An introduction to *Klebsiella* genomics & strain typing

Assistant Professor Zoe A. Dyson

London School of Hygiene and Tropical Medicine

zoe.dyson@lshtm.ac.uk

@msmicrobiocode

Today's schedule

Time	Activity
11:15-12:00 (45 mins)	**Lecture: Introduction to *Klebsiella* genomics & strain typing** • Genomics and sequencing technologies • Species typing and the *Klebsiella* genome • Strain typing and the *Klebsiella* population structure • Case study: *Klebsiella* strain typing in Kathmandu, Nepal
12:00-12:10 (10 mins)	**Class discussion**
12:10-12:50 (40 mins)	**Lecture: *Klebsiella* virulence typing - part I** • An introduction to *Klebsiella* virulence determinants • The capsule and K-/KL-types • Lipopolysaccharides (LPS) and O-types • An introduction to Kaptive
12:50-13:00 (10 mins)	**Class discussion**
13:00-14:00 (1 hour)	**Lunch**
14:00-15:15 (1 hour 15 mins)	**Kaptive hands on practical**
15:15-15:30 (15 mins)	**Break**
15:30-16:00 (30 mins)	**Kaptive hands on practical (continued)**
16:00-16:30 (30 mins)	**Data sharing workflow mapping (Nicole Dagata)**

Lecture outline: An introduction to *Klebsiella* genomics and strain typing

1. Genomics and sequencing technologies

2. Species typing and the *Klebsiella* genome

3. Strain typing and the *Klebsiella* population structure

4. Case study: *Klebsiella* strain typing in Kathmandu, Nepal

Genomics & sequencing technologies

Why use genomics to study *Klebsiella* epidemiology?

Genomics is increasingly used as a **core method for pathogen characterisation** in research and public health laboratories
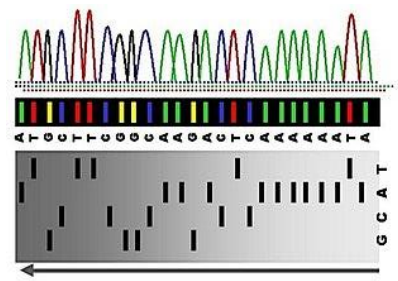
Genomic characterisation is **robust, reproducible, and informative**

Genome data are **easily stored, shared, re-analysed, and re-interpreted** as knowledge develops

Timeline of bacterial whole genome sequencing (WGS)

Capillary sequencing

1977: Sanger sequencing

1980   1990   2000   2010   2020

1995: Free-living bacterial genomes
(*M. genitalium* & *H. influenzae*)

1997: *E. coli* & *B. subtilis*
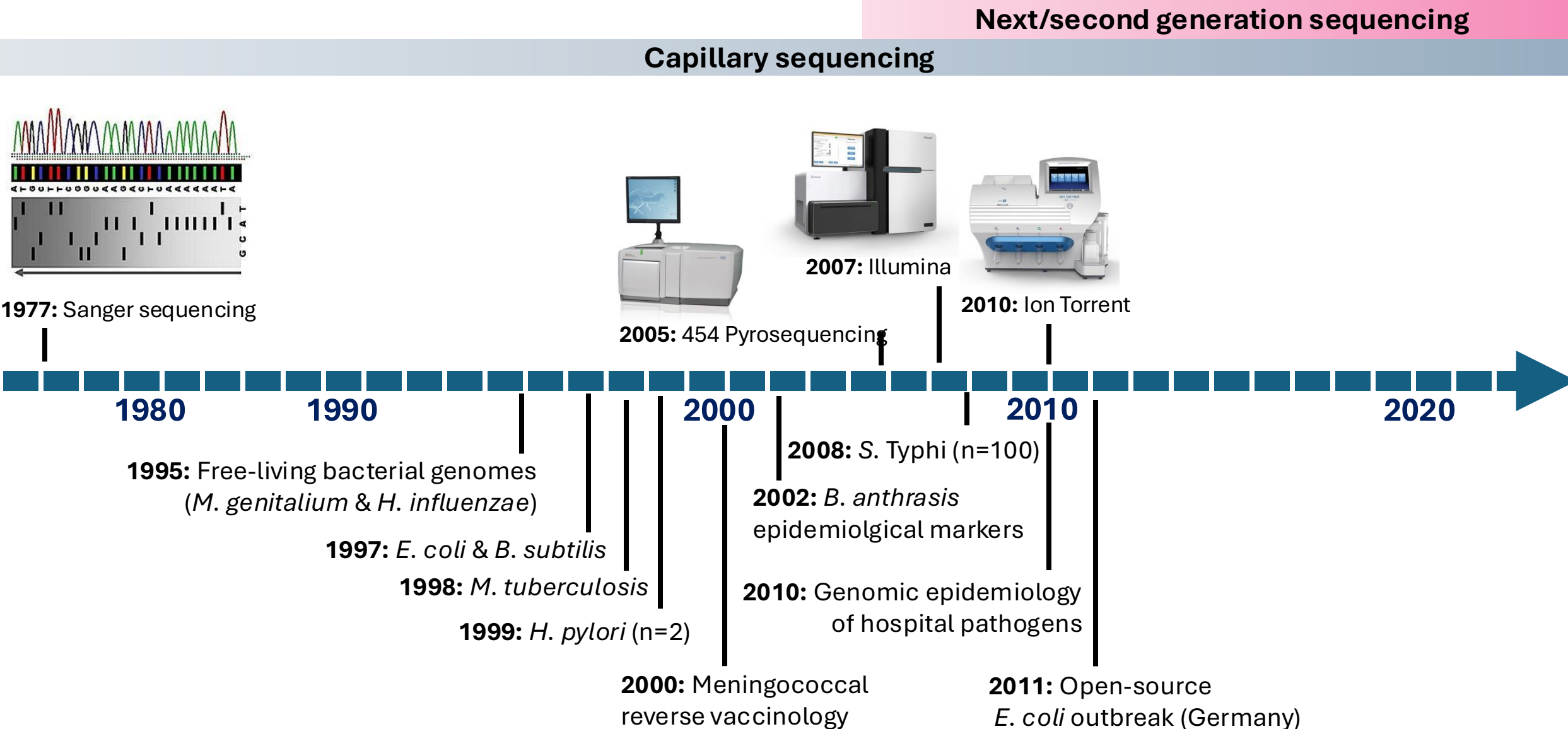
1998: *M. tuberculosis*

1999: *H. pylori* (n=2)

2000: Meningococcal
reverse vaccinology
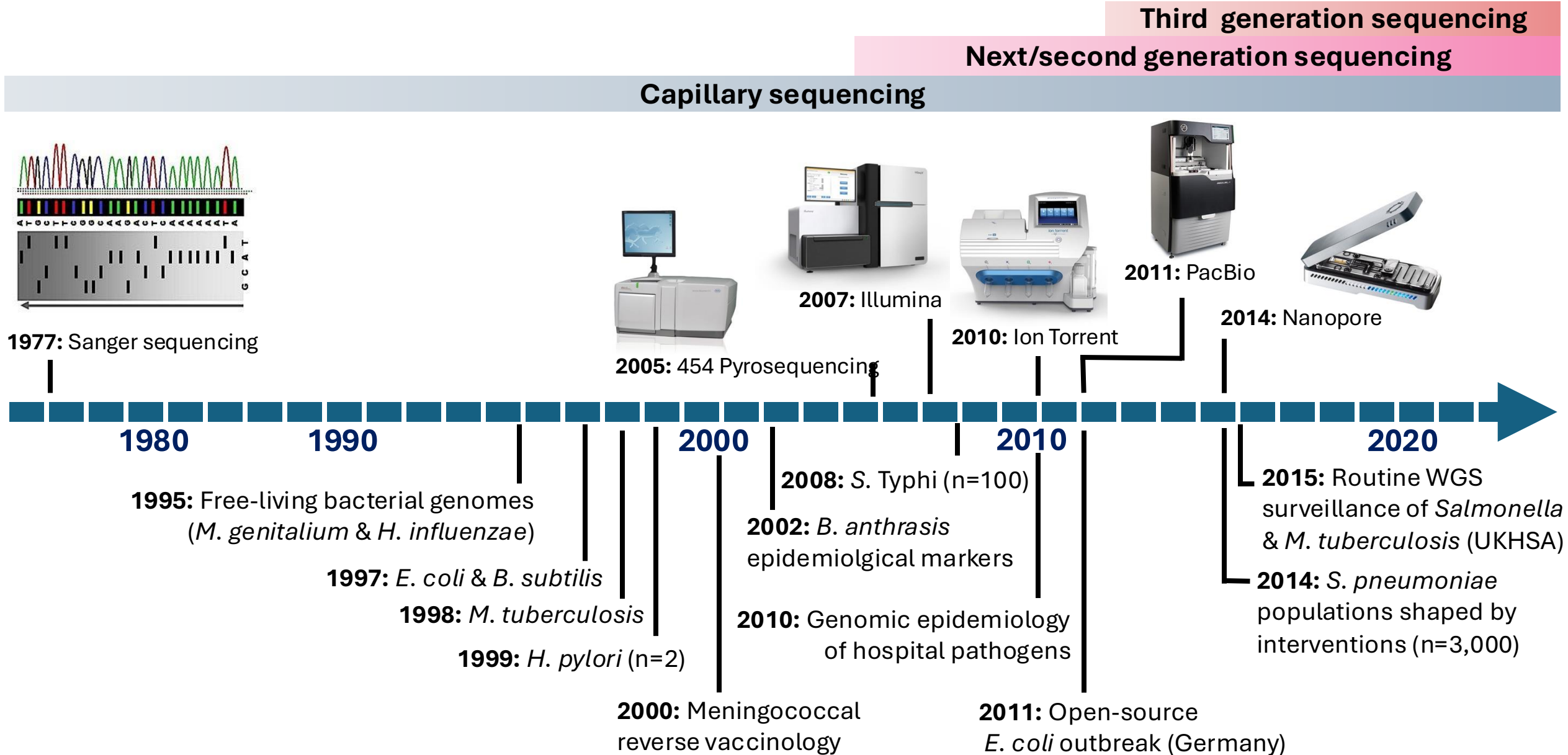
Adapted from Loman & Pallen 2015
Nat Rev Microbiol

Comparative genomics

Timeline of bacterial whole genome sequencing (WGS)

Next/second generation sequencing

Capillary sequencing

2007: Illumina

2010: Ion Torrent

2005: 454 Pyrosequencing

1977: Sanger sequencing

1980   1990   2000   2010   2020

2008: *S.* Typhi (n=100)

1995: Free-living bacterial genomes
(*M. genitalium* & *H. influenzae*)

2002: *B. anthrasis*
epidemiolgical markers

1997: *E. coli* & *B. subtilis*

2010: Genomic epidemiology
of hospital pathogens

1998: *M. tuberculosis*

1999: *H. pylori* (n=2)

2000: Meningococcal
reverse vaccinology

2011: Open-source
E. coli outbreak (Germany)

Comparative genomics   +   Genetic epidemiology

Adapted from Loman & Pallen 2015
Nat Rev Microbiol

Timeline of bacterial whole genome sequencing (WGS)

Third generation sequencing

Next/second generation sequencing

Capillary sequencing

2011: PacBio

2007: Illumina

2014: Nanopore

2010: Ion Torrent

1977: Sanger sequencing

2005: 454 Pyrosequencing

1980   1990   2000   2010   2020

2008: *S.* Typhi (n=100)

1995: Free-living bacterial genomes
(*M. genitalium* & *H. influenzae*)

2002: *B. anthrasis*
epidemiolgical markers

2015: Routine WGS
surveillance of *Salmonella*
& *M. tuberculosis* (UKHSA)

1997: *E. coli* & *B. subtilis*

1998: *M. tuberculosis*

2010: Genomic epidemiology
of hospital pathogens

2014: *S. pneumoniae*
populations shaped by
interventions (n=3,000)

1999: *H. pylori* (n=2)

2000: Meningococcal
reverse vaccinology

2011: Open-source
E. coli outbreak (Germany)

Comparative genomics   +   Genetic epidemiology   +   Surveillance

Decline of sequencing costs over time

genome.gov/about-genomics/fact-sheets/DNA-Sequencing-Costs-Data
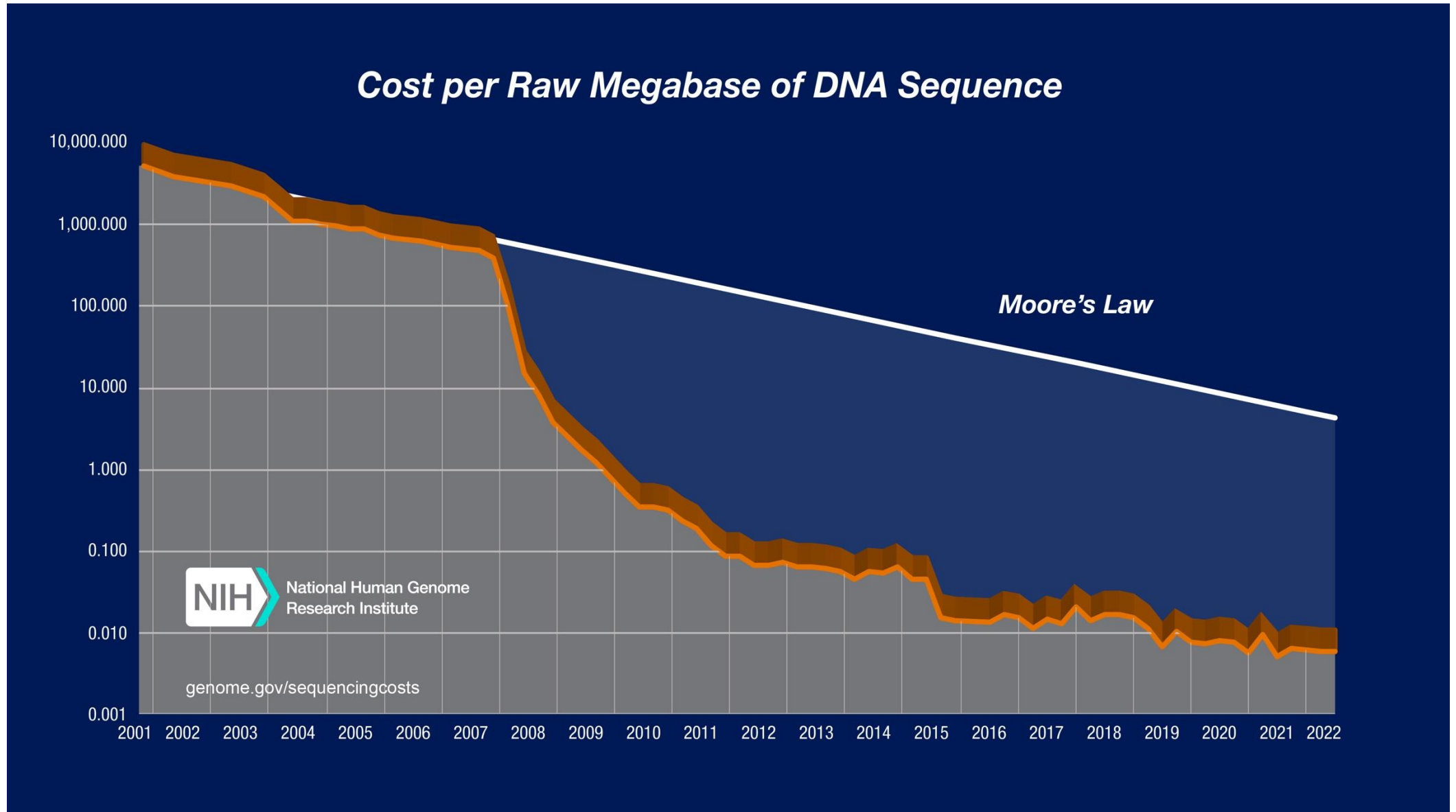
Platforms commonly used for WGS

Loman & Pallen 2015, Nat Rev Microbiol

R9 Nanopore chemistry

- ONT only assemblies were comparable to Illumina only and Illumina-ONT hybrid assemblies

- Reliable capsule (K) type calls for all strains (100% exact or best matching locus)

- Reliable multi-locus sequence type (MLST) assignment (98.3% exact match or single-locus variants)

- Good detection of acquired AMR genes and mutations (88–100% correct identification across the various drug classes)

- Calling outbreak clusters was problematic due to inflation of SNP counts

Nanopore-only assemblies for genomic surveillance of the global priority drug-resistant pathogen, *Klebsiella pneumoniae*

Ebenezer Foster-Nyarko[1,*], Hugh Cottingham[2], Ryan R. Wick[2], Louise M. Judd[2], Margaret M. C. Lam[2], Kelly L. Wyres[2], Thomas D. Stanton[1], Kara K. Tsang[1], Sophia David[3], David M. Aanensen[3], Sylvain Brisse[4] and Kathryn E. Holt[1,2]
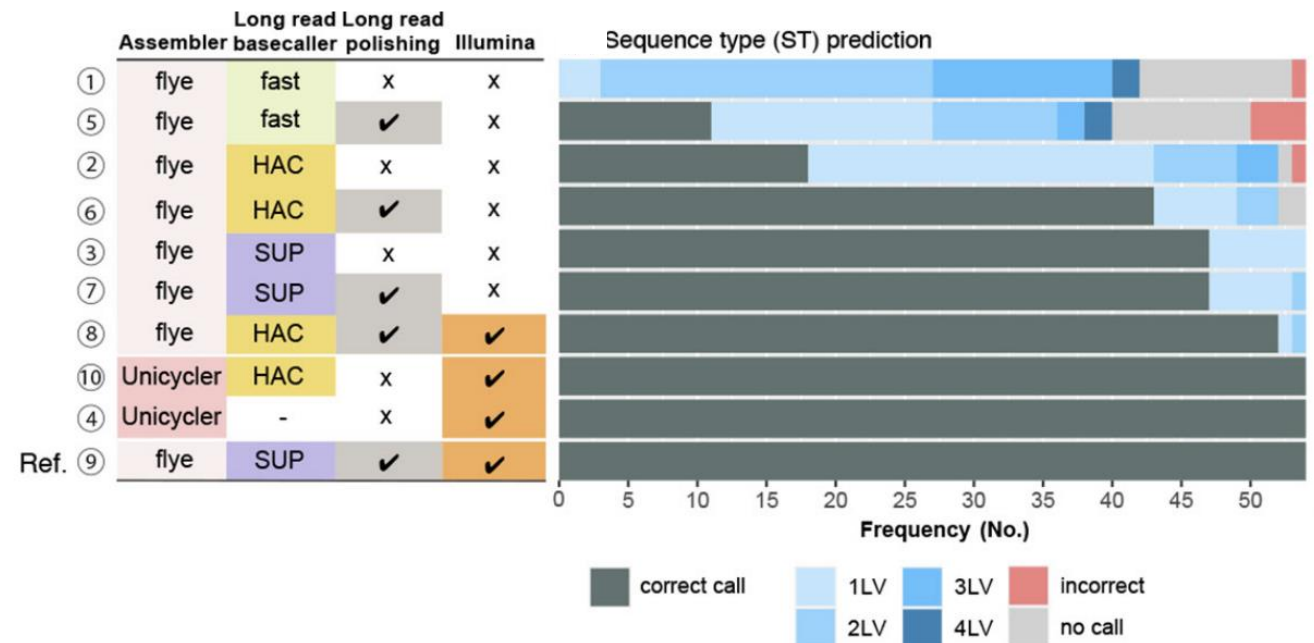
R10 Nanopore chemistry

frontiers | Frontiers in Microbiology

Check for updates

...ity, China
...ustafa,
...Pennsylvania, United States

...NCE

...cn

Oxford nanopore long-read sequencing enables the generation of complete bacterial and plasmid genomes without short-read sequencing

Wenxuan Zhao[1,2], Wei Zeng[1,3], Bo Pang[1], Ming Luo[4], Yao Peng[1], Jialiang Xu[5], Biao Kan[1,3]*, Zhenpeng Li[1]*and Xin Lu[1]*

nature methods

BRIEF COMMUNICATION

Check for updates

OPEN

Oxford Nanopore R10.4 long-read sequencing enables the generation of near-finished bacterial genomes from pure cultures and metagenomes without short-read or reference polishing

Mantas Sereika[1,4], Rasmus Hansen Kirkegaard[1,2,4], Søren Michael Karst[1], Thomas Yssing Michaelsen[1], Emil Aarre Sørensen[1], Rasmus Dam Wollenberg[3] and Mads Albertsen[1]✉

Most commonly used sequencing platforms

- **Illumina (most common)**
  - Highly accurate short reads
  - Cost effective in some settings
  - Appropriate for most common applications (mapping, phylogenetics, gene screening, draft assemblies) and downstream applications

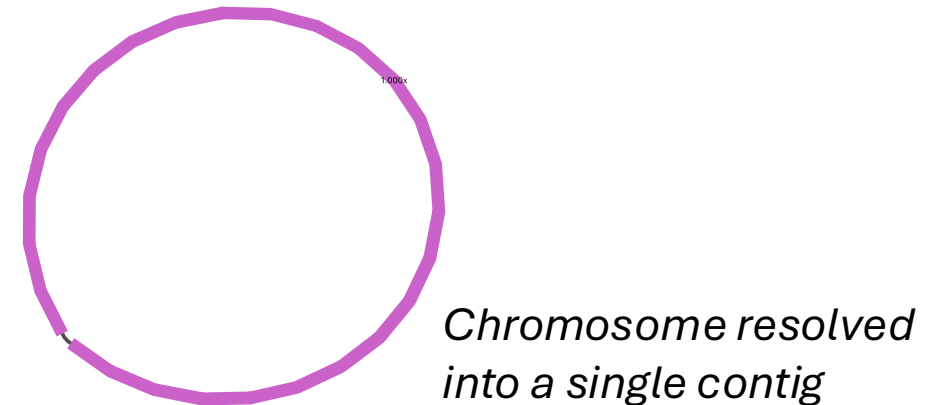- **Nanopore (increasingly common)**
  - Longer reads with systematic errors
  - Portable
  - Finishing genomes
  - Resolving mobile elements e.g. plasmids
  - Large-scale rearrangements

- Often used in combination

  e.g. **hybrid** genome assembly

Chromosome fragmented into multiple contigs – some connections are poorly resolved
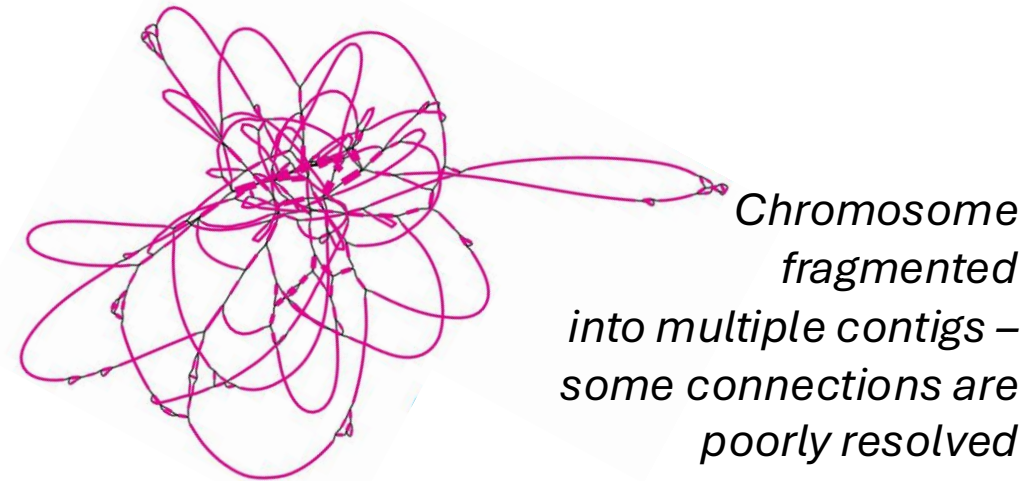
Illumina only de Bruijn genome assembly graph

Chromosome resolved into a single contig

Hybrid (Illumina + Nanopore) de Bruijn genome assembly graph

Khedher et al. 2022, Int. J. Mol. Sci.

Species typing & the *Klebsiella* genome

The *Klebsiella pneumoniae* species complex

- Whole genome sequencing has revealed that many organisms previously classified as *Klebsiella pneumoniae* belong to closely related species that share 95-96% average nucleotide identity

- Members of the *Klebsiella pneumoniae* species complex (KpSC) share 90% nucleotide identity with other *Klebsiella* species

- New KpSC species defined by ≥3% genome-wide average nucleotide identity

- *K. pneumoniae sensu stricto* cause ~85% of clinical cases
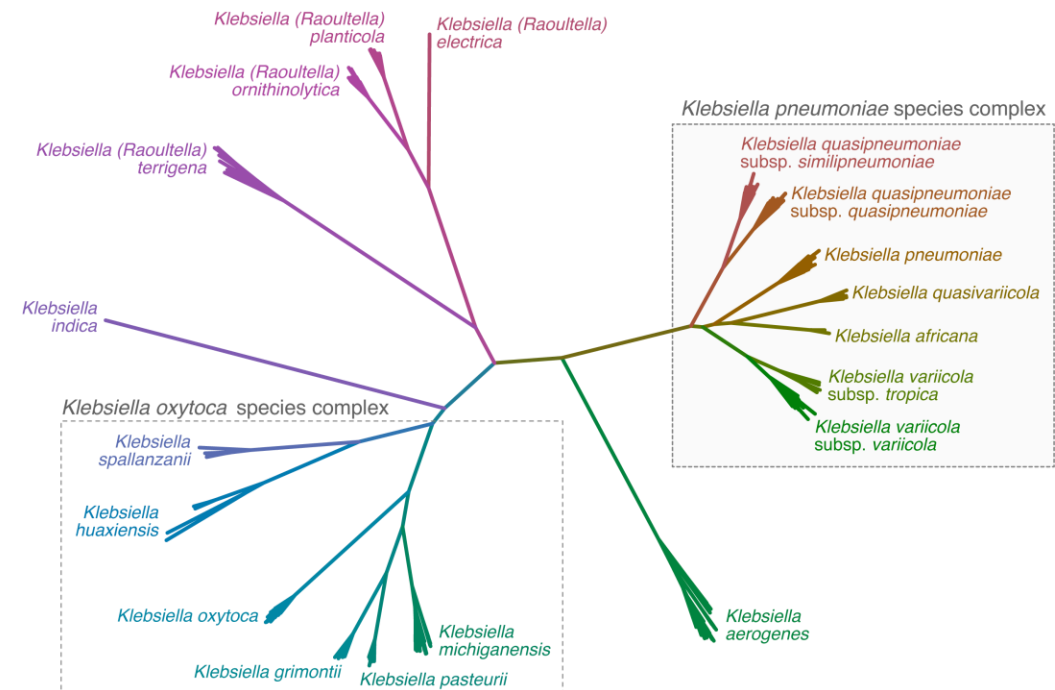
Phylogroup	Phylogroup (sub)species
Kp1	*K. pneumoniae*
Kp3	*K. variicola* subsp.*variicola*
Kp5	*K. variicola* subsp.*tropica*
Kp2	*K. quasipneumoniae* subsp. *quasipneumoniae*
Kp4	*K. quasipneumoniae* subsp. *similipneumoniae*
Kp6	*K. quasivariicola*
Kp7	*K. africana*

The *Klebsiella* genome is diverse

- *K. pneumoniae genomes*
  - *~5-6 Mbp in size*
  - *Encodes ~5,000-6,000 genes*
    - *~1700 genes conserved*
    - *Remainder are variable*

- Extremely diverse pangenome
  - Likely exceeds 100,000 genes
  - Majority of accessory genes are rare (present in <10% of genomes)

- Horizontal gene transfer common
  - Mobile genetic elements (IS, plasmids, phage)
  - 4-6 plasmids common, up to 10 reported
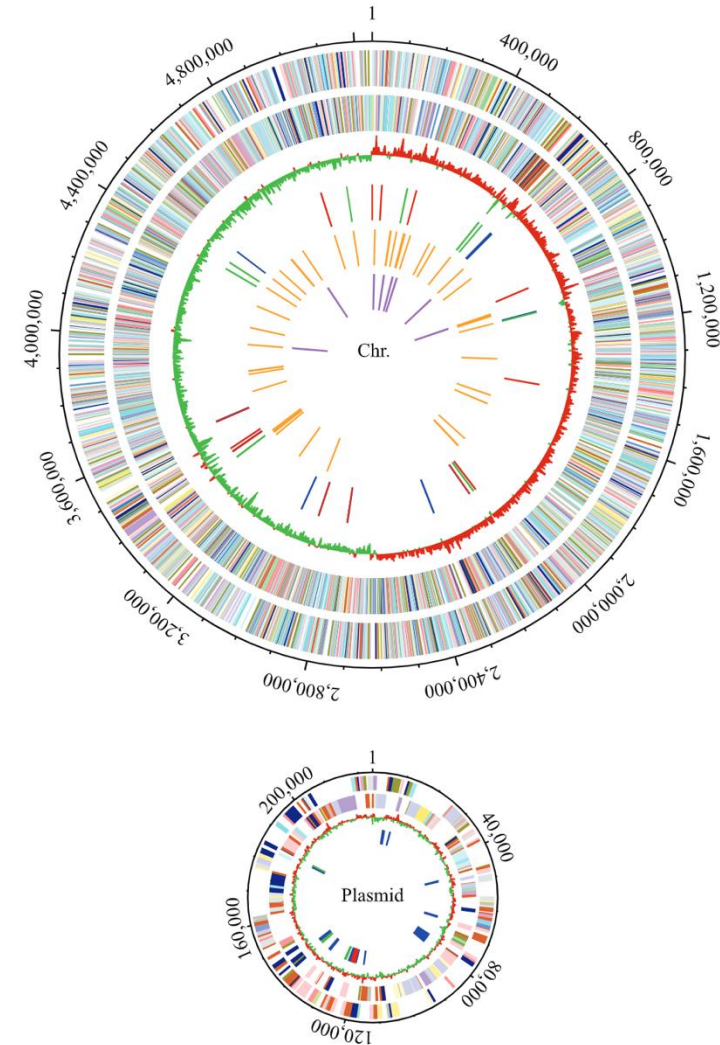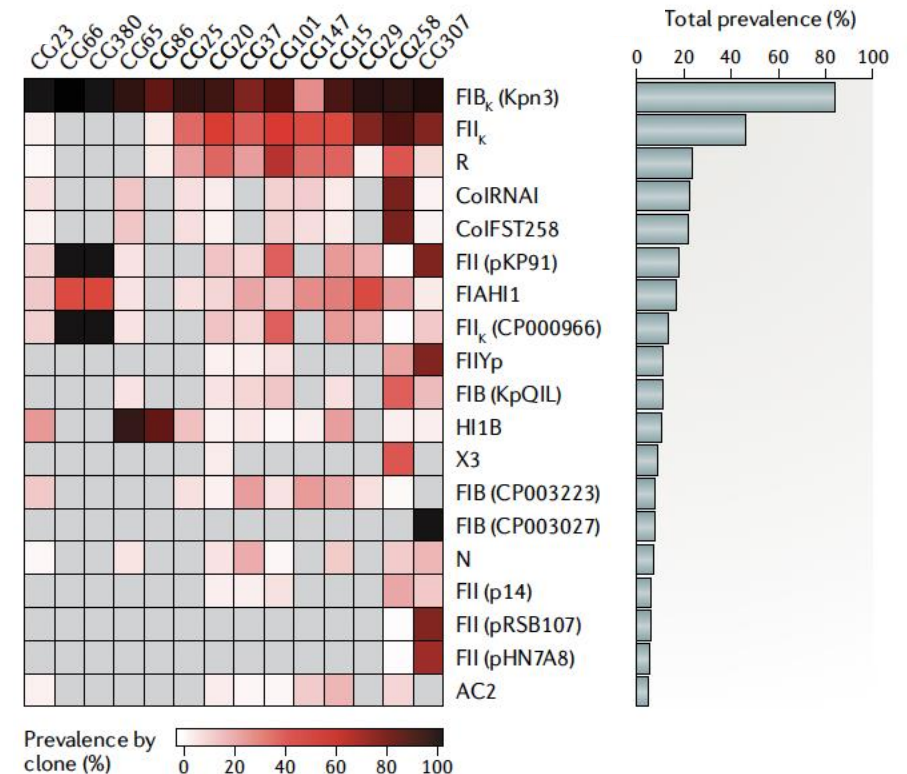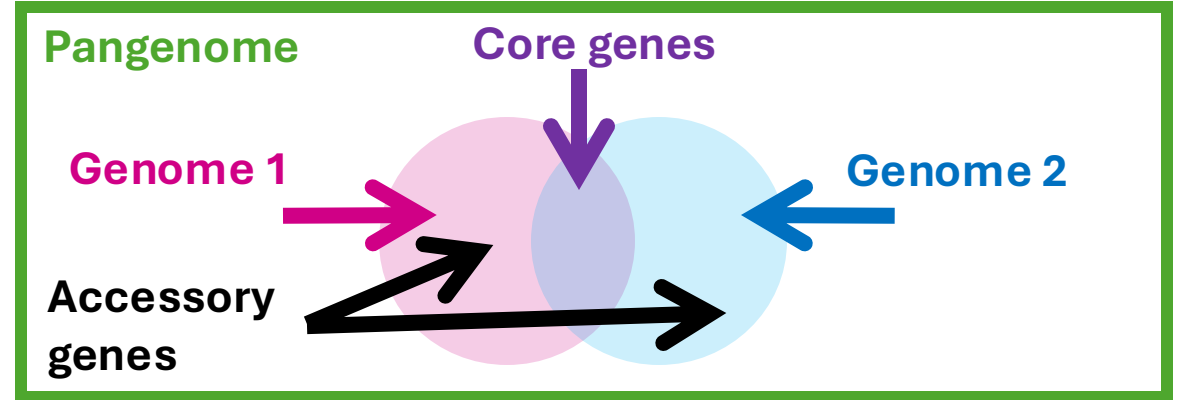 - Homologous recombination common

FIG. 1. Genomic maps of the *K. pneumoniae* NTUH-K2044 chromosome and plasmid. From the outside in, the first and second circles show the predicted protein-encoding regions on the plus and minus strands, by role, using the colors for the COG functional categories (http://www.ncbi.nlm.nih.gov/COG/grace/fiew.cgi). The third circle shows the GC skew. The fourth circle shows the transposases/transposons (blue), integrases/recombinases (green), and insertion sequences (red). The fifth and sixth circles show tRNAs and rRNAs, respectively.

Wyres et al. 2020, Nat Rev Microbiol; Wu et al. 2009, J Bact

The *Klebsiella* genome is diverse

- *K. pneumoniae genomes*
  - *~5-6 Mbp in size*
  - *Encode ~5,000-6,000 genes*
    - *~1700 genes conserved*
    - *Remainder are variable*

- Extremely diverse pangenome
  - Likely exceeds 100,000 genes
  - Majority of accessory genes are rare (present in <10% of geomes)

- Horizontal gene transfer common
  - Mobile genetic elements (IS, plasmids, phage)
  - 4-6 plasmids common, up to 10 reported
  - Homologous recombination common

Wyres et al. 2020, Nat Rev Microbiol

Strain typing & the *Klebsiella* population structure

Reference frameworks: databases & schemes

Schemes for identifying and naming <u>sub-species level variants</u> are essential for recognition and communication about variants of clinical or public health concern

- **Genotype schemes**
  - based on marker SNPs that define clades, subclades, etc in the global tree
  - hierarchical names, e.g. 1.2.1 and 1.2.2 are sister subclades, within the parent clade 1.2
  - used for slow-evolving pathogens with limited diversity
    - e.g. *M. tuberculosis, Salmonella* Typhi, *Shigella sonnei*

- **Multi-locus sequence typing (MLST)**
  - based on common genes, unique combination of gene seqs define a unique ST
  - organism-specific databases, curated by research communities
  - all databases hosted via ***BIGSdb*** at ***pubmlst.org***, incorporated into many tools
  - **commonly used for KpSC**

Multi-locus sequence typing (MLST)

- Defined set of seven core genes for typing (e.g. *rpoB, gapA, mdh, pgi, phoE, infB, tonB* for *Klebsiella*)

- For each gene, every unique allele is assigned a number (e.g. *gapA*-1, *gapA*-2, *gapA*-3)

locus	allele id	sequence		
gapA	1	AACCTGAAGTGGGAC	. . .	ACCGGTATGGCGTTC
gapA	2	AACCTGAAGTGGGAC	. . .	ACCGGTATGGCGTTC
gapA	3	AACCTGAAGTGGGAC	. . .	ACCGGTATGGCGTTC
gapA	4	AACCTGAAGTGGGAC	. . .	ACCGGTATGGCGTTC
gapA	5	AACCTGAAGTGGGAC	. . .	ACCGGTATGGCGTTC
gapA	6	AACCTGAAGTGGGAC	. . .	ACCGGTATGGCGTTC
gapA	7	AACCTGAAGTGGGAC	. . .	ACCGGTATGGCGTTC
gapA	8	AATCTGAAGTGGGAC	. . .	ACCGGTATGGCGTTC
gapA	9	AACCTGAAGTGGGAC	. . .	ACCGGTATGGCGTTC
gapA	10	AACCTGAAGTGGGAC	. . .	ACCGGTATGGCGTTC
gapA	11	AACCTGAAGTGGGAC	. . .	ACCGGTATGGCGTTC
gapA	12	AACCTGAAGTGGGAC	. . .	ACCGGTATGGCGTTC

***Klebsiella gapA* alleles in MLST scheme**
- *gapA* currently has 392 unique alleles

Multilocus sequence typing (MLST)

- Defined set of seven core genes for typing (e.g. *rpoB, gapA, mdh, pgi, phoE, infB, tonB* for *Klebsiella*)

- For each gene, every unique allele is assigned a number (e.g. *gapA*-1, *gapA*-2, *gapA*-3)

- Each unique combination of gene alleles defines a unique sequence type (ST)

- Each genome can then be represented by the set of allele numbers across these genes

- MLST database made up of
    - (i) set of all allele sequences
    - (ii) lookup table of allele number combinations to ST

ST	*gapA*	*infB*	*mdh*	*pgi*	*phoE*	*rpoB*	*tonB*
1	4	4	1	1	7	4	10
2	3	4	1	1	9	4	17
3	5	5	1	1	9	6	11
4	3	1	1	1	3	3	1
5	2	2	1	1	3	3	3

***Klebsiella* MLST scheme**
- Currently has >7500 unique allelic profiles

Multilocus Sequence Typing (MLST)

- Originally developed for use with PCR primers and Sanger sequencing

Locus	Putative function of gene	Primer sequence[b,c]	Size (bp)	Location[d]	Temp (°C)	No. of alleles	Nucleotide diversity	Polymorphic sites (nonsynonymous substitutions)
rpoB	Beta-subunit of RNA polymerase B	VIC3: GGC GAA ATG GCW GAG AAC CA	501	4,771,502–4,772,002	50	8	0.00166	7 (1)
		VIC2: GAG TCT TCG AAG TTG TAA CC						
gapA	Glyceraldehyde 3-phosphate dehydrogenase	gapA173: TGA AAT ATG ACT CCA CTC ACG G	450	1,347,540–1,347,091	60	6	0.00136	5 (0)
		gapA181: CTT CAG AAG CGG CTT TGA TGG CTT						
mdh	Malate dehydrogenase	mdh130: CCC AAC TCG CTT CAG GTT CAG	477	4,004,045–4,003,569	50	10	0.00161	10 (3)
		mdh867: CCG TTT TTC CCC AGC AGC AG						
pgi	Phosphoglucose isomerase	pgi1F: GAG AAA AAC CTG CCT GTA CTG CTG GC	432	4,831,091–4,831,522	50	6	0.00092	5 (0)
		pgi1R: CGC GCC ACG CTT TAT AGC GGT TAA T						
		pgi2F(seq): CTG CTG GCG CTG ATC GGC AT						
		pgi2R(seq): TTA TAG CGG TTA ATC AGG CCG T						
phoE	Phosphoporine E	phoE604.1: ACC TAC CGC AAC ACC GAC TTC TTC GG	420	320,309–320,728	50	14	0.00727	18 (2)
		phoE604.2: TGA TCA GAA CTG GTA GGT GAT						
infB	Translation initiation factor 2	infB1F: CTC GCT GCT GGA CTA TAT TCG	318	3,937,568–3,937,885	50	10	0.0038	11 (0)
		infB1R: CGC TTT CAG CTC AAG AAC TTC						
		infB2F(seq): ACT AAG GTT GCC TCC GGC GAA GC						
tonB	Periplasmic energy transducer	tonB1F: CTT TAT ACC TCG GTA CAT CAG GTT	414	2,394,251–2,394,664	45	21	0.01019	14 (5)
		tonB2R: ATT CGC CGG CTG RGC RGA GAG						

Multilocus Sequence Typing (MLST)

- Several general software tools have been developed that can use MLST schemes to type isolates from WGS data

- These software tools can be used to analyse WGS data for any pathogen where an MLST scheme has been developed
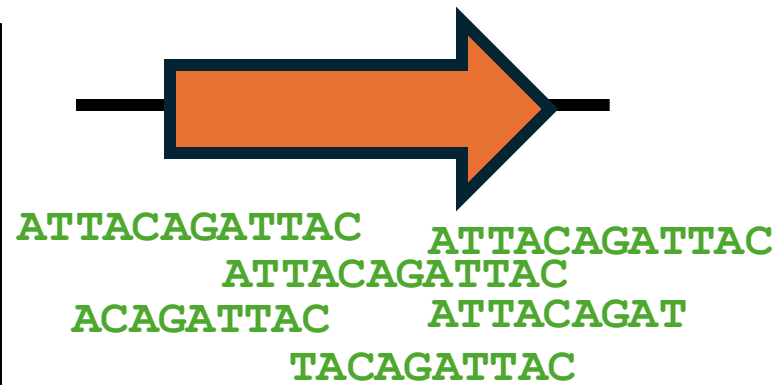
Genome **Medicine**

SOFTWARE   Open Access

SRST2: Rapid genomic surveillance for public health and hospital microbiology labs

Michael Inouye[1,2], Harriet Dashnow[3,4], Lesley-Ann Raven[1], Mark B Schultz[3], Bernard J Pope[4,5], Takehiro Tomita[2,6], Justin Zobel[5] and Kathryn E Holt[3*]

MLST https://github.com/tseemann/mlst

ARIBA: rapid antimicrobial resistance genotyping directly from sequencing reads

Martin Hunt,[1] Alison E Mather,[1,2] Leonor Sánchez-Busó,[1] Andrew J Page,[1] Julian Parkhill,[1] Jacqueline A Keane[1] and Simon R Harris[1,*]
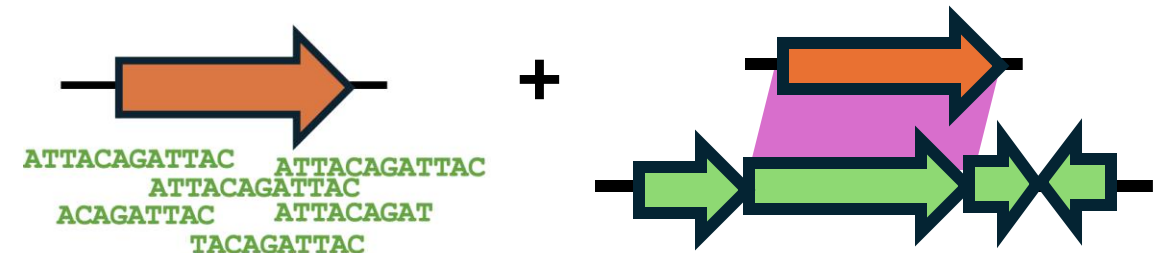
Multilocus Sequence Typing (MLST)

- Specialist software tools have been developed specifically for *Klebsiella* that include MLST typing

Multilocus Sequence Typing (MLST)

In Klebsiella the population structure is comprised of hundreds of deep branching lineages

Sequences types correspond to broad phylogenetic lineages

Sequence types provide useful nomenclature to discuss transmission, spread, and biological traits e.g. AMR, virulence

Holt et al. 2015, PNAS

Core Genome MLST (cgMLST)

- Uses ~700 core genes (defined using pangenome approaches)

- Same principle as for MLST

- ~100x more resolution

- **Clonal groups (CGs)** correspond to deep branching lineages that share ≥594 alleles with at least one other member of the group (~0.5% nucleotide divergence)
  - e.g. CG258 includes closely related STs (ST258, ST11, ST512, ST340)
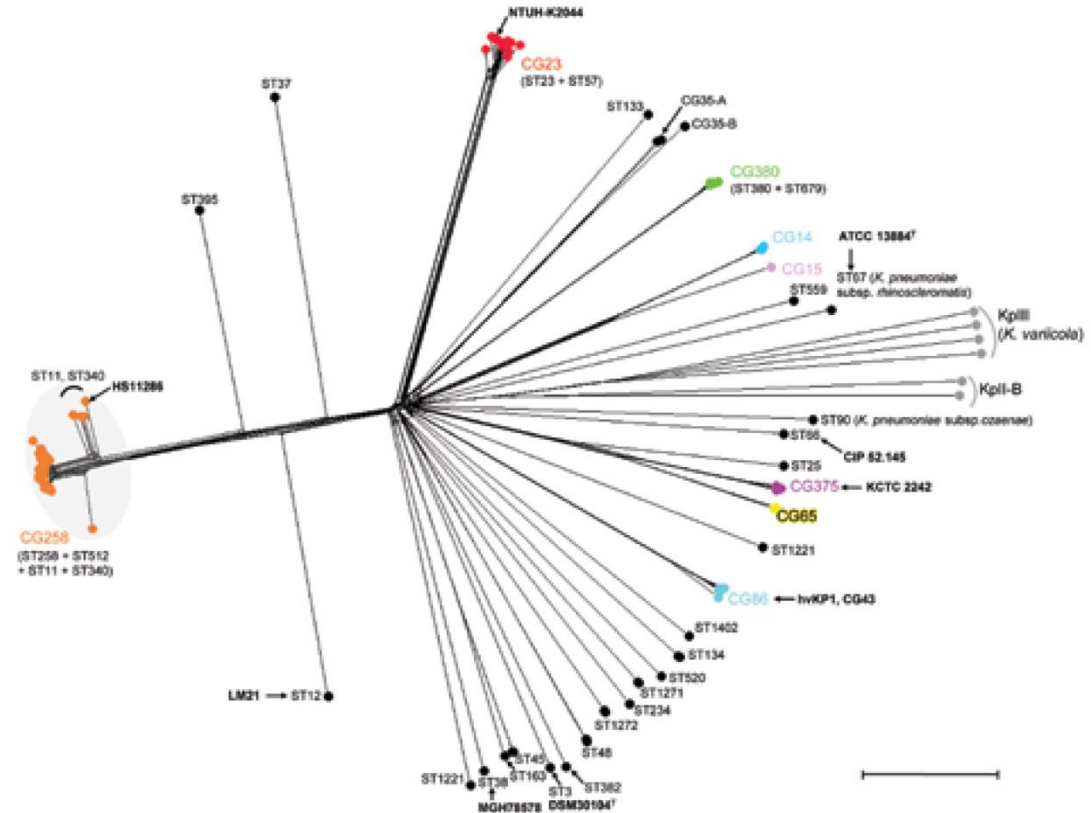
Suzanne Bialek-Davenet,[1] Alexis Criscuolo,[1] Florent Ailloud, Virginie Passet, Louis Jones, Anne-Sophie Delannoy-Vieillard, Benoit Garin, Simon Le Hello, Guillaume Arlet, Marie-Hélène Nicolas-Chanoine, Dominique Decré, and Sylvain Brisse

Other MLST schemes

- Using the same principles, MLST schemes have been developed for many different genetic loci, including plasmids and virulence factors

- Kleborate includes typing for major virulence determinants e.g. Salmochelin, Aerobactin, Yersiniabactin, Colibactin, *rmpA/D/C*

Schemes are collections of loci. They may be indexed, in which case they have a primary key field that identifies unique combinations of alleles. The following schemes are indexed.

Name	Download	Profiles	Description	Curator(s)	Last updated
AbST	⬇	99	MLST-style typing of the aerobactin locus	Margaret Lam, Kat Holt, Federica Palma	2024-04-16
MLST	⬇	7,608	The standard 7-gene MLST scheme, initially defined by Diancourt et al. in 2005.	Margaret Lam, Kat Holt, Radek Izdebski, Marit Andrea Klokkhammer Hetland, Virginie Passet, Carla Rodrigues, Federica Palma, Mélanie Hennart	2024-08-26
CbST	⬇	82	Colibactin typing scheme using allele combinations from the clbABCDEFGHILMNOP loci.	Margaret Lam, Kat Holt, Federica Palma	2024-04-16
RmST	⬇	171	rmpA, rmpD & rmpC	Margaret Lam	2024-04-16
scgMLST629_S	⬇	49,050	An update of scheme scgMLST initially identified in Bialek-Davenet et al, 2014. This 629-loci scheme is described in Hennart et al, 2021.	Federica Palma	2024-08-27
SmST	⬇	49	MLST style typing of salmochelin locus	Margaret Lam, Kat Holt, Federica Palma	2024-04-16
wzi	⬇	618	This scheme contains a unique gene, wzi. Profiles numbers are identical to wzi alleles, and some of them are linked to capsular types as defined by phenotypic serotyping.	Kat Holt, Virginie Passet, Carla Rodrigues, Federica Palma	2023-09-04
YbST	⬇	600	Typing scheme for yersiniabactin virulence operon (ybtS ybtX ybtQ ybtP ybtA irp2 irp1 ybtU ybtT ybtE fyuA).	Margaret Lam, Kat Holt, Federica Palma	2024-04-16

https://bigsdb.pasteur.fr/cgi-bin/bigsdb/bigsdb.pl?db=pubmlst_klebsiella_seqdef&page=schemes

LIN (Life Identification Number) codes

- Extension of cgMLST using ~600 core genes

- Multi-position integer-based code attributed to each genome

- Preserves species typing and MLST typing using LIN code prefixes and lookup tables (backwards compatibility)

- Better handling of interphylogroup hybrid strains
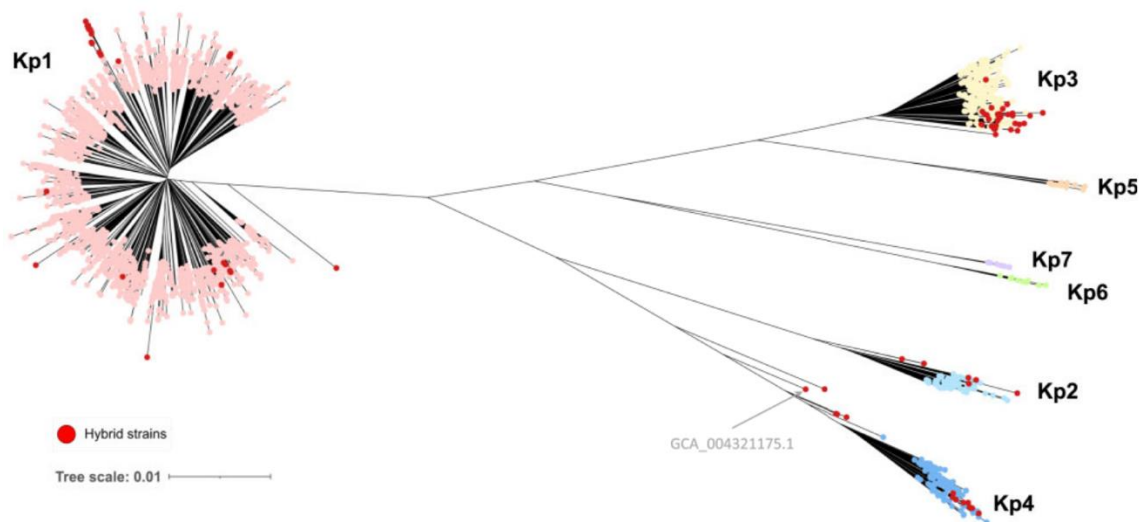
A Dual Barcoding Approach to Bacterial Strain Nomenclature: Genomic Taxonomy of *Klebsiella pneumoniae* Strains

Melanie Hennart [ID],[1,2] Julien Guglielmini [ID],[3] Sébastien Bridel [ID],[1] Martin C.J. Maiden [ID],[4] Keith A. Jolley [ID],[4] Alexis Criscuolo [ID],[3] and Sylvain Brisse [ID]*,[1]

bin	classification	No. allele mismatches
1	Species	[629-610]
2	Subspecies	[610-585]
3	Sublineage (SL)	[585-190]
4	Clonal Group (CG)	[190-43]
5	-	[43-10]
6	-	[10-7]
7	-	[7-4]
8	-	[4-2]
9	-	[2-1]
10	-	[1-0]

https://bigsdb.pasteur.fr/klebsiella/cgmlst-lincodes/

LIN (Life Identification Number) codes

LIN Prefix	Phylogroup	Phylogroup (sub)species
0_0	Kp1	*K. pneumoniae*
1_0	Kp3	*K. variicola* subsp.*variicola*
1_1	Kp5	*K. variicola* subsp.*tropica*
2_0	Kp2	*K. quasipneumoniae* subsp. *quasipneumoniae*
2_1	Kp4	*K. quasipneumoniae* subsp. *similipneumoniae*
3_0	Kp6	*K. quasivariicola*
4_0	Kp7	*K. africana*

First two digits correspond to phylogroup & species/subspecies

Palma et al. 2024, bioRxiv; Hennart et al. 2022

bigsdb.pasteur.fr/klebsiella/cgmlst-lincodes/

LIN (Life Identification Number) codes

LIN Prefix	Sublineage (SL)	Main ST
0_0_0	SL15	ST15
0_0_429	SL23	ST23
0_0_105	SL258	ST258
0_0_158	SL45	ST45
0_0_197	SL147	ST147
0_0_369	SL307	ST307
0_0_84	SL101	ST101
0_0_1	SL14	ST14

Next digit corresponds to MLST profiles (referred to as sublineages SL's)

Palma et al. 2024, bioRxiv; Hennart et al. 2022

https://bigsdb.pasteur.fr/klebsiella/cgmlst-lincodes/

LIN (Life Identification Number) codes

LIN Prefix	Clonal Group (CG)	Main ST
0_0_0_0	CG15	ST15
0_0_429_0	CG23	ST23
0_0_105_6	CG258	ST258
0_0_158_8	CG45	ST45
0_0_197_0	CG147	ST147
0_0_369_0	CG307	ST307
0_0_84_0	CG101	ST101
0_0_1_1	CG14	ST14

*Next digit corresponds to MLST profiles
(Clonal group/CG level)*

Palma et al. 2024, bioRxiv; Hennart et al. 2022

https://bigsdb.pasteur.fr/klebsiella/cgmlst-lincodes/
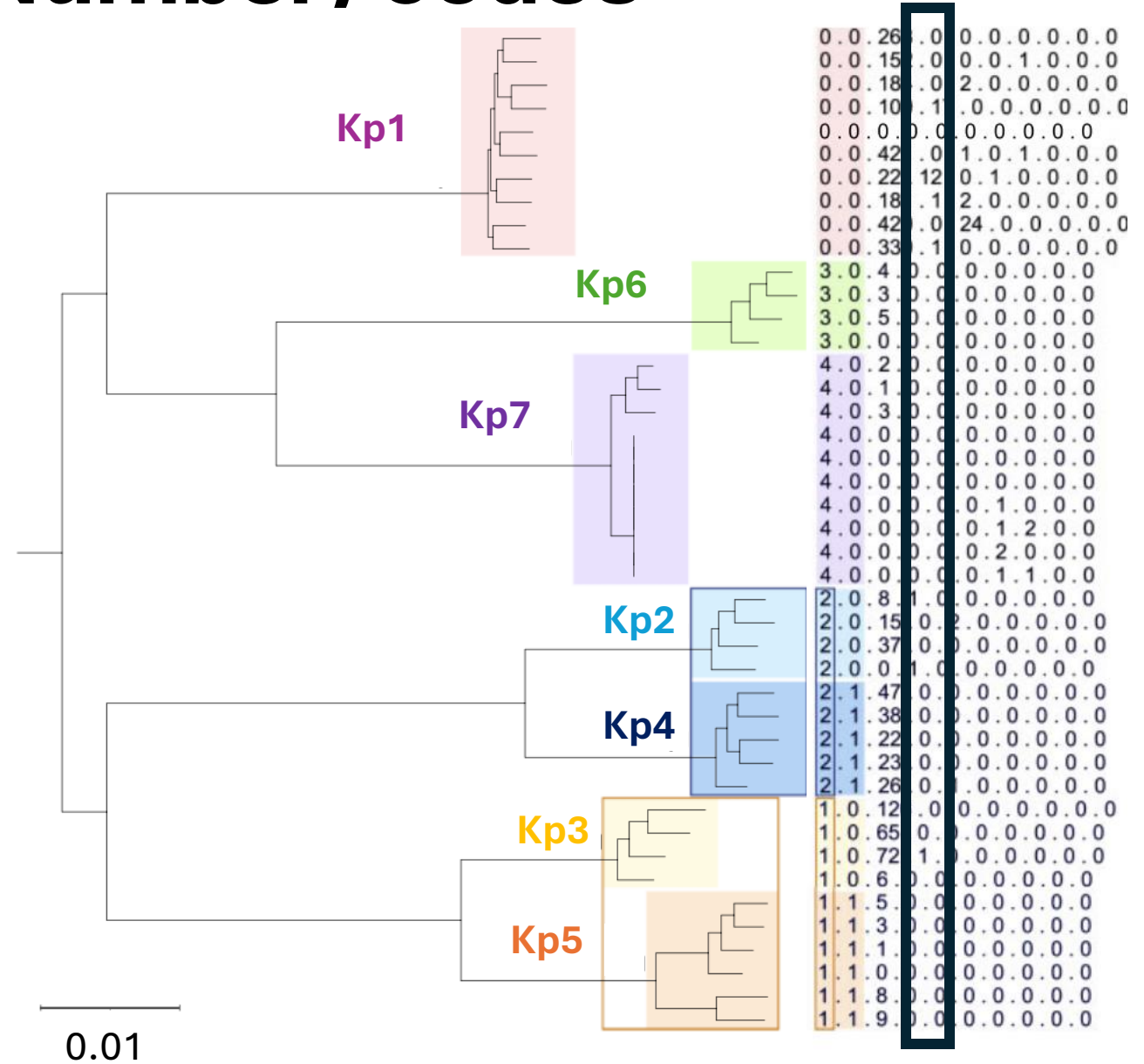
LIN (Life Identification Number) codes

bin	classification	No. allele mismatches
1	Species	[629-610]
2	Subspecies	[610-585]
3	Sublineage (SL)	[585-190]
4	Clonal Group (CG)	[190-43]
5	-	[43-10]
6	-	[10-7]
7	-	[7-4]
8	-	[4-2]
9	-	[2-1]
10	-	[1-0]

Remaining digits give higher resolution data on allelic differences based on the number of mismatches

Palma et al. 2024, bioRxiv; Hennart et al. 2022

https://bigsdb.pasteur.fr/klebsiella/cgmlst-lincodes/
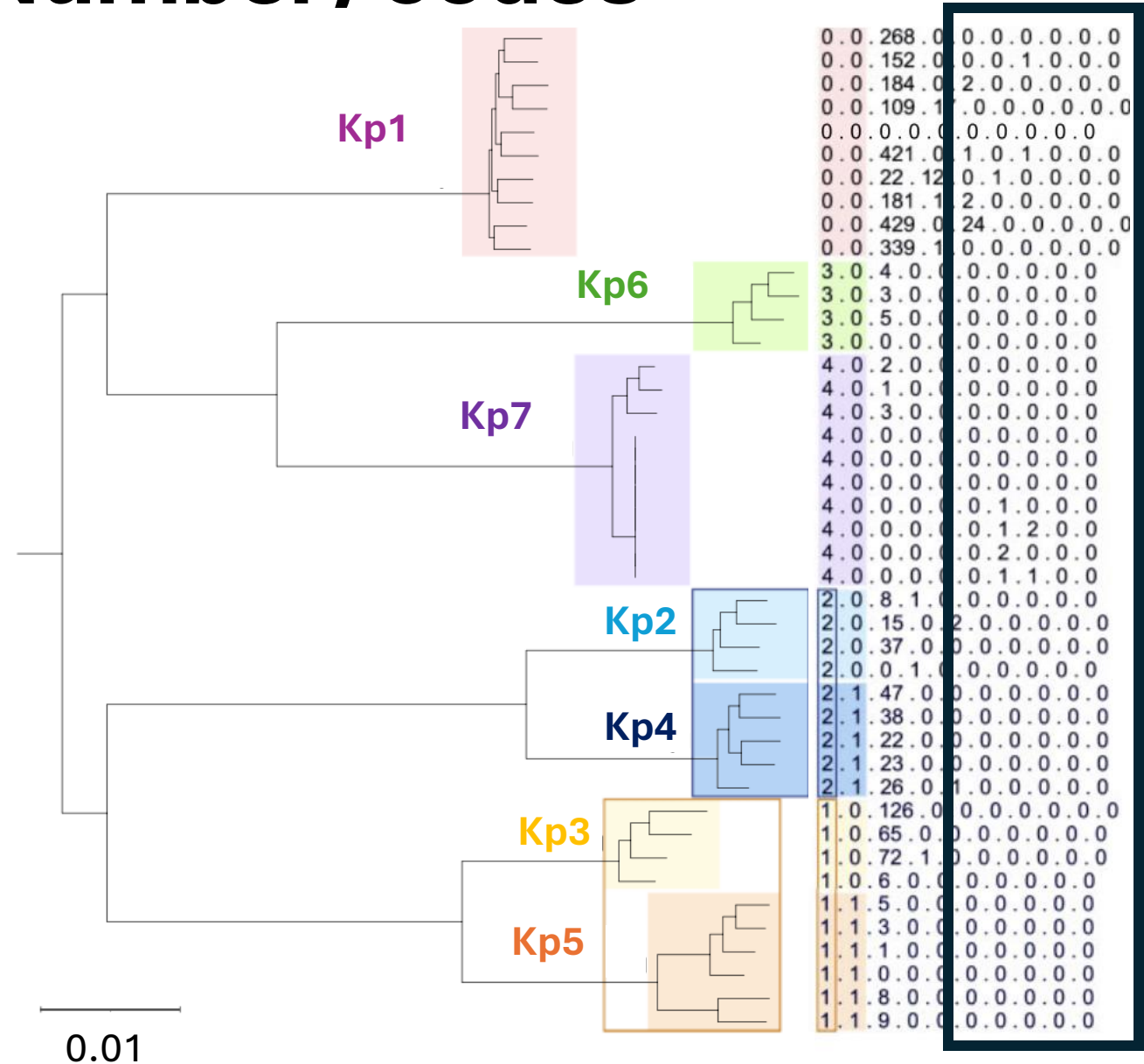
Typing databases freely available online

- All databases hosted or mirrored via **BIGSdb** software at **pubmlst.org**

https://bigsdb.pasteur.fr/klebsiella/

Typing methods provide useful nomenclature

1. To <u>stratify</u> cases into pathogen subtypes
   - To identify / define those with different genomic / biological traits and assess whether they have distinct epidemiology, so they can be managed in a targeted way
   - May consider phylogenetic relatedness to define groups, or use non-phylogenetic groupings

2. To investigate <u>emergence</u> and <u>spread</u>
   - Of the infectious disease generally, or variants of special clinical interest such as drug resistant or hypervirulent strains
   - Identify sources of infection, track transmission events, investigate outbreaks

Typing methods provide useful nomenclature

For example, CG23 is a known hypervirulent strain type, whereas CG258 is often described as a 'classical' MDR strain type. These classifications are due to the presence of marker genes, and corresponding phenotypes, for either hypervirulence (blue) or drug resistance (red).


**Wyres et al. 2019, PLOS Genet**
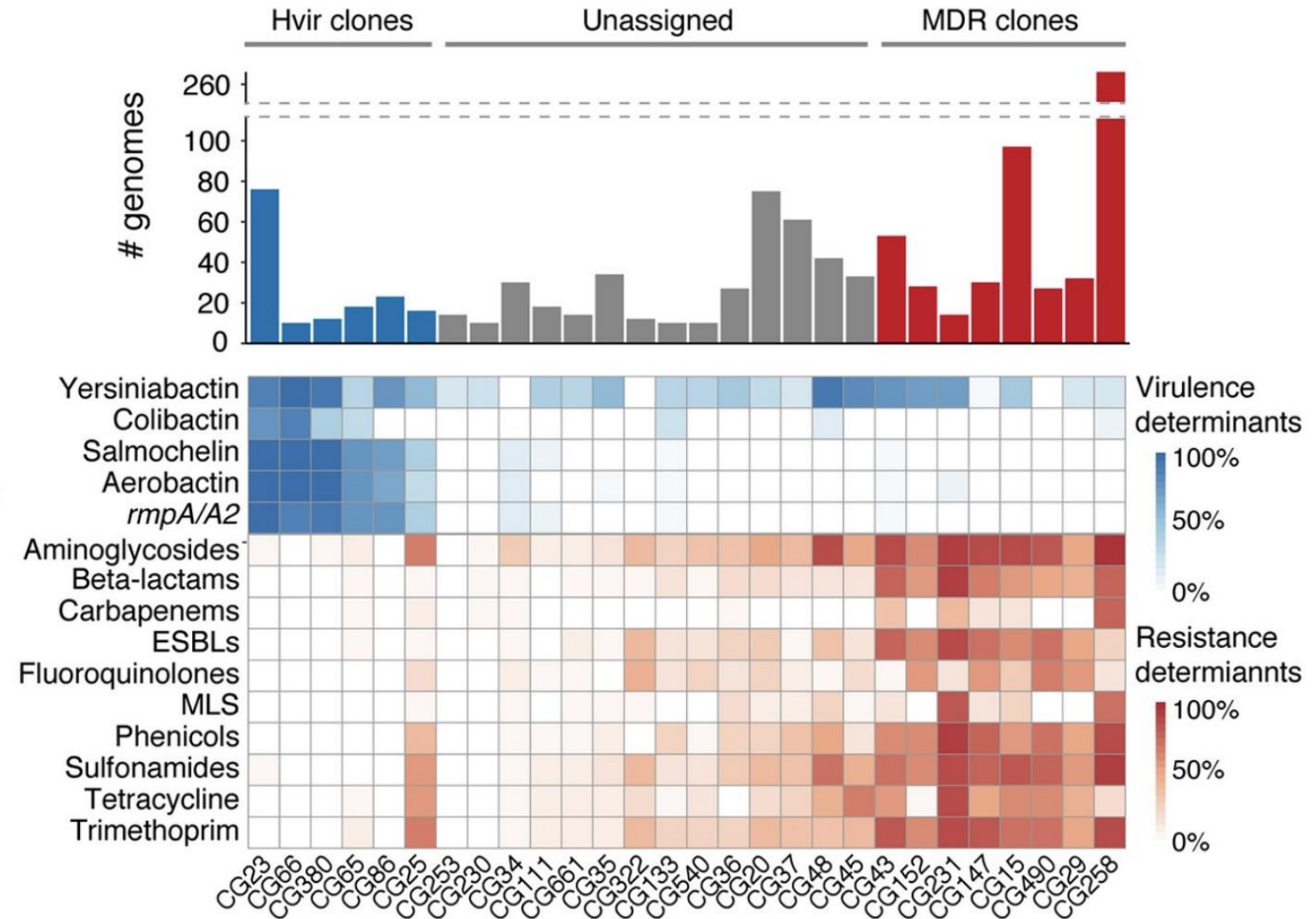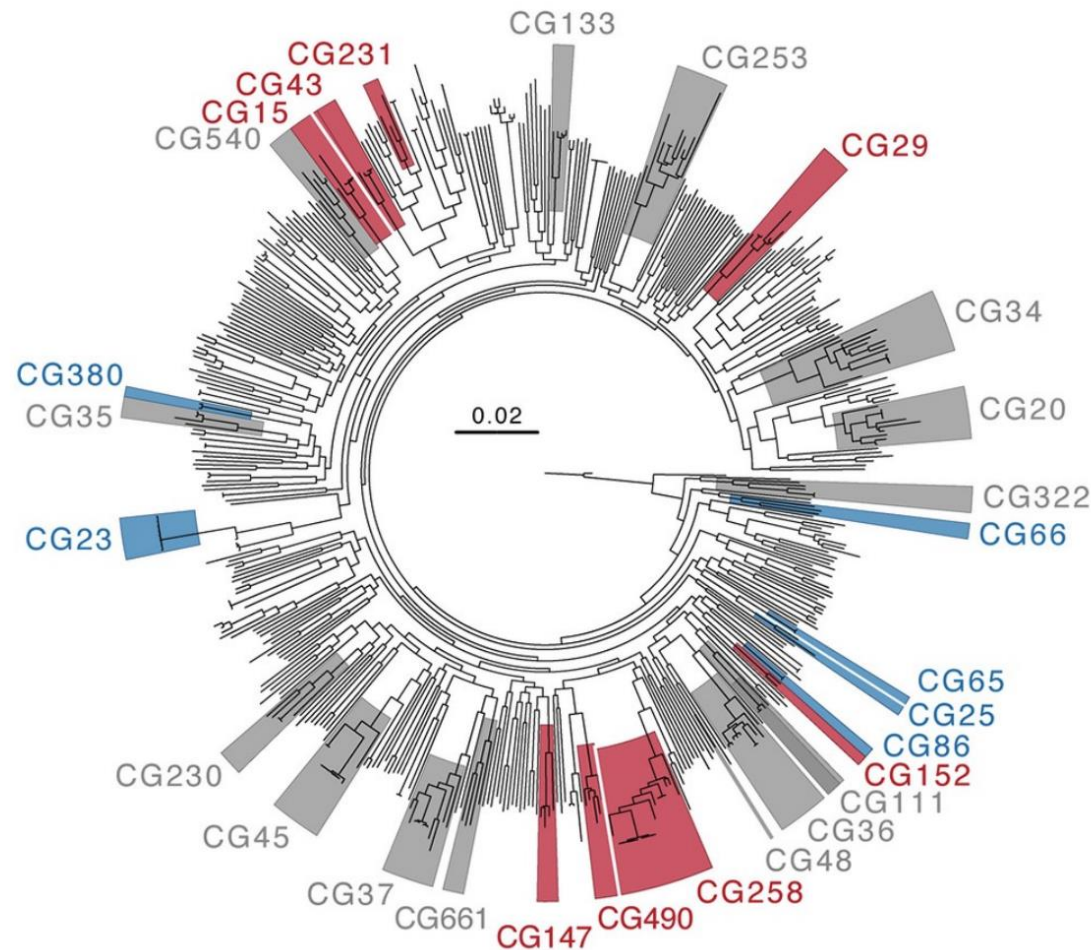
Case study

Case study: *Klebsiella* strain typing

- Setting: Patan Hospital, Kathmandu, Nepal

- Increase in blood isolates of *Klebsiella pneumoniae* from neonatal and pediatric intensive care units

- Sequencing investigation:
  - 29 suspected outbreak isolates
    - N=8 from NICU
    - N=7 from PICU
    - N=14 from nurseries
  - 60 randomly selected from other wards

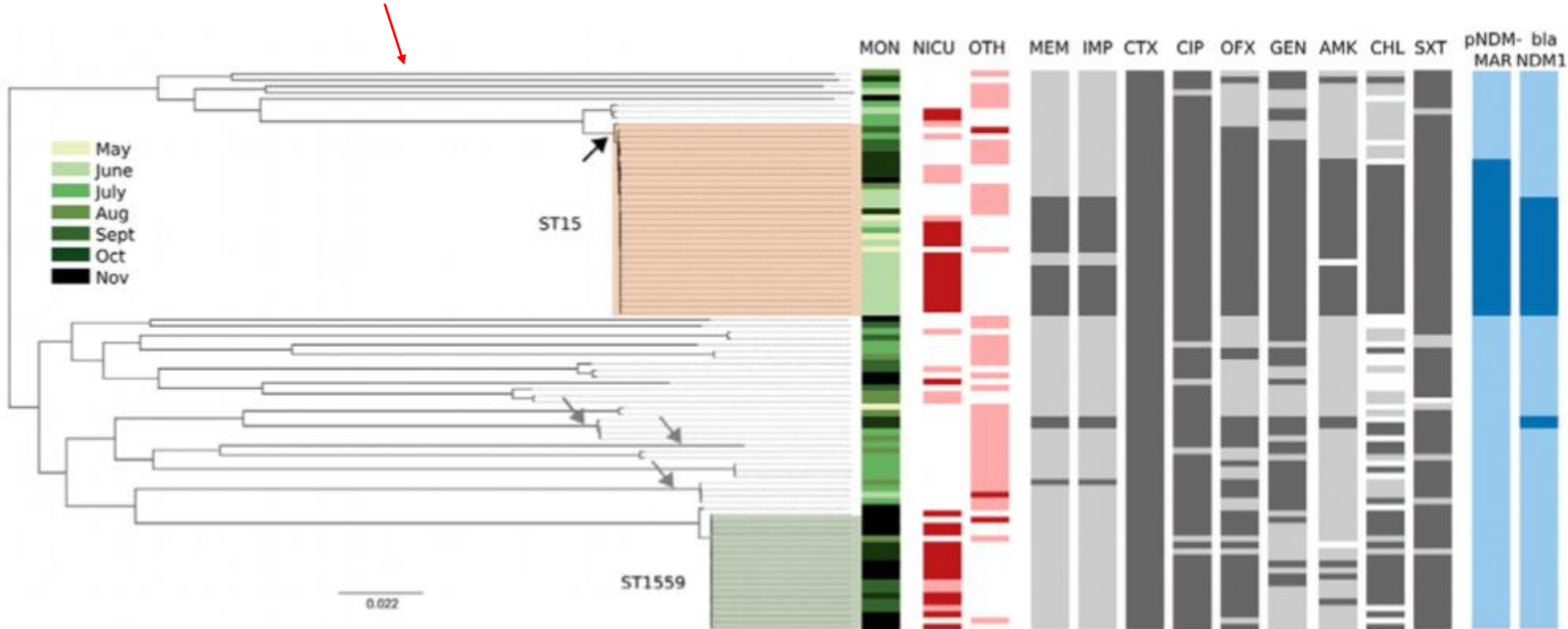**Monthly isolations of *K. pneumoniae* from blood**
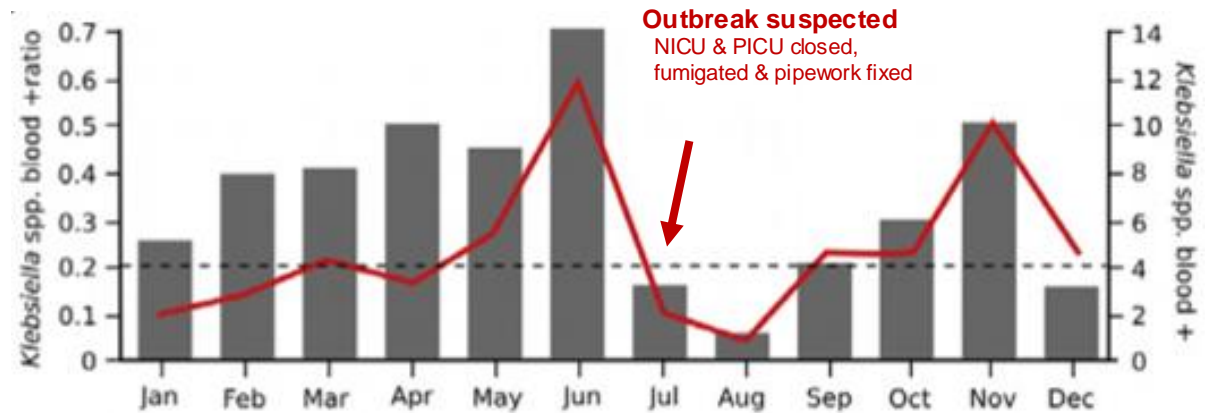
Wards affected by *K. pneumoniae* outbreak

Pediatric ICU
Neonatal ICU
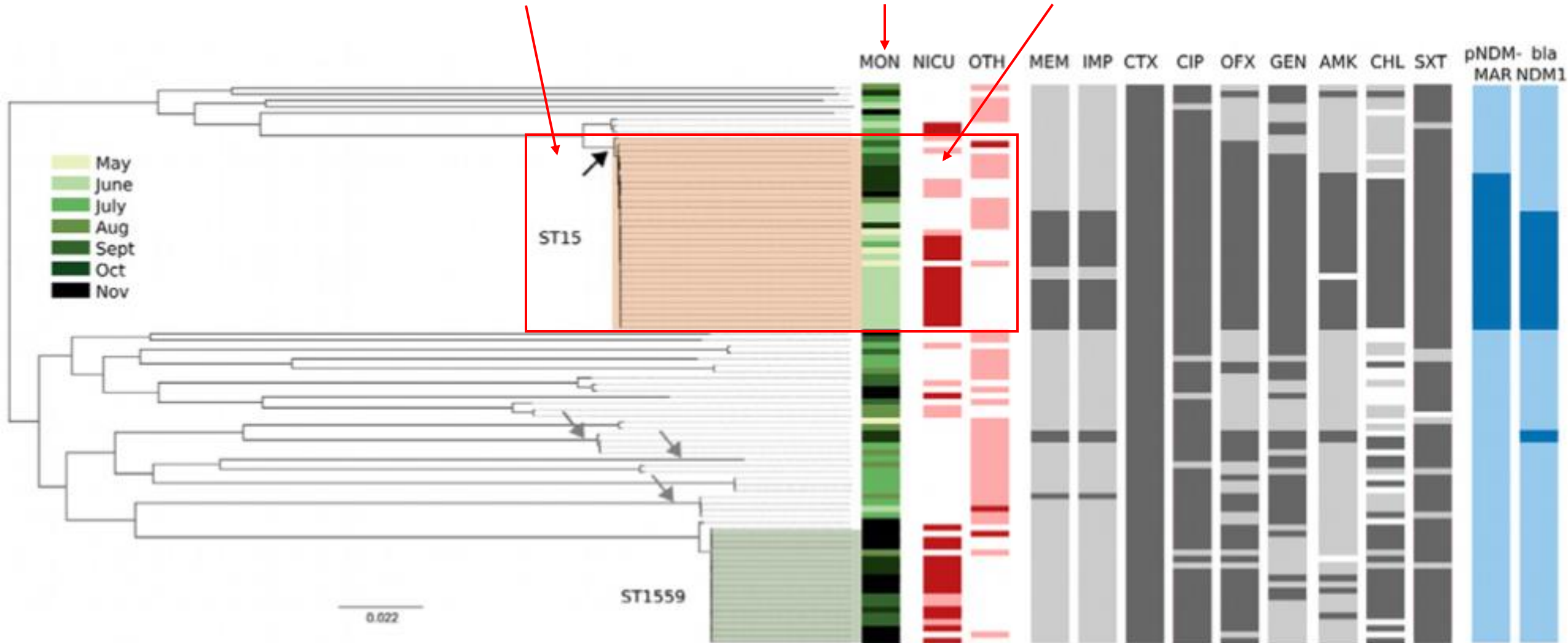**Nurseries**
Adult ICU
Medical
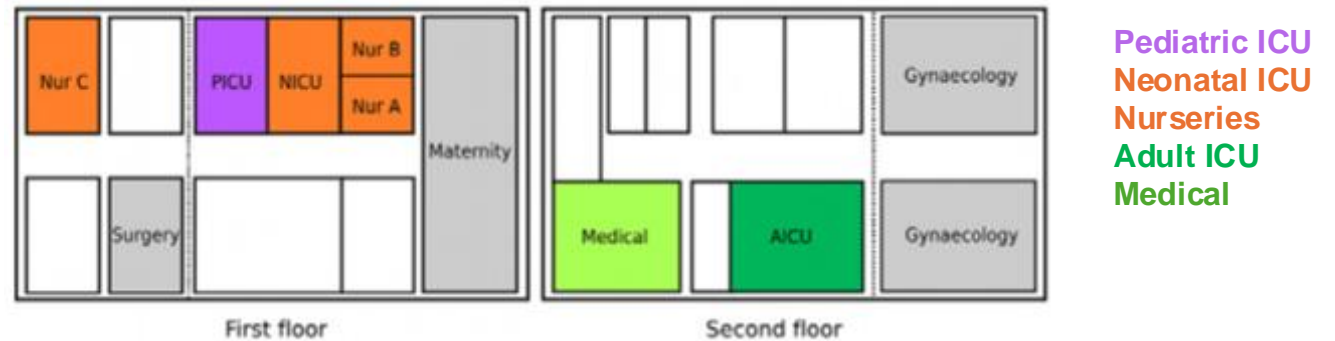
Case study: *Klebsiella* strain typing
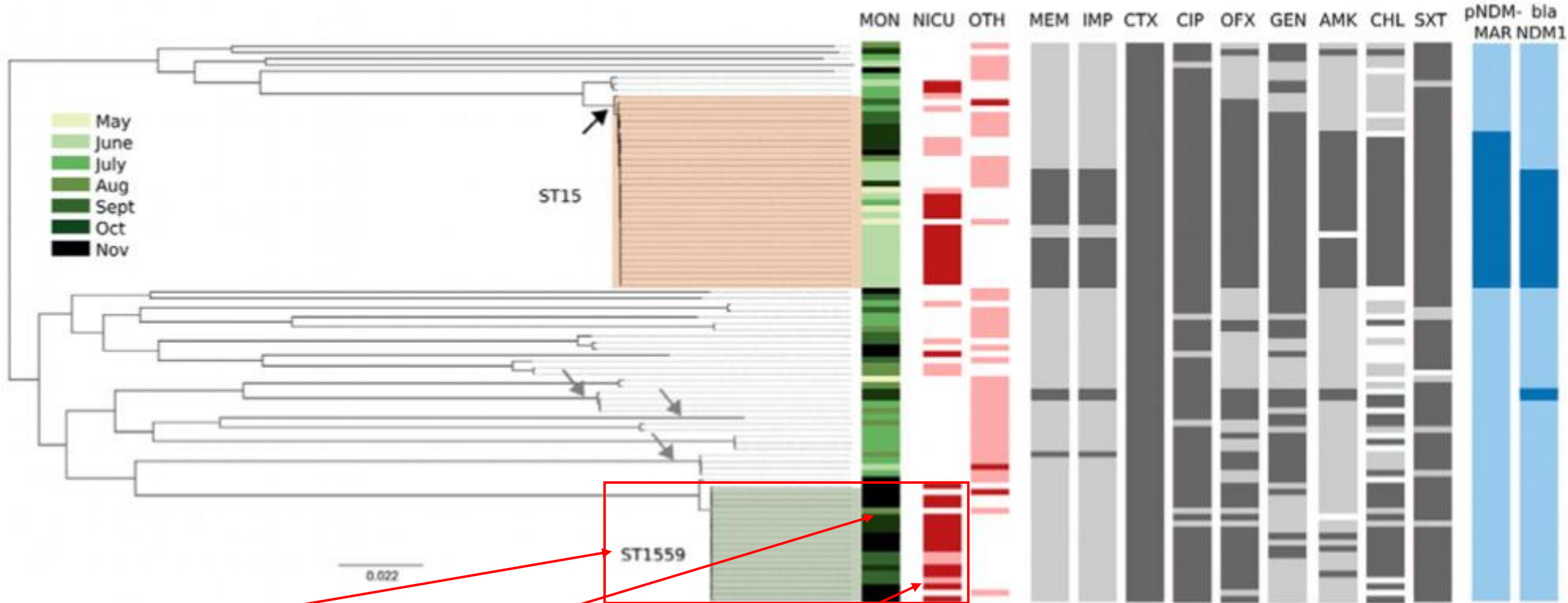

Whole-genome SNP tree
(tips = cases / genomes)

Case study: *Klebsiella* strain typing

Cluster 1: ST15, isolated mainly May-June, from NICU & nurseries

Case study: *Klebsiella* strain typing

Carbapenem resistance (meropenem, imipenem) in NICU cluster, due to NDM-1 carbapenemase

Case study: *Klebsiella* strain typing

Cluster 2: ST1559, isolated August-November, mainly from NICU

Case study: *Klebsiella* strain typing

A high-resolution genomic analysis of multidrug-resistant hospital outbreaks of *Klebsiella pneumoniae*

Hao Chung The[1,†], Abhilasha Karkey[2,†], Duy Pham Thanh[1], Christine J Boinett[3], Amy K Cain[3], Matthew Ellington[3,4], Kate S Baker[3], Sabina Dongol[2], Corinne Thompson[1,5], Simon R Harris[3], Thibaut Jombart[6], Tu Le Thi Phuong[1], Nhu Tran Do Hoang[1], Tuyen Ha Thanh[1], Shrijana Shretha[2], Suchita Joshi[2], Buddha Basnyat[2], Guy Thwaites[1,5], Nicholas R Thomson[3,7,‡], Maia A Rabaa[1,8,‡] & Stephen Baker[1,5,7,‡,*]

Any questions or reflections?