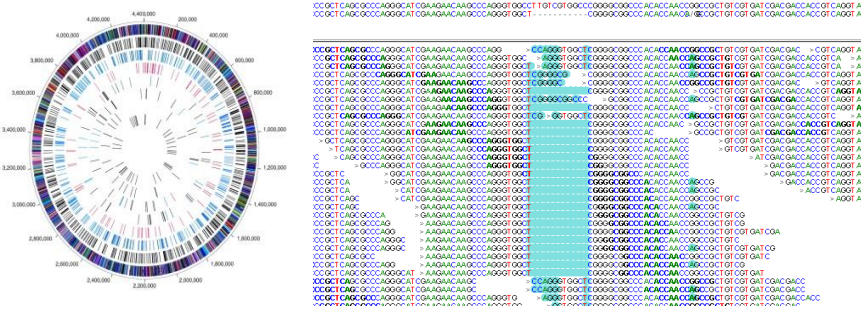


Transmission
CLUSTER



Orphan cases

Genomic Epidemiology



Number of SNPs between bacteria
from different patients

Quantitative
analysis

Number of SNPs

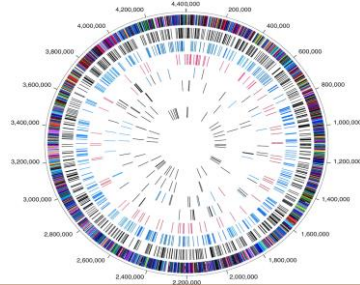


Transmission
CLUSTER



Orphan cases

Genomic epidemiology in TB



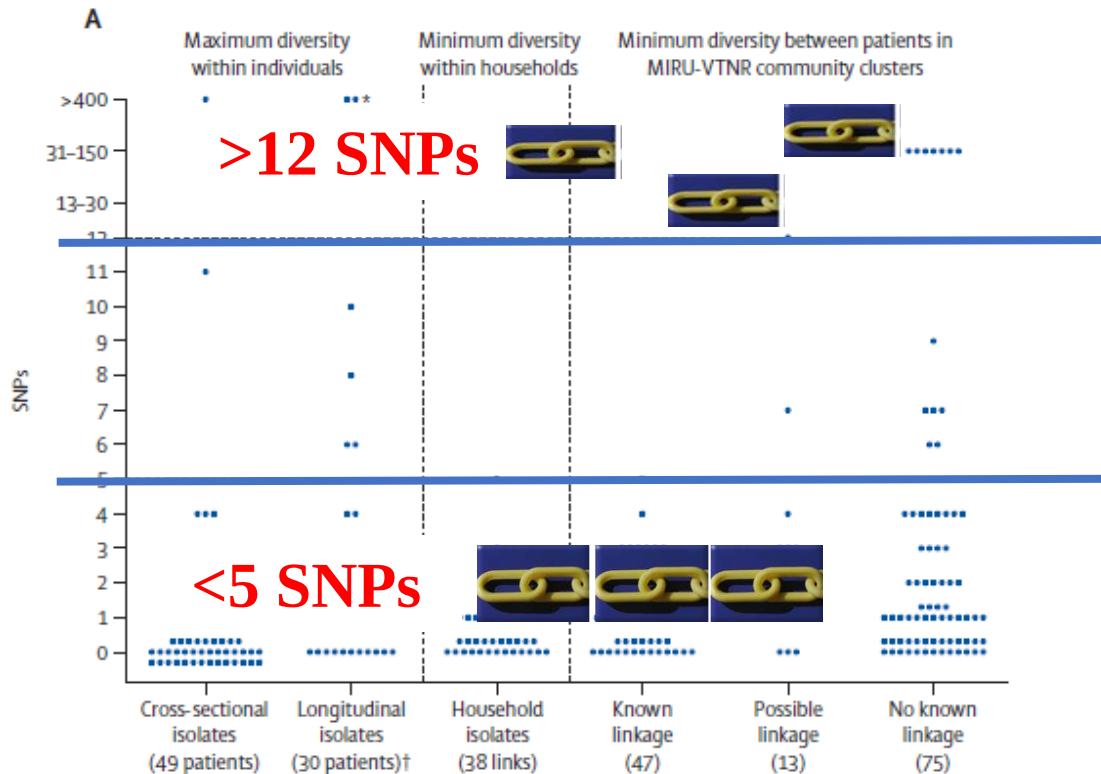
Whole Genome Sequencing

SNPs similarity thresholds to define clusters

Lancet ID, Nov 2012

Whole-genome sequencing to delineate *Mycobacterium tuberculosis* outbreaks: a retrospective observational study

Timothy M Walker*, Camilla L C Ip*, Ruth H Harrell*, Jason T Evans, Georgia Kapatai, Martin J Dedicoat, David W Eyre, Daniel J Wilson, Peter M Hawkey, Derrick W Crook, Julian Parkhill, David Harris, A Sarah Walker, Rory Bowden, Philip Monk†, E Grace Smith†, Tim E A Peto†



Different SNP thresholds for different bacteria

Genomic Epidemiology

HOSPITAL OUTBREAK **ALERT**

Higher number of cases
than expected

1

**Quantitative Genomic
analysis**

NO
CLUSTER

Number
of SNPs

CLUSTER

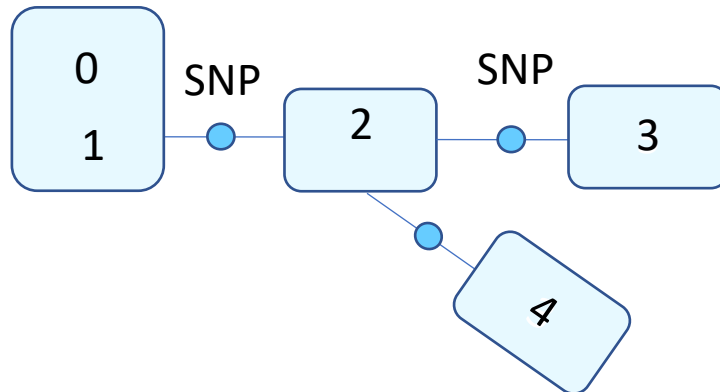
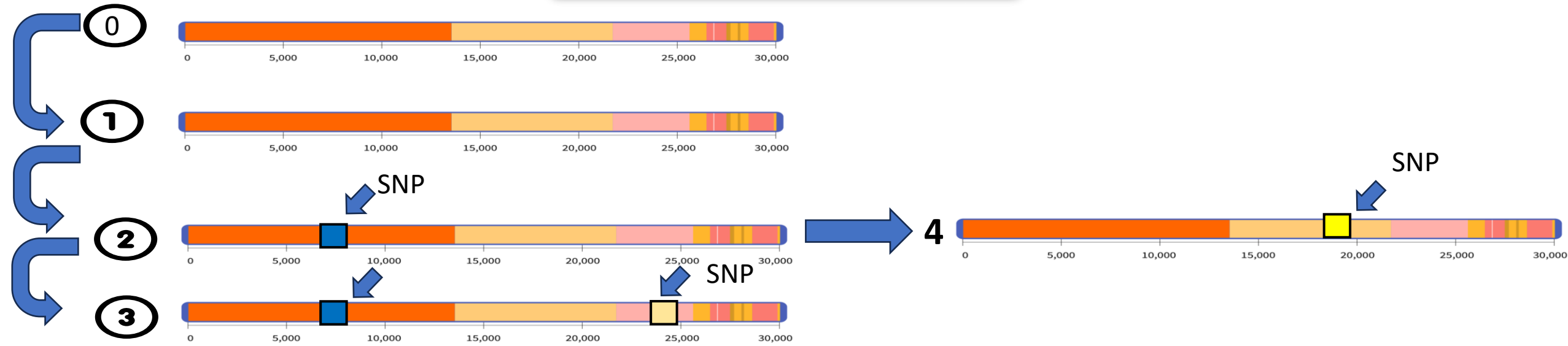
2

**Qualitative/Evolutionary
Genomic analysis**



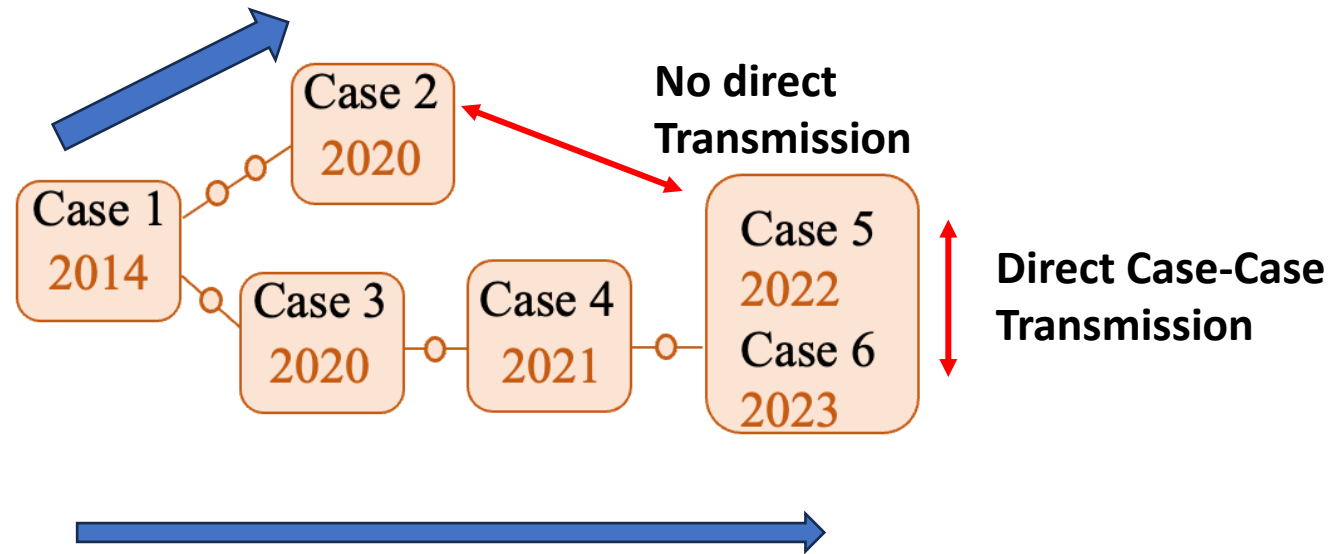
Qualitative evolutionary analysis

CLUSTER



Evolutionary analysis

Analysis of the
distribution of SNPs



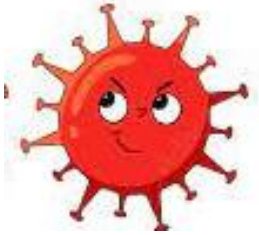
Genomic epidemiology

1. Mycobacterium tuberculosis

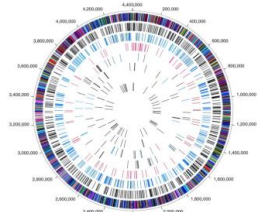
Genomic epidemiology

1. *Mycobacterium tuberculosis*

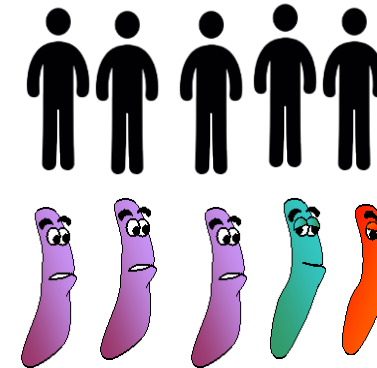
2. SARS-CoV-2



Genomic epidemiology

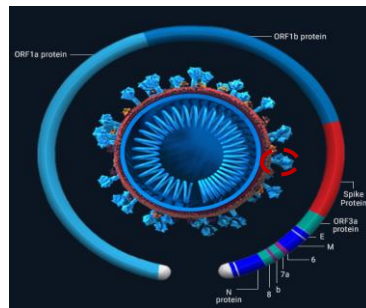
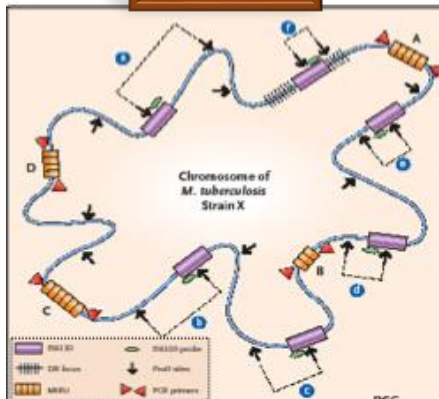


Mycobacterium tuberculosis



4.4 Mb

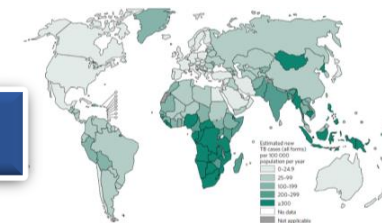
SARS-CoV-2



30Kb

Populational

Global



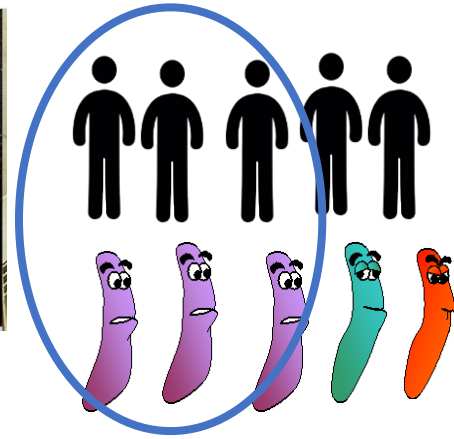
Local



Hospital



**Hospital
(Nosocomial)
transmission**

[illegible]

Tailor specific Control Measures

Replicate the model

Hospital



**Control of Hospital
Transmission**

Microbiology and Infectious Diseases

Preventive Health

Laboral Risks

Genomic Research

Direction

Outbreaks identification
Nosocomial cases
HCWs infected

Sequencing

Sequencing

Lunes	Martes	Miércoles	Jueves	Viernes	Sábado	Domingo
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

Analysis of
Results

All-parts
discussion

Genomic confirmation of suspected outbreaks

RULE-IN Cases

0 SNPs

10 patients
7 HCWs

Case 1	(14)	
Case 2	(17)	
Case 3	(18)	
Case 4	(18)	
Case 7	(24)	
Case 9	(27)	
Case 10	(30)	
Case 11	(27)	
Case 12	(28)	
Case 13	(28)	
		Case 15 (HCW)(17)
		Case 16 (HCW)(18)
		Case 17 (HCW)(18)
		Case 19 (HCW)(19)
		Case 20 (HCW)(19)
		Case 21 (HCW)(19)
		Case 22 (HCW)(19)

Case 5 (24)

Case 6 (19)
Case 14 (s) (17)

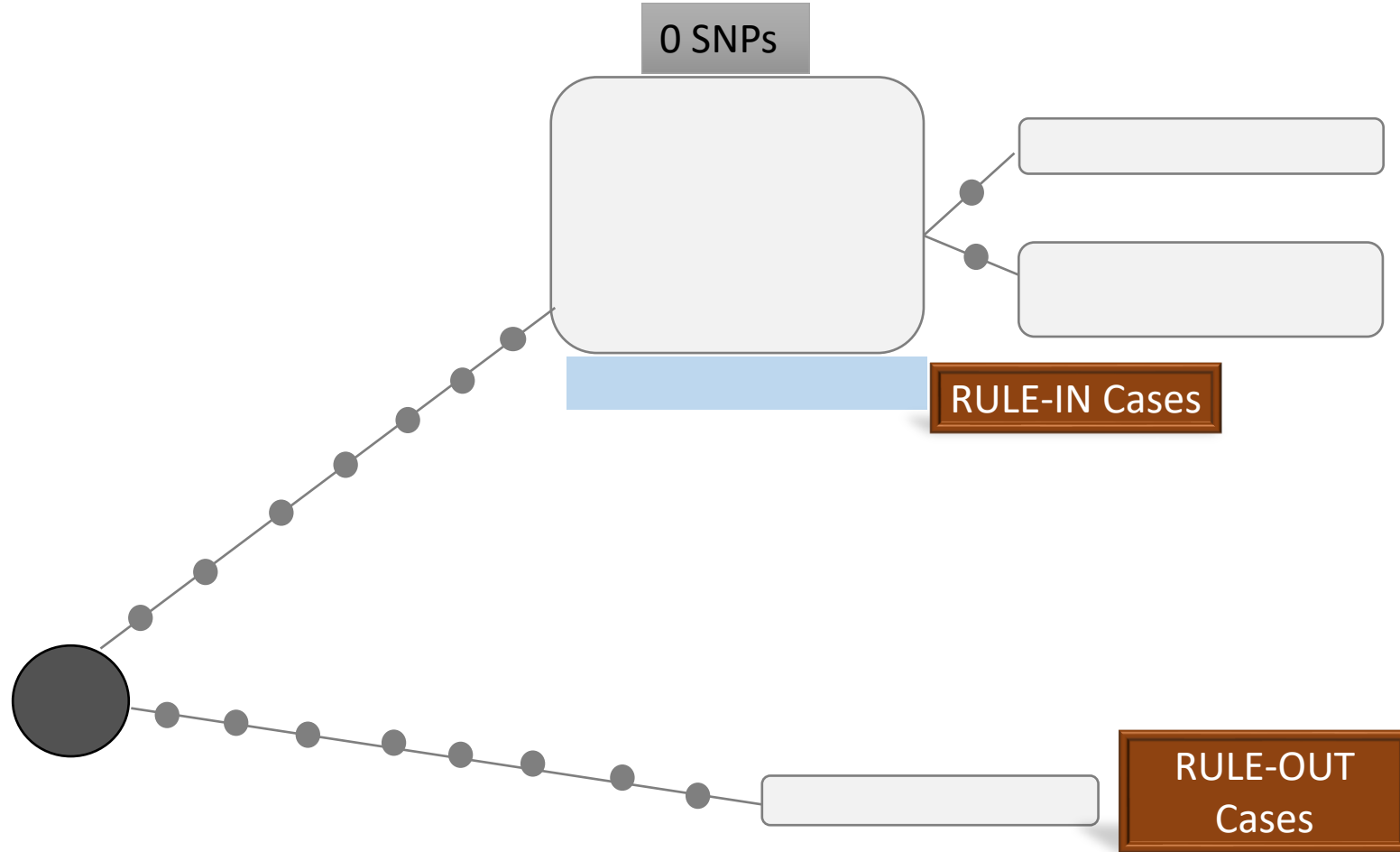
Case 23 (s) (19)

Case 18 (s) (25)

RULE-OUT
Cases

Major nosocomial outbreaks

Monitoring outbreaks after implementing control measures



Chracterization of complex outbreaks

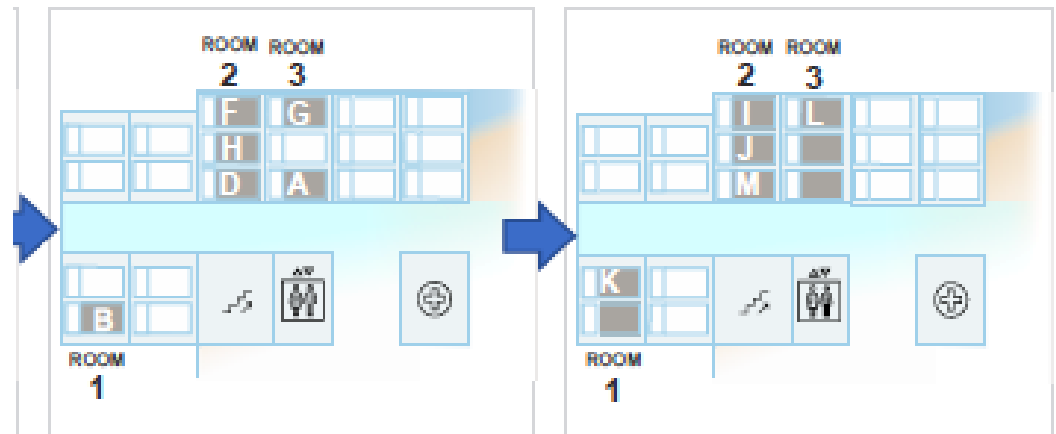
Suspected outbreak

Department A

12 patients

1 HCW

Cases from 09/21/2020 to 09/27/2020 Cases from 10/05/2020 to 10/11/2020

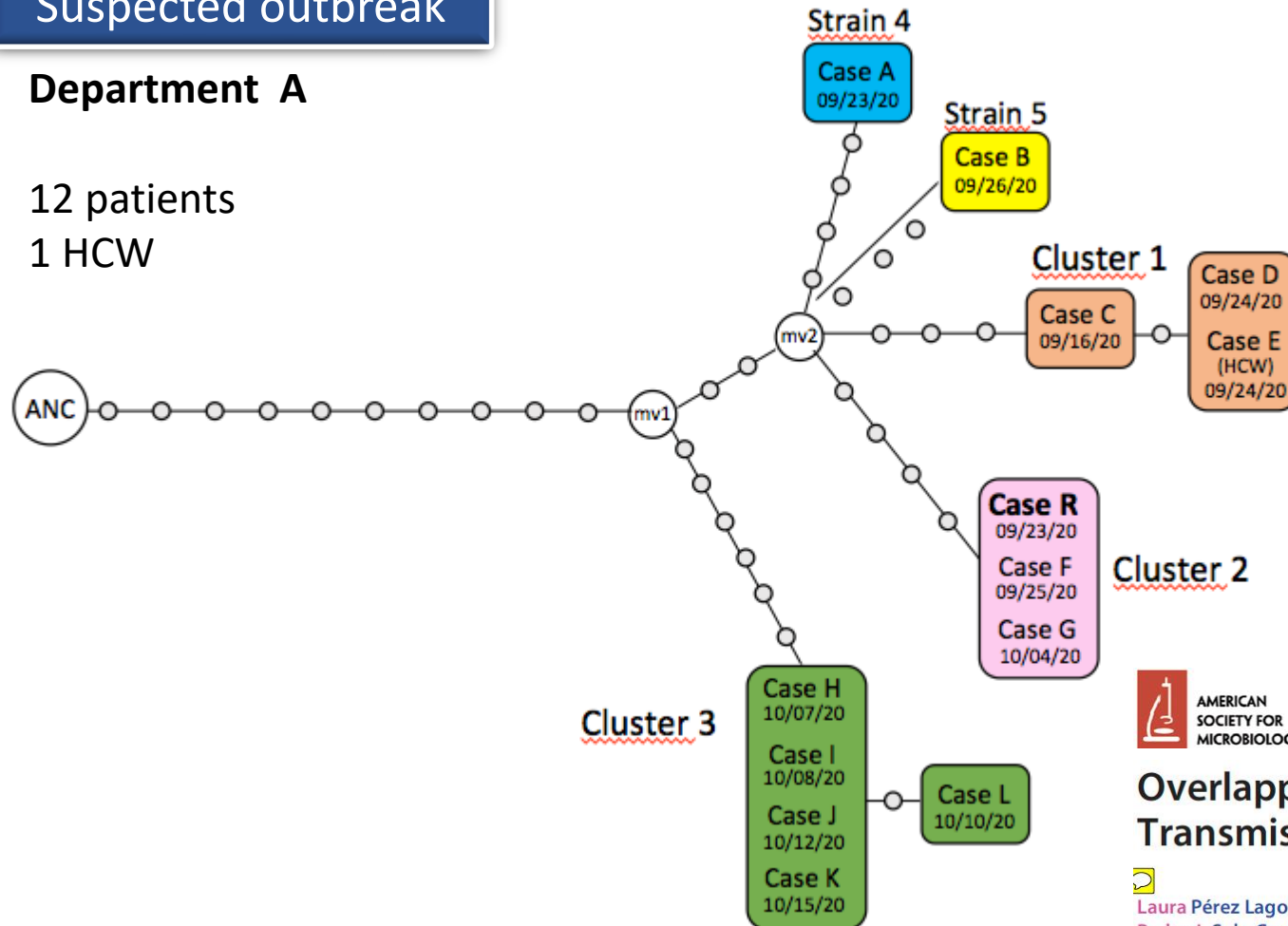


Chracterization of complex outbreaks

Suspected outbreak

Department A

12 patients
1 HCW



Independent
introductions

Overlapping
outbreaks



Overlapping of Independent SARS-CoV-2 Nosocomial Transmissions in a Complex Outbreak

Laura Pérez Lago,^{a,b} Helena Martínez Lozano,^{b,c} Jose Antonio Pajares Díaz,^{b,c} Arantxa Díaz Gómez,^{b,c} Marina Machado,^{a,b} Pedro J. Sola-Campoy,^{a,b} Marta Herranz,^{a,b,d} Maricela Valerio,^{a,b} María Olmedo,^{a,b} Julia Suárez González,^{b,g} Víctor Quesada Cubo,^b María del Mar Gómez Ruiz,^{b,f} Nieves López Fresneña,^{b,e} Ignacio Sánchez Arcilla,^{b,f} Iñaki Comas,^{h,j} Fernando González Candelas,ⁱ Sonia García de San José,^k Rafael Bañares,^{b,c,l,m} Pilar Catalán,^{a,b,d} Patricia Muñoz,^{a,b,d,l} Darío García de Viedma,^{a,b,d} on behalf of Gregorio Marañón Microbiology-ID COVID-19 Study Group

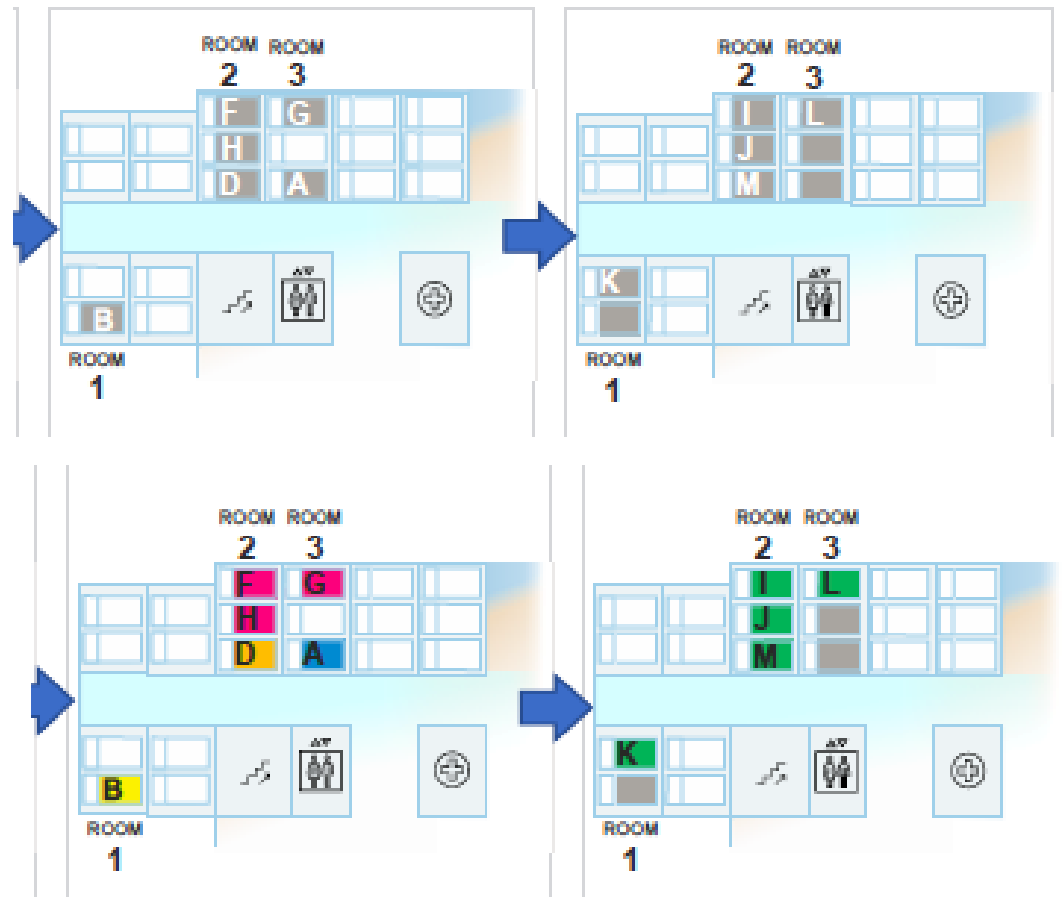
Chracterization of complex outbreaks

Suspected outbreak

Department A

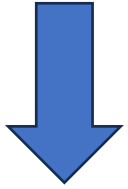
12 patients
1 HCW

Cases from 09/21/2020 to 09/27/2020 Cases from 10/05/2020 to 10/11/2020

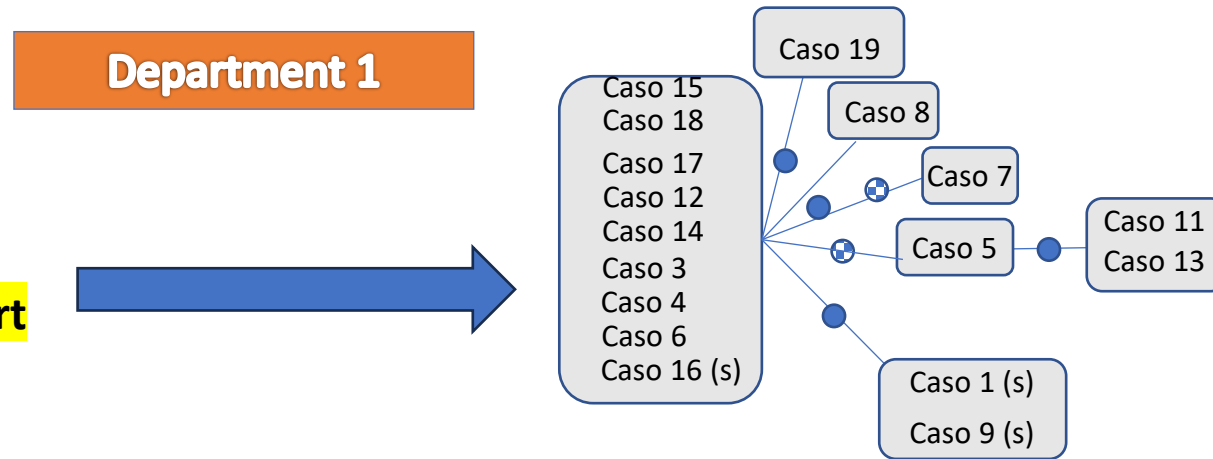


Chracterization of complex outbreaks

Firstly: Genomic analysis
guided by an **outbreak alert**



Compare all sequences
from different departments
among them, **without
previous assumptions or
suspicions**

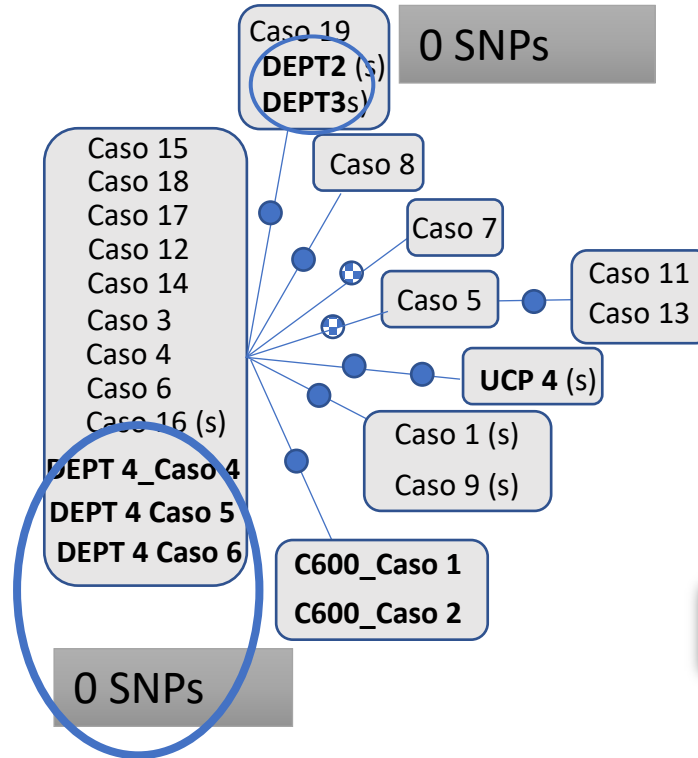


Characterization of complex outbreaks

Firstly: Genomic analysis
guided by an **outbreak alert**

Compare all sequences
from different departments
among them, **without
previous assumptions or
suspicions**

Department 1



**Multidepartment
transversal outbreak**

Transversal links

Outbreak Department 1
Cases Department 2
Cases Department 3
Cases department 4

Multidepartment transversal outbreaks

0 SNPs

, 09/11/21)

, 10/11/21)

, 10/11/21)

, 10/11/21)

1, 12/11/21) (

, 15/11/21)

, 15/11/21)

, 15/11/21)

09, 16/11/21)

, 16/11/21

, 16/11/21)

, 16/11/21)

, 17/11/21)

, 23/11/21)

, 23/11/21)

, 22/11/21)

, 23/11/21)

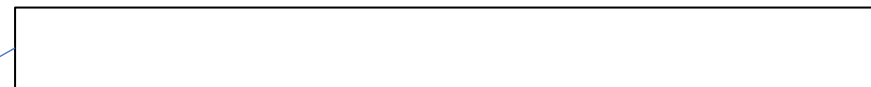
Infectious
diseases

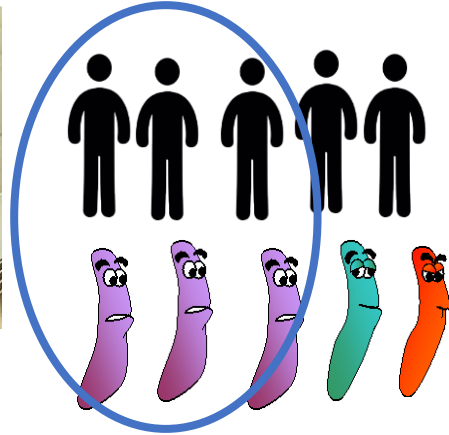
Residents

Radiology

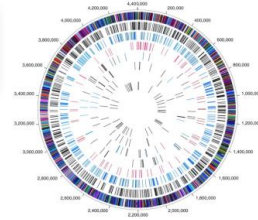
Technicians

Cardiology





Genomic epidemiology



+

Epidemiological data

Multidepartment transversal outbreaks

Multilnstitutions transversal outbreaks

20/10/21)

Hospital Ward X

, 20/10/21) (S)

22/10/21)

Elderly residence 1

GRESADO

, 06/10/21)
, 08/10/21)

, 10/10/21)

Elderly residence 2

, 13/10/21) (

COINCIDENCE in
EMERGENCY DEPT
BEFORE DECIDING
WHERE THEY WILL BE
HOSPITALIZED

Hospital



Control of Nosocomial Transmission

Microbiology and Infectious Diseases

Preventive Health

Laboral Risks

Genomic Research

Direction

Precise knowledge of nosocomial dynamics



Tailored interventions

Visitors control

HCWs active screening

Reduction of intra-hospital mobility

New Multidisciplinary working dynamic sharing a new genomic language

Genomic surveillance Circuit at a Hospital

(Not a research Centre)
And within the pandemic

Response Time

Lunes	Martes	Miércoles	Jueves	Viernes	Sábado	Domingo
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

72 h

Prolonged
quarantine

Emphasized Contact
tracing

Illumina sequencing

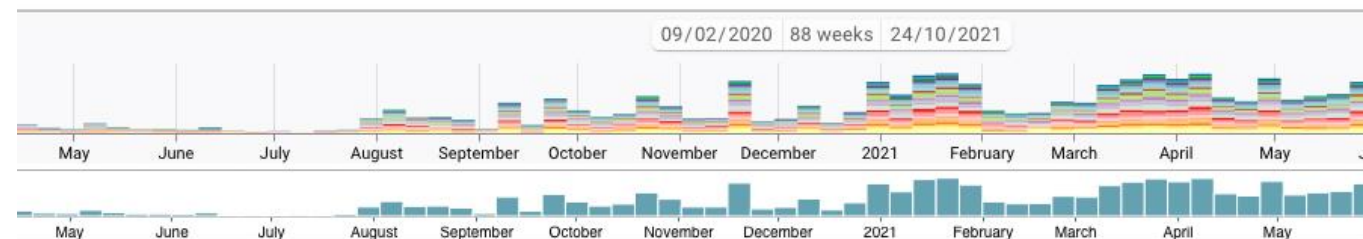
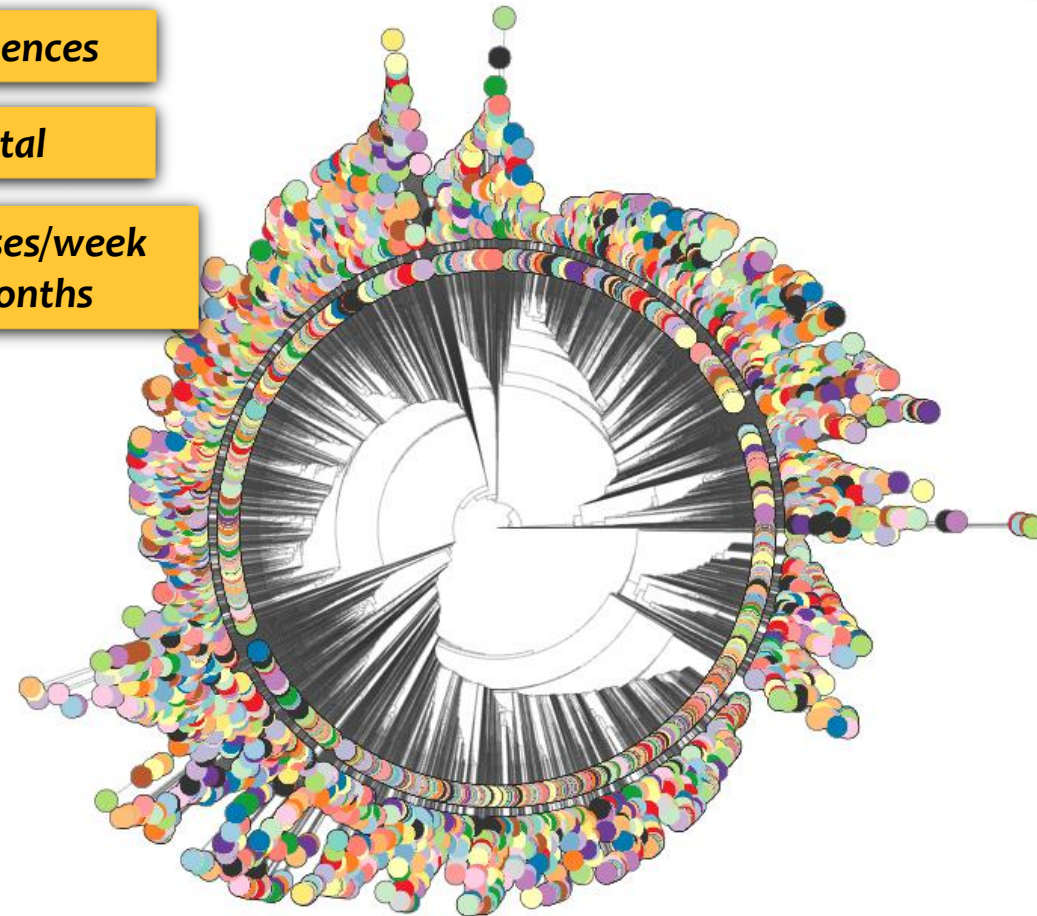
96-120 sequences/week

MiSeq/NextSeq

6074 sequences

15% total

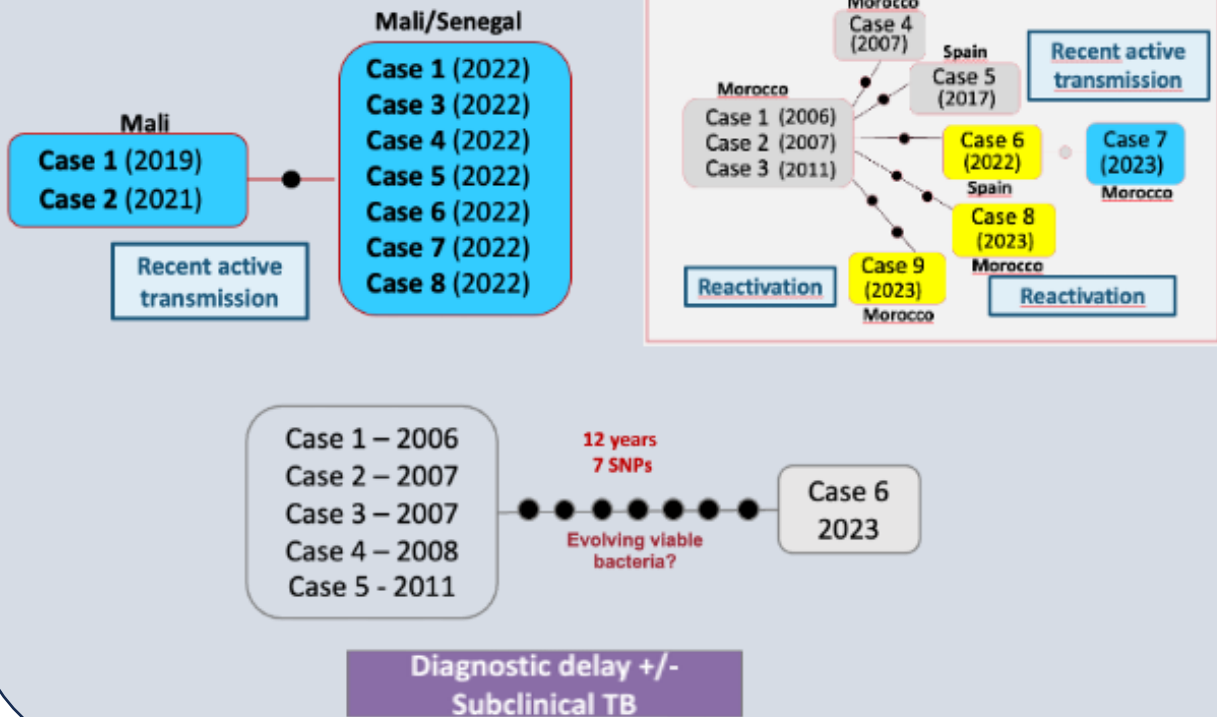
75-100% cases/week
last 5 months



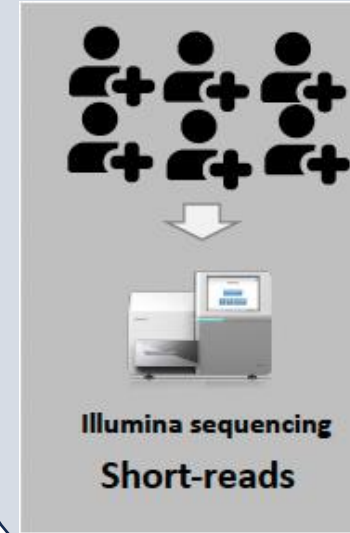
Valuable information: Faster analysis

Evolutionary analysis

Analysis of the distribution of SNPs



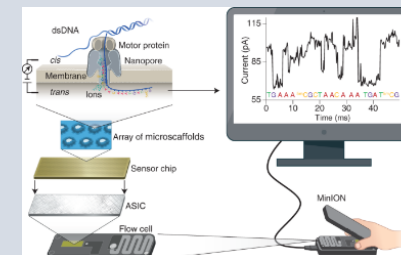
Illumina sequencing



-Pooled in the same run
-Subcultured isolates

Delayed results

Nanopore sequencing

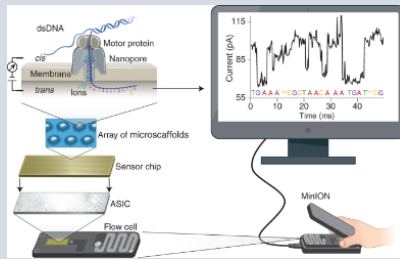


Real-time analysis

Speed
Flexibility

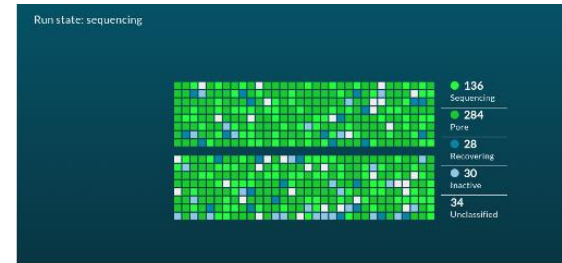
Genomic surveillance Circuit from a Hospital

Nanopore sequencing



Real-time analysis

Speed
Flexibility



Minion Sequencing

1-16 sequences/run

Illumina
sequencing

-Pooled in the same run
-Subcultured isolates

Nanopore
sequencing

One incident case,
immediate analysis



Speed
Flexibility

March-July

2023

Isolate

Flow-cell
usages

1	A
2	B
3	C
4	C
5	C
6	C
7	C
8	C
9	C
10	C
11	D
12	D
13	D
14	D
15	E
16	F
17	E
18	F
19	E
20	F
21	E
22	F
23	G

Mean
coverage

% Genome
coverage
>20X

Run time

80,88	96,49	1h 13min	Orphan
48,51	94,6	24h 48min	Clustered
91	95,91	1h 50min	Orphan
50,33	93,02	1h 50min	Orphan
48,47	94,05	4h 4 min	Orphan
36,02	92,18	2h 37 min	Orphan
76,68	96,63	1h 13 min	Orphan
72,73	95,64		Clustered
81,94	96,29	50% < 2 hours	Orphan
54,91	95,01		Orphan
70,91	95,59	51 min	Orphan
86,82	96,53	1h 23 min	Clustered
59,68	95,42	2h 49 min	Orphan
72,36	95,84	1h 35 min	Clustered
76,84	94,69	1h 11min	Clustered
74,74	96,49	2h 28 min	Orphan
75,32	95,99	3h 11min	Clustered
87,58	96,46	3h 58min	Orphan
78,72	97,27	1h 24 min	Clustered
72,59	96,76	1h 29 min	Clustered
73,42	97,34	3h 4min	Clustered
73,65	97,46	2h 24min	Orphan
68,24	96,1	2h 18min	Orphan

Genomic epidemiology

1. *Mycobacterium tuberculosis*

2. SARS-CoV-2

3. Nosocomial transmission

Vulnerable patients
MDR bacteria

Klebsiella michiganensis VIM Padiatric Oncology

Pseudomonas aeruginosa XDR ICU

Serratia UCCQ

Pseudomonas UCCQ

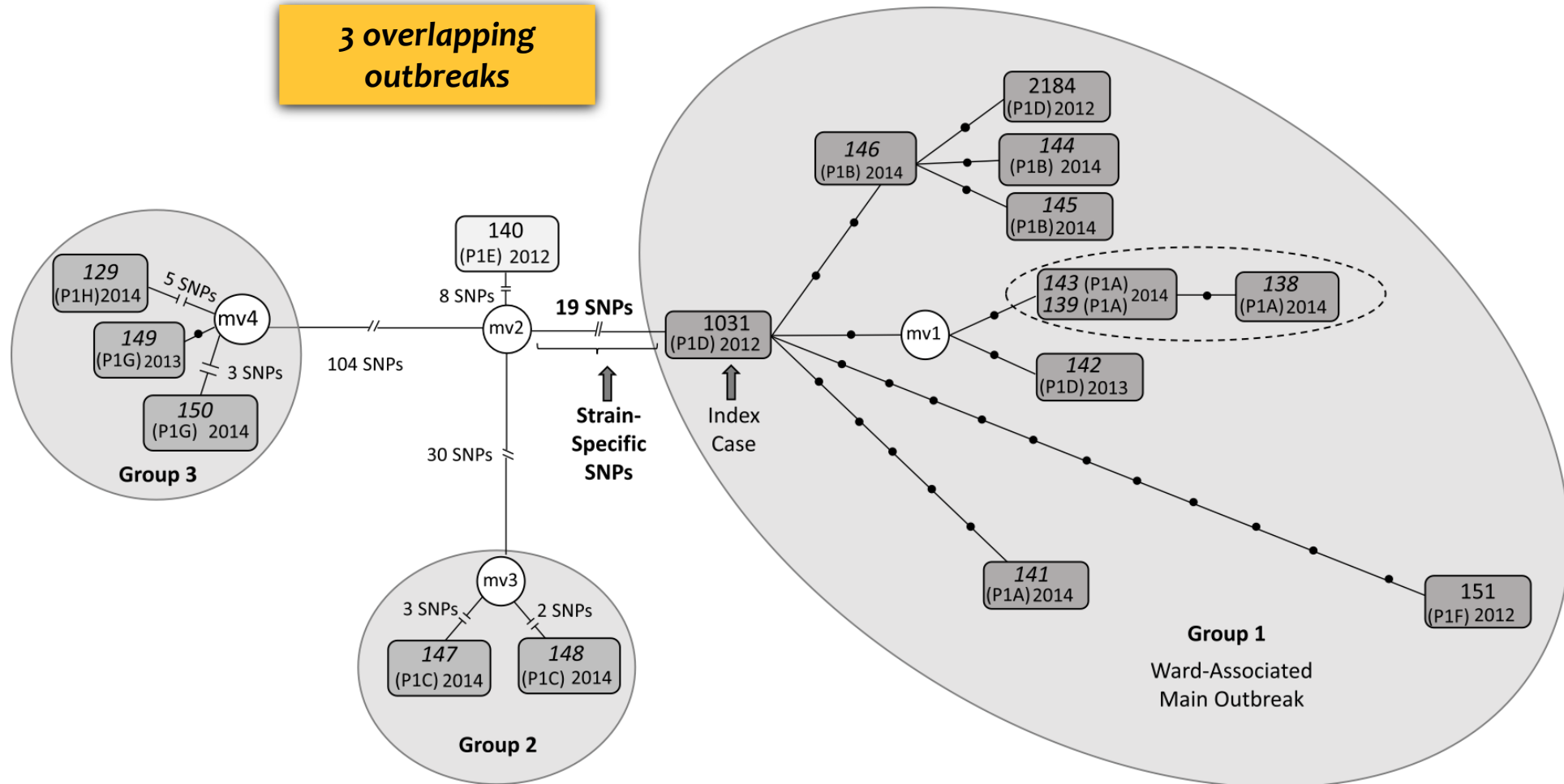
Serratia UCI Neonatology

MDR *Pseudomonas aeruginosa*

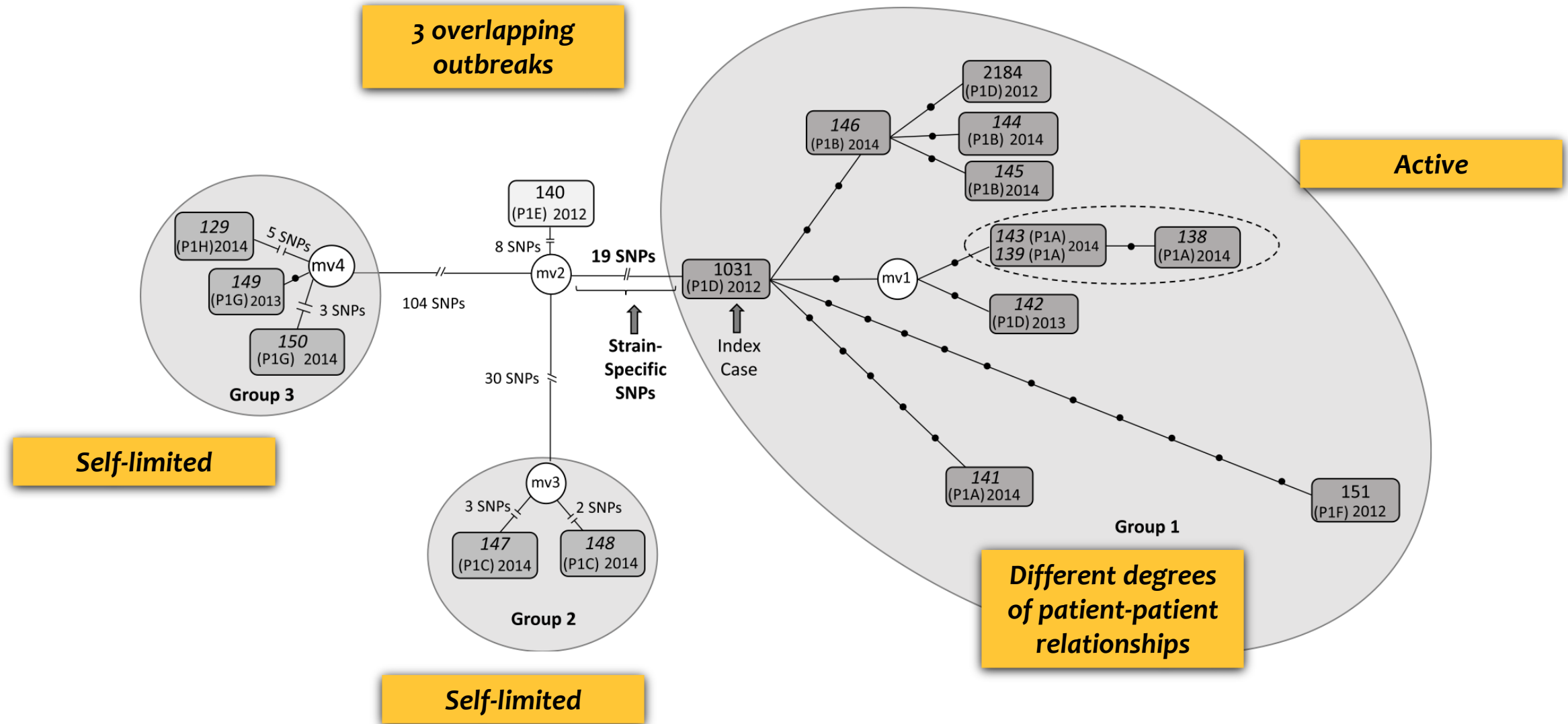
outbreak alert

in Haematology ward

MDR *Pseudomonas aeruginosa* outbreak alert in Hematology ward



MDR *Pseudomonas aeruginosa* outbreak alert in Hematology ward



***Serratia marcescens* ICU Neonatology**

along 5 months

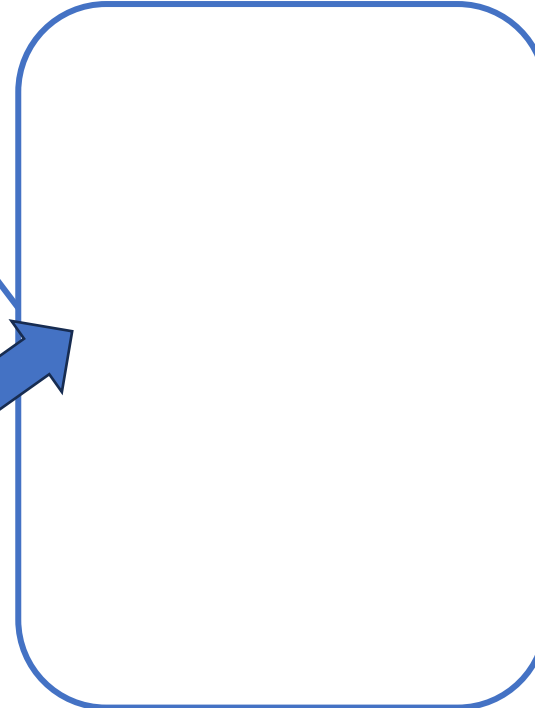
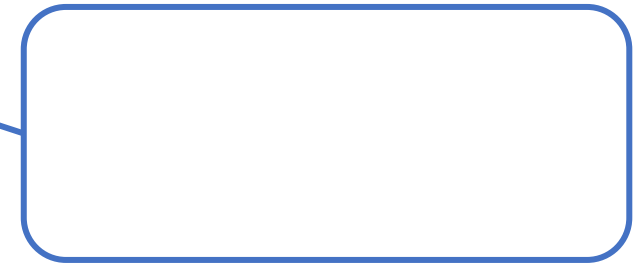
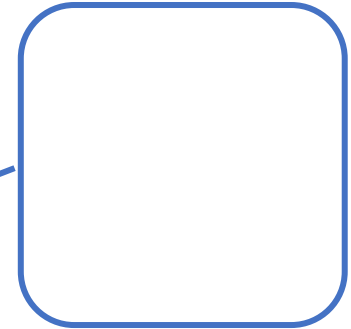
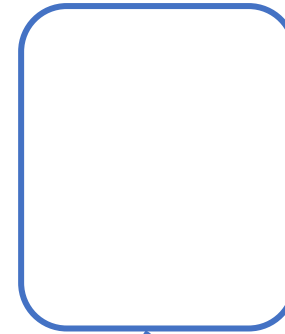
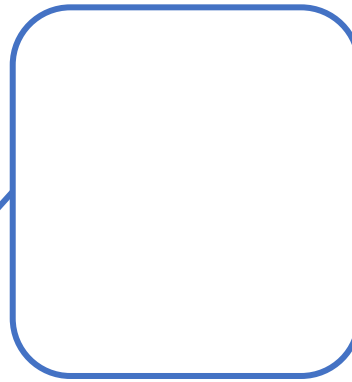
Outbreak 1

Serratia ureilytica

17 cases

Serratia ureilytica

Brote 1

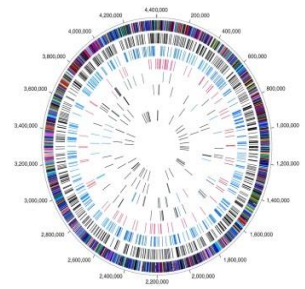


Alta similitud
pero
Secuenciación
subóptima

Only 1
environmental
(Sink)

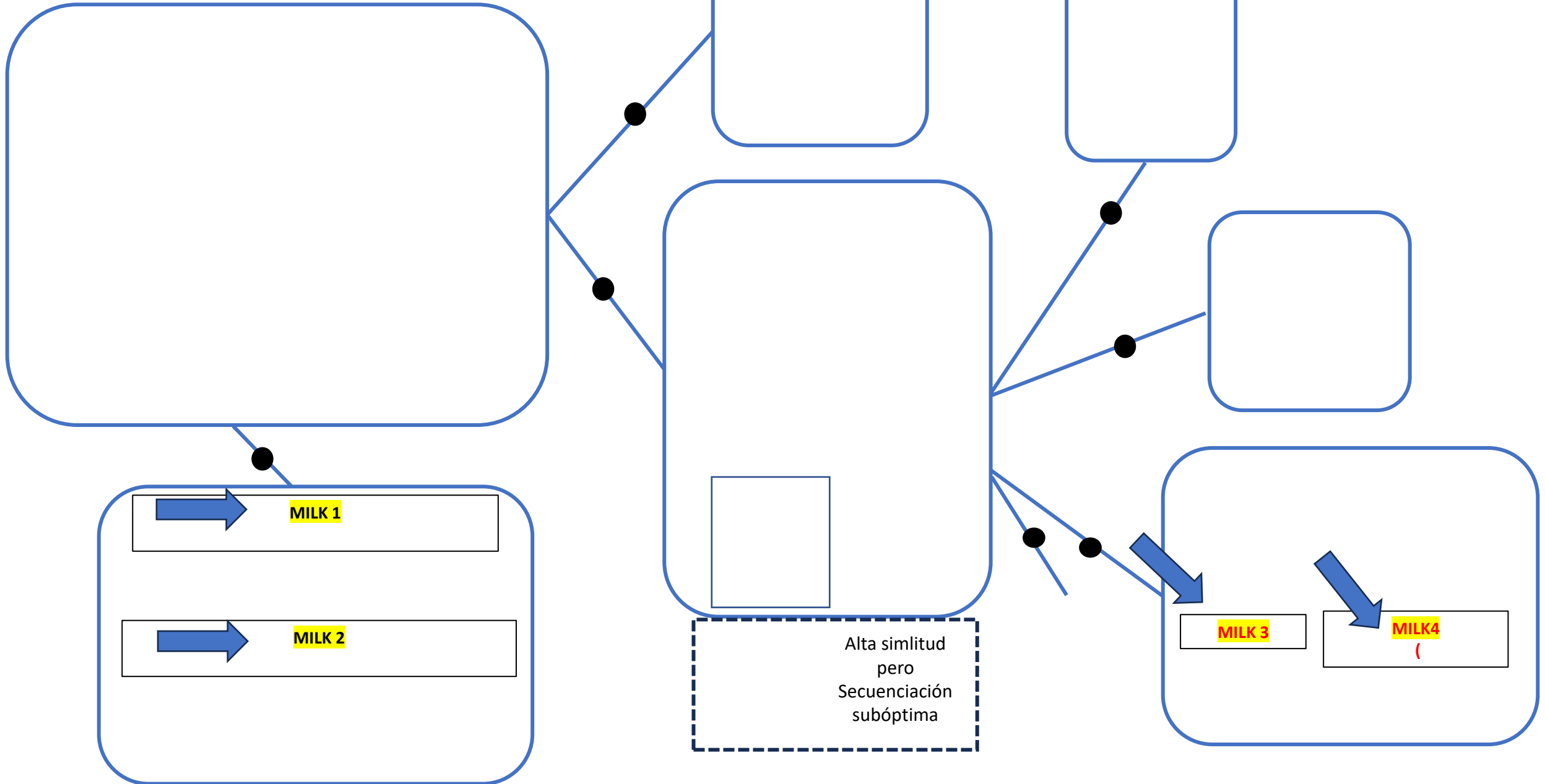
Reasons for
persistence?

Breast milk donated for other kids (MILK bank): Sterilized but control cultures

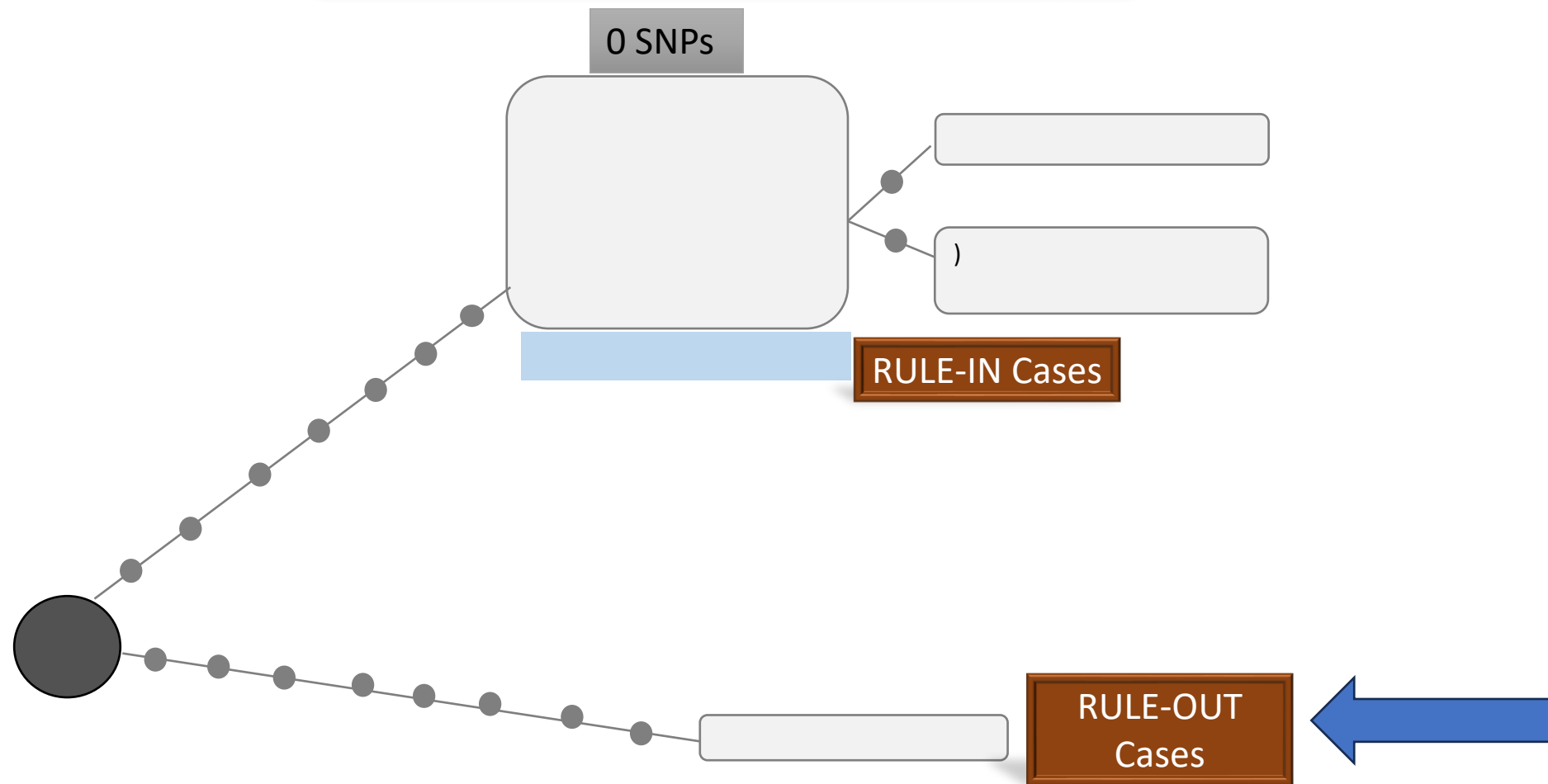


Serratia ureilytica

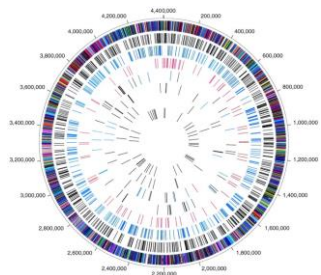
Brote 1



Monitoring outbreaks after implementing control measures



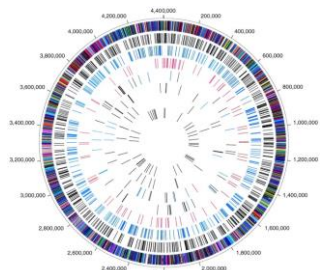




***Identify informative
simple markers***



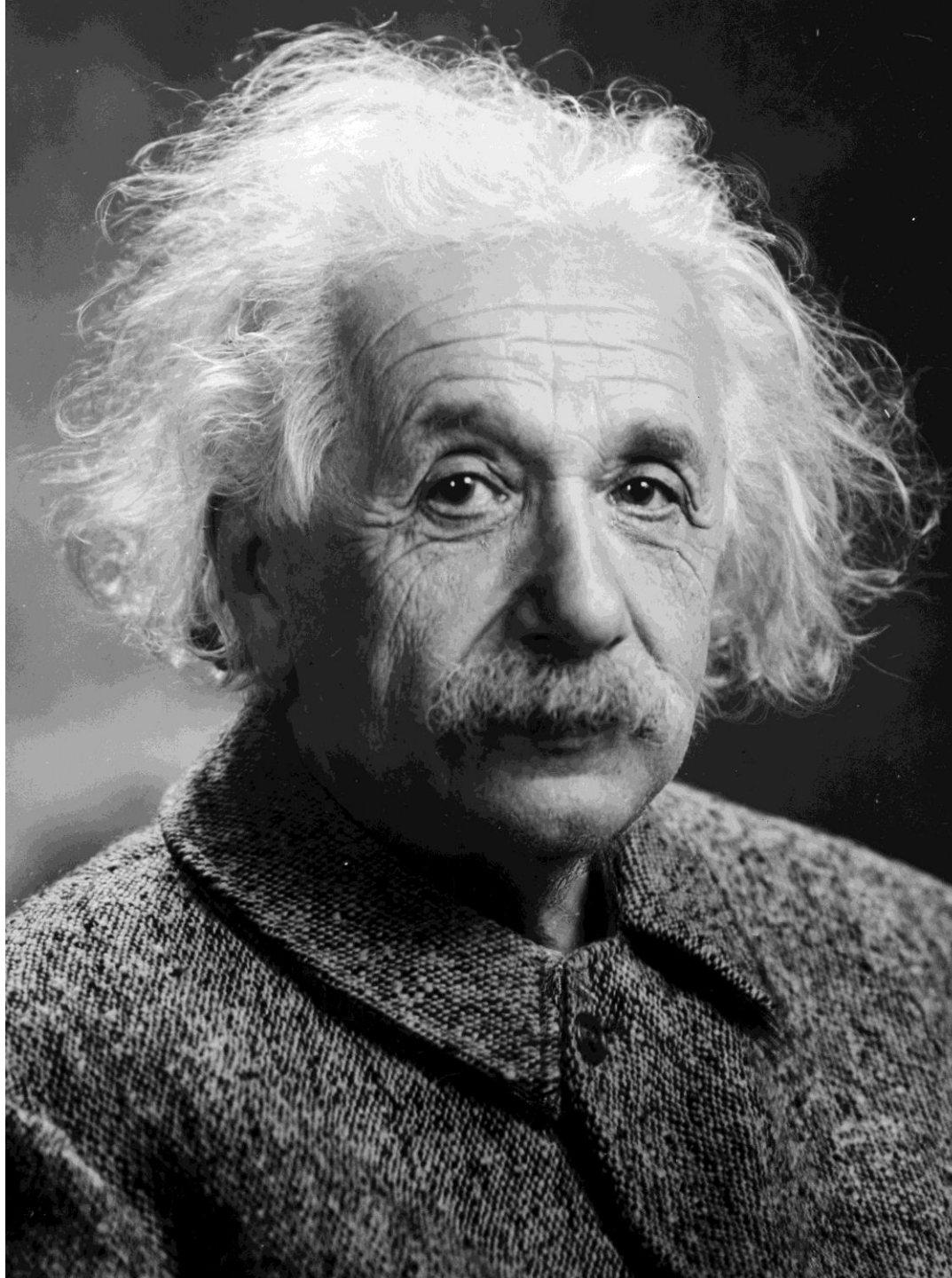
***Target them with
simple tools to allow
FAST high-confident
pre-identification***



**Identify informative
simple markers**

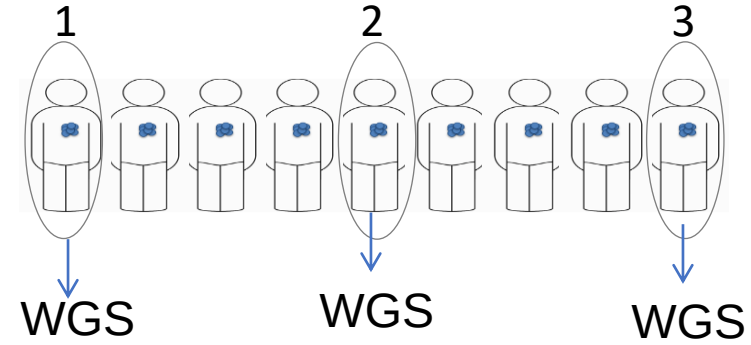
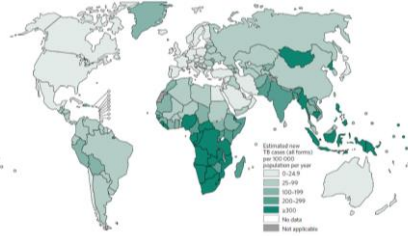
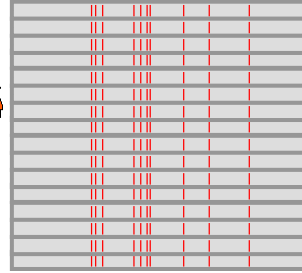


**Target them with
simpler tests to allow
FAST high-confident
pre-identification**

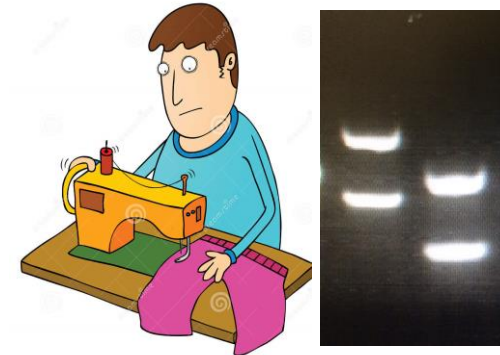
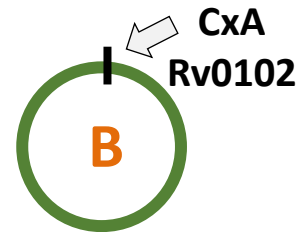
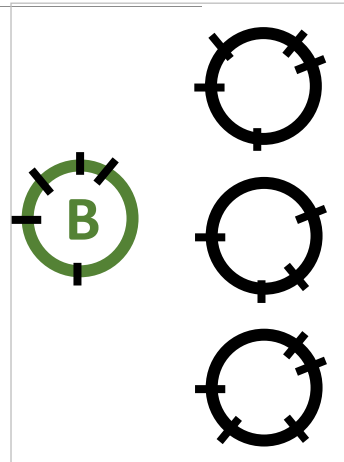
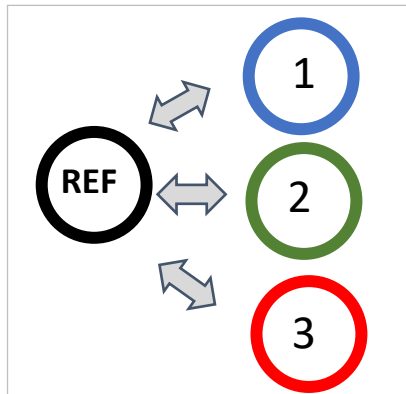


Our proposal

1



2



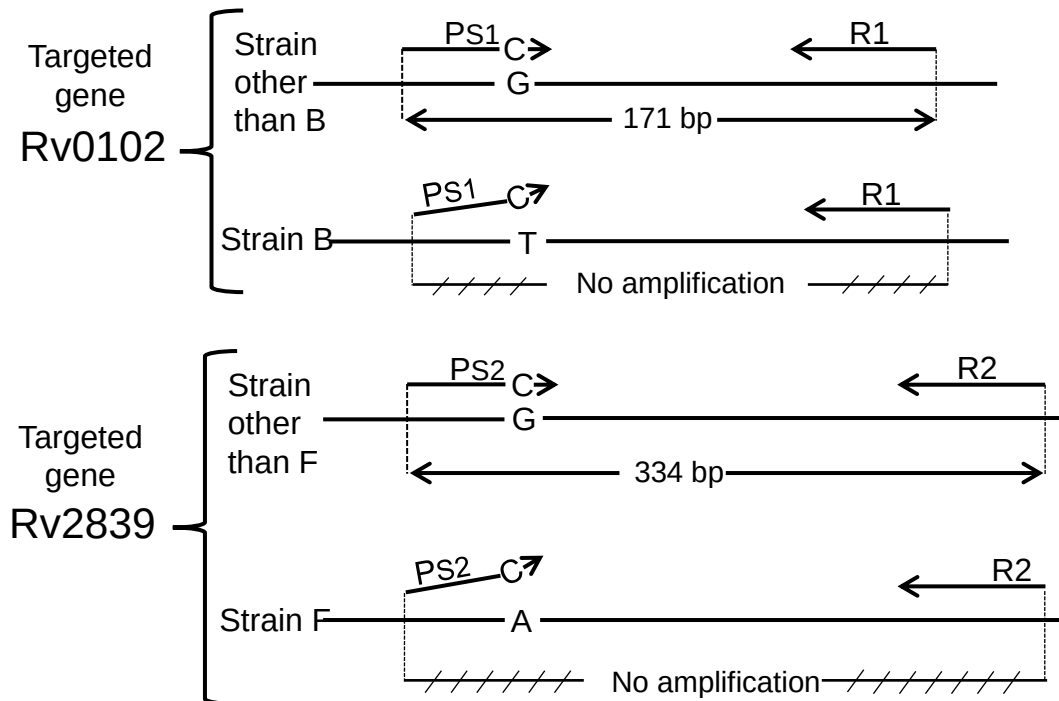
Strain Specific
SNPs

User-friendly approach

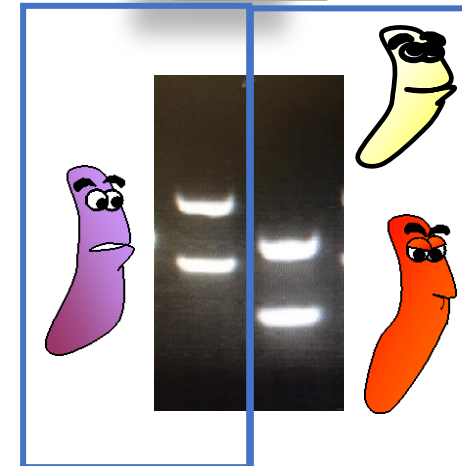
Targeted Regional Allele-specific PCR (TRAP)



Strain-specific PCRs



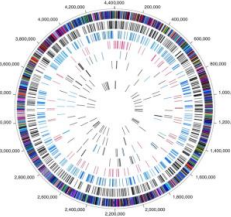
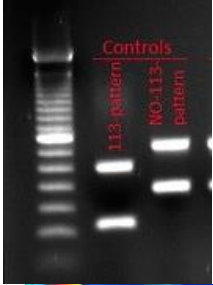
TRAP



TRAP



designed by freepik.com



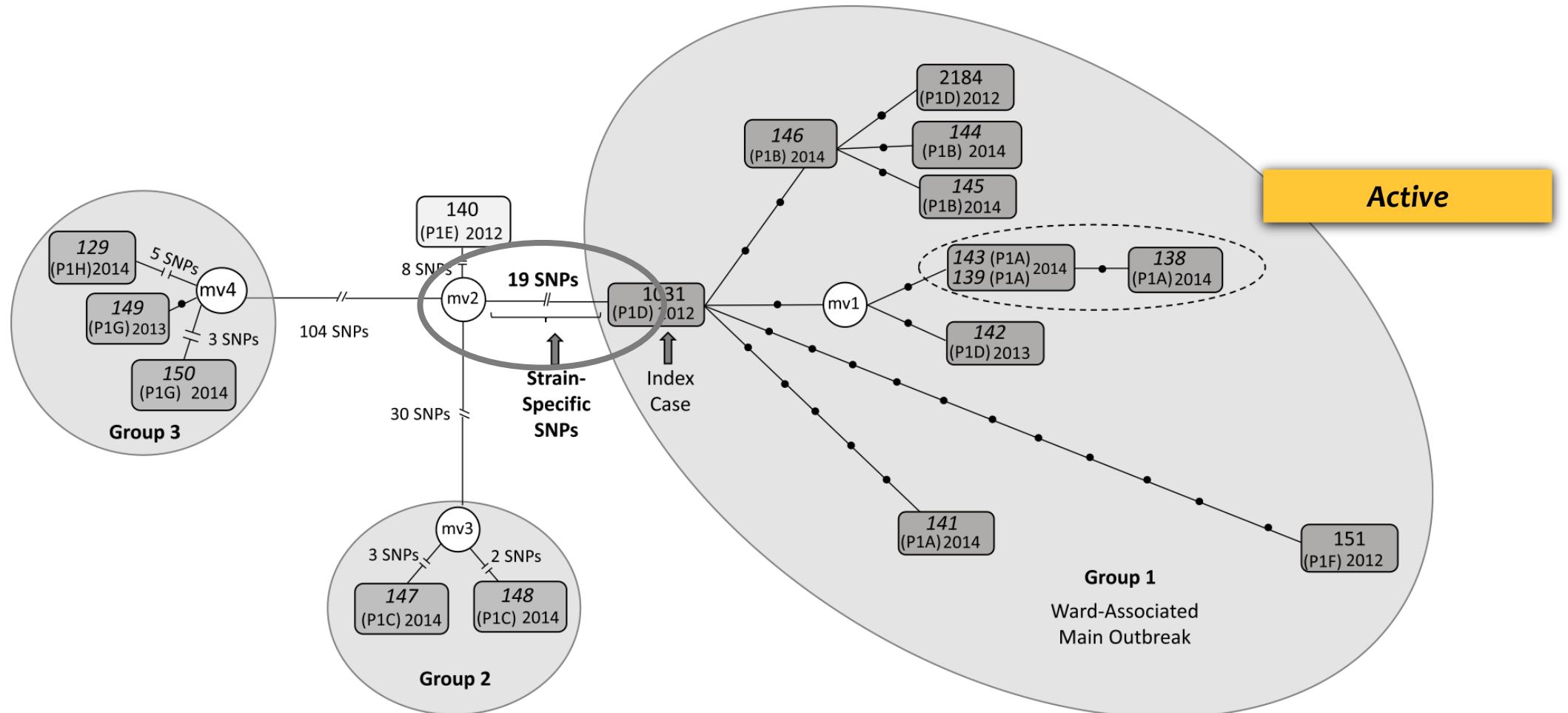
Mycobacterium tuberculosis



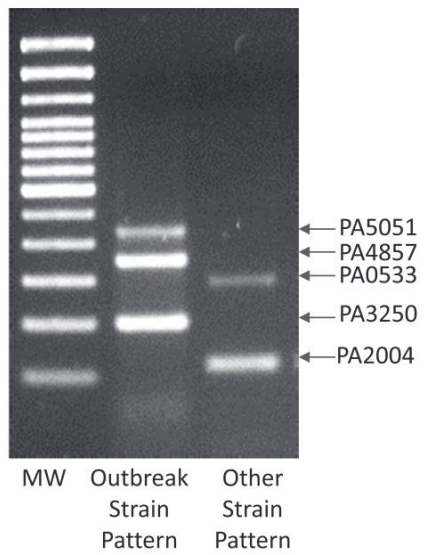
Peru
Panama
Costa Rica
Somalia

Italy
France
Portugal

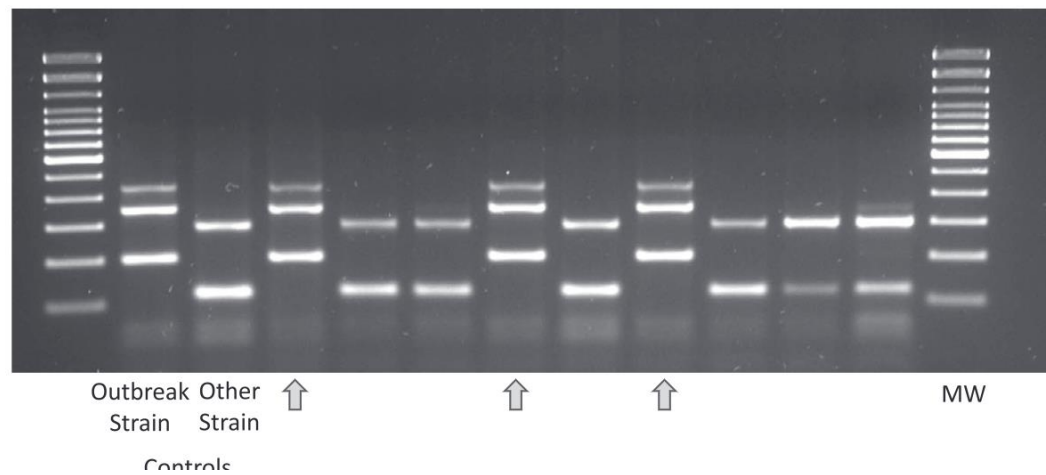
MDR *Pseudomonas aeruginosa* outbreak alert in Hematology ward



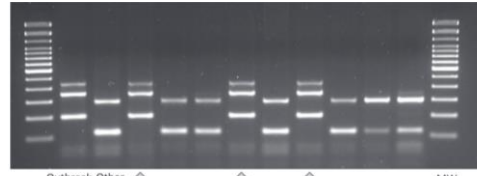
A)



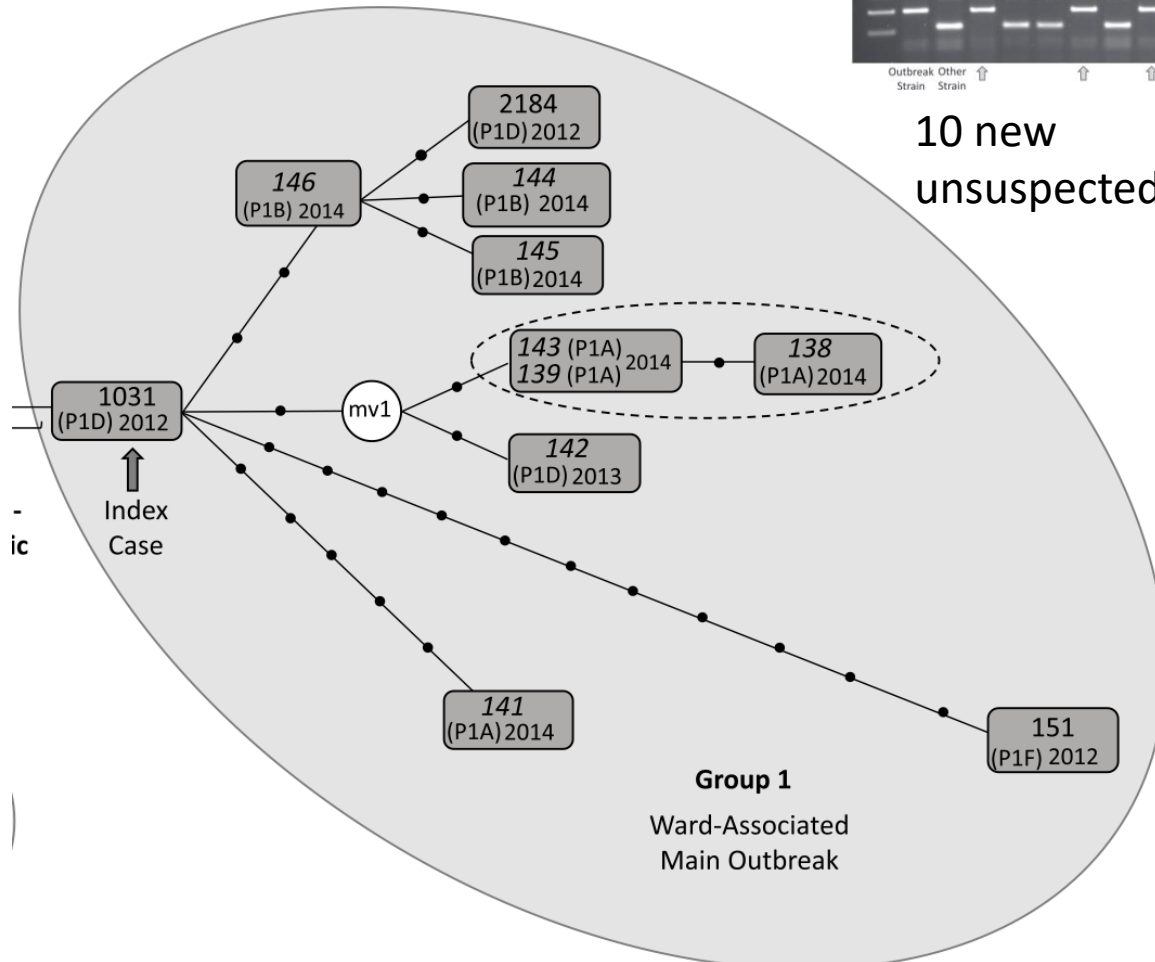
B)

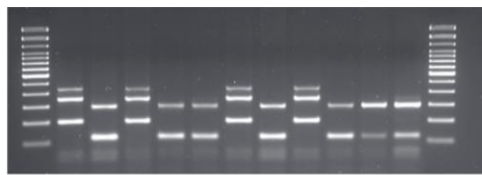


Active



10 new
unsuspected cases





10 new
unsuspected cases

