



MGEII

**Plasmids** : Structure, diversity, evolution/recombination,  
medically important plasmids

# Intended Learning Objectives

Specific objectives of this session:

1. Learn about plasmid structure and identification
2. Learn about plasmid with clinical relevance
3. Learn about resistance plasmid evolution

Related to the course objectives:

- A. Enhancing participants' knowledge and skills in genomic epidemiology and bioinformatics
- B. Supporting participants' deeper understanding of how the interdisciplinary interpretation of such integrated results can inform infectious disease prevention and control

# Outline

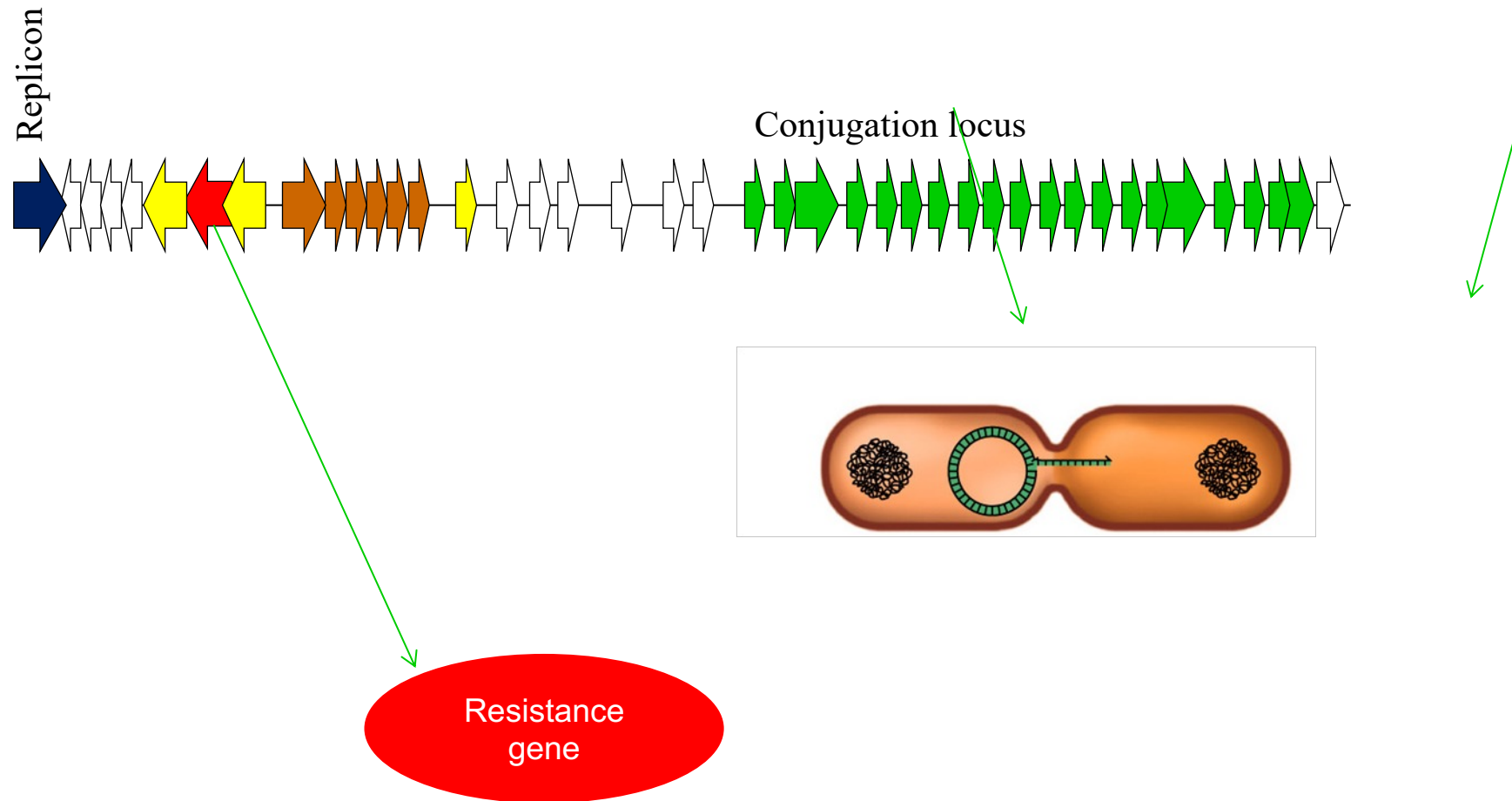
This session consists of the following elements

1. Introduction to plasmid biology
2. Explanation of plasmid relevance
3. Examples of plasmid evolution

# Content slides 1-2: **Bacterial sex**



# Self-conjugative plasmid (30-300 kb)



■ replication   
 ■ stability   
 ■ conjugation   
 ■ resistance   
 ■ Mobile elements   
 □ other

# Architecture of Type IV secretion system (T4SS)



## FIGURES

## **Content slides 3-4:**

**Plasmids control the initiation of replication independently by the replication of the bacterial chromosome**

# control by Iterons

Konieczny et al., S., Microbiol Spectr. 2014 ;2(6)



## FIGURES

The iteron-containing plasmid origin is recognized by the plasmid-encoded initiator (Rep), which binds cooperatively to the iterons.  
plasmid Rep +host DnaA proteins are sufficient to open the plasmid origin

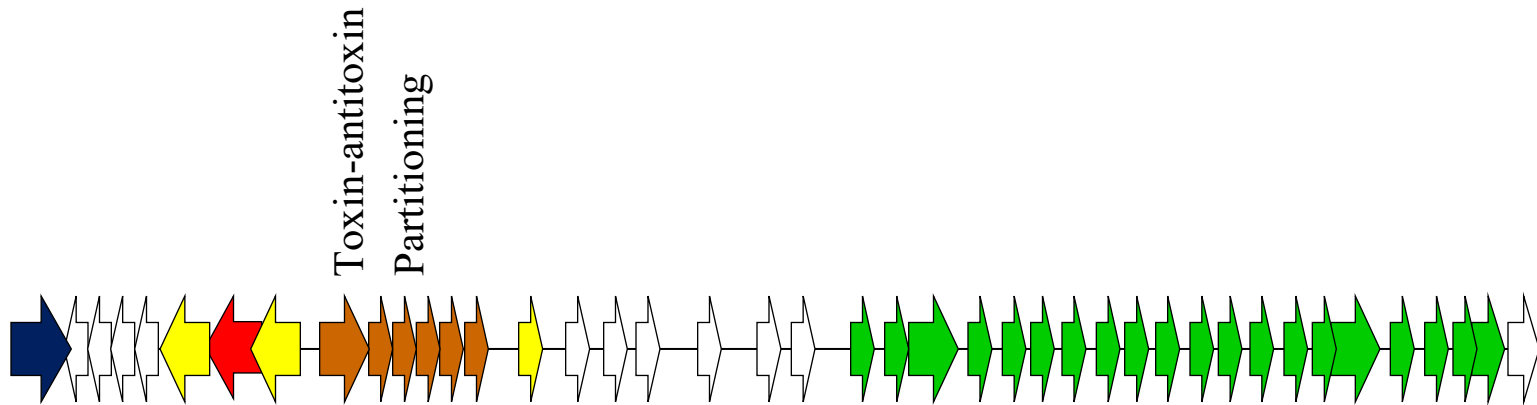
Regulation of iteron-containing plasmid replication initiation by the auto-repression mechanism. Binding of Rep dimers to inverted repeats inhibits the initiation of transcription starting from the *rep* gene promoter. Proteases limit the amount of both dimer and monomer forms of the Rep protein.

# PLASMID REPLICATION CONTROL BY ANTISENSE

- CopR represses transcription from the *repR* promoter
- Binding of Inc RNA to the *repZ* RNA inhibits formation of the pseudoknot and inhibits *repY* translation
- Translation inhibition by inhibition of ribosome binding.
- The CopB protein represses transcription from the *repA* promoter
- The antisense RNA interacts via three loops with the nascent *repA* mRNA resulting in a stem-loop structure that sequesters the ribosome binding site

## FIGURES

# Content slides 5-6 Stability and partitioning



FIGURES

# Plasmids control their segregation



## FIGURES

**Model of R1 plasmid segregation.**

Szardenings F et al., 2011. Regular distribution of plasmids on the bacterial nucleoid confers genetic stabilisation of plasmids by type I *par* loci. *Current Opinion in Microbiology* 14 (6): 712-718

**Structural analysis of the ParR/*parC* plasmid partition complex** J Møller-Jensen, S Ringgaard, CP Mercogliano, K Gerdes and J Löwe *The EMBO Journal* (2007) 26, 4413-4422

# Plasmid addiction systems

## FIGURES

Van Melder et al., 2009 Bacterial toxin-antitoxin systems: more than selfish entities? PLoS Genet. 5(3):e1000437

Kenn Gerdes et al., 2005. PROKARYOTIC  
TOXIN-ANTITOXIN STRESS RESPONSE  
LOCI *Nature Reviews Microbiology* **3**, 371-382



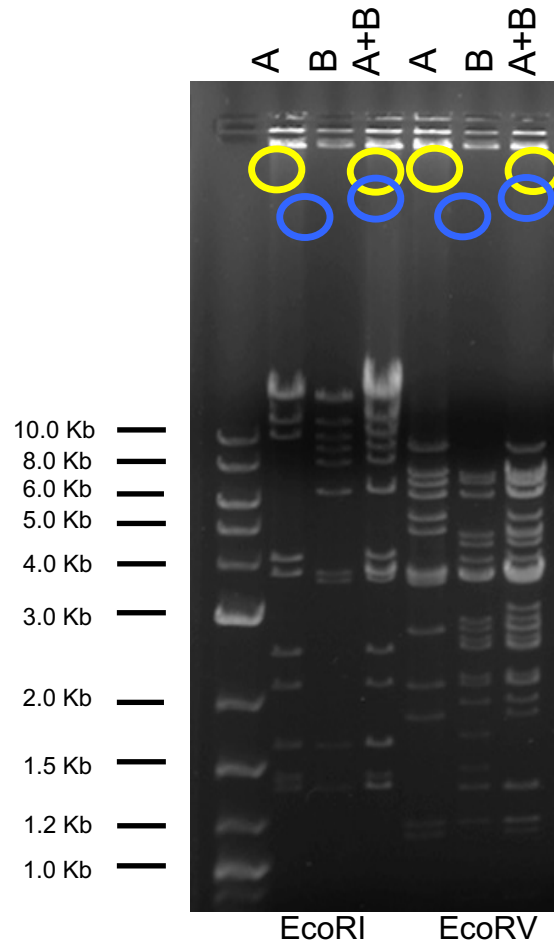
# Content slides 7-14 PLASMID TYPING



- Plasmid detection
- Plasmid evolution
- Plasmid success

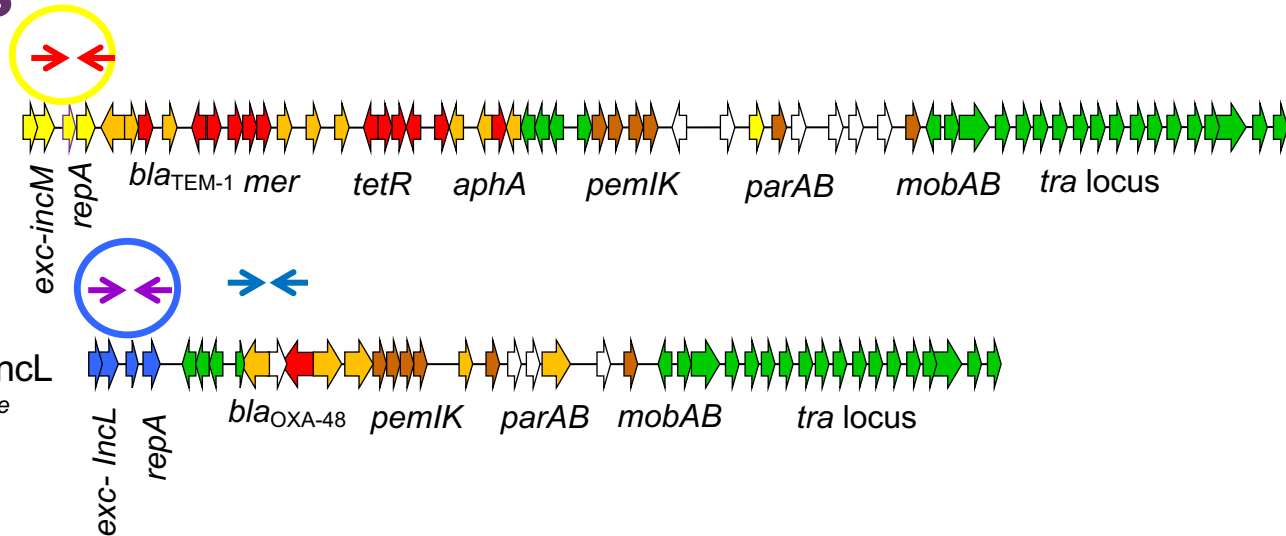
# Plasmid typing by conjugation- PCR-Based Replicon Typing (PBRT)

## Incompatibility groups



### A- R69 IncM

*Salmonella paratyphi B*  
78899 bp

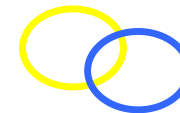
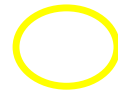


### B- pOXA-48 IncL

*Klebsiella pneumoniae*  
63,581 bp

**A**

**B**



FIGURES

IncM

IncL + OXA-48

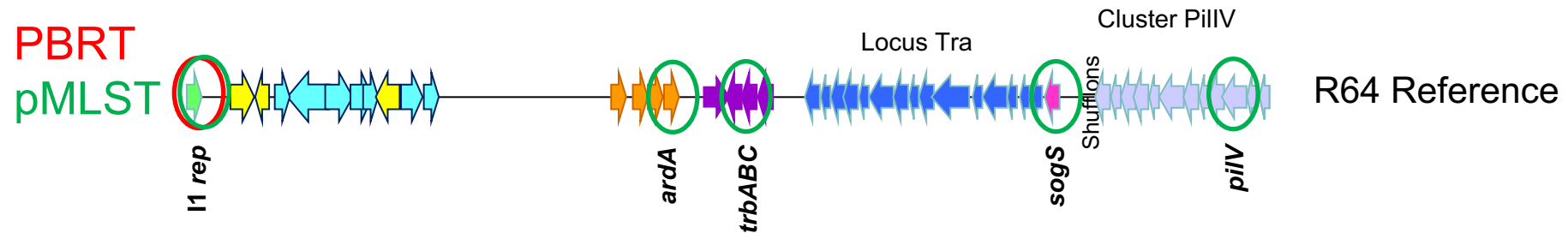
PCR-Based Replicon Typing (PBRT)

MOBp13

MOB typing by relaxases

# Incl1 plasmid MultiLocus Sequence Typing

## FIGURES



# Plasmid MultiLocus Sequence Typing

<http://pubmlst.org/plasmid/>



## Incl1

García-Fernández *et al.* 2008

**repl**: replicase  
**ardA**: type I restriction-modification  
**trbA**: plasmid transfer  
**sogS**: DNA primase  
**pilL**: type IV pilus biogenesis

## IncHI2

García-Fernández, Carattoli 2010

**smr 0018** hyp protein  
**smr 0199** hyp protein

## IncF

Villa *et al.* 2010

**FII**: *copA* of FII replicon  
**FIA**: *repE* of FIA replicon  
**FIB**: *repB* gene of the FIB replicon  
**FIC**: *copA* of FIC replicon

## IncN

García-Fernández *et al.* 2011

**repN**: replicase  
**traJ**: conjugative  
**korA**: conjugation

## IncA/C

Hancock *et al.*, 2016

**repA**: replication protein  
**parA**: plasmid partitioning  
**parB**: plasmid partitioning  
**053**: hyp protein

## IncHI1

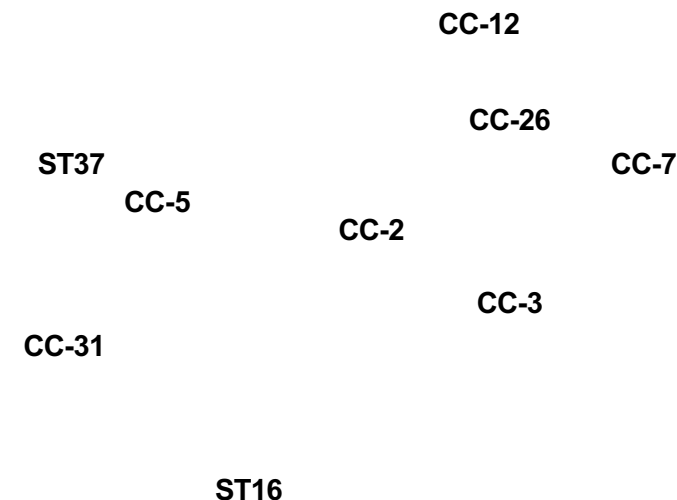
Phan *et al.* 2009

**HCM1 043**: hyp protein  
**HCM1 064**: *repA2* of HI1A replicon  
**HCM1 099**: *trhW* H-pilus production  
**HCM1 116**: hyp protein  
**HCM1 178ac**: hyp protein  
**HCM1 259**: hyp protein

GrapeTree of IncI1 and IncIy plasmid STs and country of isolation. A minimum spanning tree based on allelic profiles of 774 IncI1 and IncIy plasmids was downloaded from the pMLST website. Pie size corresponds to number of isolates. Colours indicate country of isolation, and the legend shows the number of isolates from each country.

## FIGURES

## FIGURES



Carattoli A, Villa L, Fortini D, García-Fernández A. Contemporary IncI1 plasmids involved in the transmission and spread of antimicrobial resistance in Enterobacteriaceae. *Plasmid*. 2021 Nov;118:102392. doi: 10.1016/j.plasmid.2018.12.001. Epub 2018 Dec 5. PMID: 30529488

# Plasmid identification in WGS: PlasmidFinder and pMLST *in silico*



National Food Institute  
Technical University of Denmark



## PlasmidFinder Results

### SETTINGS:

Selected %ID threshold: 95.00

PlasmidFinder - Gram-negativ						
Plasmid	%Identity	Query/HSP length	Contig	Position in contig	Note	Accession number
FIA	100.00%	388/388	AP001918	48305..48692		<a href="#">AP001918</a>
FIB	100.00%	682/682	AP001918	37018..37699		<a href="#">AP001918</a>
FIC	100.00%	240/240	AP001918	3421..3660		<a href="#">AP001918</a>
FII	95.02%	261/261	AP001918	3659..3919		<a href="#">AY458016</a>

extended output

<http://cge.cbs.dtu.dk/services/PlasmidFinder/>  
<http://cge.cbs.dtu.dk/services/pMLST/>

*In silico* detection and typing of plasmids using PlasmidFinder and plasmid multilocus sequence typing  
A Carattoli et al.2014, AAC 58: 3895-3903

59896 plasmid sequences

31101 plasmids from *Enterobacterales*

# Plasmid Database PLSD



## ResFinder & PlasmidFinder

<https://ccb-microbe.cs.uni-saarland.de/plsdb/>

<https://cge.food.dtu.dk/services/ResFinder/>

<https://cge.cbs.dtu.dk/services/PlasmidFinder/>

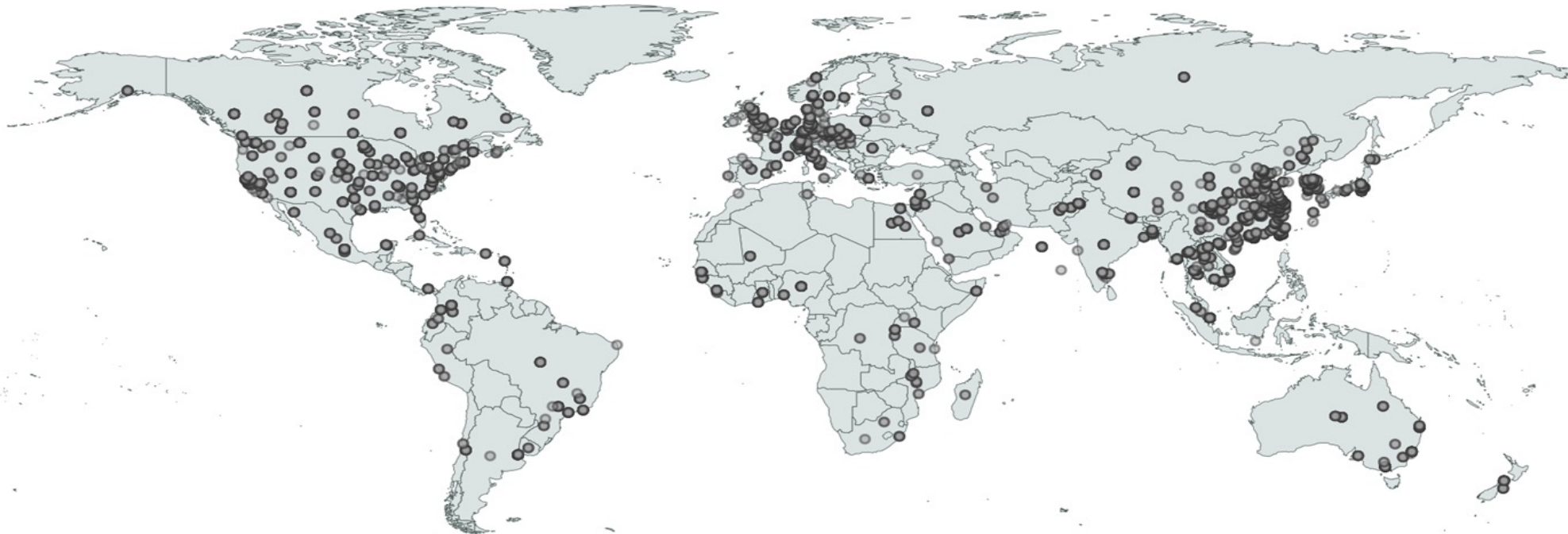
<https://www.ncbi.nlm.nih.gov/genome/browse/#!/plasmids/815/>

Schmartz GP, *et al.* PLSDb: advancing a comprehensive database of bacterial plasmids, NAR, 2021

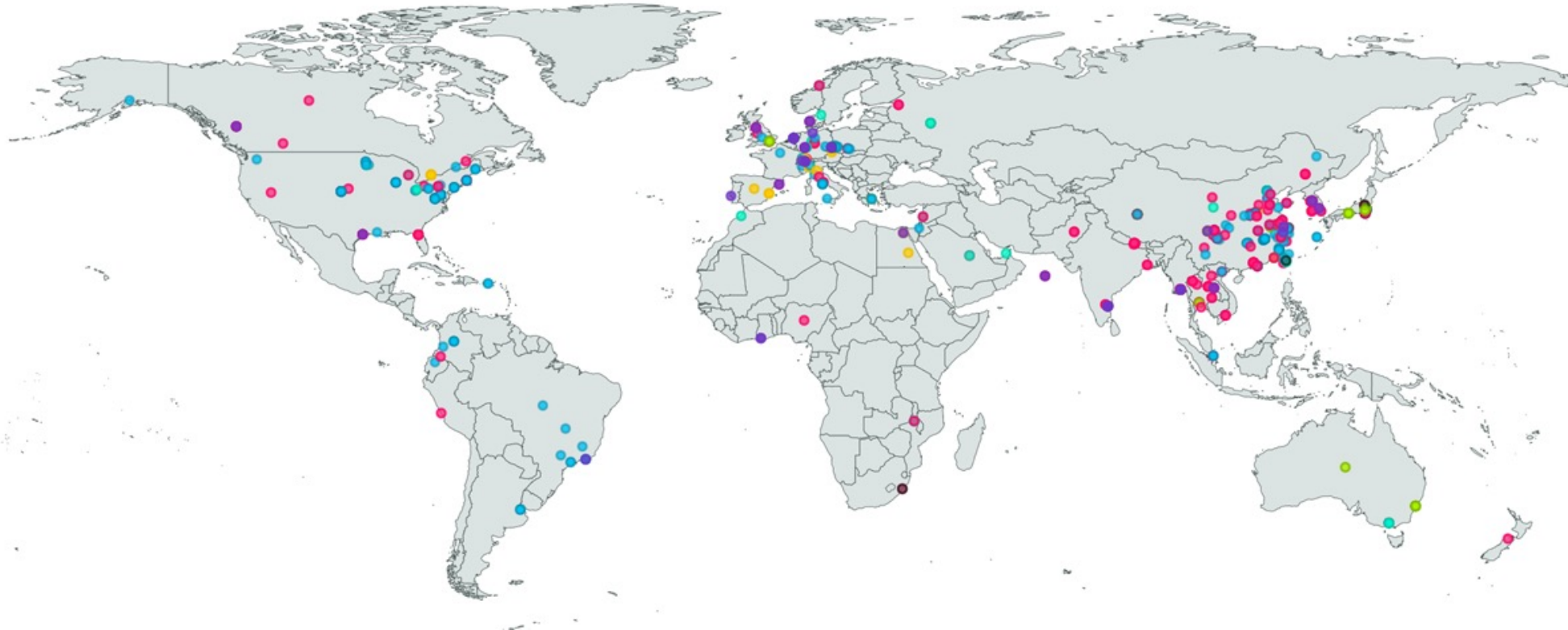
Galata V, *et al.* PLSDb: a resource of complete bacterial plasmids, NAR, 2018

Bortolaia V, *et al.* ResFinder 4.0 for predictions of phenotypes from genotypes. JAC,








Carattoli A, *et al.* PlasmidFinder and pMLST: in silico detection and typing of plasmids. AAC 2014



# 4626 plasmid sequences with carbapenemase genes in *Enterobacterales*

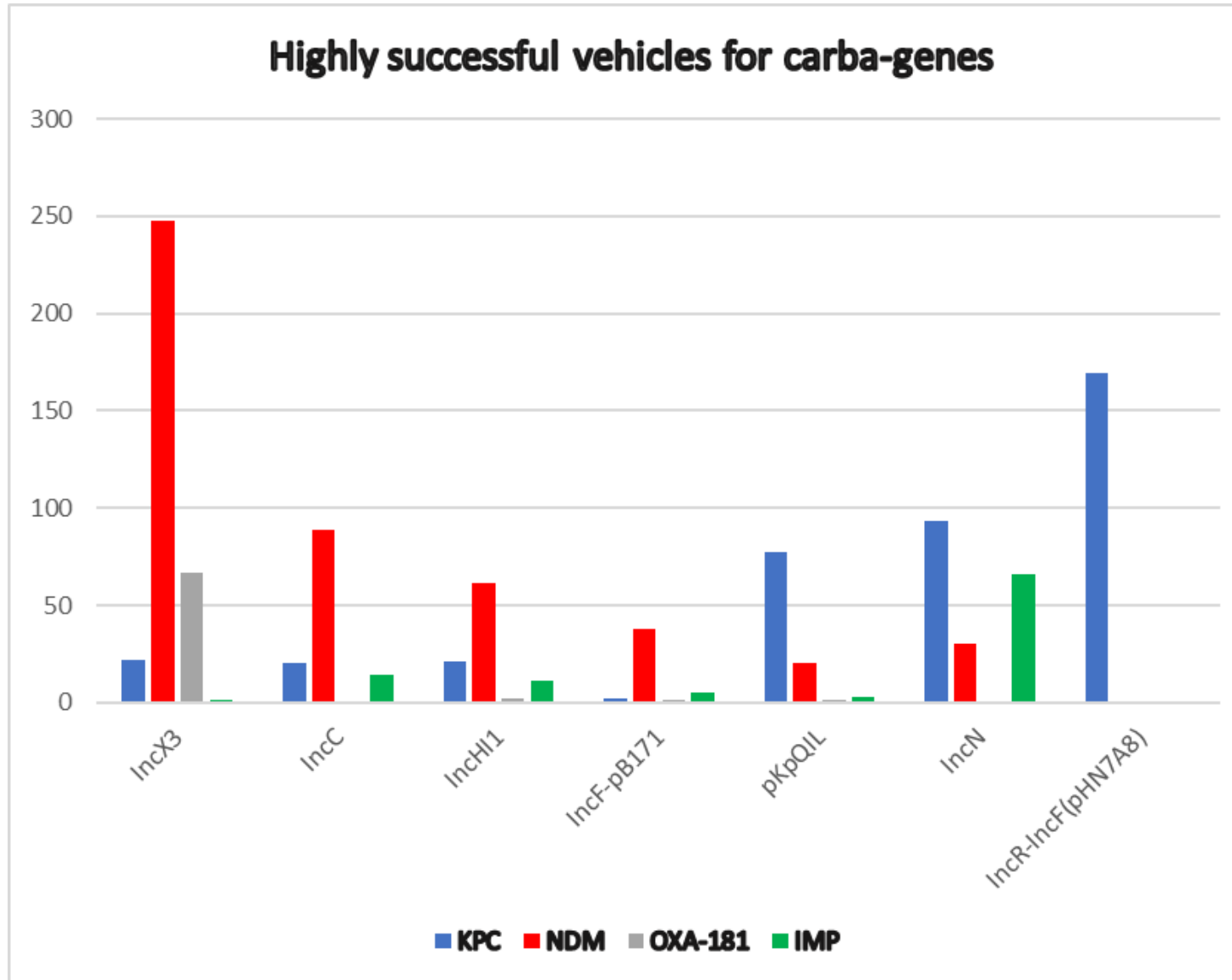


Carba

-  GES
-  IMP
-  KPC
-  NDM
-  OXA-181
-  OXA-48
-  VIM



# >1100 plasmids with KPC, NDM, OXA-181, IMP carba-genes in 8 plasmid types



## PLASMID DETECTION and TYPING Machine Learning era

# Clustering of 10,634 complete plasmid genomes along taxonomic boundaries



## FIGURES

Redondo-Salvo S, Fernández-López R, Ruiz R, Vielva L, de Toro M, Rocha EPC, Garcillán-Barcia MP, de la Cruz F. Pathways for horizontal gene transfer in bacteria revealed by a global map of their plasmids. Nat Commun. 2020 Jul 17;11(1):3602.

Plasmids in discrete clusters, called plasmid taxonomic units (PTUs), measuring plasmid similarity by average nucleotide identity ( $ANI_{L50}$ )

Nodes, corresponding to plasmid genomes, are colored according to their cognate host taxonomy (a) or MOB class, as defined by MOBscan (b).

# PTUs vs Inc groups



# Diverse plasmid systems and their ecology across human gut metagenomes revealed by PlasX and MobMess

Received: 21 July 2022

Michael K. Yu<sup>1,2</sup>, Emily C. Fogarty<sup>2,3,4</sup> & A. Murat Eren<sup>1,5,6,7,8</sup>

Accepted: 17 January 2024

Published online: 4 March 2024

 Check for updates

Plasmids alter microbial evolution and lifestyles by mobilizing genes that often confer fitness in changing environments across clades. Yet our ecological and evolutionary understanding of naturally occurring plasmids is far from complete. Here we developed a machine-learning

## A machine-learning model for classifying plasmids

PF10609 is a broad family of genes related to *parA*, a gene that drives the partitioning of not only chromosomes but also plasmids

This could be subdivided into two de novo gene families, **one of which was plasmid-specific and the other chromosome-specific.**

## FIGURES

- a, Pangenomics workflow to characterize gene functions in a reference set of plasmids and chromosomes.
- b, Fraction of all plasmids or all chromosomal genes that are annotated using known families, de novo families or a combination of both.
- c, Training of PlasX.
- d, Precision–recall curves comparing PlasX, Platon, PlasClass and PPR-Meta
- e, Coefficients of the 200 gene families with the highest PlasX coefficients and that are thus most important for identifying plasmids.
- f, Maximum-likelihood phylogenetic tree of genes that are in PF10609 as well as either the plasmid-specific de novo subfamily mmseqs\_5\_1535552 or chromosome-specific de novo subfamily mmseqs\_70\_40217271.
- g, Sequence alignment of ten representative genes from each subfamily (arrows in f).



## Diverse plasmid systems and their ecology across human gut metagenomes revealed by PlasX and MobMess

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Plasmids alter microbial evolution and lifestyles by mobilizing genes that often confer fitness in changing environments across clades. Yet our ecological and evolutionary understanding of naturally occurring plasmids is far from complete. Here we developed a machine-learning

## FIGURES

### Identification of plasmid systems

**a, b**, Distribution of model coefficients for backbone and cargo genes in the non-redundant set of 68,350 predicted plasmids.

**c**, Network of all plasmid systems that contain  $\geq 3$  non-redundant and high-confidence plasmids

**d**, Genetic architecture of plasmids in PS486, encased by a red box in **c**.

# FIGURES

nature microbiology



Analysis

<https://doi.org/10.1038/s41564-024-01610-3>

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# Content slides 20-24

**IncFlk**

***Klebsiella pneumoniae***



# ST258 ST512 - CG258



USA

FIGURES

Italy

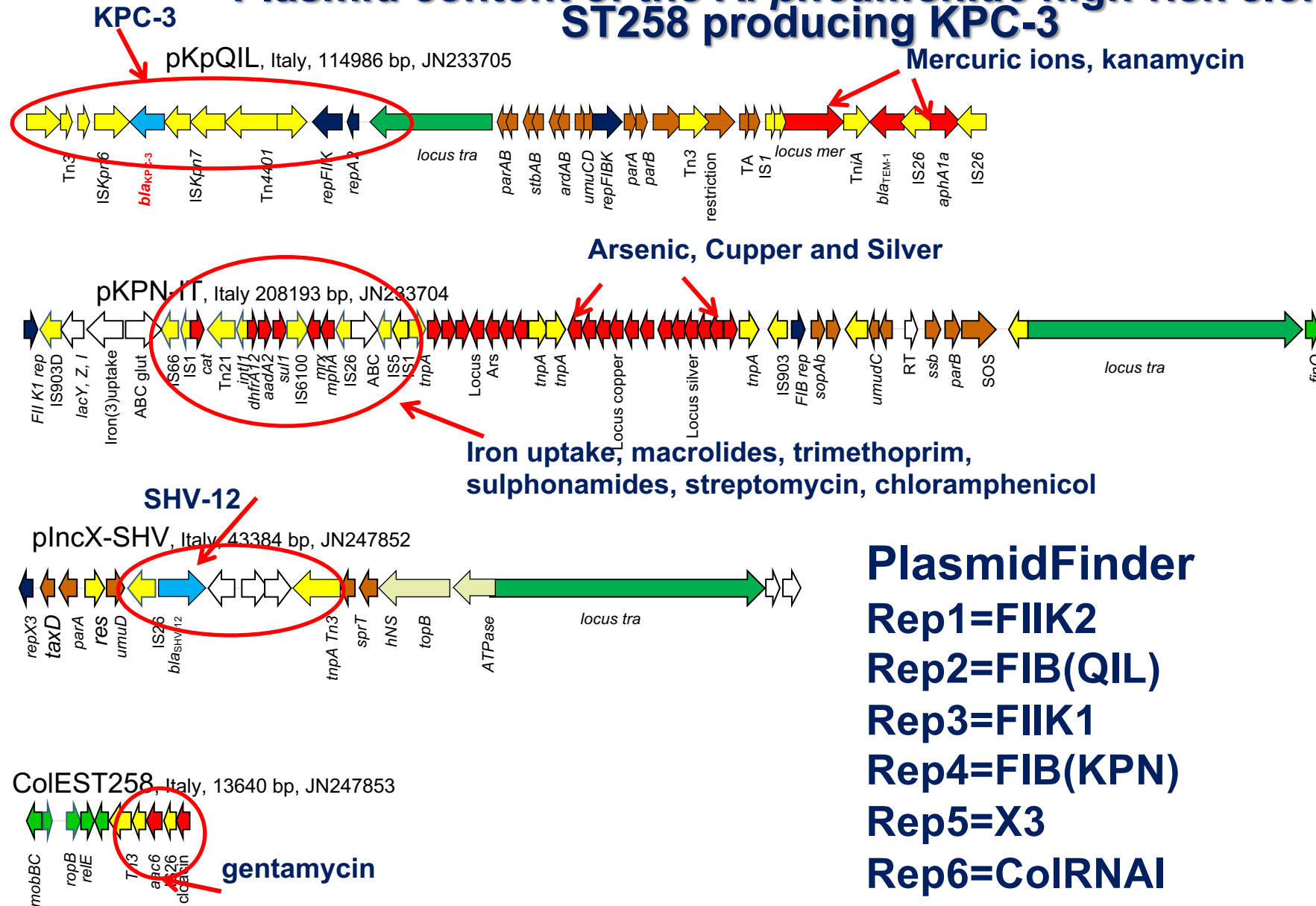
Israel

Italy

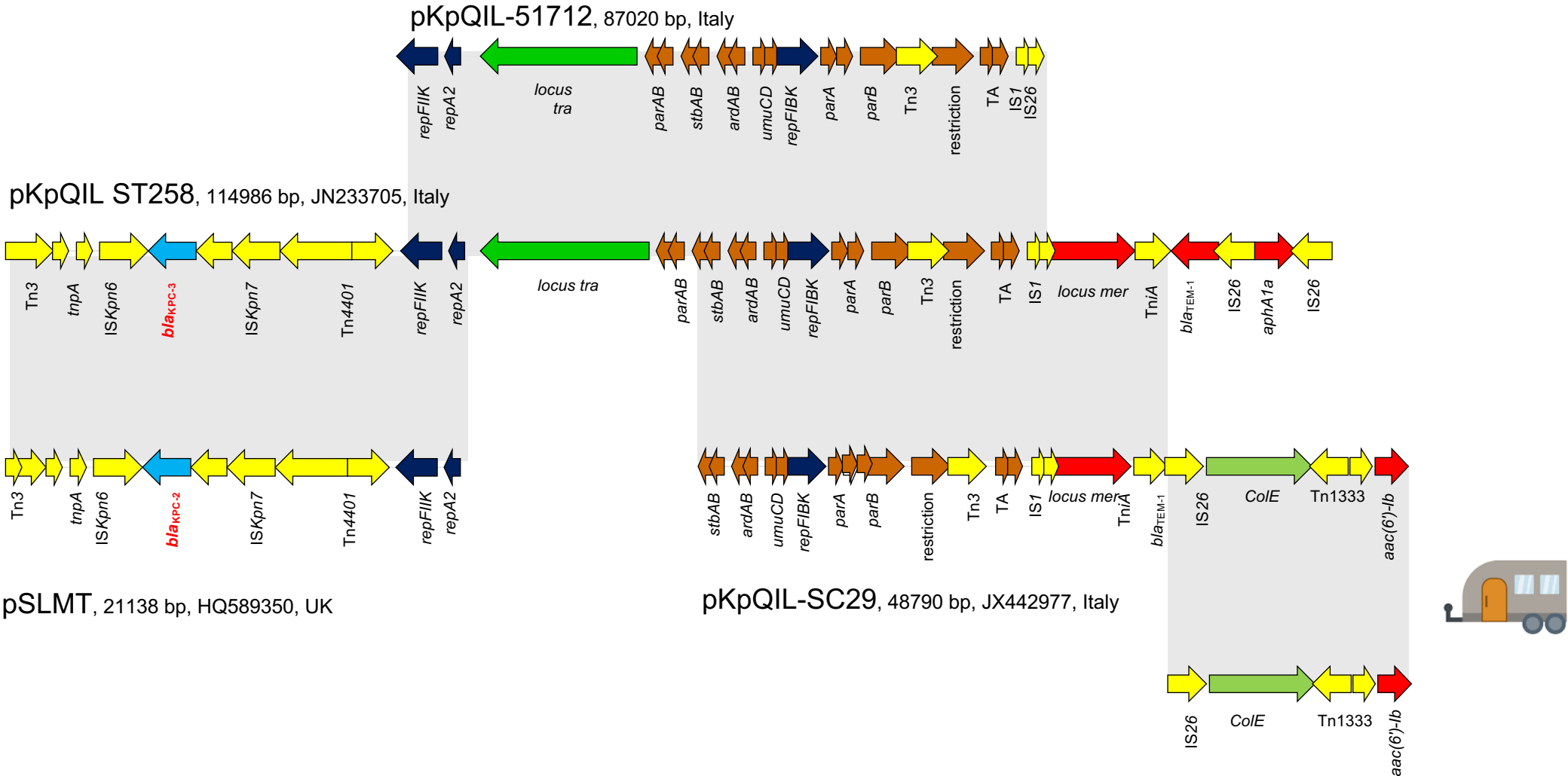
David et al., 2019. Epidemic of carbapenem-resistant *Klebsiella pneumoniae* in Europe is driven by nosocomial spread  
Nat Microbiol. 4:1919-1929

nature  
microbiology

# Plasmid content of the *K. pneumoniae* high-risk clone ST258 producing KPC-3



García-Fernández *et al.*, Antimicrob Agents Chemother. 2012 ; 56:2143-5





### Horizontal transmission of pKpQIL

CG258 (47.4%), CG307 (19.9%), ST101 (15.4%) and ST395 (5.1%)

The changing epidemiology of carbapenemase-producing *Klebsiella pneumoniae* in Italy: toward polyclonal evolution with emergence of high-risk lineages.

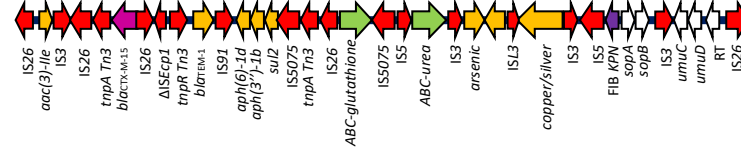
Di Pilato V et al., JAC 2021;76:355-361

# pKPN in ST307 *K. pneumoniae*



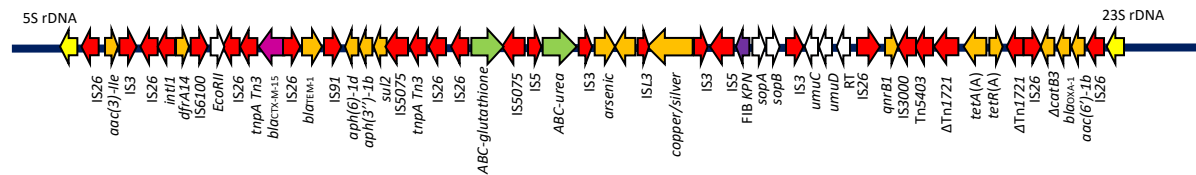
PlasmidFinder  
Rep1=FIB(KPN)

pKPN3-307\_typeB, 2016, 133069 bp (KY271405)



Rep1=FIB(KPN) in  
the chromosome

pKPN-1203, 2019 (chromosome; OM489428)



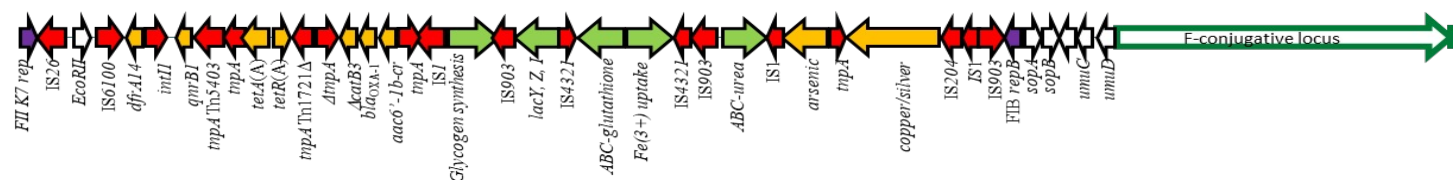
Rep1=FIB(KPN)  
Rep2=FIB (QIL)  
Rep3=FIK2

pKPN-27B, 2020, 238655 bp (MW650887)



Rep1=FIB(KPN)  
Rep2=FIK1

pKPN3-307 Type C, 2016, 212319 bp (KY271406)



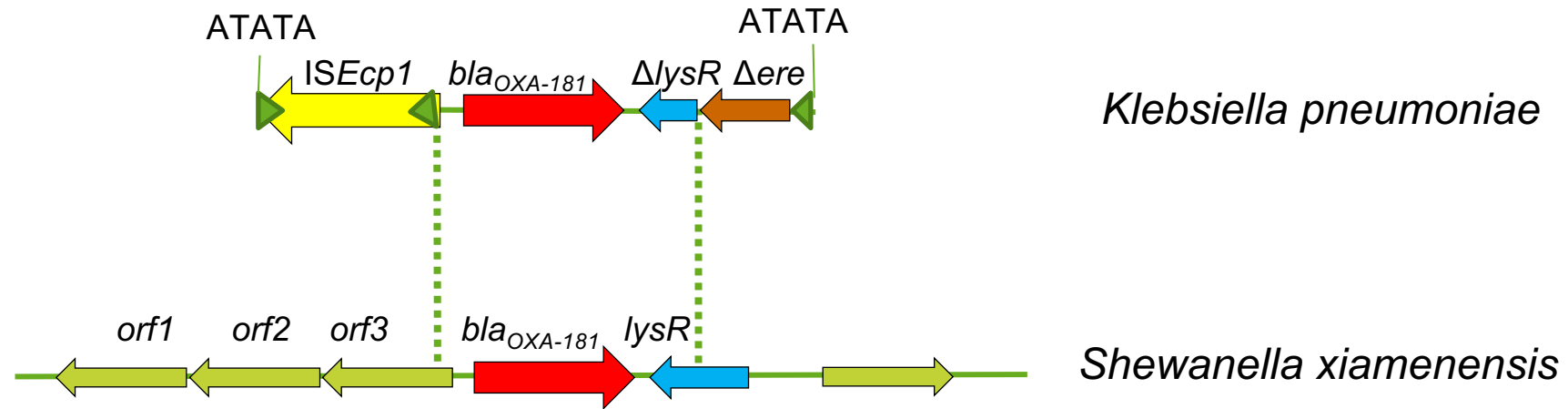
# Content slides 25-32

The origin of *bla*<sub>OXA-181</sub> and the impact of the plasmid type change

# Class D carbapenemases

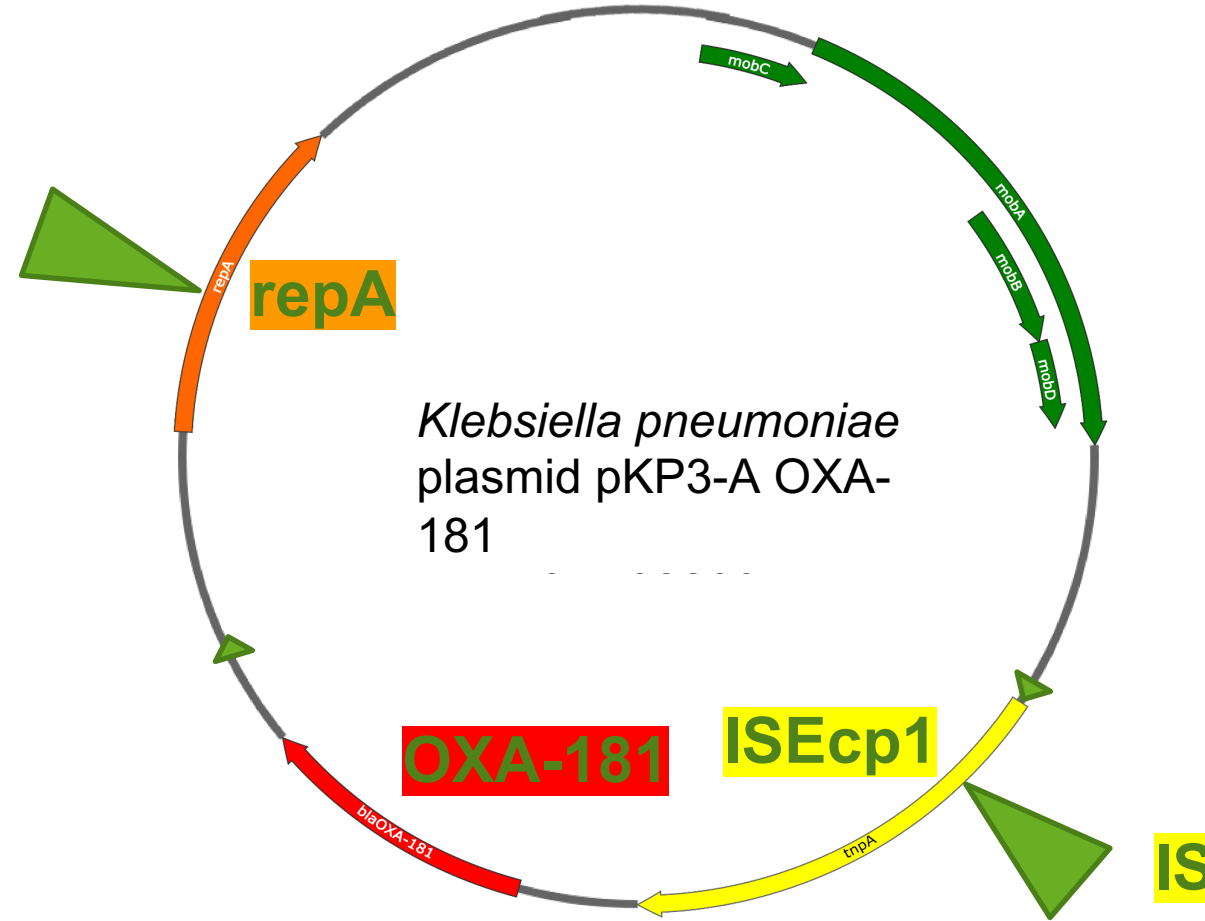


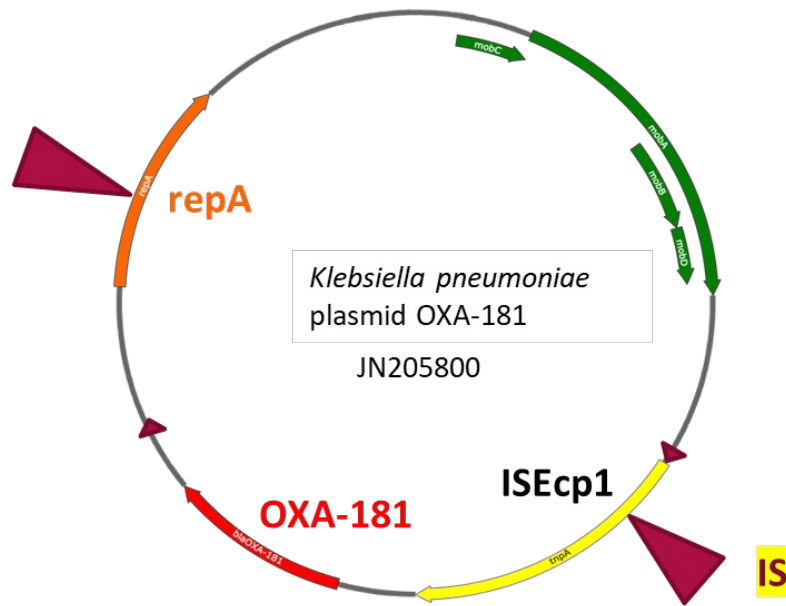
## FIGURES





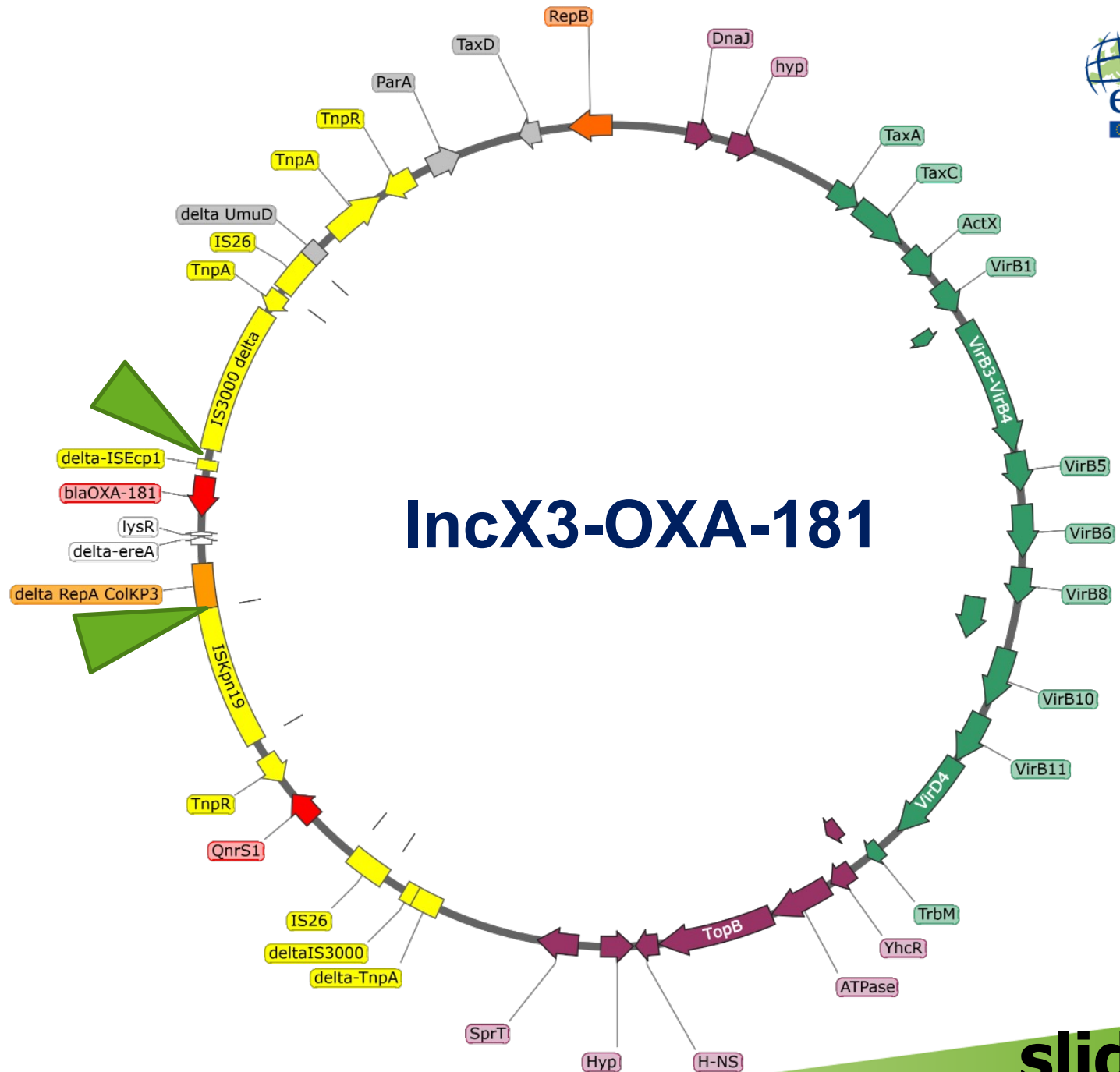
# ColKP3 9 Kb





ColKP3 :  
mobilizable 9 Kb plasmid

PlasmidFinder  
Rep1=X3  
Rep2=deltaColKP3



# FIGURES

## IncX3

**IncX-SHV**, JN247852, 43380 bp  
*Klebsiella pneumoniae* ST258,  
2012

**pEC14\_35**, JN935899, 34945 bp  
*Escherichia coli*, 1989



García-Fernández A, Villa L, Carta C, Venditti C, Giordano A, Venditti M, Mancini C, Carattoli A. *Klebsiella pneumoniae* ST258 producing KPC-3 identified in Italy carries novel plasmids and OmpK36/OmpK35 porin variants. *Antimicrob Agents Chemother*. 2012 Apr;56(4):2143-5.

Johnson TJ, Bielak EM, Fortini D, Hansen LH, Hasman H, Debroy C, Nolan LK, Carattoli A. Expansion of the IncX plasmid family for improved identification and typing of novel plasmids in drug-resistant Enterobacteriaceae. *Plasmid*. 2012 Jul;68(1):43-50.

# Content slide 16 Global distribution of *Enterobacterales* with OXA-181



Pitout JDD, Peirano G, Kock MM, Strydom KA, Matsumura Y. The Global Ascendancy of OXA-48-Type Carbapenemases. Clin. Microbiol. Rev. 2019;33:e00102-19.

## FIGURES

### Global distribution of IncX3 plasmids with OXA-181

$2.0 \times 10^{-4} - 3.0 \times 10^{-5}$   
IncX3 plasmids were  
demonstrated to be highly  
conserved, and highly  
stable,  
no fitness cost on their  
bacterial host  
no virulence

Arcari G, Carattoli A 2023

## Animals

### *Escherichia coli*

**pOXA-181-IHIT35346**, KX894452, Germany

Pulss S, et al. First report of an *Escherichia coli* strain from swine carrying an OXA-181 carbapenemase and the colistin resistance determinant MCR-1. Int J Antimicrob Agents. 2017 Aug;50(2):232-236

## FIGURES

## Environment

### *Escherichia coli*

**p124\_B-OXA181**, CP048346, Switzerland

Bleichenbacher S et al., Environmental dissemination of carbapenemase-producing Enterobacteriaceae in rivers in Switzerland, Environmental Pollution, 265B,2020,115081

## ESBL shift in Enterobacterales from broilers

*bla*<sub>SHV-12</sub> plasmids



- flock prevalence of ESBL-producers at farm level reduced  
**21% in 2023**  
**63% in 2012**
- *bla*<sub>SHV-12</sub> prevalence **increased from 19% to 92%** within the last decade
- *bla*<sub>CTX-M-1</sub> prevalence **decreased from 71% to 3%**, suggesting a replacement of *bla*<sub>CTX-M-1</sub> and a shift towards *bla*<sub>SHV-12</sub> in Swiss broiler flock
- *bla*<sub>SHV-12</sub> is mediated primarily by **a specific IncX3 plasmid lineage** rather than by the spread of Enterobacterales clones

Nüesch-Inderbinen M, Heyvaert L, Cernela N, Zurfluh K, Biggel M, Stephan R.

**Emergence of *bla*<sub>SHV-12</sub> and *qnrS1* encoded on IncX3 plasmids: changing epidemiology of extended-spectrum  $\beta$ -lactamases among Enterobacterales isolated from broilers.**

J Glob Antimicrob Resist. 2023 Mar 25:S2213-7165(23)00054-1

## FIGURES

The first genetic characterization of IncX3 plasmids of animal origin, as well as the first functional analysis of human- and animal-derived plasmids of this subgroup, including their conjugation frequencies, stability, fitness cost and virulence potential.

Liakopoulos A, van der Goot J, Bossers A, Betts J, Brouwer MSM, Kant A, Smith H, Ceccarelli D, & Mevius D

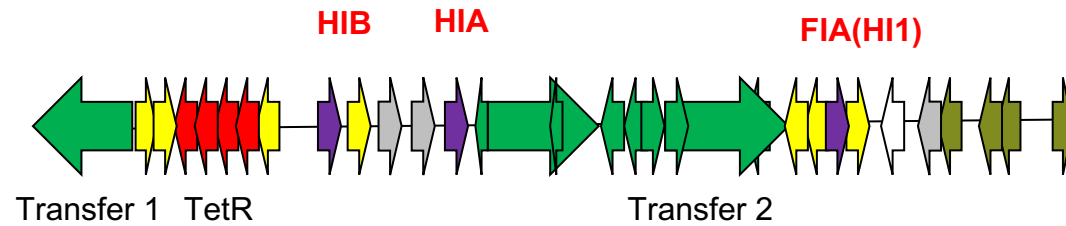
**Genomic and functional characterisation of IncX3 plasmids encoding *bla*<sub>SHV-12</sub> in *Escherichia coli* from human and animal origin.**

Scientific Reports. 2018 May;8(1):7674

# Content slides 33-41

IncHI1B plasmids: resistance & virulence

R27 Reference IncHI1, *Salmonella enterica* Typhi,, 180461 bp, AF250878 human



replicon

stability

conjugation

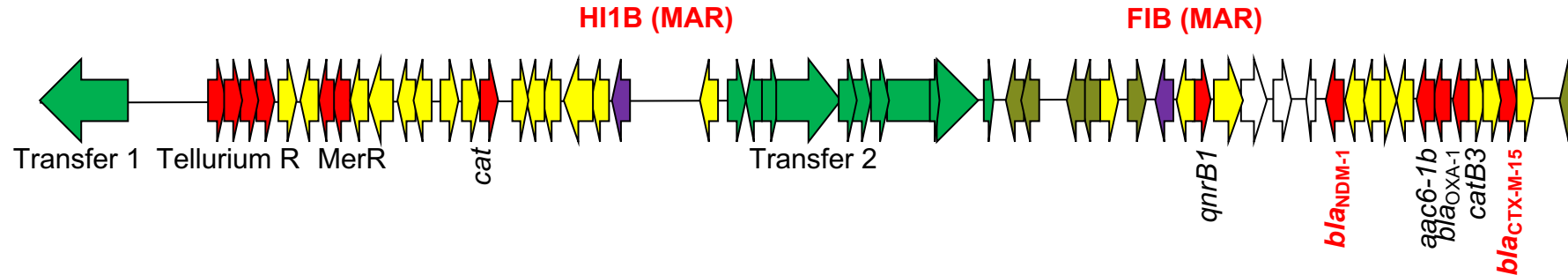
resistance

mobile elements

virulence



pNDM-MAR, IncHI1-like *Klebsiella pneumoniae*, Morocco, 267242 bp, JN420336 human

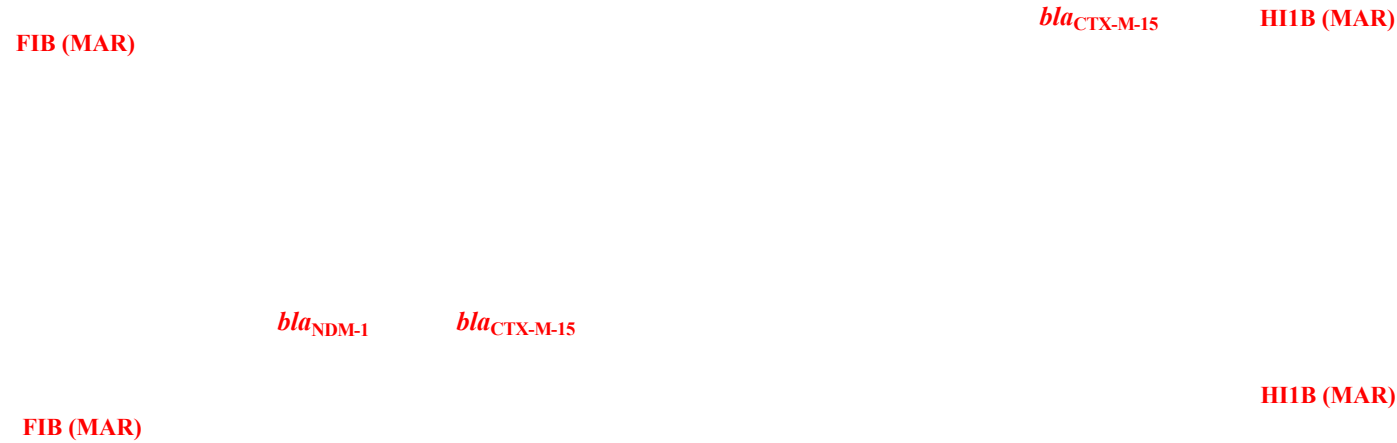


Plasmid pNDM-MAR encoded 177 predicted proteins. It harboured novel replicons and transfer loci, defining a novel plasmid type within the IncH plasmid family.

Villa L, et al, Complete sequencing of an IncH plasmid carrying the bla<sub>NDM-1</sub>, bla<sub>CTX-M-15</sub> and qnrB1 genes. J Antimicrob Chemother. 2012 Jul;67(7):1645-50.



# pENVA recovered from dogs, cats, sheep, hedgehog in CTX-M-15-producing ST254 *Klebsiella pneumoniae* from animals in France



## FIGURES

*bla*<sub>CTX-M-15</sub>

Locus Tra 1

## FIGURES

HI1B (Mar)

***Klebsiella pneumoniae***  
**ST147**

pKP-1PI\_HIB-FIB, 340568 bp,  
CP071028, Italy

Locus Tra 2

*armA*  
*mphE*  
*sul1*  
*dfrA5*  
*aph(3')*  
*mphA*

Tellurium R

Iron ABC

$\Delta rmpA$

2

ABC transporter

*rmpACD* mucoid phenotype regulators

*iucABCD-iutA* hydroxamate siderophore  
aerobactin

# IncHIB-MAR replicon and hypervirulent *Klebsiella pneumoniae*



Silver R

Copper R

## FIGURES

repB (VIR)

ABC transporter

HI1B (Mar)

**Hv *Klebsiella*  
*pneumoniae* pLVPK**, 219385  
bp, AY378100, China

*iucABCD-iutA*  
hydroxamate  
siderophore  
aerobactin

*iroBCDN* salmochelin

*rmpACD* mucoid  
phenotype regulators

Iron ABC transporter

Tellurium R

*rmpA2*

Chen YT et al.  
Sequencing and analysis  
of the large virulence  
plasmid pLVPK of  
*Klebsiella pneumoniae*  
CG43. Gene 337, 189-  
198 (2004)

## FIGURES

*aac(6')1b-cr5*  
*bla<sub>OXA-1</sub>*  
*catB3*  
*arr-3*  
*sul1*  
*bla<sub>CTX-M-15</sub>*

***K. pneumoniae* ST147**  
**pKP-1PI\_FIB**  
 54064 bp  
 CP071030

*bla<sub>TEM-1</sub>*  
*bla<sub>OXA-9</sub>*  
*aadA1*  
*aac(6')1b*

***K. pneumoniae***  
**ST147**  
**pKP-12PI\_R**  
 39637 bp  
 CP072922

R

*aph(3')-VI*

*qnrS1*

*bla<sub>NDM-1</sub>*

Di Pilato,V Resistome and virulome accretion in an NDM-1-producing ST147 sublineage of *Klebsiella pneumoniae* associated with an outbreak in Tuscany, Italy: a genotypic and phenotypic characterisation *Lancet Microbe* 3 (3), e224-e234 (2022)

FIB(Mar)



R

*bla*<sub>CTX-M-15</sub>

pKP-12PI\_R,  
39637 bp,  
CP072922

Locus Tra 1

## ***Klebsiella pneumoniae* ST147**

pKP-1PI\_HIB-FIB,  
340568 bp, CP071028, Italy

HI1B (Mar)

Locus Tra 2

*armA*  
*mphE*  
*sul1*  
*dfrA5*  
*aph(3')*  
*mphA*

Tellurium R

$\Delta$ *rmpA2* Iron ABC

ABC transporter

*rmpACD*

*iucABCD-iutA*

FIB(Mar)

R *aac(6')1b*,  
*aadA1*, *bla*<sub>OXA-9</sub>, *bla*<sub>TEM-1</sub>

*bla*<sub>CTX-M-15</sub>

Locus Tra 1

## FIGURES

***Klebsiella pneumoniae* ST147**  
pPAP<sub>I</sub>vir, 382377 bp, Italy  
CP084985

HI1B (Mar)

Locus Tra 2

*armA*  
*mphE*  
*sul1*  
*dfrA5*  
*aph(3')*  
*mphA*

Tellurium R

Iron ABC

$\Delta$ *rmpA2*

ABC transporter

*rmpACD*

*iucABCD-iutA*

Falcone M, et al. Spread of hypervirulent multidrug resistant ST147 *Klebsiella pneumoniae* in patients with severe COVID-19: an observational study from Italy, 2020-21. J Antimicrob Chemother. 2022 1;77(4):1140-1145

Locus Tra 1

## FIGURES

Locus Tra 2

HI1B (Mar)

*Klebsiella pneumoniae*

ST395

phvKpST395\_NDM1\_1657,  
388104 bp, Russia CP072809

armA  
mphE  
qnrS1  
aph(3')

R

ABC transporter

rmpACD

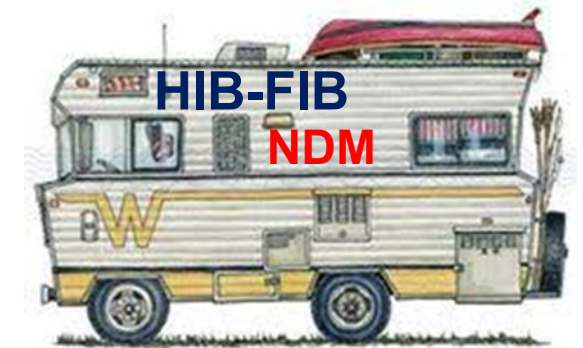
Iron ABC

iucABCD-iutA

 $\Delta$ rmpA2

bla<sub>NDM-1</sub>  
sul1, dfrA5  
mphA

Tellurium R



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# Worldwide distribution of the HI1B replicon type of *bla*<sub>NDM</sub>-carrying plasmids in *Enterobacteriaceae*

## FIGURES

Wu W et al., NDM Metallo- $\beta$ -  
Lactamases and Their Bacterial  
Producers in Health Care  
Settings.  
Clin Microbiol Rev.  
2019;32(2):e00115-18.

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# Content slides 42-47

IncF plasmids carrying *bla*<sub>NDM</sub>

resistance

*rmtC* FIB (pECL)

*sul1*

*bla*<sub>NDM-1</sub>



## FIGURES

FII (Yp)

***Enterobacter cloacae* pECL3-NDM-1**

99435 bp, Australia, KC887917

partitioning,  
SOS response  
restriction/antirestriction

Transfer locus

Wailan AM, et al. Mechanisms Involved in Acquisition of bla<sub>NDM</sub> Genes by IncA/C2 and IncFIIY Plasmids. Antimicrob Agents Chemother. 2016 Jun 20;60(7):4082-8.

partitioning,  
SOS response  
restriction/antirestriction

Phage

## FIGURES

phospholipase D

FII (Yp)

***Yersinia pestis* Pestoides**  
**F plasmid MT1,**  
137010 bp, CP000670

F1 capsule-anchoring  
usher Caf1A

Transfer locus

FIB (pECL)

*Leclercia adecarbovylata*  
*E. coli* Chromosome



resistance

*bla*<sub>NDM-6</sub>  
*rmtC*  
*sul1*

capsular locus

## FIGURES

***Escherichia coli* pEC4-NDM-6**  
110786 bp, New Zeland, KC887916

FII (Yp)

partitioning,  
restriction/antirestriction

Transfer locus

Wailan AM, et al. Mechanisms Involved in Acquisition of blaNDM Genes by IncA/C2 and IncFIIY Plasmids. Antimicrob Agents Chemother. 2016 Jun 20;60(7):4082-8.

resistance

*bla*<sub>NDM-1</sub>  
*rmtC*

## FIGURES

*sul1*

partitioning,  
SOS response  
restriction/antirestriction

***Klebsiella pneumoniae***  
**pKp\_Goe\_629-2**  
Germany, human, 2016  
94434 bp, CP018366

FII (Yp)

Transfer locus

*bla*<sub>NDM-1</sub>  
*rmtC*

resistance

*sul1*

FII (Yp)

Transfer locus

## FIGURES

***Klebsiella pneumoniae***  
China, river , 2019,  
2017

107590 bp, CP065342

***Klebsiella pneumoniae***  
USA, human, 2019

106853 bp, CP023914

***Escherichia coli***  
Denmark, 2020

110787 bp, MG462729

***Enterobacter cloacae***  
Canada, human, 2020

110786 bp, KJ812998

capsular locus

partitioning,  
restriction/antirestriction

# IncF plasmids with NDM



## FIGURES

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- The success of resistance genes may depend by the success of the plasmid
- Persistence, stability and conjugation are offered by the plasmid to the resistance gene



The success of a plasmid depends by multiple factors:

host-range, conjugation rate, no or low fitness cost for the bacterial cell, multi-replicons, toxin-antitoxin, partitioning



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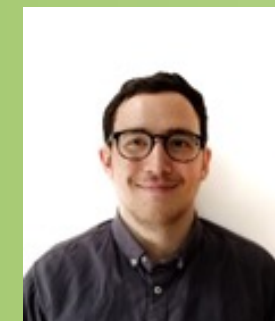


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**Aurora Garcia-Fernandez**  
**Laura Villa**



**Gabriele Arcari**

**Riccardo Polani**  
**Alice de Francesco**  
**Dario Tomolillo**  
**Valerio Capitani**  
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# Acknowledgements

The creation of this training material was commissioned by ECDC to Institut Pasteur with the direct involvement of Alessandra Carattoli