

Screening for CPO/CPE in Denmark



GÆLDENDE

BEK nr 1091 af 30/08/2018

Statens Serum Institut og Ældreministeriet

Yderligere oplysninger >

**Notifiable in Danish legislation
since September 2018**

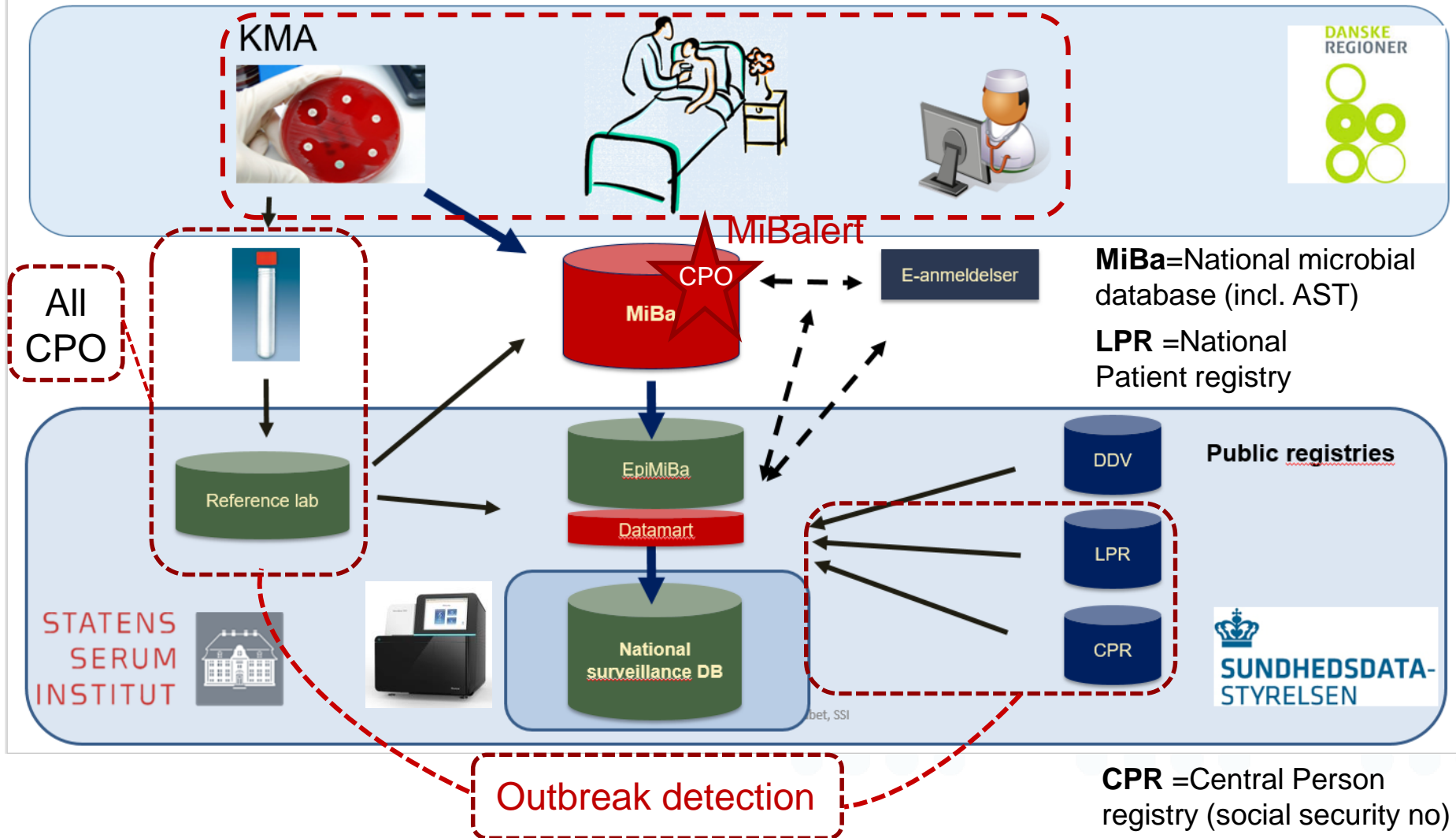
Bekendtgørelse om anmeldelse af tilfælde af Carbapenemase-
Producerende Organismer (CPO) påvist hos personer

I medfør af § 26 i lov om foranstaltninger mod smitsomme sygdomme, jf. lovbekendtgørelse nr. 814 af 27. august 2009,

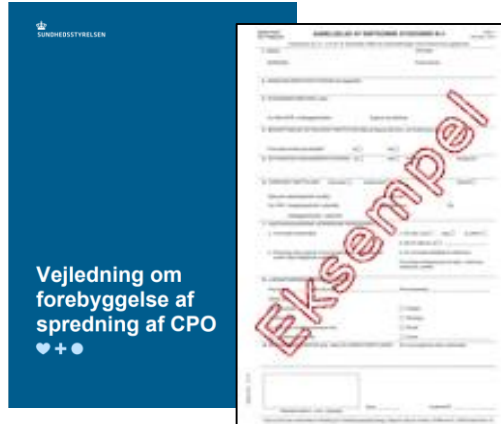
Henrik Hasman
Senior scientist
Statens Serum Institut



MiBa based surveillance: coherent data flows



• National guidelines for detection and containment of CPO (Sept., 2018)



- Mandatory reporting by clinicians of CPE
- Mandatory submission of all CPO isolates to SSI
- All submitted isolates are subjected to WGS analysis
- SSI has the mandate and obligation to investigate CPO outbreaks
- Outbreaks are tracked in a central database and reported back to the relevant hospitals.

• Three supplementary guidelines in relation to infection hygiene control

- Hospitals
- Nursing homes
- Home care

Bilag 1 Infektionshygiejniske retningslinjer: Hospitaler		
Udarbejdet på baggrund af Sundhedsstyrelsens "Vejledning om forebyggelse af spredning af CPO", 1. udgave 2018.		
Emne	Generelle infektionshygiejniske retningslinjer	Supplerende retningslinjer
Patientplacering mv.	Ikke relevant.	• Isolering af patienter med CPO • Opstilling af patienter med CPO • Adgang til patienter med CPO • Adgang til patienter med CPO • Adgang til patienter med CPO
Håndhygiejne	Hånddesinfektion er forpligtende. • Håndhygiejne skal udføres: o før alle rene procedurer o efter alle rene procedurer o efter brug af handsker. • Patient, besøgende og pårørende bør instrueres i og tilbydes at håndhygiejne og have mulighed for at gennemføre denne.	Håndhygiejne isolationsmidler er af afgørende betydning.
Værnemidler, generelt	Personlige værnemidler omfatter engangshandsker, engangsbeskyttelse, beskyttelsesbriller og visir. • Personlige værnemidler	• Værnemidler skal anvendes ved direkte kontakt med patienten, besøgende, udstyret og inventar. • Personlige værnemidler

Bilag 2 Infektionshygiejniske retningslinjer: Plejeboliger og lignende institutioner		
Udarbejdet på baggrund af Sundhedsstyrelsens "Vejledning om forebyggelse af spredning af CPO", 1. udgave 2018.		
Emne	Generelle infektionshygiejniske retningslinjer	Supplerende retningslinjer
Beboerforbrug, placering mv.	Ikke relevant.	• Adgang til patienter med CPO • Adgang til patienter med CPO • Adgang til patienter med CPO • Adgang til patienter med CPO • Adgang til patienter med CPO
Håndhygiejne	Hånddesinfektion er forpligtende. • Håndhygiejne skal udføres: o før alle rene procedurer o efter alle rene procedurer o efter brug af handsker. • Beboerforbrug, besøgende og pårørende bør instrueres i og tilbydes at håndhygiejne og have mulighed for at gennemføre denne.	Håndhygiejne isolationsmidler er af afgørende betydning.
Værnemidler, generelt	Personlige værnemidler omfatter engangshandsker, engangsbeskyttelse, beskyttelsesbriller og visir. • Personlige værnemidler	• Værnemidler skal anvendes ved direkte kontakt med patienten, besøgende, udstyret og inventar. • Personlige værnemidler

Bilag 3 Infektionshygiejniske retningslinjer: Hjemmepleje og Hjemmesygepleje		
Udarbejdet på baggrund af Sundhedsstyrelsens "Vejledning om forebyggelse af spredning af CPO", 1. udgave 2018.		
Emne	Generelle infektionshygiejniske retningslinjer	Supplerende infektionshygiejniske retningslinjer ved CPO
Patientplacering mv.	Ikke relevant.	Ikke relevant.
Håndhygiejne	Hånddesinfektion er forpligtende. • Håndhygiejne skal udføres: o før alle rene procedurer o efter alle rene procedurer o efter brug af handsker. • Borger, besøgende og pårørende bør instrueres i og tilbydes at håndhygiejne og have mulighed for at gennemføre denne.	Håndhygiejne skal udføres, når borgeren forlader, og værnemidler er afleveret.
Værnemidler, generelt	Personlige værnemidler omfatter engangshandsker, engangsbeskyttelse, beskyttelsesbriller og visir. • Personlige værnemidler	• Værnemidler skal anvendes ved direkte kontakt med borgeren, borgerens udstyret, udstyr og inventar. • Personlige værnemidler • er personlige og til engangsbrug • skiftes mellem hver borger samt mellem rene og rene procedurer • kasseres umiddelbart efter brug.

❖ Questionnaire at time of hospitalization

Form 1a: Risk situations for CPO <i>To be asked at beginning of all hospitalization events</i>	
At hospitalization please ask the following question	If the answer is yes, then the listed criteria below should also apply:
1. Is the patient known to be CPO positive?	
2. Has the patient had any direct contact with a CPO positive person (e.g. in the household or similar)?	
3. Has the patient been receiving treatment in a hospital or clinic abroad within the last 6 months (excluding The Nordic countries)?	a) The stay lasted more than 24 hours, or b) An invasive operation has been performed regardless of the length of the stay.
4. Has the patient been staying abroad outside the Nordics and received treatment with antibiotics during this stay?	

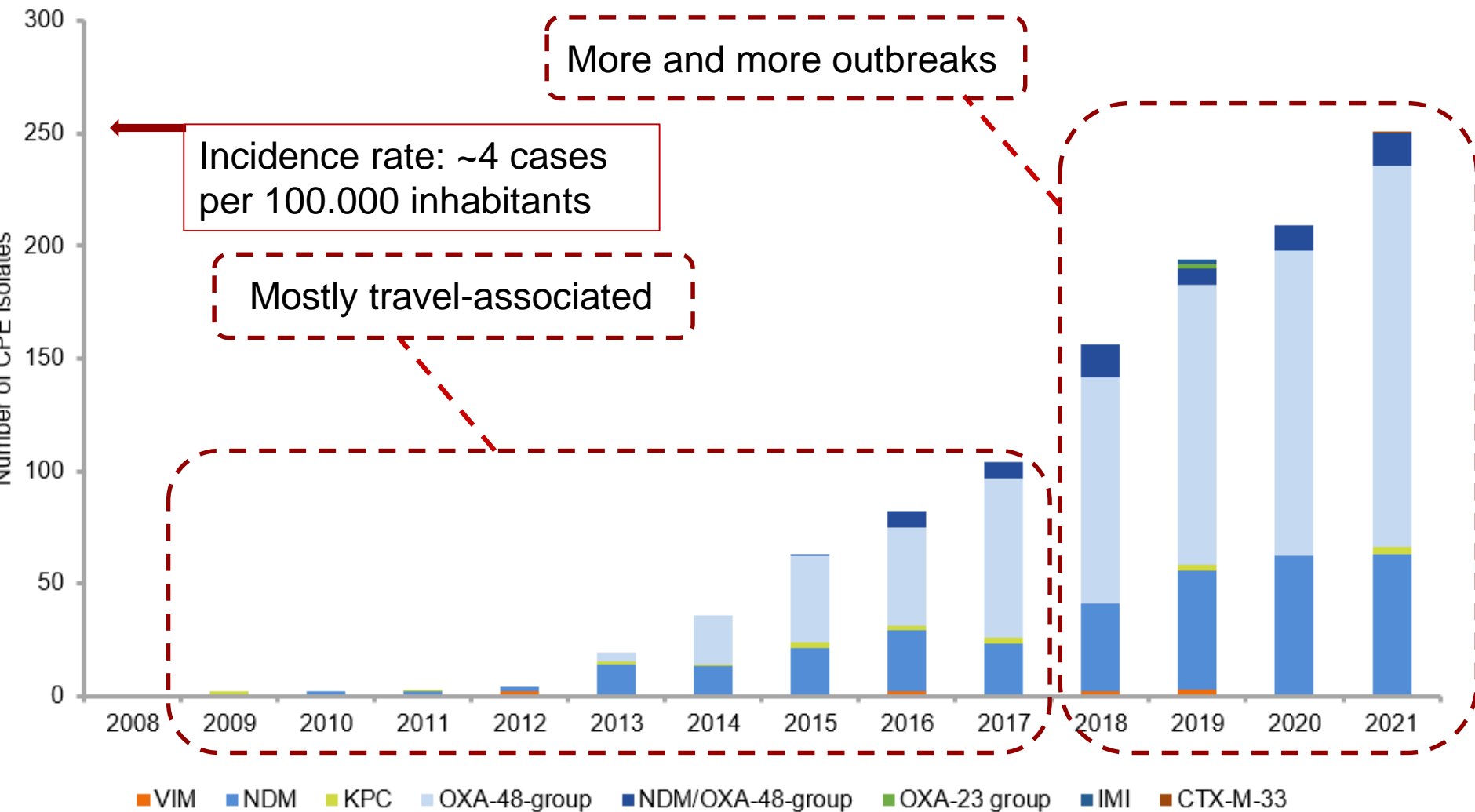
- Besides the general risk situations listed in Form 1a, certain additional known risk factors/situations may apply less frequently, thus not requiring all patients to be asked on a routinely basis. Here, the physician may have prior knowledge about the patient to suspect an increased risk for CPO carriage. In these case, the questions in Form 1b should be asked.

Form 1b: Special risk situations for CPO

To be asked at beginning of all hospitalization events, if the physician find it appropriate or if the patient is already aware that he/she/they is in a risk situation.

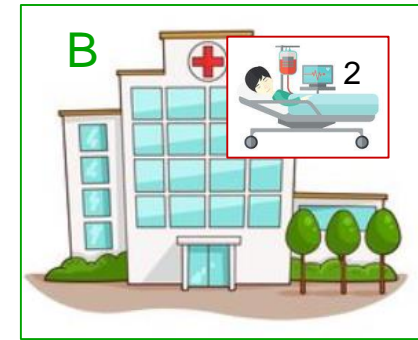
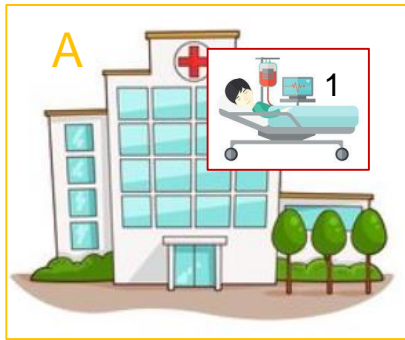
Persons who have, within the last 6 months	<ul style="list-style-type: none">- Been hospitalized in a CPO-positive department- Been staying in a CPO-positive nursing home (or similar..)- Been staying in confined spaces with poor sanitary conditions (e.g. war zones, refugee camps, foreign forster homes ect.)
Persons who have, within the last 6 months	<ul style="list-style-type: none">- Been in dialysis treatment or have received anti-neoplastic medical treatment.

CPO IN DENMARK



All isolates are submitted to WGS (Illumina) and analyzed (Ridom SeqSphere+) to detect genomic (clonal) clusters across departments, hospitals and regions.

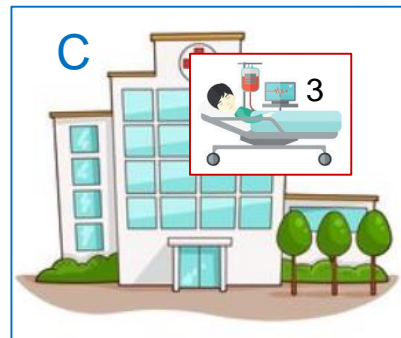
THE COMPLICATED (REGIONAL) OUTBREAK SITUATION



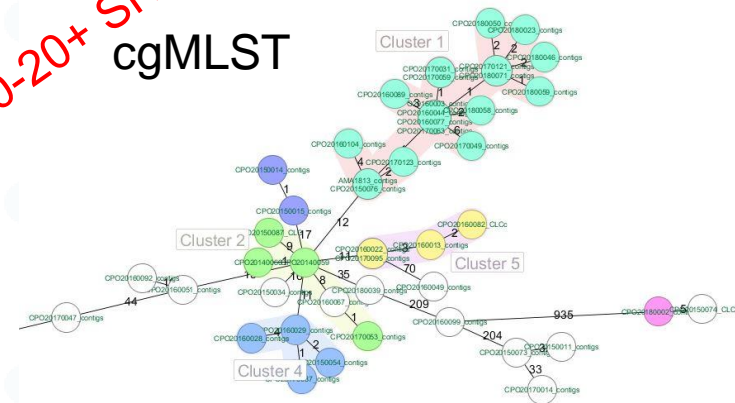
E. coli
NDM+




E. coli
ST1 (CT1)
*bla*NDM-1




~0-20+ SNPs/alleles
cgMLST





- 2013 : Pilot projekts
- 2014 - : WGS of **ESBL/pAmpC *E. coli*** from blood infections
- 2014 - : WGS of **CPO's** (all isolates)
- 2015 - : WGS of **clinical VRE + all LRE**
- 2016 - : MinION Nanopore (selected isolates but later all CPO)
- 2018 : WGS of ESBL/pAmpC ***K. pneumoniae*** from bloodinfections


**Welcome to SeqSphere+ Server on SSI001537**


Shortcuts

**New Project**
Create a new 'species-specific' Project to hold Sample data


**Import Epi Metadata**
Import epi metadata from MS Excel and CSV files into Samples of a Project


**Process Assembled Genome Data**
Process and import assembled data from local files or from NCBI Genomes into Samples of a Project

**Download FASTQ from SRA**
Download FASTQ and metadata from NCBI SRA to be processed by a pipeline

**Logout & Start Pipeline Mode**
Configure and start non-interactive data assembling and processing pipelines

**Comparison Table**
Compare and visualize Sample data (e.g., phylogenetic trees, epi curve, maps)

**Search Samples**
Search Samples by Project, epi/genotyping data, or last modified date

**User Guide**

CPO IN DENMARK – E. COLI 2014-2022



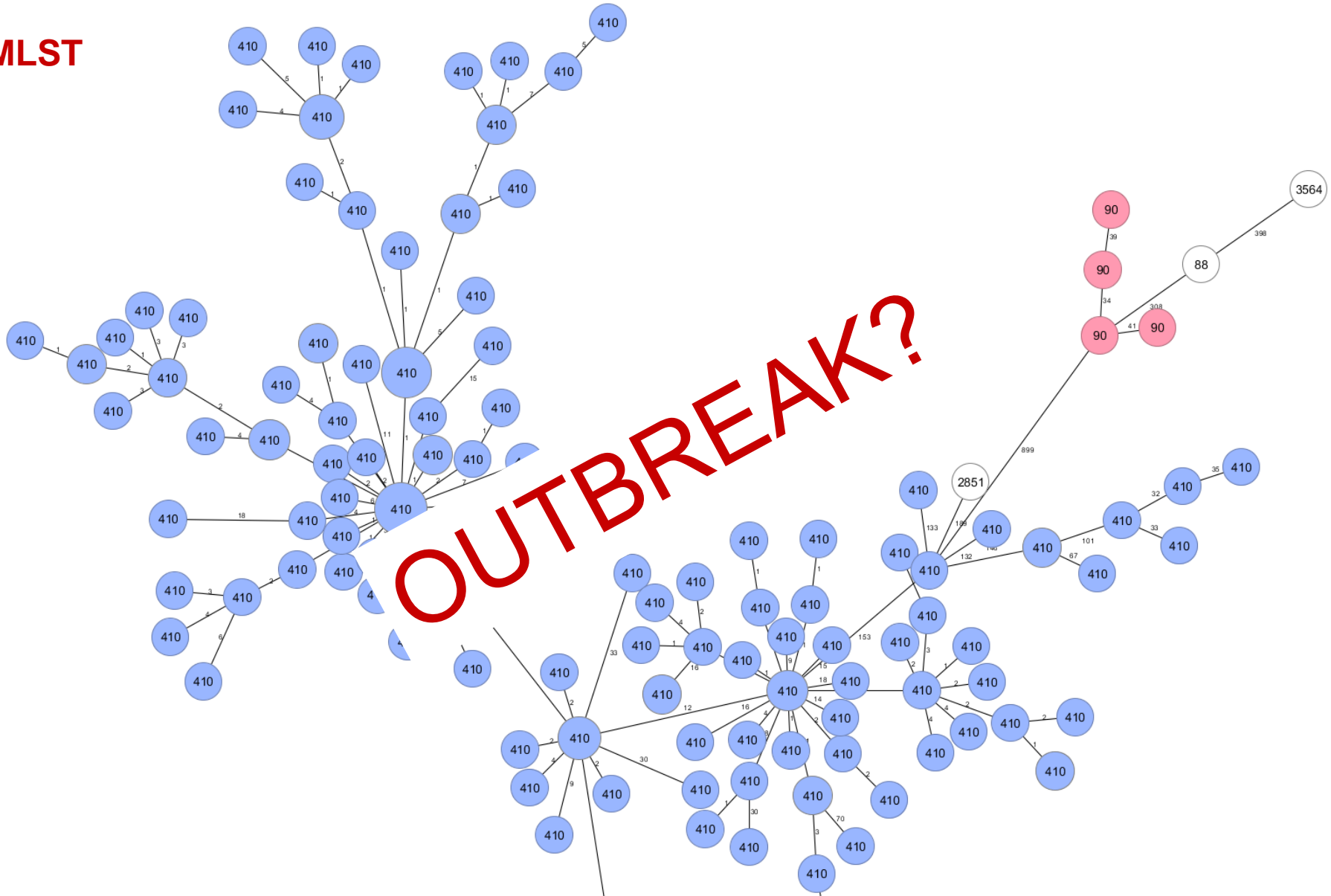
cgMLST



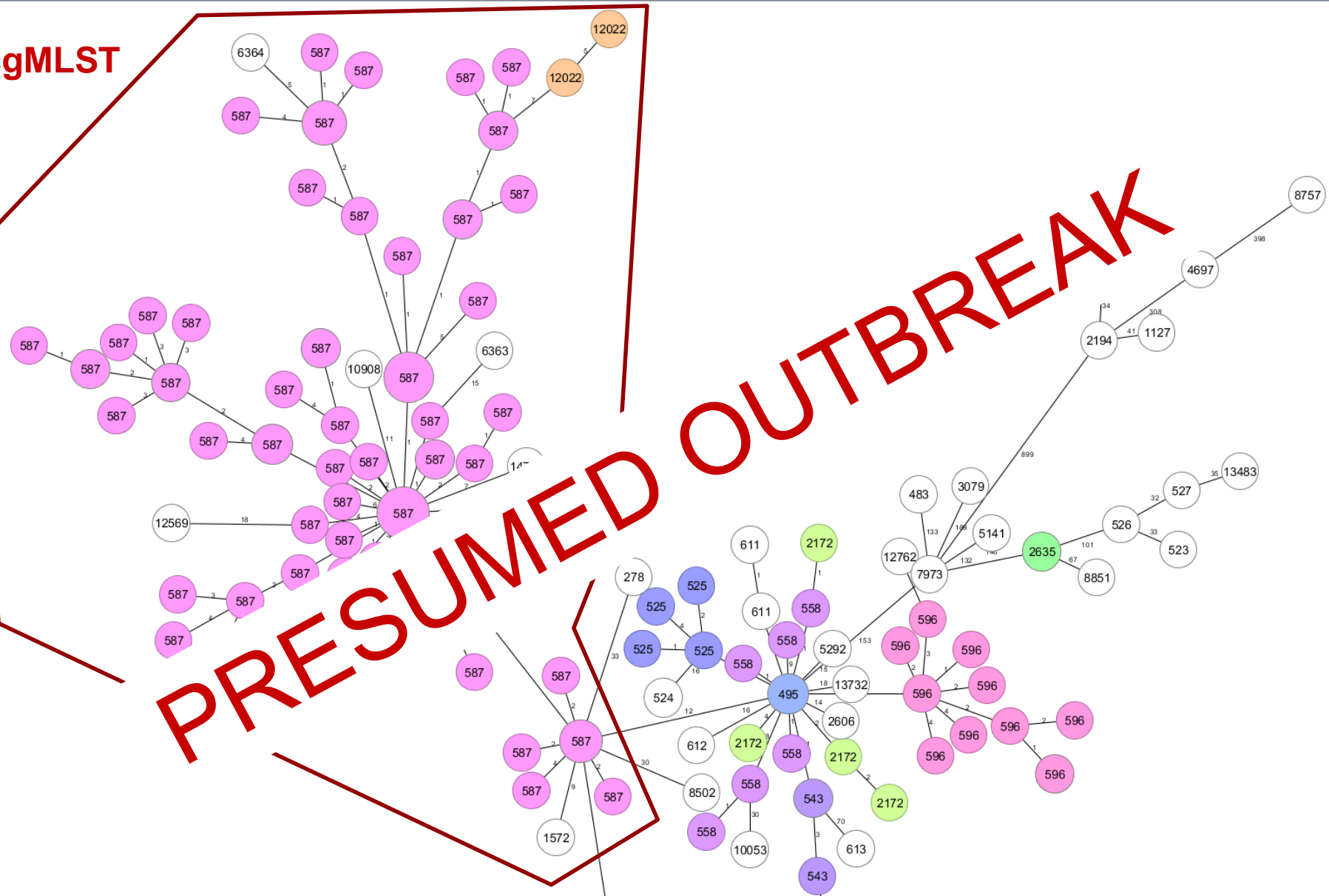
CPO IN DENMARK – E. COLI ST410



MLST



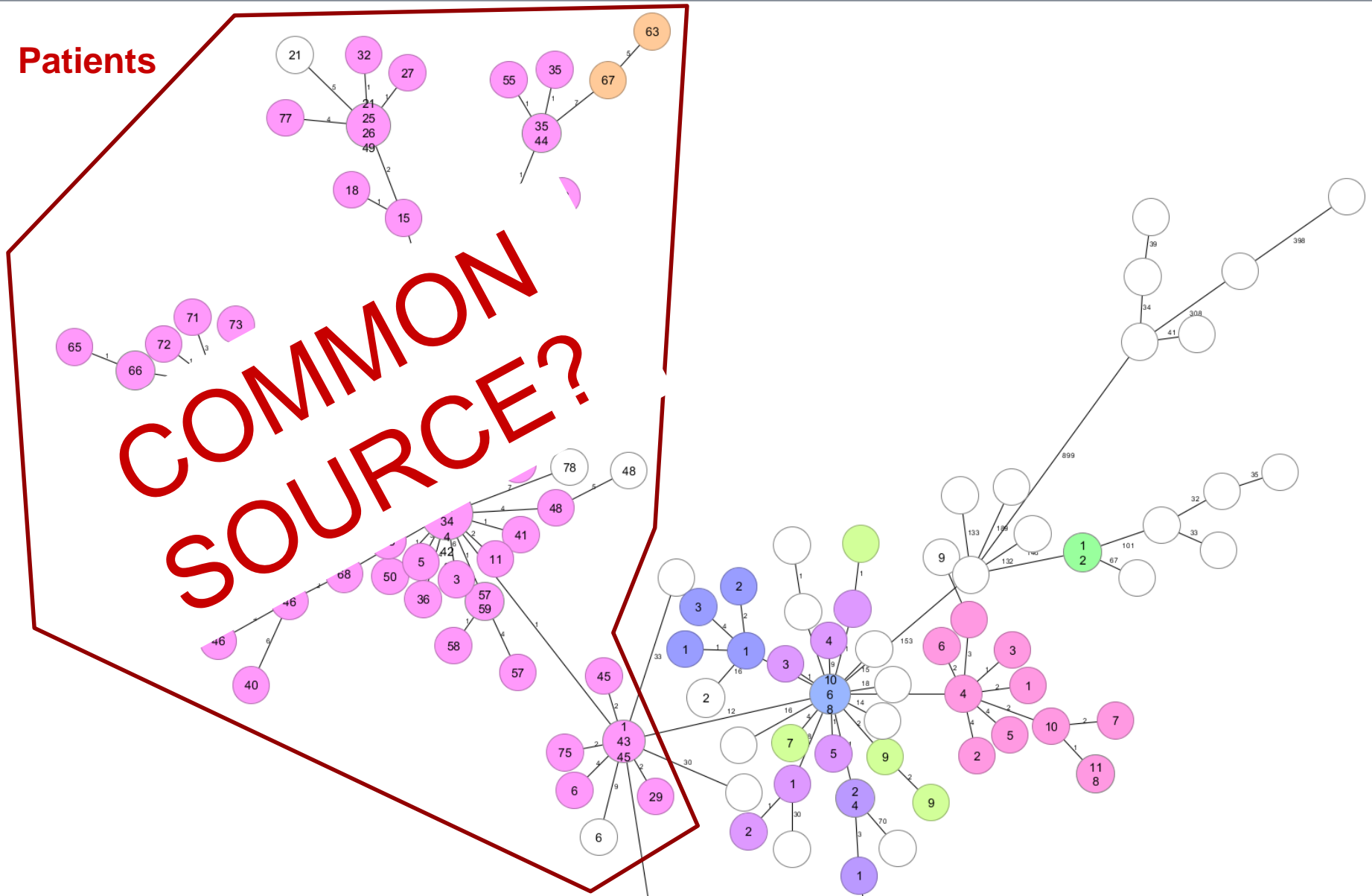
STATENS
SERUM
INSTITUT



CPO IN DENMARK – E. COLI ST410



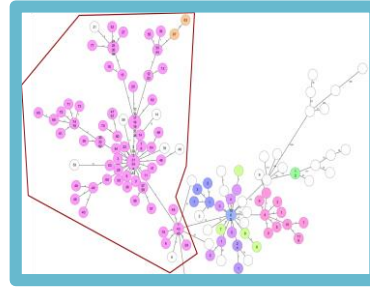
Patients



NOSOCOMIAL OUTBREAKS



Epidemiology

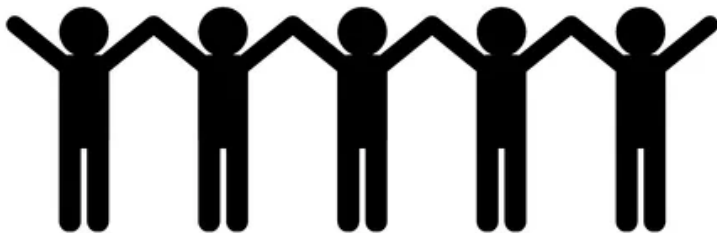


Molecular typing



Evasive action

Central dogma of (hospital) epidemiology



Direct chain of transmission



Indirect chain of transmission

DAI – DRAIN ASSOCIATED INFECTIONS

Journal of Hospital Infection 93 (2016) 152–154

Available online at www.sciencedirect.com

Journal of Hospital Infection

journals/jhin



ELSEVIER

Short report

Carbapenem resistance in sink drain as a potential source of DAI

J.S. Soothill*

Great Ormond Street

**FECHE A TAMPA
PARA DESCARGA DO
AUTOCLISMO**



**CLOSE THE LID FOR
TOILET TO FLUSH**

Safe
travels

Safe
travels

Clean
& Safe

SEARCH

Use sink as a source of transmission of carbapenem-resistant *Enterobacteriaceae* in the hospital

Shah De Geyter^{1*}, Lieve B. J. J. van Duin¹, Denis Piérard¹ and

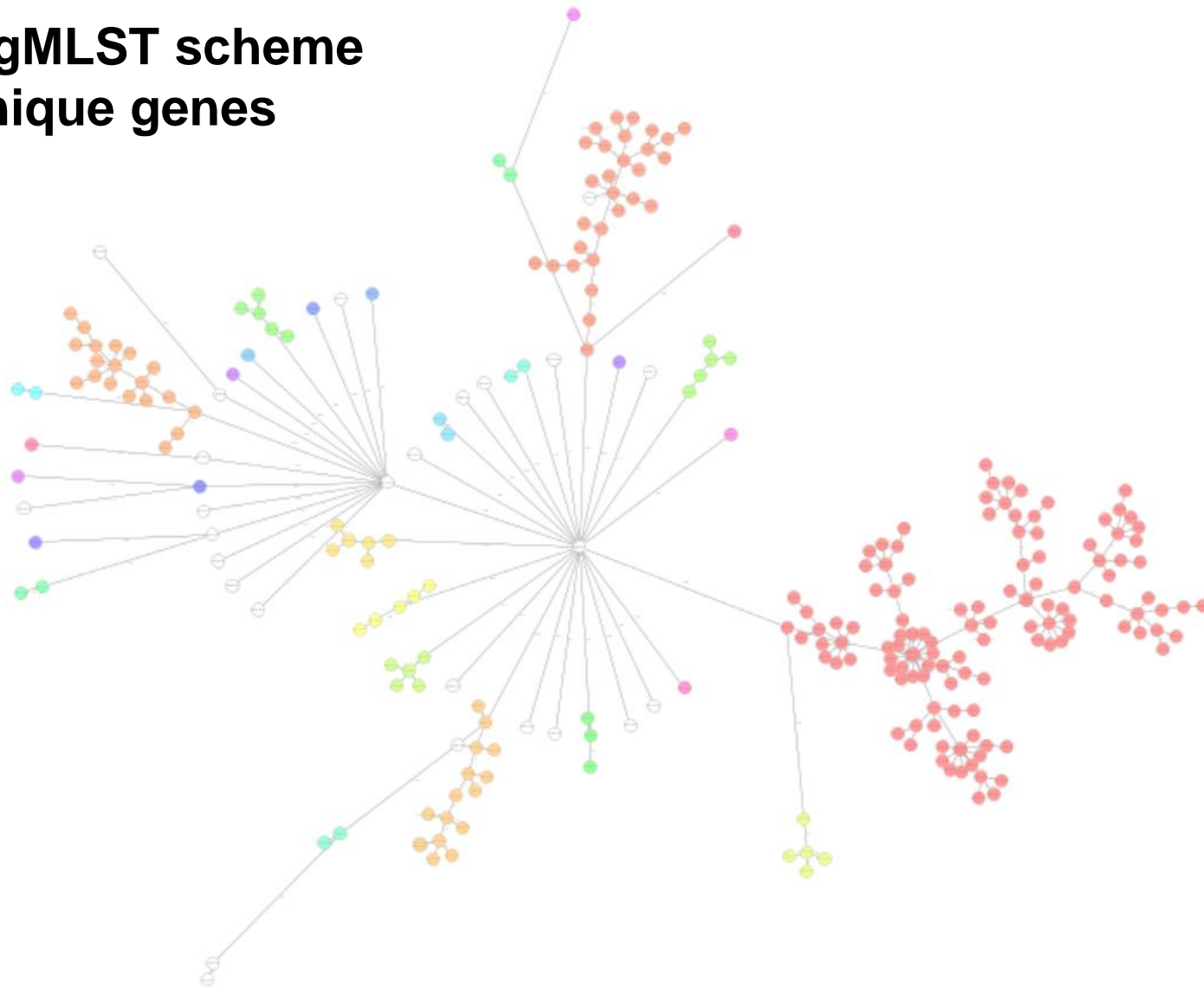
Antimicrobial Resistance
Infection Control

Open Access



Helena Martini¹,

RIVM cgMLST scheme 2965 unique genes



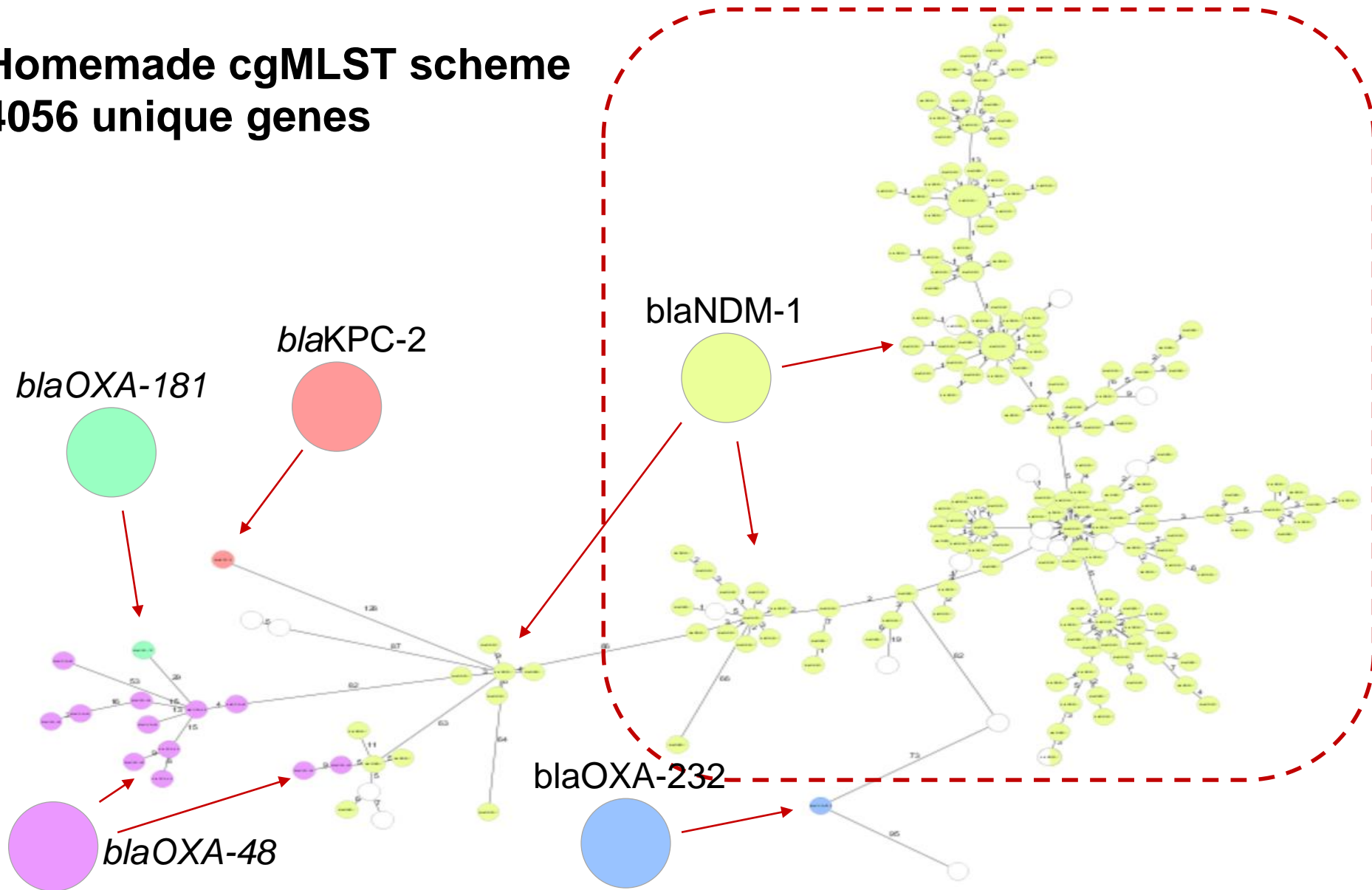
CPE CITROBACTER FREUNDII IN DENMARK



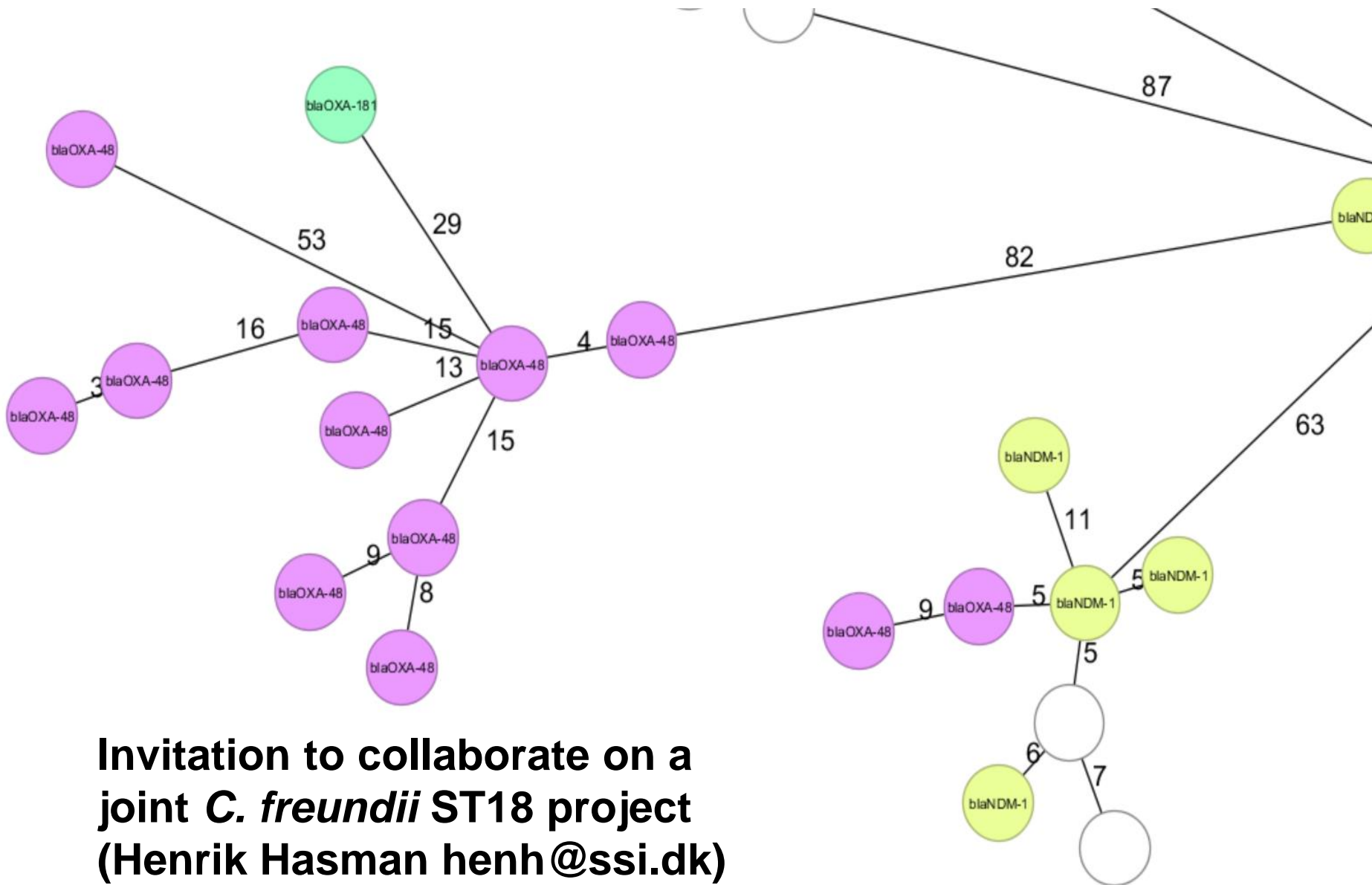
C. FREUNDII ST18 – JOINT PROJECT?



Homemade cgMLST scheme
4056 unique genes

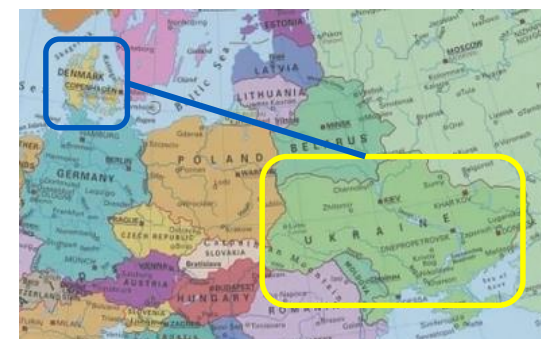


C. FREUNDII ST18 – JOINT PROJECT?



Invitation to collaborate on a joint *C. freundii* ST18 project (Henrik Hasman henh@ssi.dk)

CPO ISOLATES (2022) AND UKRAINE



Patient	Species	Proveart	Rejse	CarbapenemaseNGS	MLST1
7	<i>K. pneumoniae</i>	podning axil	Ukraine	blaNDM-1, blaOXA-48	ST23
7	<i>K. pneumoniae</i>	podning axil	Ukraine	blaNDM-1	ST307
7	<i>P. aeruginosa</i>	podning axil	Ukraine	blaNDM-1	ST773
6	<i>K. pneumoniae</i>	urin	Ukraine	negativ	ST23
6	<i>A. baumannii</i>	cicatrice	Ukraine	blaOXA-72	STNovel
5	<i>K. pneumoniae</i>	podning rectum	Ukraine	blaNDM-1, blaOXA-232	ST5859
5	<i>E. coli</i>	podning rectum	Ukraine	blaOXA-181	ST101
4	<i>E. coli</i>	podning rectum	Ukraine	blaNDM-5	ST361
3	<i>E. coli</i>	podning rectum	Ukraine	blaOXA-48	ST405
2	<i>A. baumannii</i>	cicatrice	Ukraine	blaOXA-72	STNovel
1	<i>E. coli</i>	podning rectum	Ukraine	blaKPC-3	ST131



Report

Manage

Explore

Collaborate

≡ (o)



All ARHAI Molec. typing

Search by text

in Please select



Announcement

Event

Forum

Long-Term Monitoring

News

Signal

Threat

Closed

Open

+ Advanced search criteria

Create item

Edit flags



Column visibility

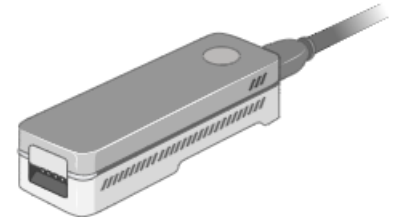
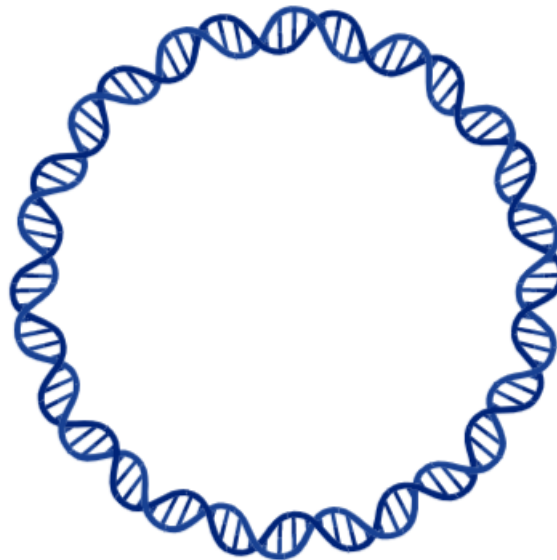
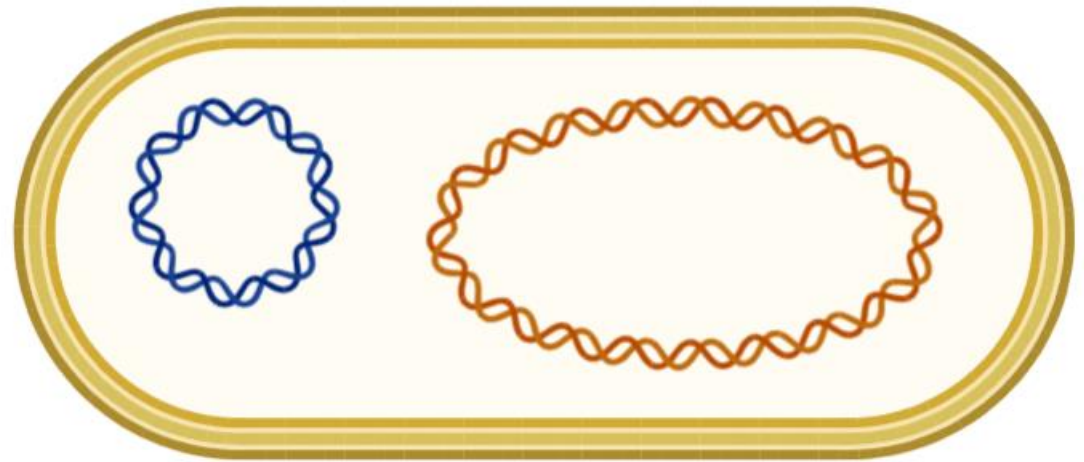
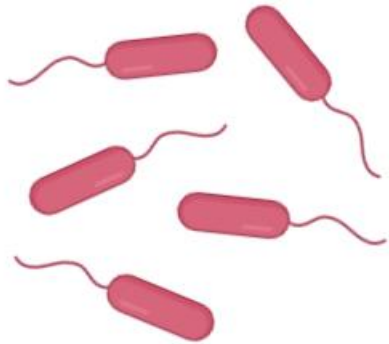
Show 25 rows

<input type="checkbox"/>	ID	Participating domain	Type	Title	Created by	Pathogens	Diseases	Modified time	Flags
<input type="checkbox"/>	2022-ARH-00005	ARHAI	Event	Increase in New Delhi metallo-beta-lactamase (NDM)-5-producing Escherichia coli in European countries	ECDC/Public Health	Escherichia coli	Infection/Colonisation /Other	2022-06-27 11:03	

QUESTIONS PLEASE?

ANY
QUESTIONS
?

PLASMID SEQUENCING

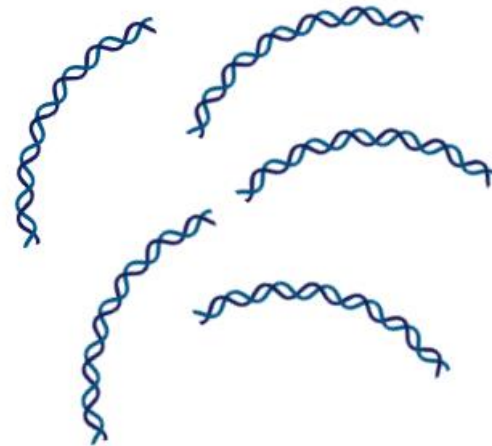
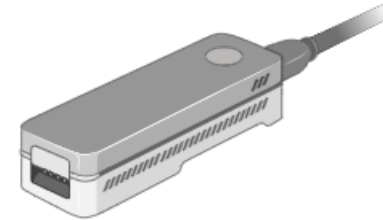


ILLUMINA VS MINION DATA



Read error rate: 0.1% – 1%

Genome coverage: 98%* - 100%



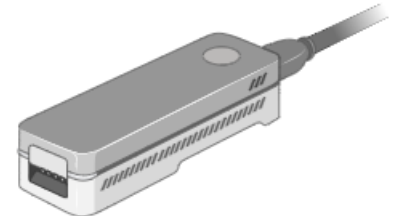
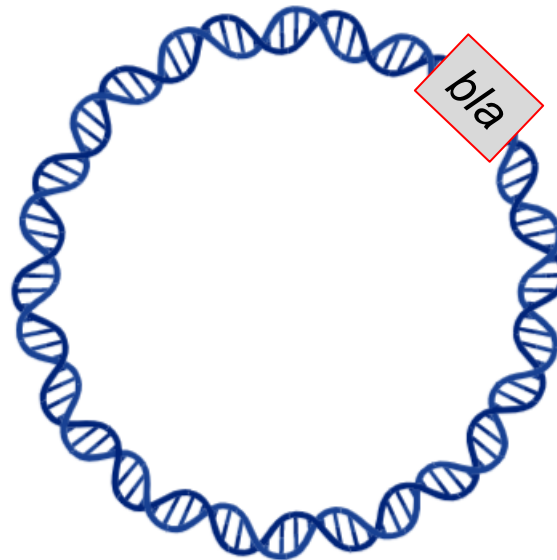
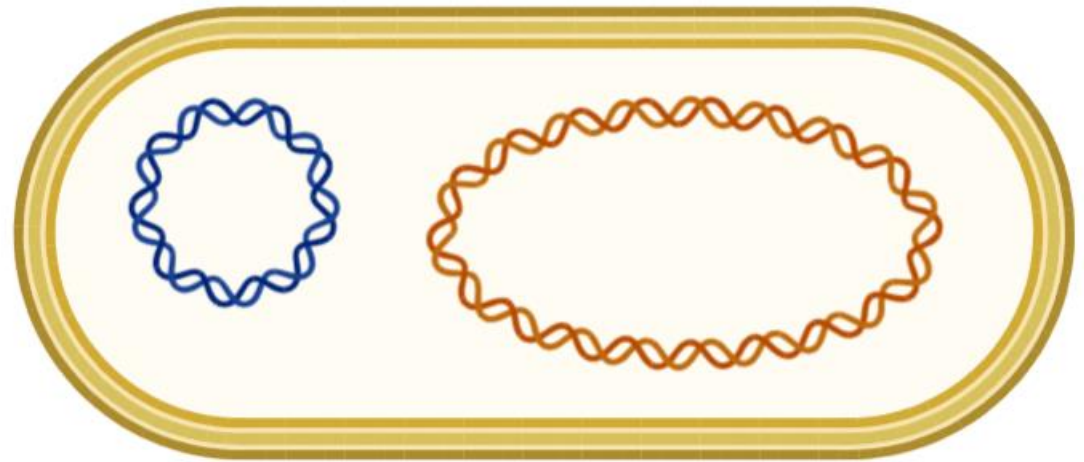
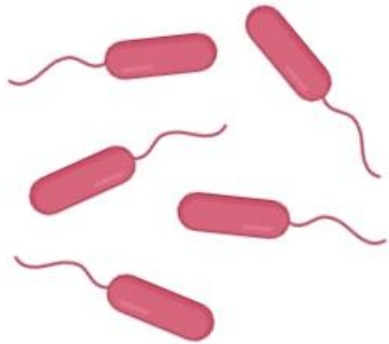
Read error rate: 5% – 15%

Genome coverage: ~100%**

* Bias from Tagmentation insertion sites

** Small plasmids may be missed

PLASMID SEQUENCING

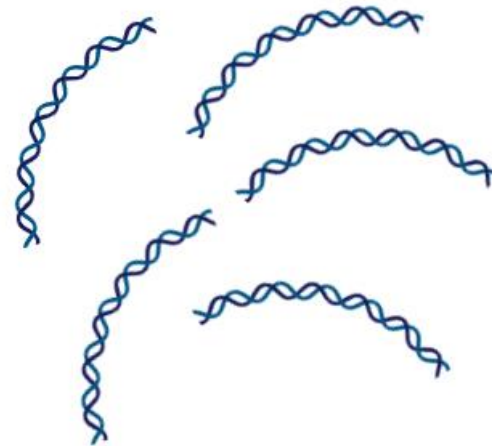
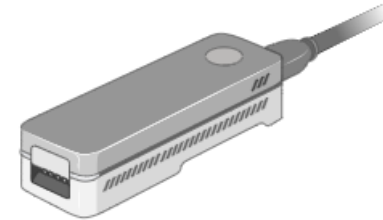


ILLUMINA VS MINION DATA



Read error rate: 0.1% – 1%

Genome coverage: 98%* - 100%



Read error rate: 5% – 15%

Genome coverage: ~100%**

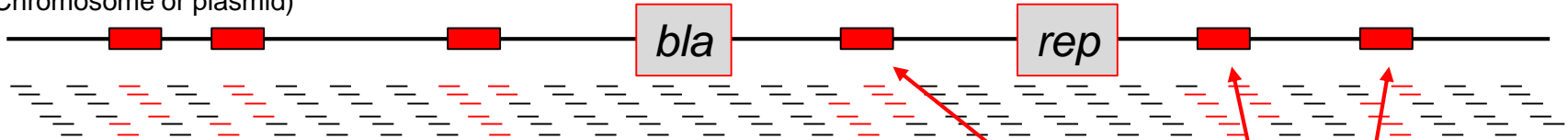
* Bias from Tagmentation insertion sites

** Small plasmids may be missed

ILLUMINA ASSEMBLY USING SPADES

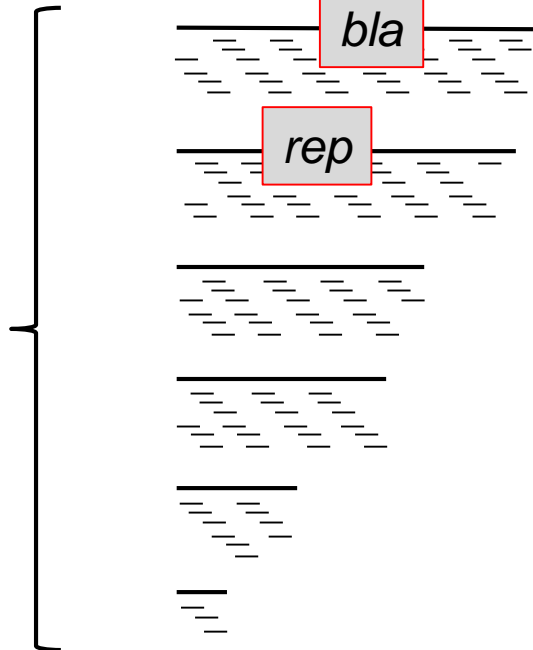
DNA

(Chromosome or plasmid)

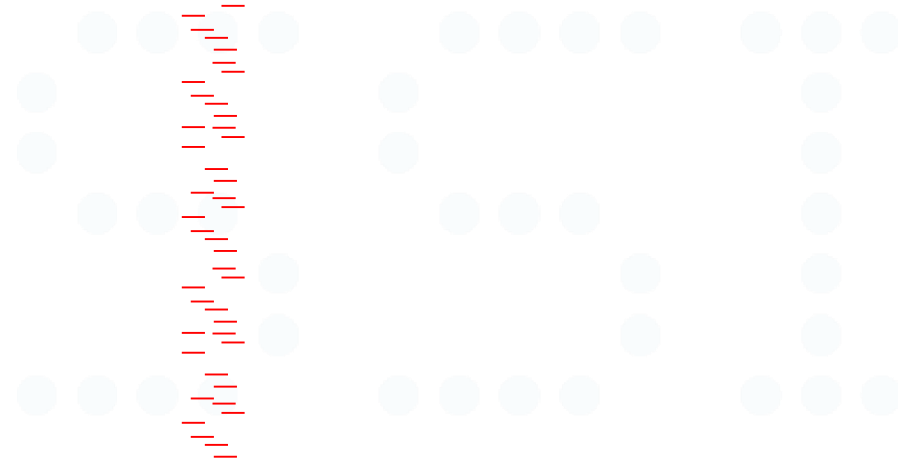


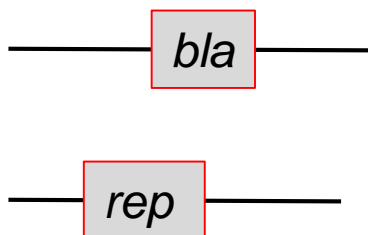
SPAdes assembly

N numbers of contigs



Repetitive element
(IS or transposons)





Other reports [Distance tree of results](#) [MSA viewer](#) ?

Descriptions

Graphic Summary

Alignments

Taxonomy

Sequences producing significant alignments

DownloadSelect columnsShow100?

☒ select all

100 sequences selected

GenBank

Graphics

Distance tree of results

MSA Viewer

	Description	Scientific Name	Max Score	Total Score	Query Cover	E value	Per. Ident	Acc. Len	Accession
<input checked="" type="checkbox"/>	Klebsiella quasipneumoniae subsp. quasipneumoniae SHB035 plasmid pYUSBH035 DNA complete sequence	Klebsiella quasip...	73.1	73.1	100%	6e-10	100.00%	46161	LC716358.1
<input checked="" type="checkbox"/>	Enterobacter hormaechei strain Eh27 plasmid pEh27_3 complete sequence	Enterobacter hor...	73.1	73.1	100%	6e-10	100.00%	53096	CP053694.1
<input checked="" type="checkbox"/>	Klebsiella pneumoniae strain dm664b plasmid p1_dm664b_NDM5 complete sequence	Klebsiella pneum...	73.1	73.1	100%	6e-10	100.00%	163355	CP095682.1
<input checked="" type="checkbox"/>	Enterobacter hormaechei strain beb_c250b plasmid p1_beb_c250b_NDM5 complete sequence	Enterobacter hor...	73.1	73.1	100%	6e-10	100.00%	94643	CP095681.1
<input checked="" type="checkbox"/>	Klebsiella pneumoniae subsp. pneumoniae strain MMGX21 subclass B1 metallo-beta-lactamase NDM-5 (blaND...	Klebsiella pneum...	73.1	73.1	100%	6e-10	100.00%	813	ON553466.1
<input checked="" type="checkbox"/>	Klebsiella pneumoniae subsp. pneumoniae strain MMGN70 subclass B1 metallo-beta-lactamase NDM-5 (blaND...	Klebsiella pneum...	73.1	73.1	100%	6e-10	100.00%	813	ON553465.1
<input checked="" type="checkbox"/>	Klebsiella pneumoniae subsp. pneumoniae strain MMGN224 subclass B1 metallo-beta-lactamase NDM-1 (blaND...	Klebsiella pneum...	73.1	73.1	100%	6e-10	100.00%	813	ON511106.1
<input checked="" type="checkbox"/>	Klebsiella pneumoniae subsp. pneumoniae strain MMGA96 subclass B1 metallo-beta-lactamase NDM-1 (blaND...	Klebsiella pneum...	73.1	73.1	100%	6e-10	100.00%	820	ON511105.1
<input checked="" type="checkbox"/>	Klebsiella pneumoniae subsp. pneumoniae strain MMGX130 subclass B1 metallo-beta-lactamase NDM-1 (blaND...	Klebsiella pneum...	73.1	73.1	100%	6e-10	100.00%	813	ON511104.1
<input checked="" type="checkbox"/>	Klebsiella pneumoniae subsp. pneumoniae strain MMGK9 subclass B1 metallo-beta-lactamase NDM-1 (blaND...	Klebsiella pneum...	73.1	73.1	100%	6e-10	100.00%	813	ON511103.1
<input checked="" type="checkbox"/>	Klebsiella pneumoniae subsp. pneumoniae strain MMGK6 subclass B1 metallo-beta-lactamase NDM-1 (blaND...	Klebsiella pneum...	73.1	73.1	100%	6e-10	100.00%	813	ON511102.1

GView Server

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GView Server is a comparative genomics server and front end to [GView](#), a circular and linear genome viewer. It allows sequence information to be analyzed, results visualized in an intuitive manner. A single reference genome (in GenBank, EMBL) can be uploaded and the appearance customized, or multiple genomes uploaded to perform comparative analysis. GView Server uses BLAST to compare the reference with any other genomes uploaded and contains a number of predefined BLAST analysis types for different use cases.

Step 1: Choose Analysis and Upload Reference

Choose the analysis type to perform and select a reference sequence file to upload. Accepted formats are GenBank and EMBL, and the file should contain a nucleotide genome. If you would like to have your results e-mailed to you upon completion, enter your e-mail address below.

February 9, 2021: Job submission for GView Server is back to normal.

Analysis Type **BLAST atlas**
Select analysis type to see a description below

Select a sequence file **Browse...** pT1.gb
Upload your reference genome (in GenBank)

E-mail **henh@ssi.dk**
A valid e-mail address (optional)

Create a BLAST atlas

Create a BLAST atlas by uploading a reference genome and one or more related genomes. Regions will be displayed where there is similarity between the reference genome and one of the related genomes.

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