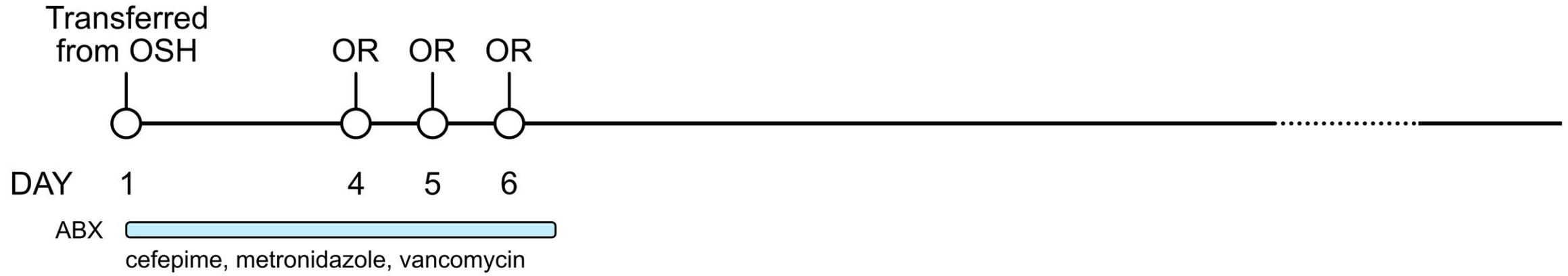
The background of the slide is a microscopic image of several rod-shaped bacteria, likely Enterobacter cloacae, with numerous thin, hair-like flagella extending from their surfaces. The bacteria are rendered in shades of red and pink against a light, hazy background.

Prevalence and genetics of cefepime resistance among the AmpC-producing organisms *Citrobacter freundii*, *Enterobacter cloacae*, and *Klebsiella aerogenes*

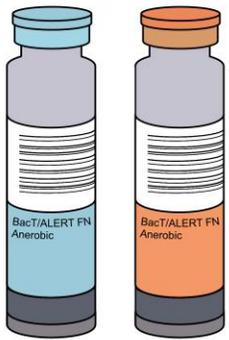
Sarah Schrader, MD, PhD
PGY-3 CP resident, Mass General Brigham

9th Annual Texas Medical Center Antimicrobial Resistance and Stewardship Conference
January 14th, 2026

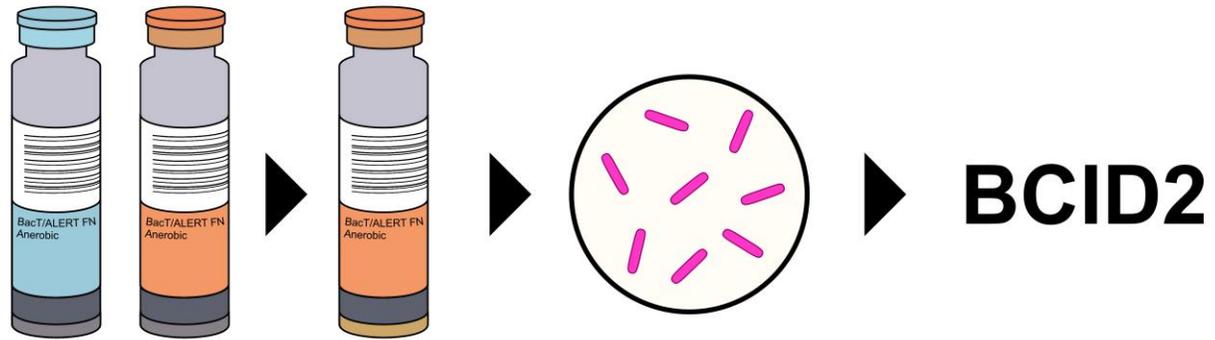
A case



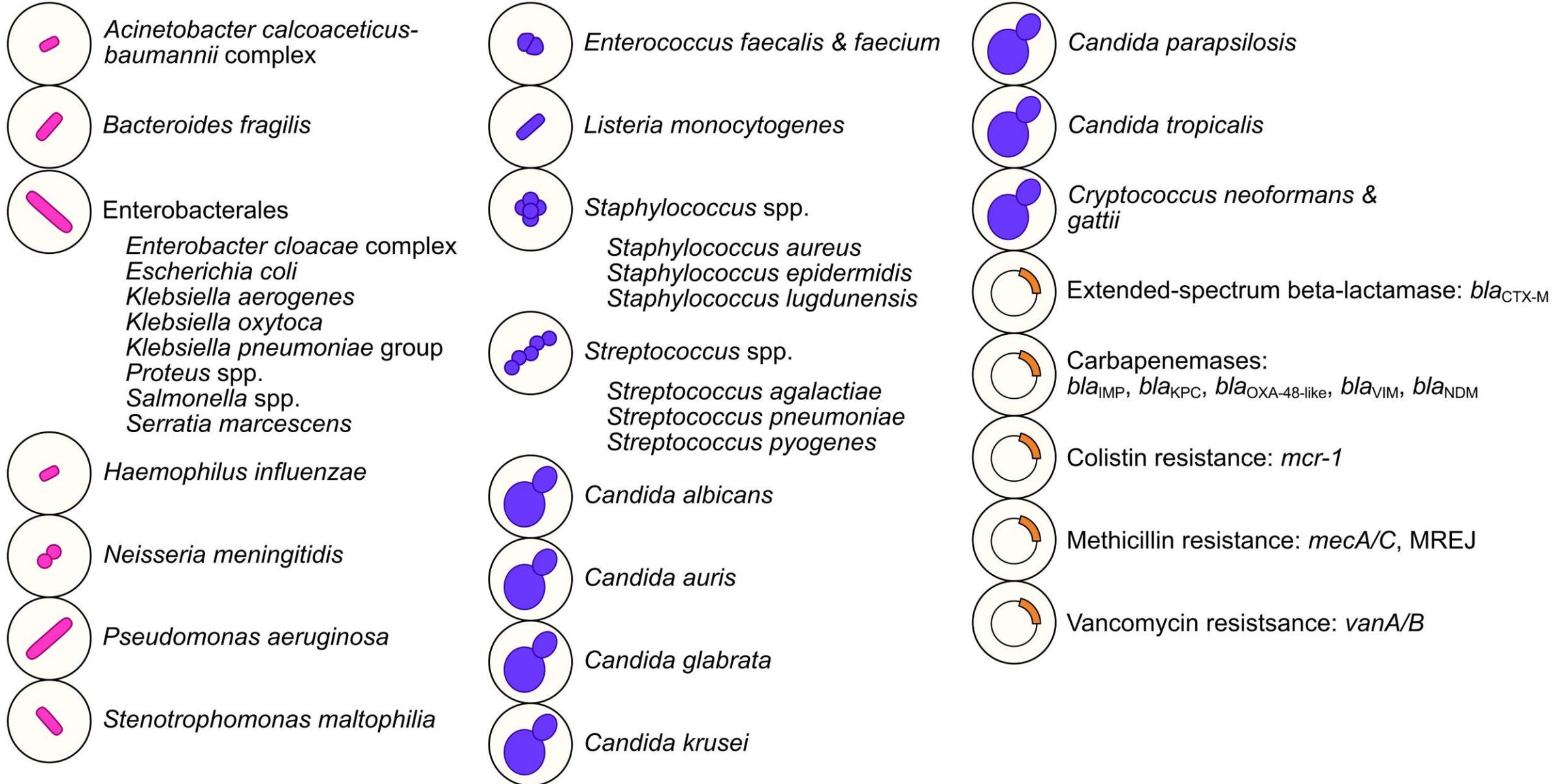
A case



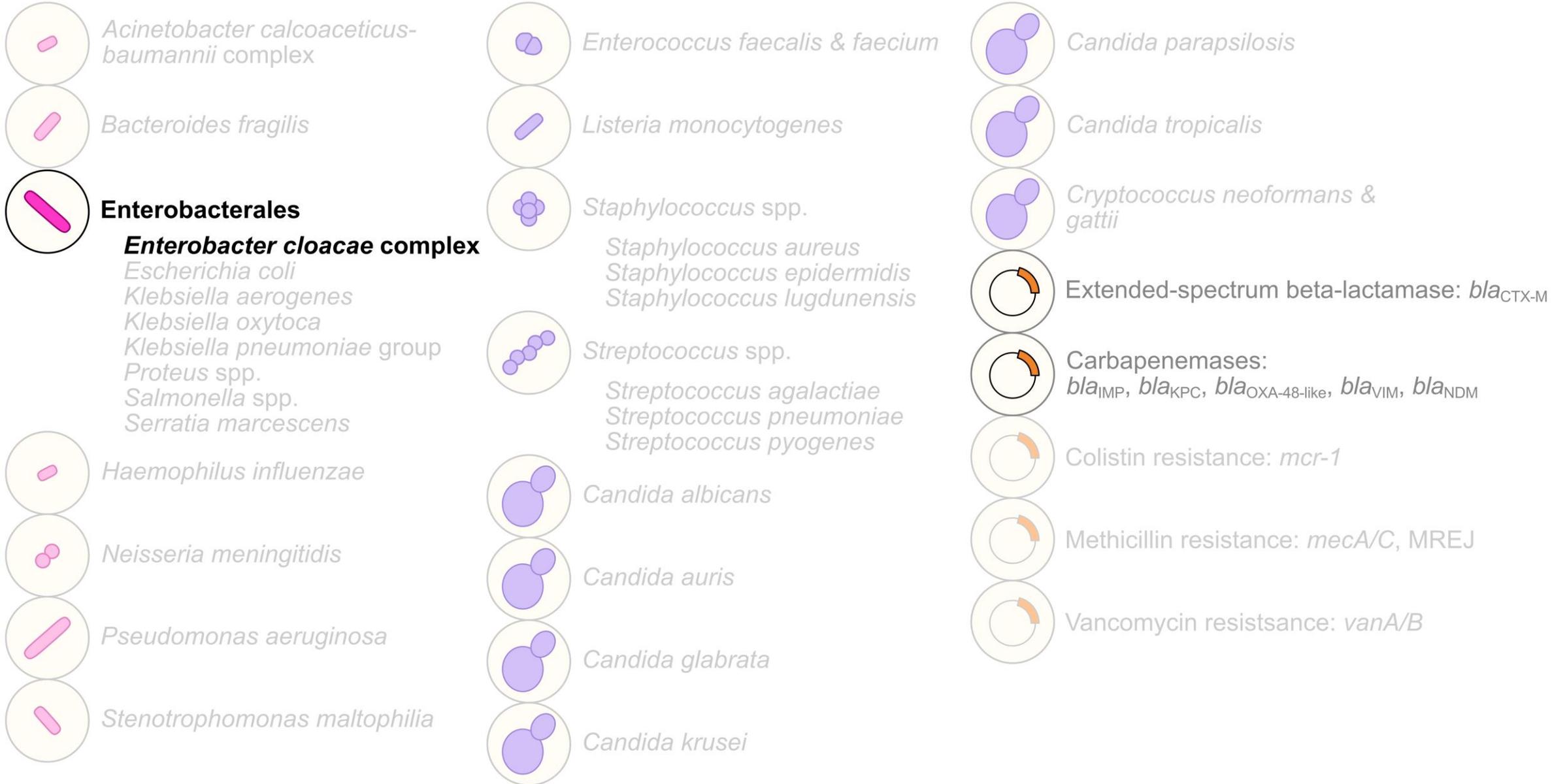
A case



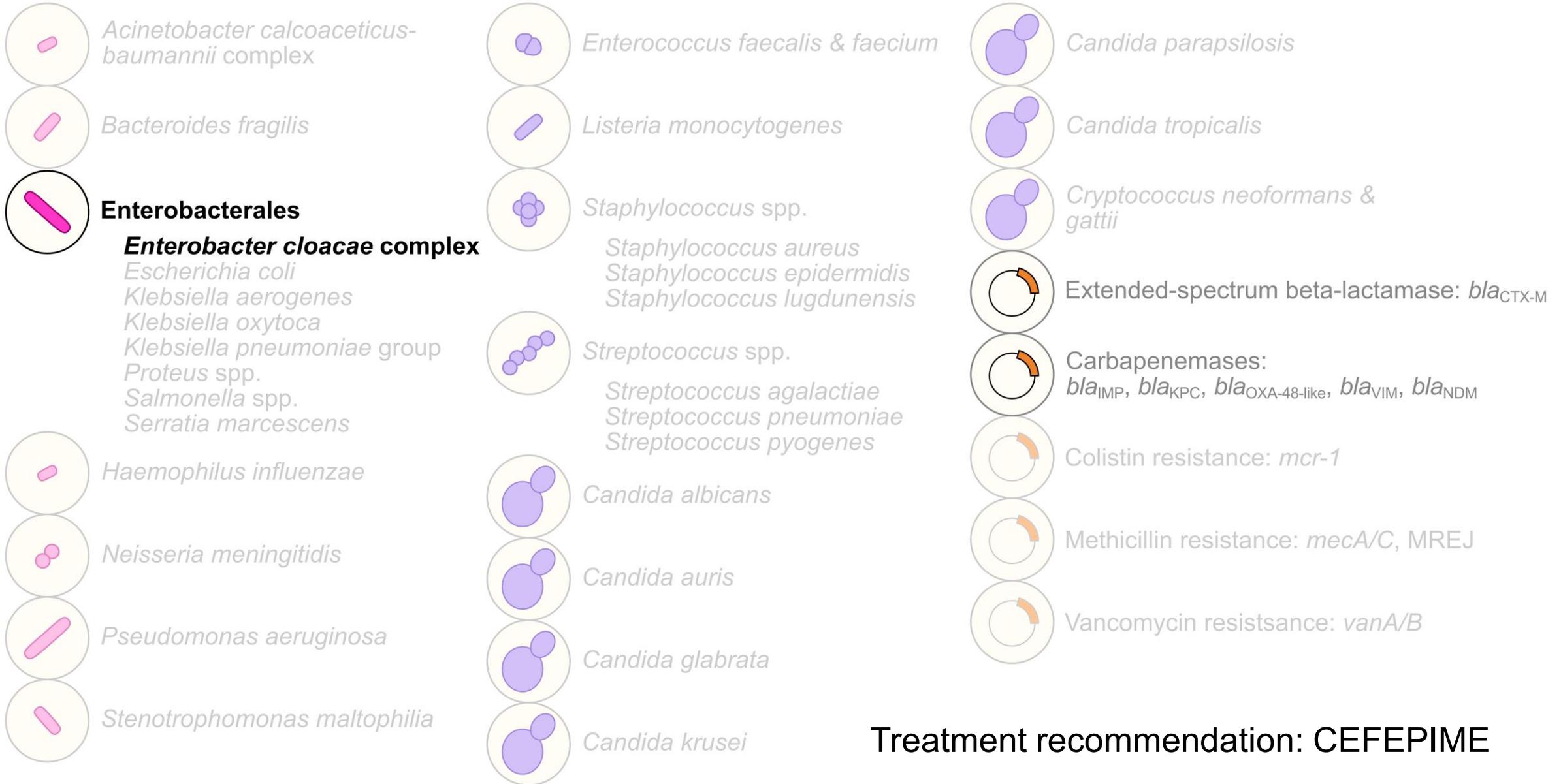
Targets for Blood Culture Identification 2 panel (bioMérieux)



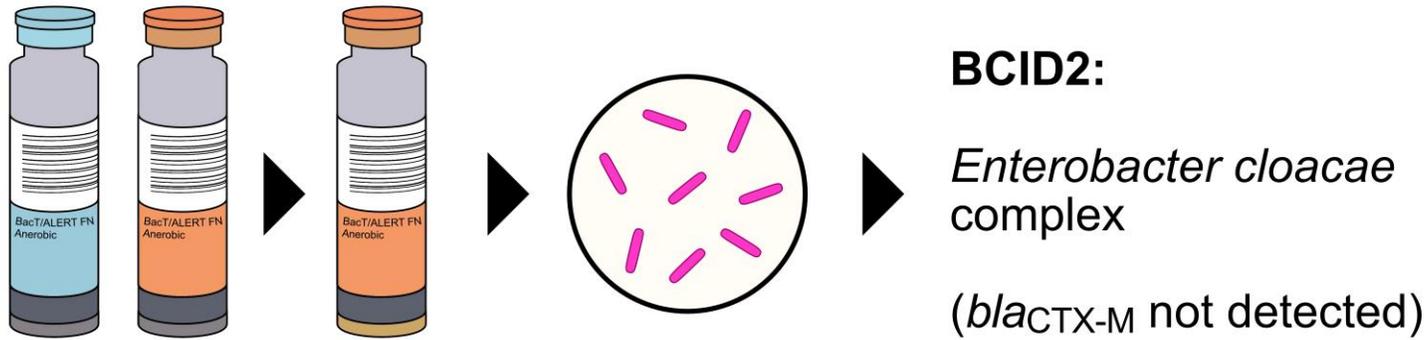
BCID2 results



BCID2 results



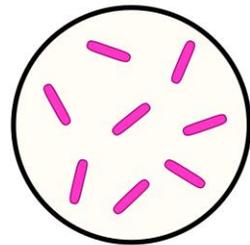
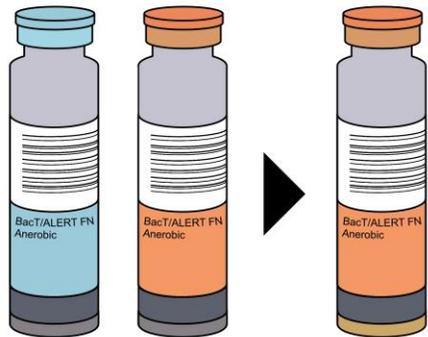
A case



A case



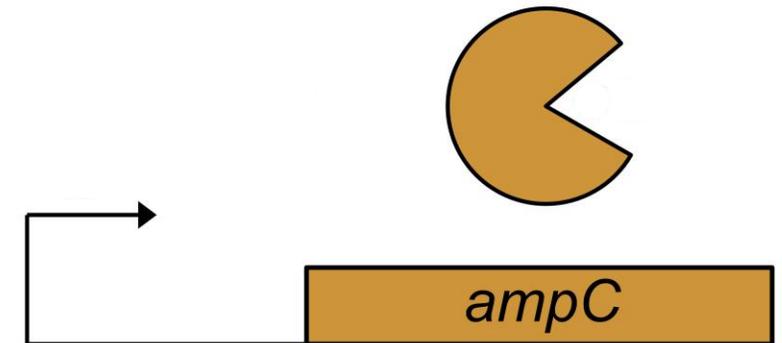
Inducible AmpC



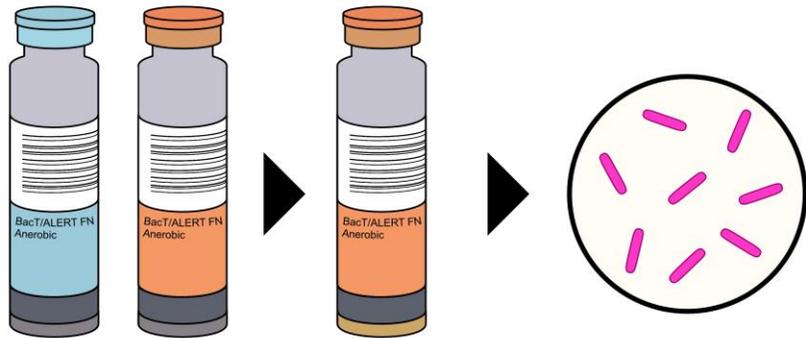
BCID2:

Enterobacter cloacae
complex

(*bla*_{CTX-M} not detected)



A case



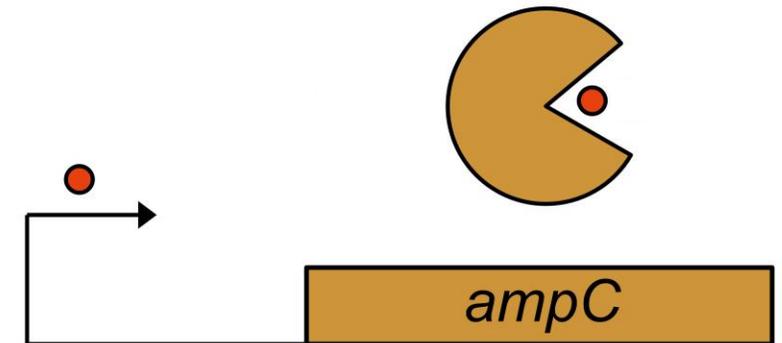
BCID2:

Enterobacter cloacae complex

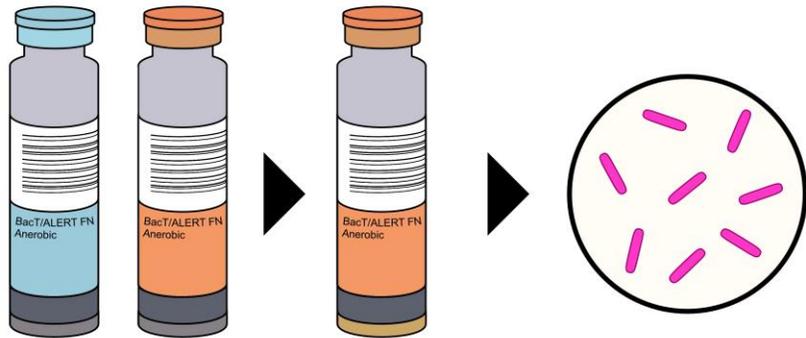
(*bla*_{CTX-M} not detected)

Inducible AmpC

- aminopenicillins
- first-gen cephalosporins
- cephamycins



A case



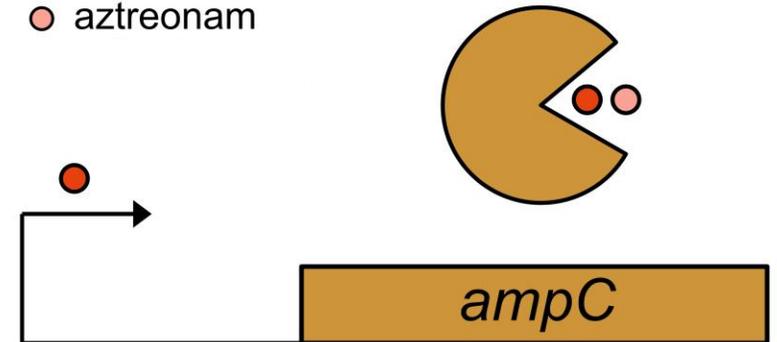
BCID2:

Enterobacter cloacae complex

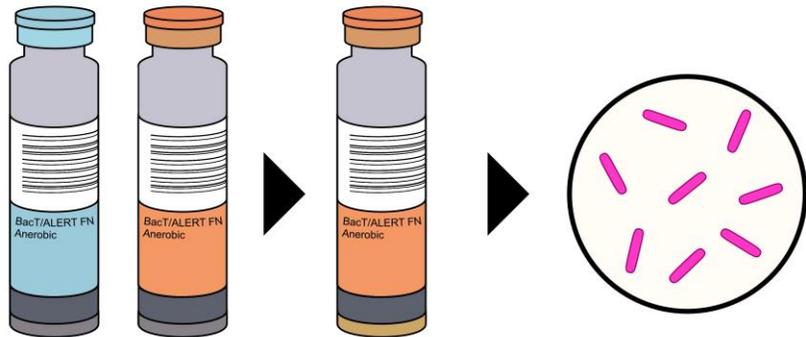
(*bla*_{CTX-M} not detected)

Inducible AmpC

- aminopenicillins
- first-gen cephalosporins
- cephamycins
- pip-tazo
- ceftriaxone
- ceftazidime
- aztreonam



A case



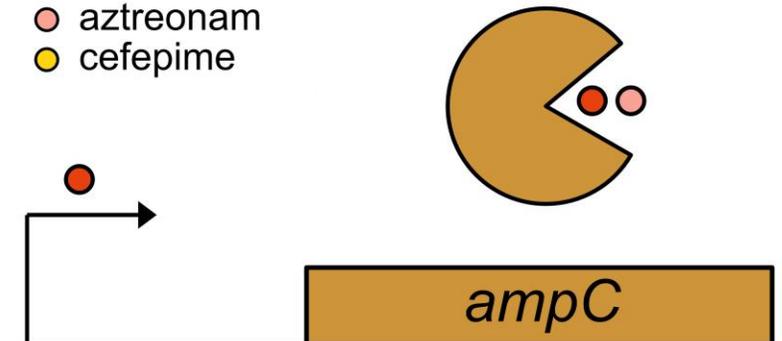
BCID2:

Enterobacter cloacae complex

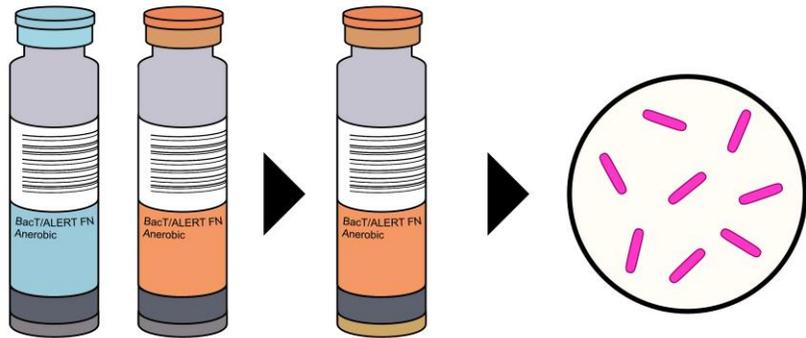
(*bla*_{CTX-M} not detected)

Inducible AmpC

- aminopenicillins
- first-gen cephalosporins
- cephamycins
- pip-tazo
- ceftriaxone
- ceftazidime
- aztreonam
- cefepime



A case



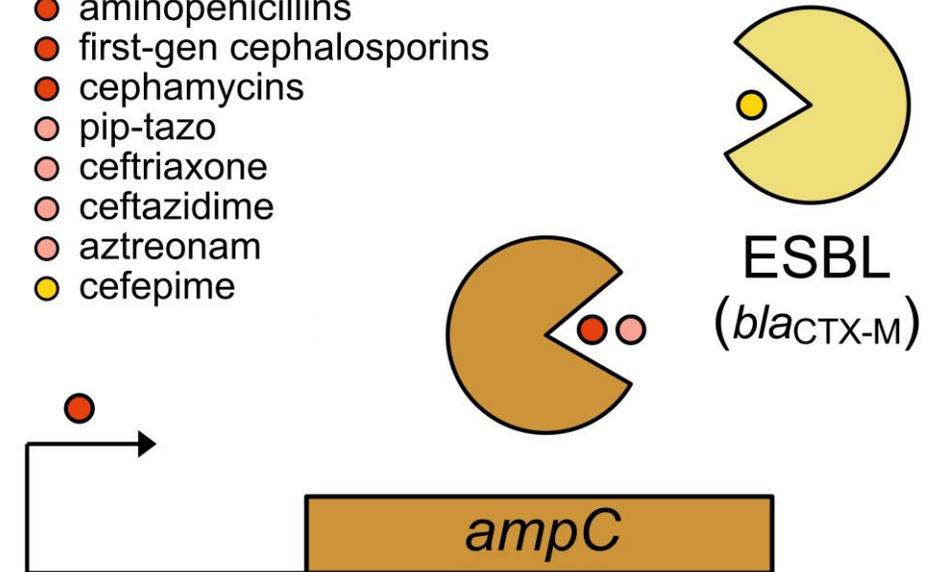
BCID2:

Enterobacter cloacae complex

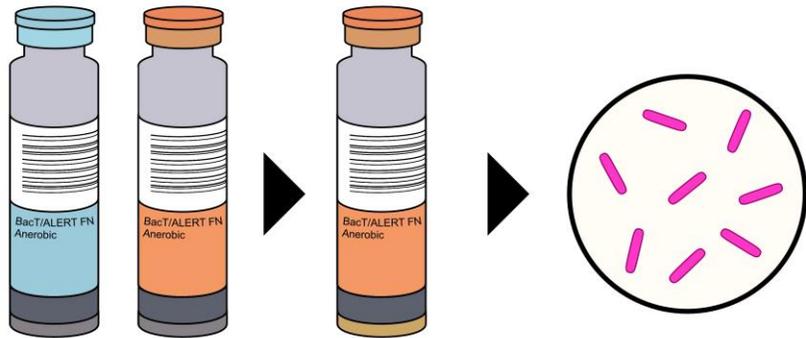
(*bla*_{CTX-M} not detected)

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- first-gen cephalosporins
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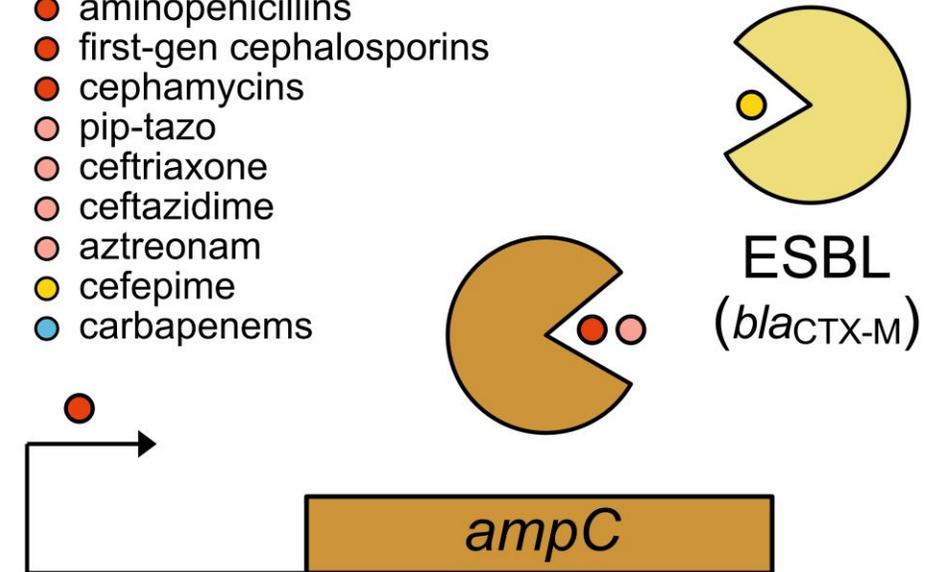
A case



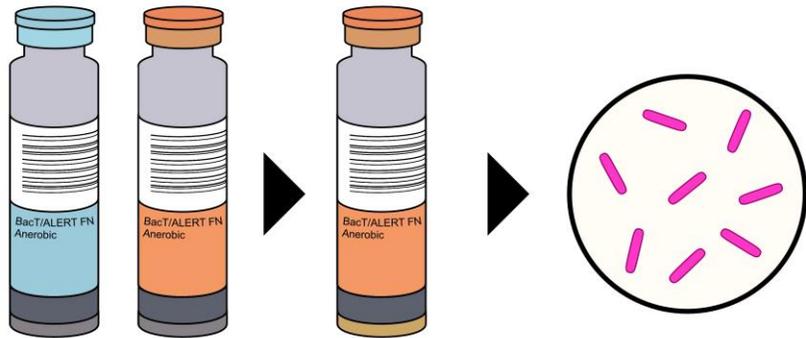
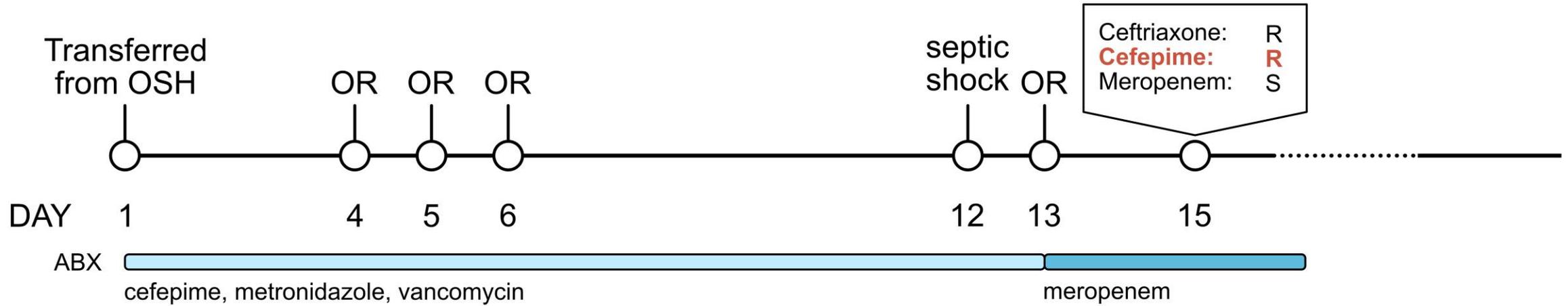
BCID2:
Enterobacter cloacae
complex
(*bla*_{CTX-M} not detected)

Inducible AmpC

- aminopenicillins
- first-gen cephalosporins
- cephamycins
- pip-tazo
- ceftriaxone
- ceftazidime
- aztreonam
- cefepime
- carbapenems



A case



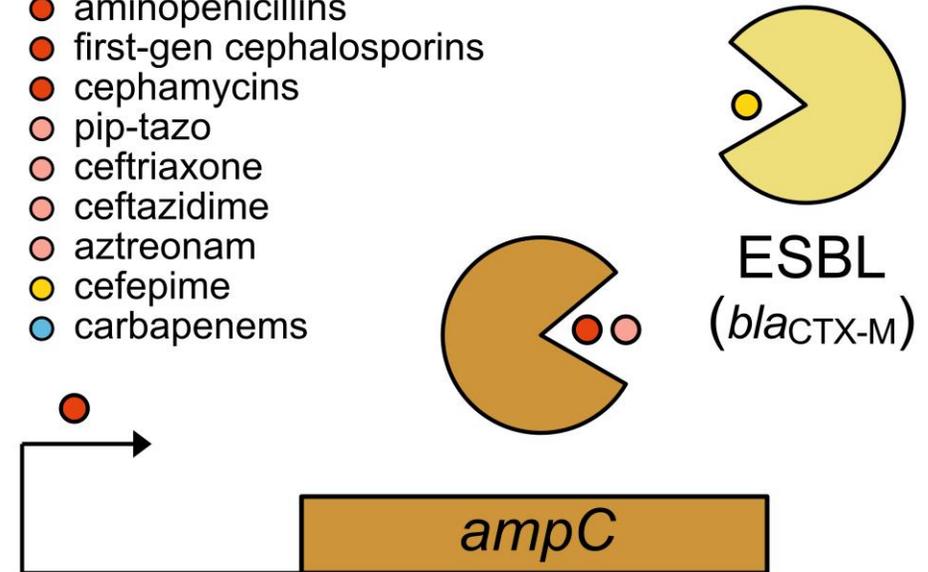
BCID2:

Enterobacter cloacae
complex

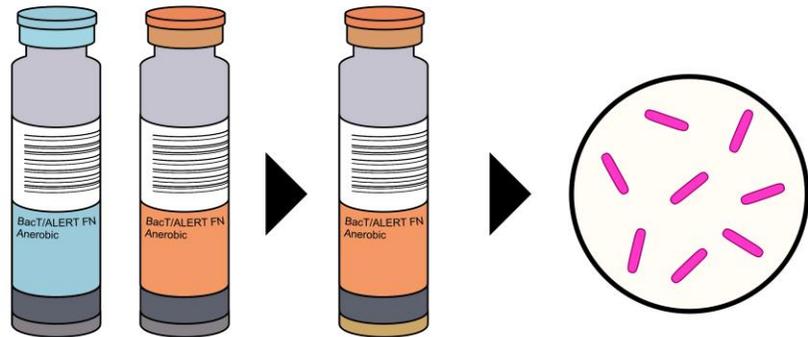
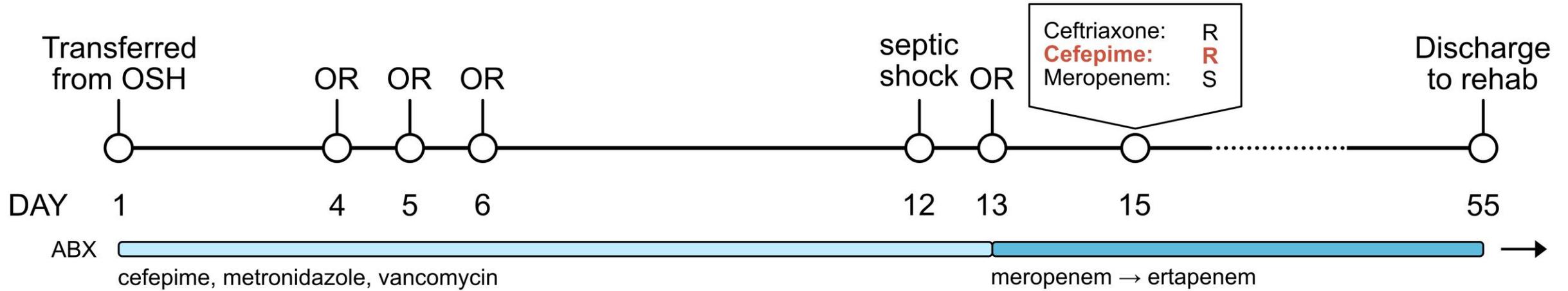
(*bla*_{CTX-M} not detected)

Inducible AmpC

- aminopenicillins
- first-gen cephalosporins
- cephamycins
- pip-tazo
- ceftriaxone
- ceftazidime
- aztreonam
- cefepime
- carbapenems



A case



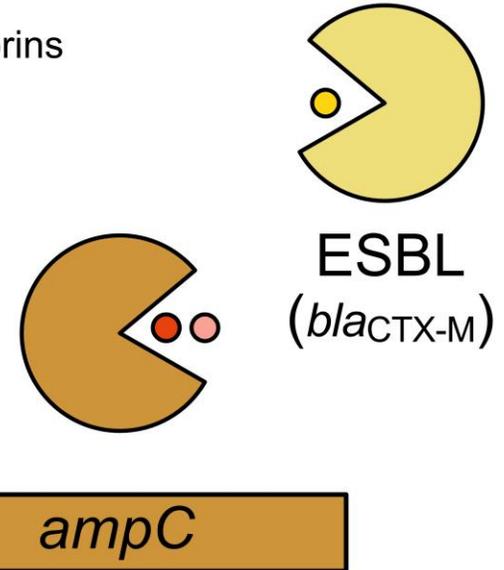
BCID2:

Enterobacter cloacae complex

(*bla*_{CTX-M} not detected)

Inducible AmpC

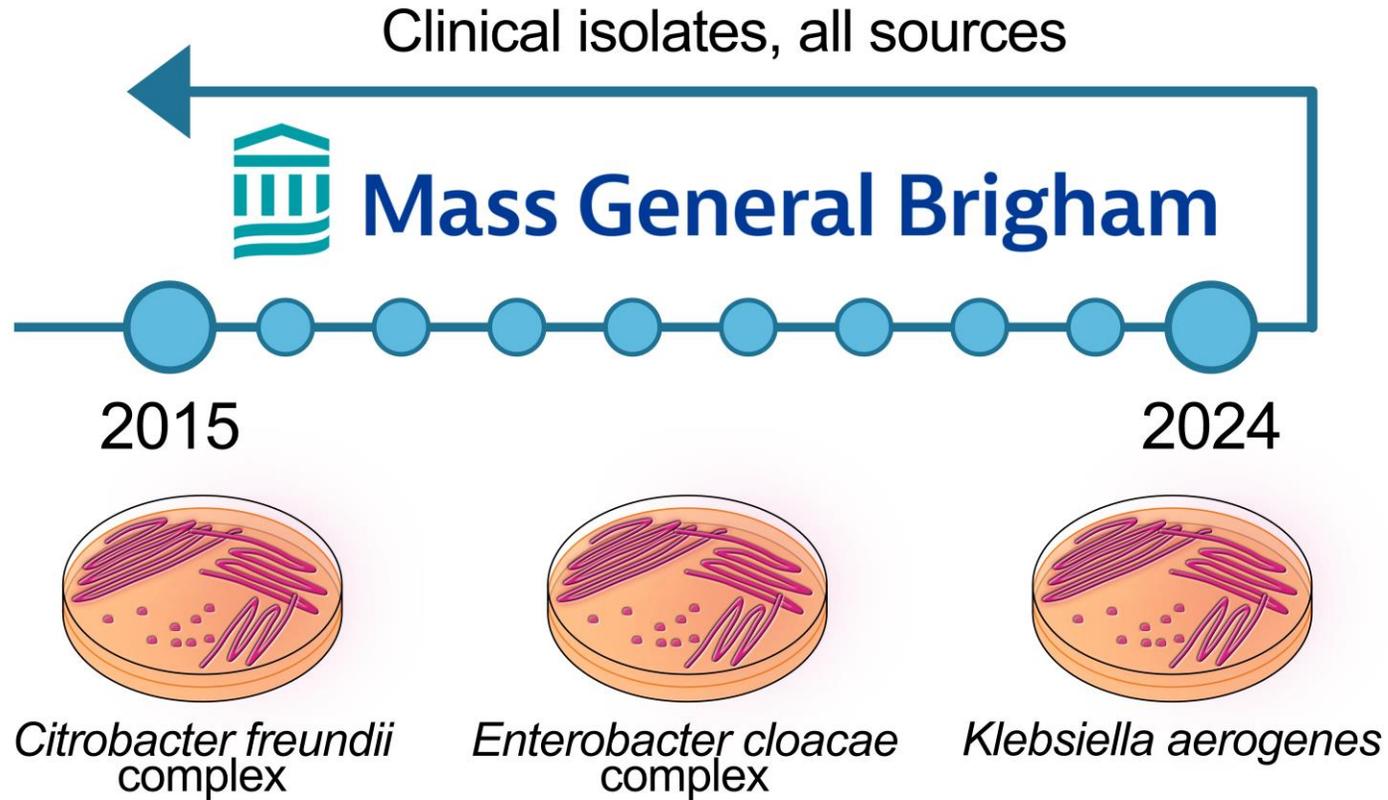
- aminopenicillins
- first-gen cephalosporins
- cephamycins
- pip-tazo
- ceftriaxone
- ceftazidime
- aztreonam
- cefepime
- carbapenems



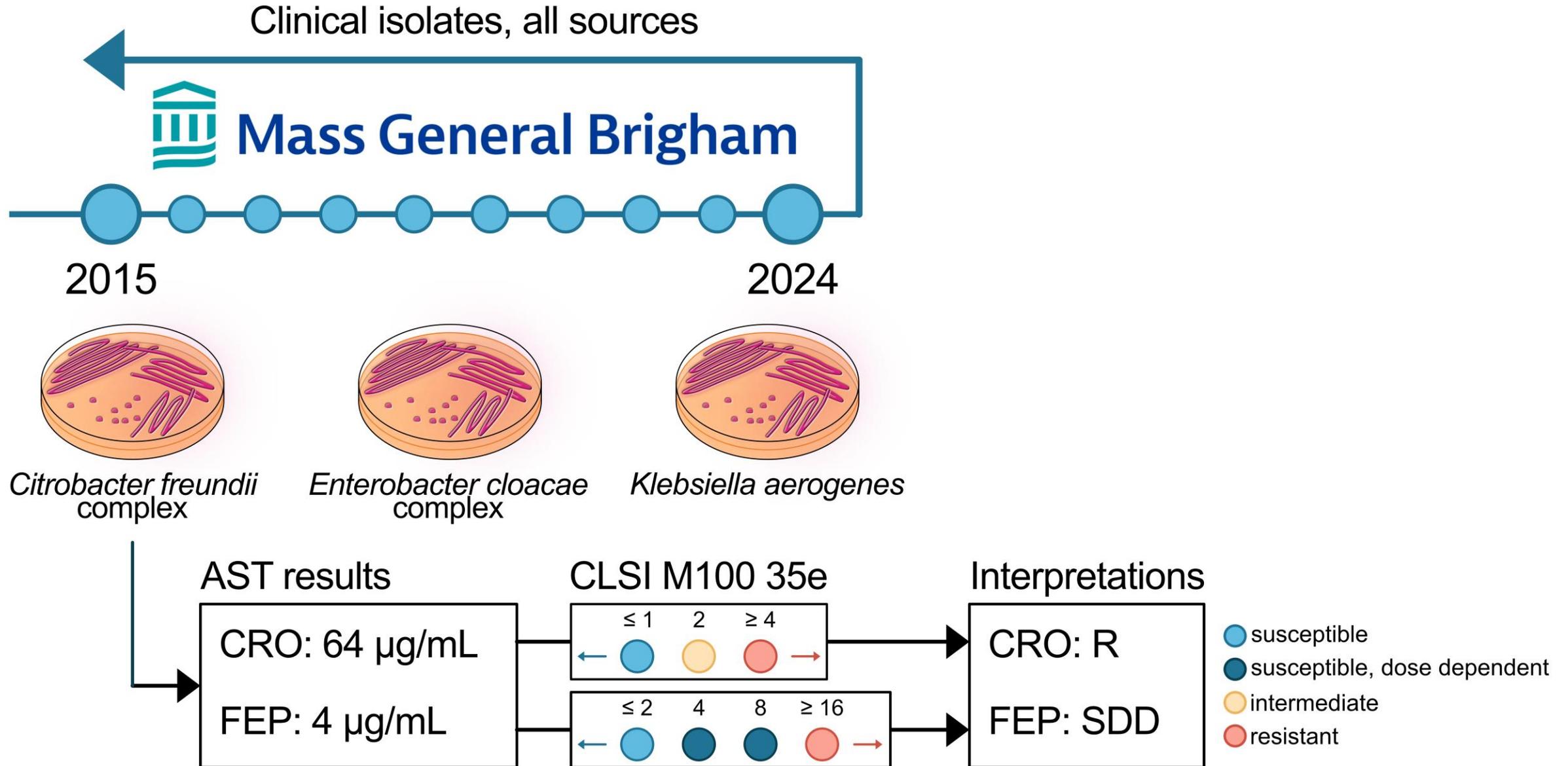
What is the prevalence of cefepime resistance among AmpC producers?

What are the molecular mechanisms underlying elevated cefepime MICs?

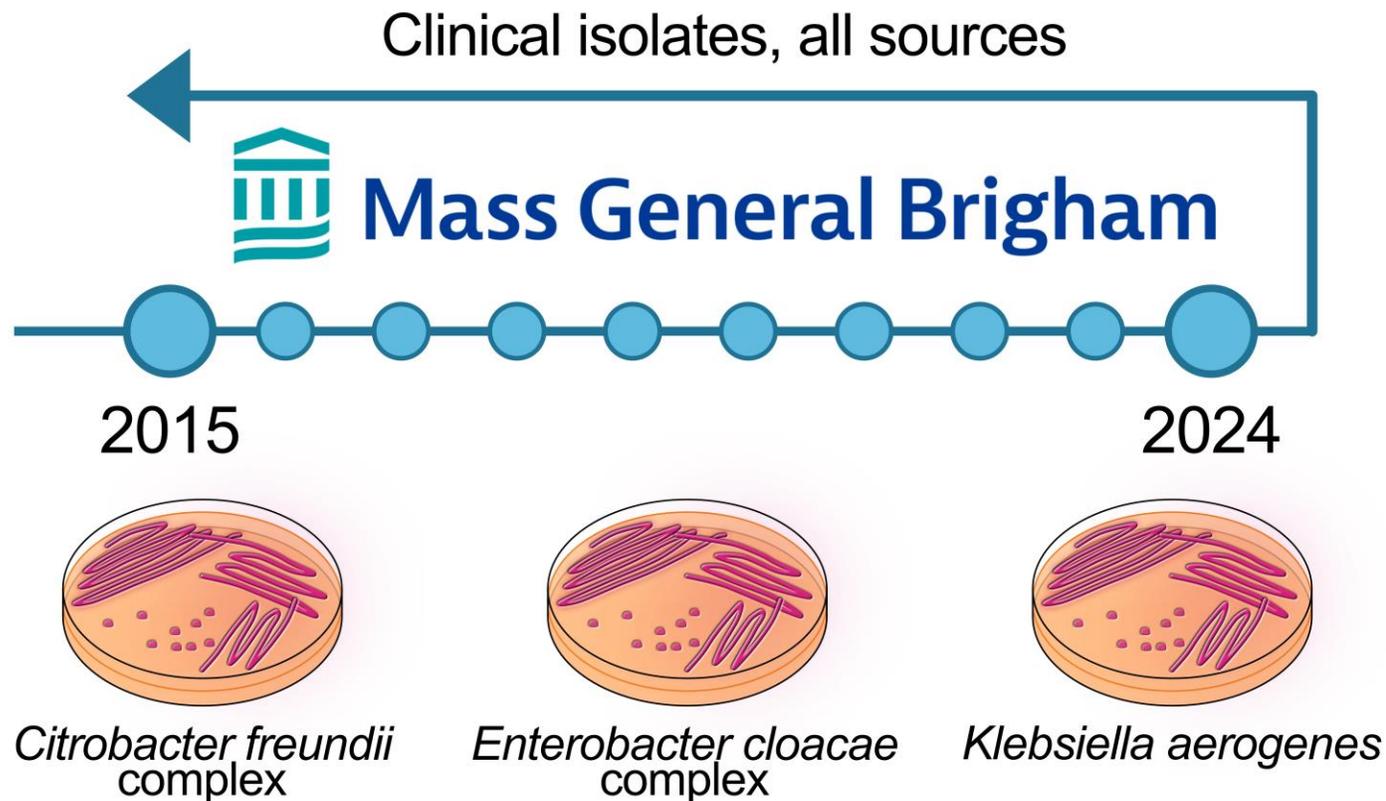
Study design, part 1: prevalence of cefepime resistance



Study design, part 1: prevalence of cefepime resistance



Study design, part 1: prevalence of cefepime resistance

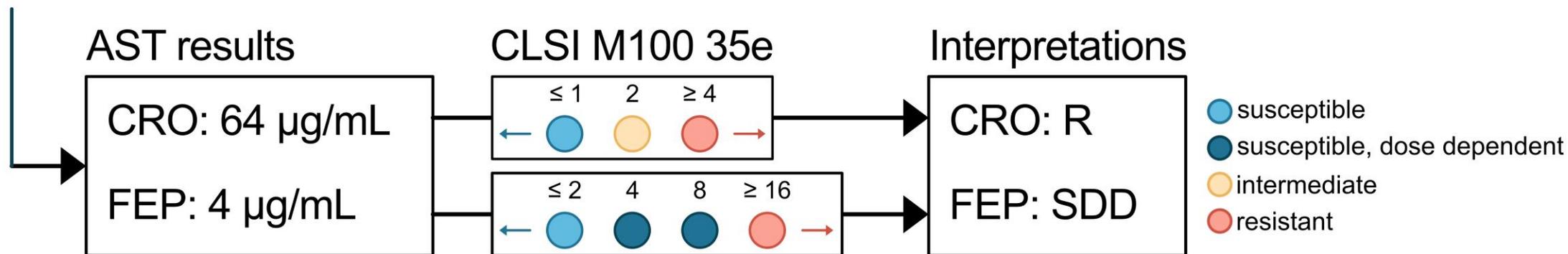


19,366 ISOLATES

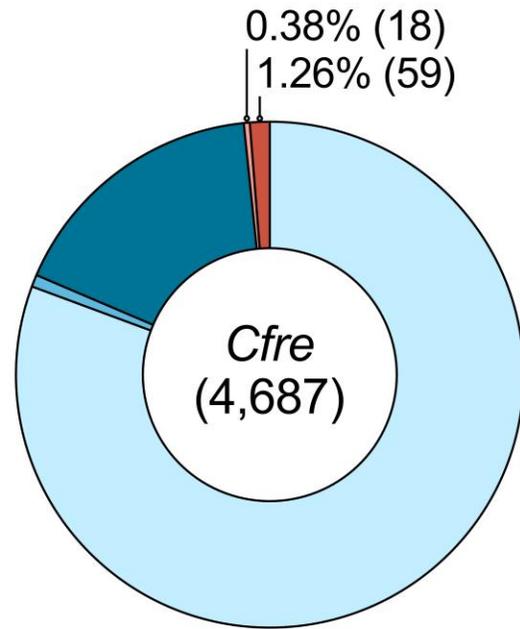
Cfre 4,687

Eclo 9,879

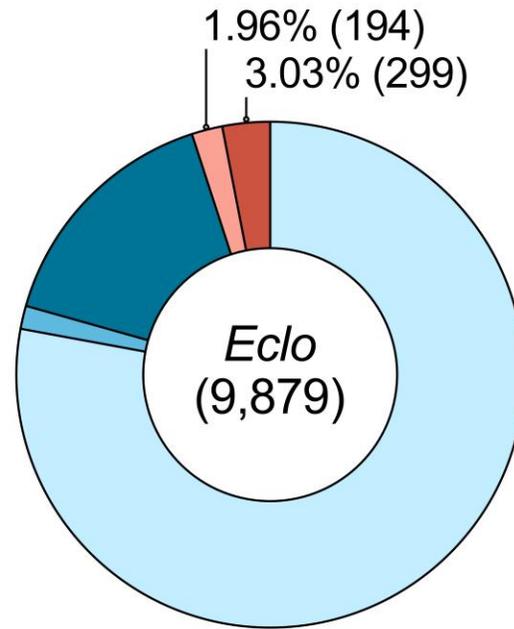
Kaer 4,800



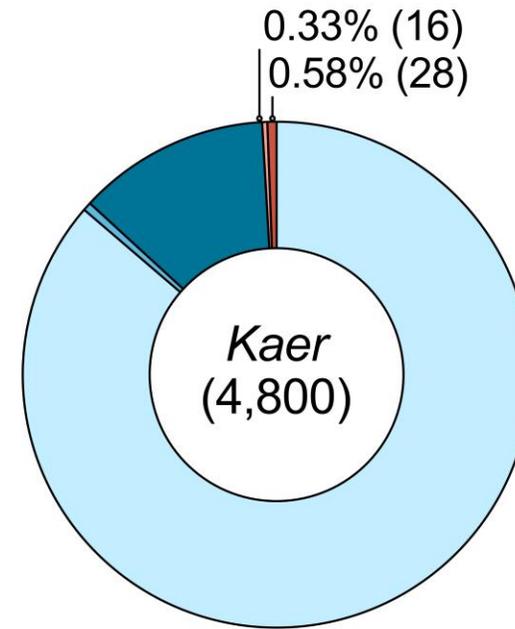
Cefepime susceptibility profiles in AmpC producers



Total = 100.00%



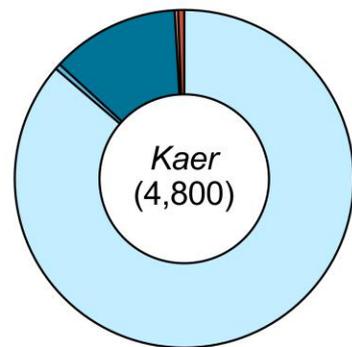
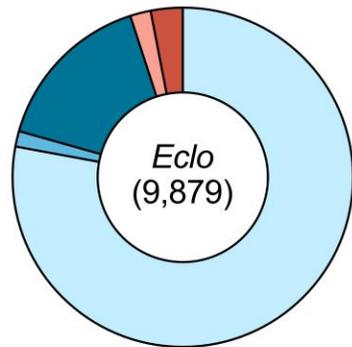
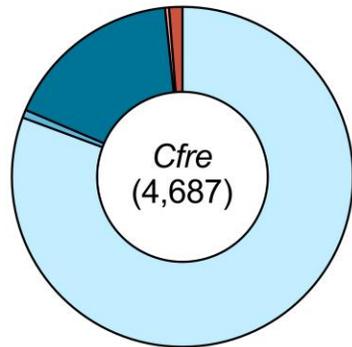
Total = 99.99%
0.01% CRO-S, FEP-SDD



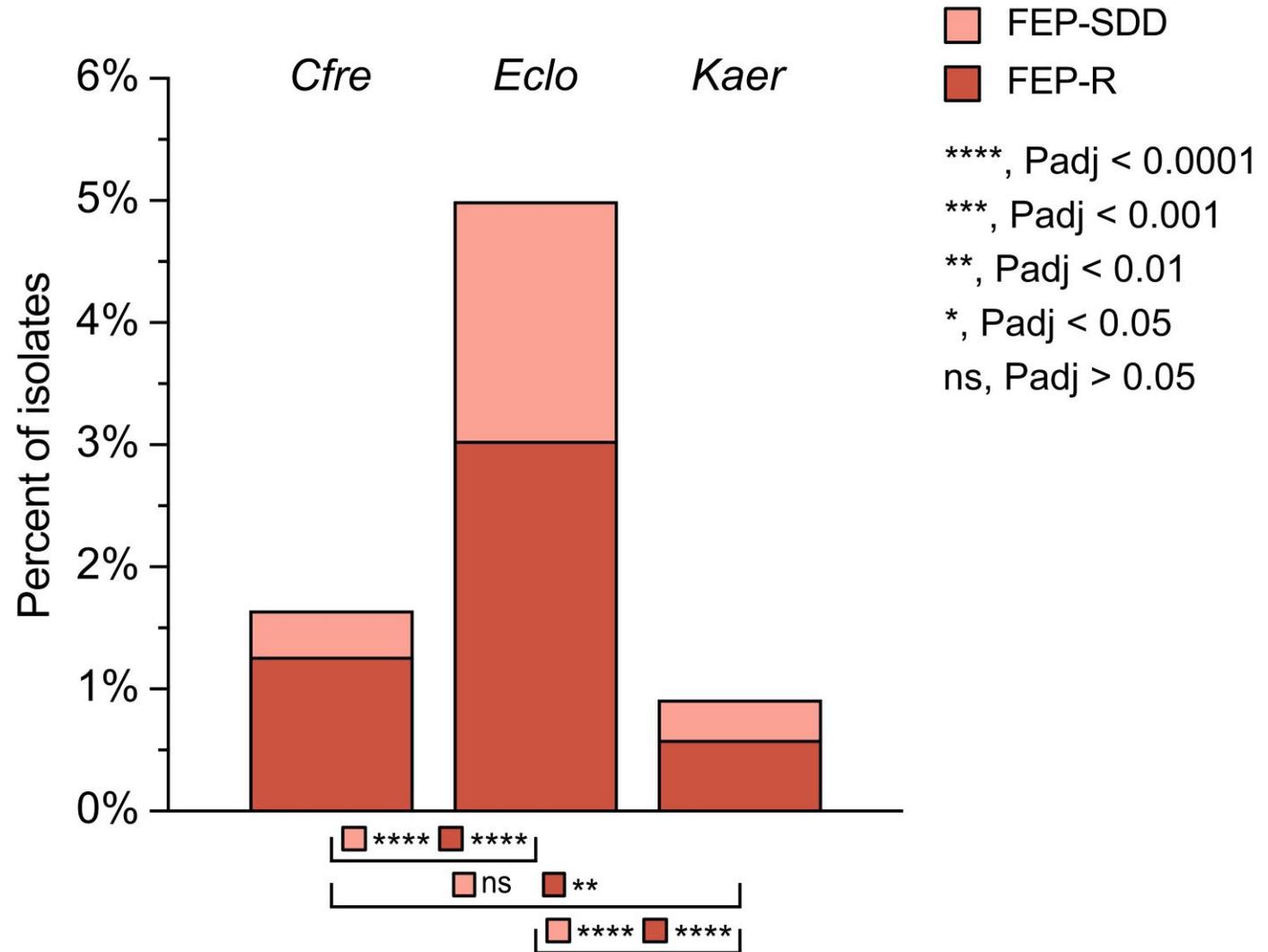
Total = 99.92%
0.06% CRO-S, FEP-SDD
0.02% CRO-S, FEP-R

- CRO-S, FEP-S
- CRO-I, FEP-S
- CRO-R, FEP-S
- CRO-R, FEP-SDD
- CRO-R, FEP-R

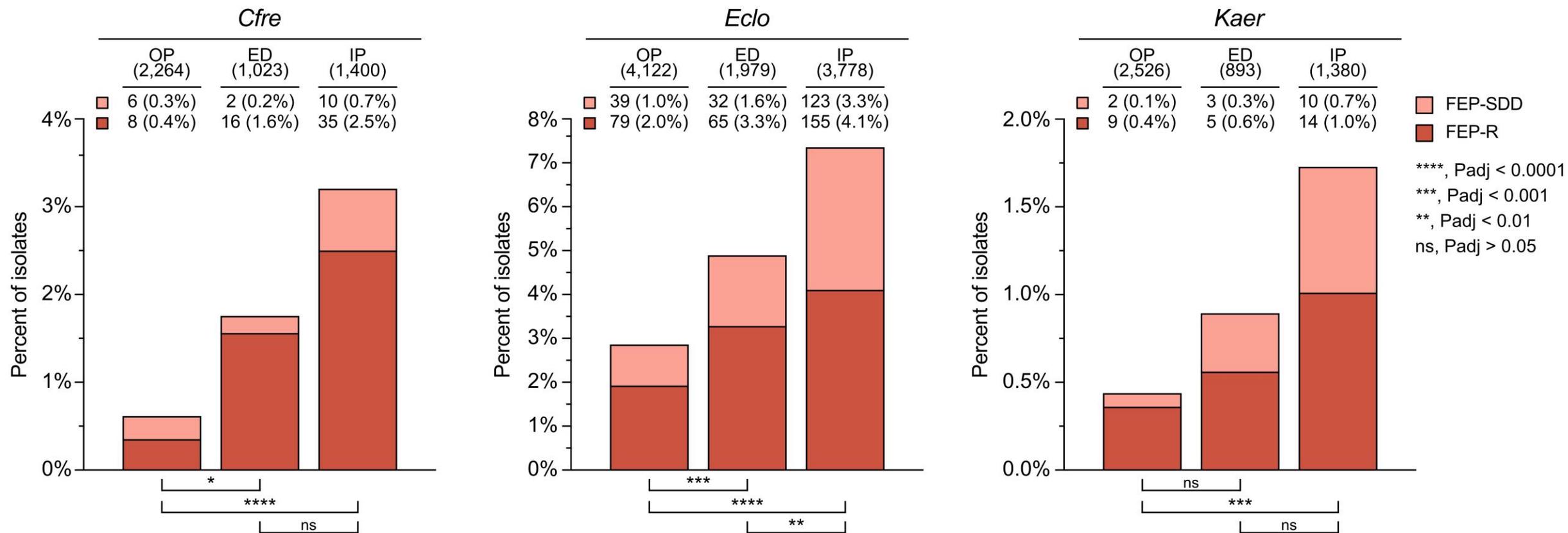
Cefepime susceptibility profiles in AmpC producers



FEP-SDD and FEP-R percentages

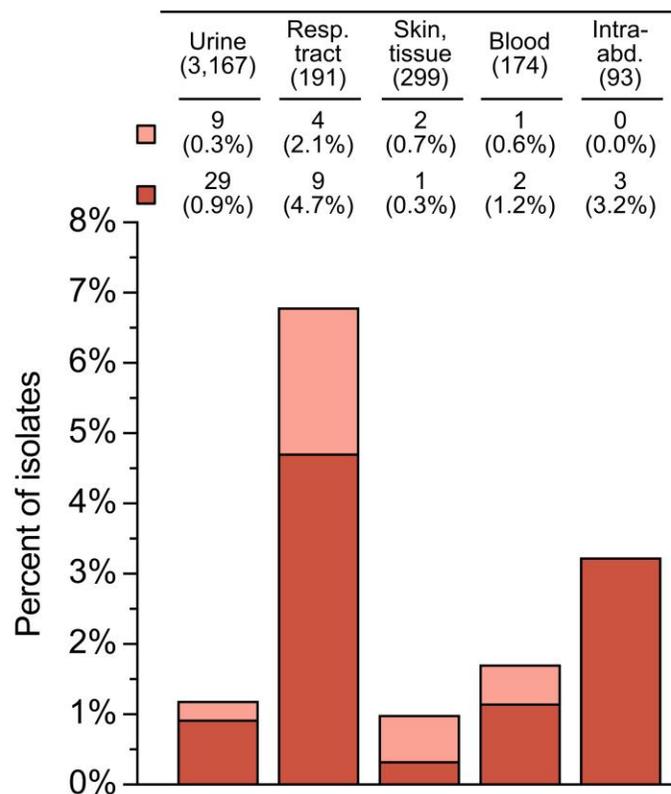


Prevalence of cefepime SDD/R by patient location

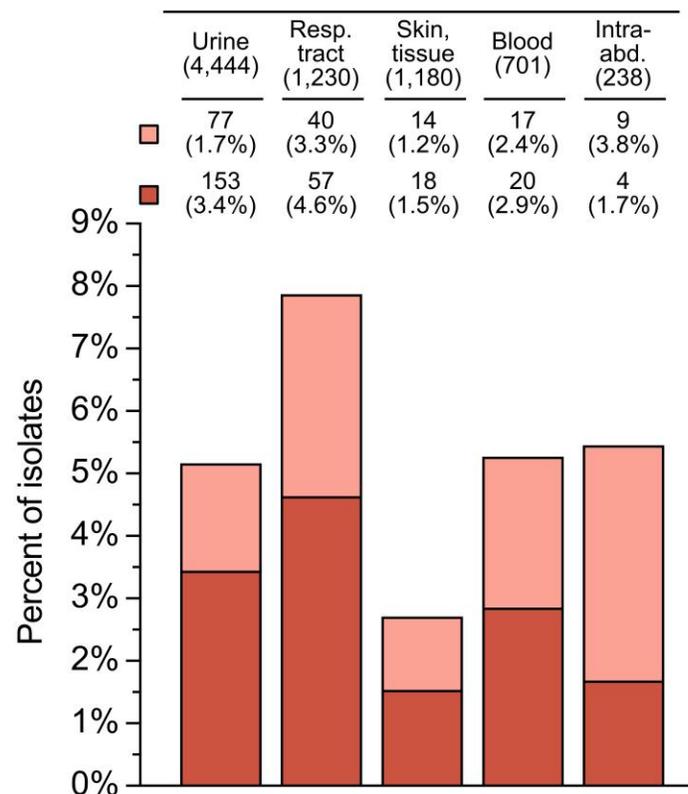


Prevalence of cefepime SDD/R by specimen type

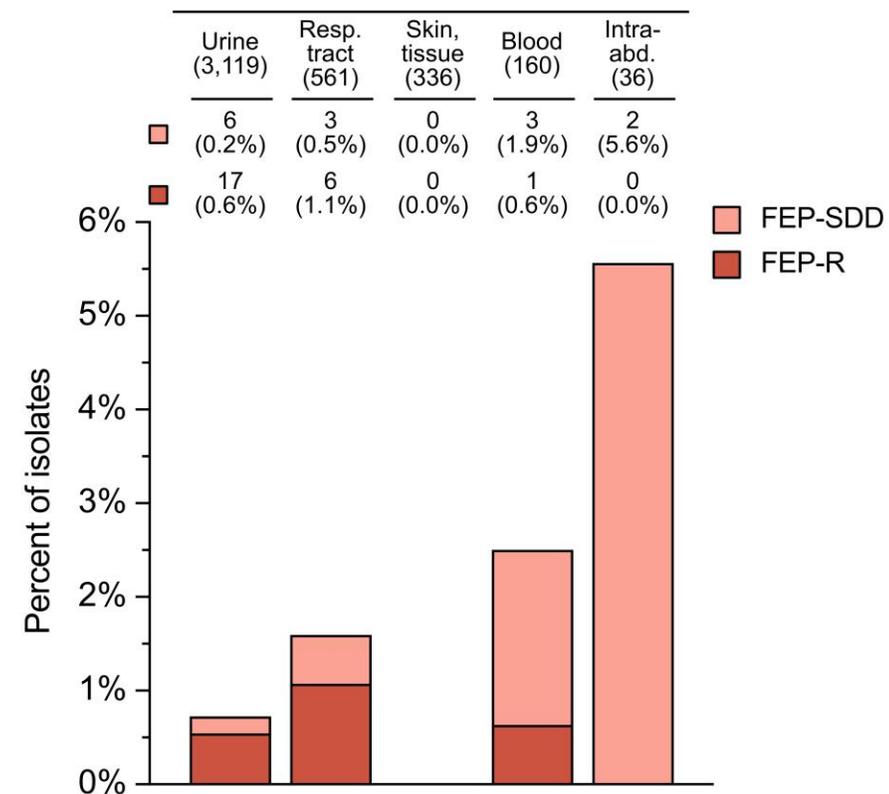
Cfr



Eclo

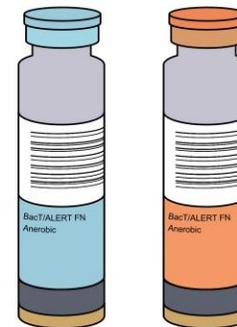
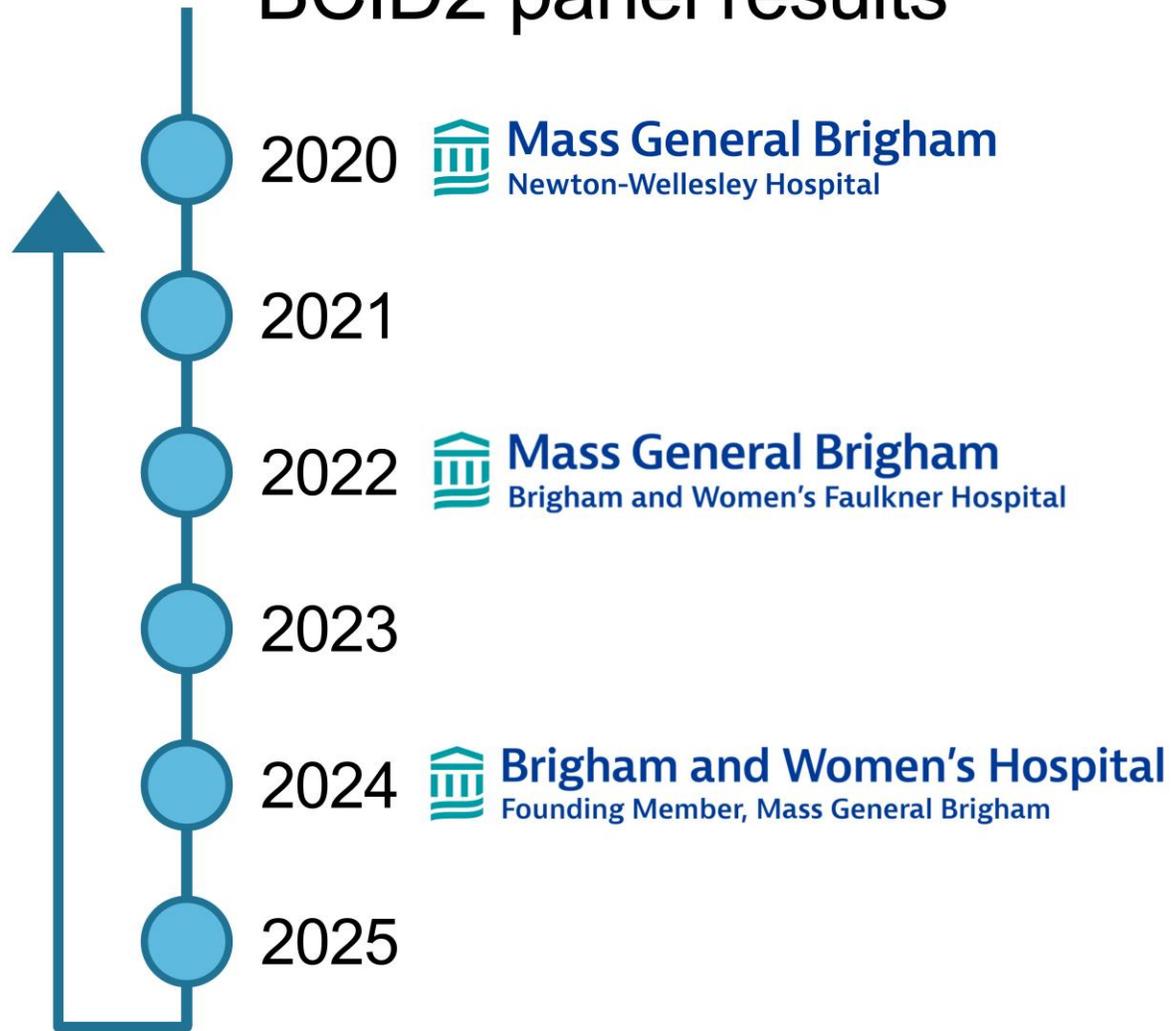


Kaer



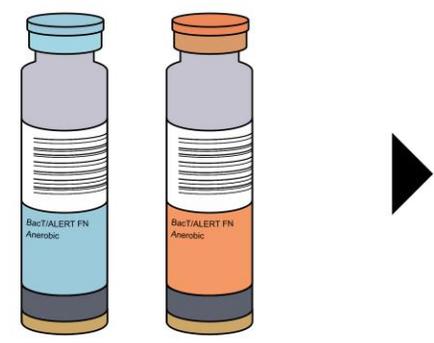
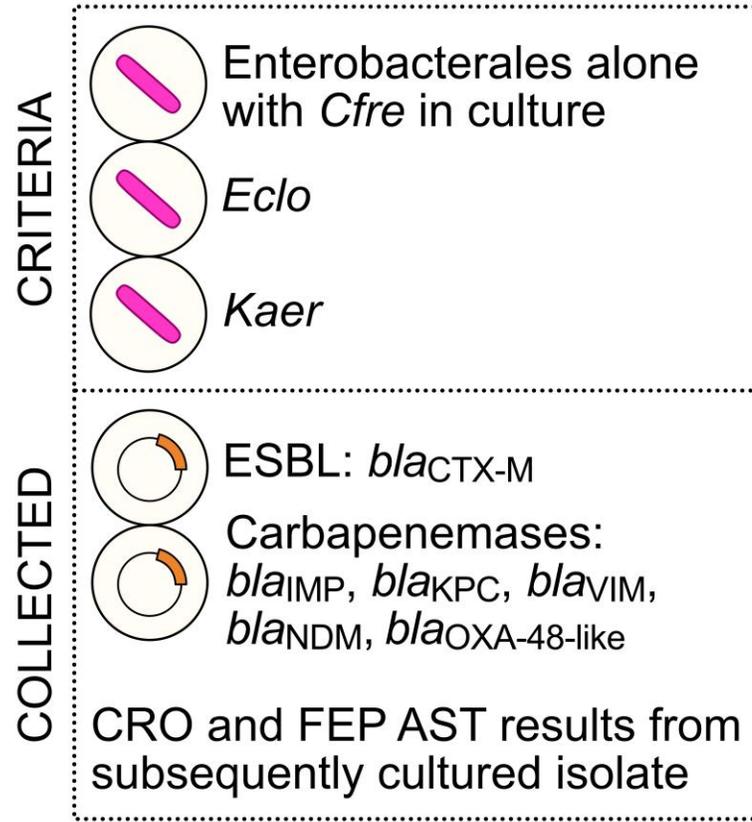
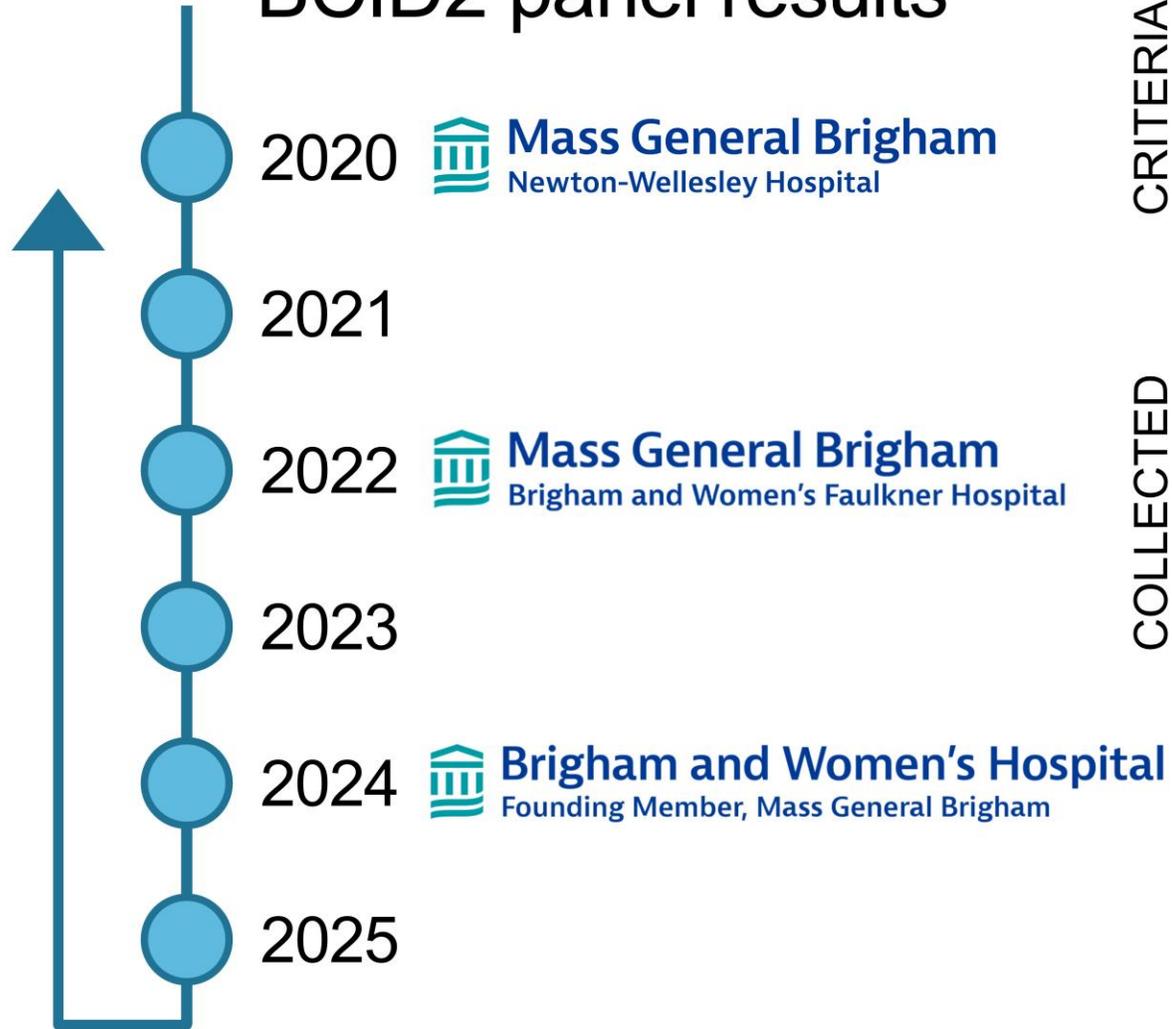
Study design, part 2: bloodstream isolates detected on BCID2

BCID2 panel results



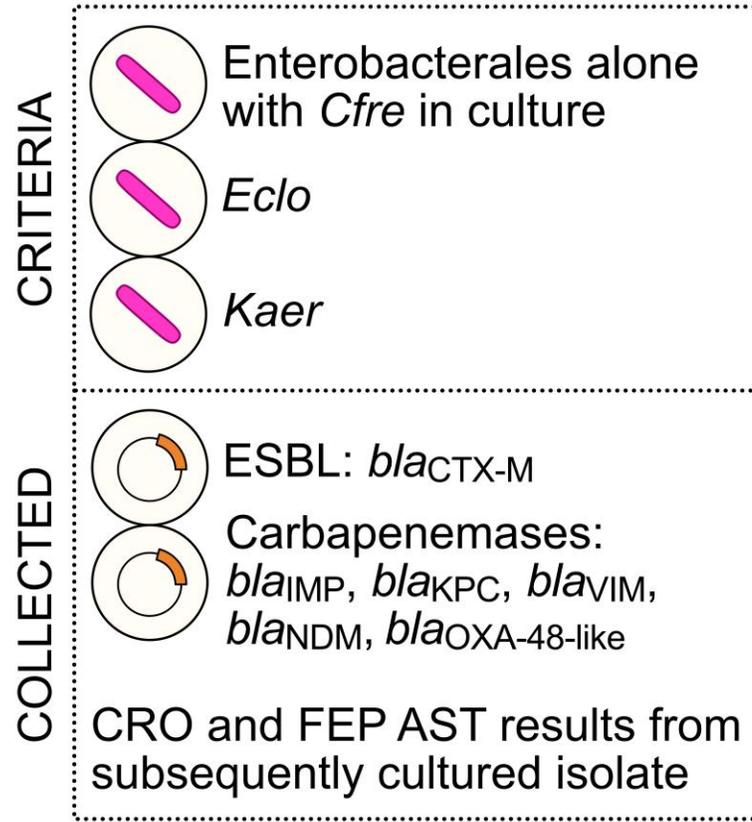
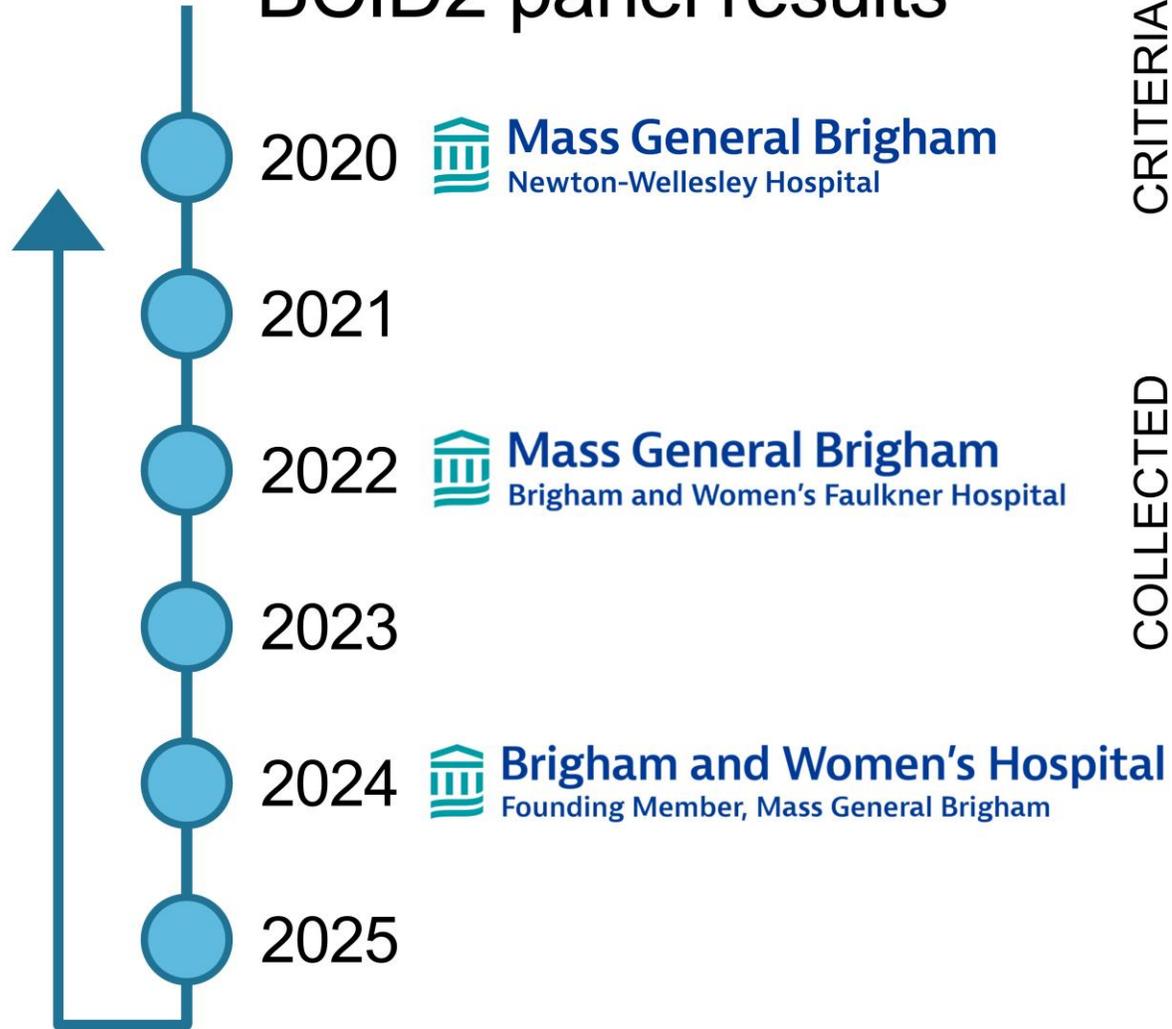
Study design, part 2: bloodstream isolates detected on BCID2

BCID2 panel results



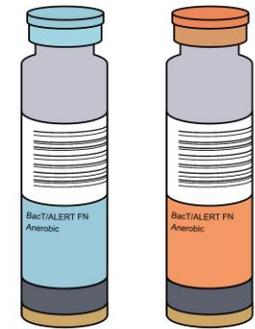
Study design, part 2: bloodstream isolates detected on BCID2

BCID2 panel results

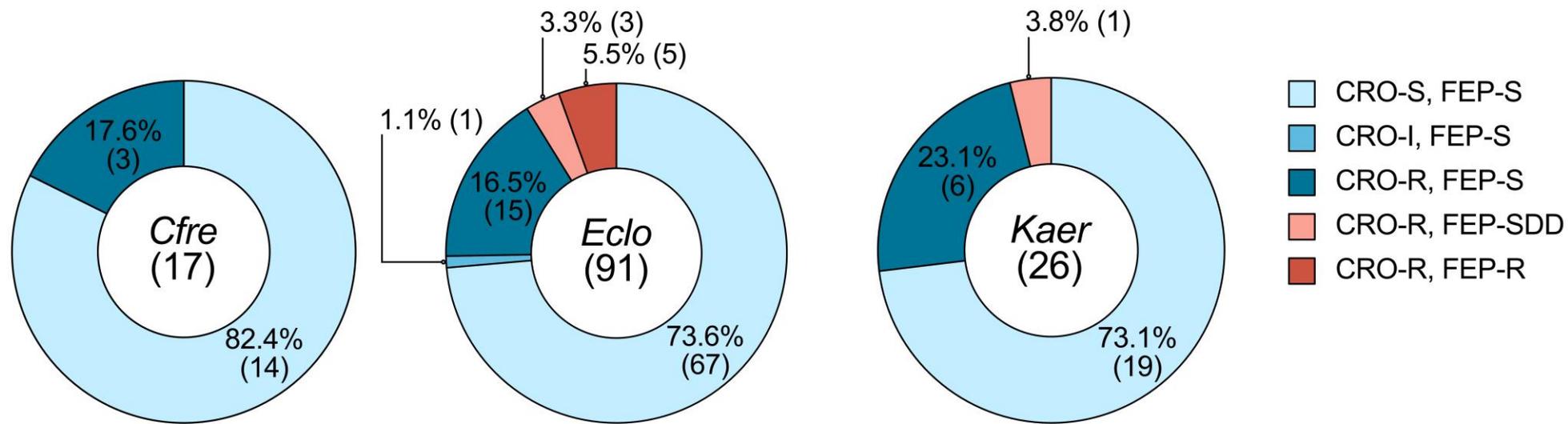


134 ISOLATES

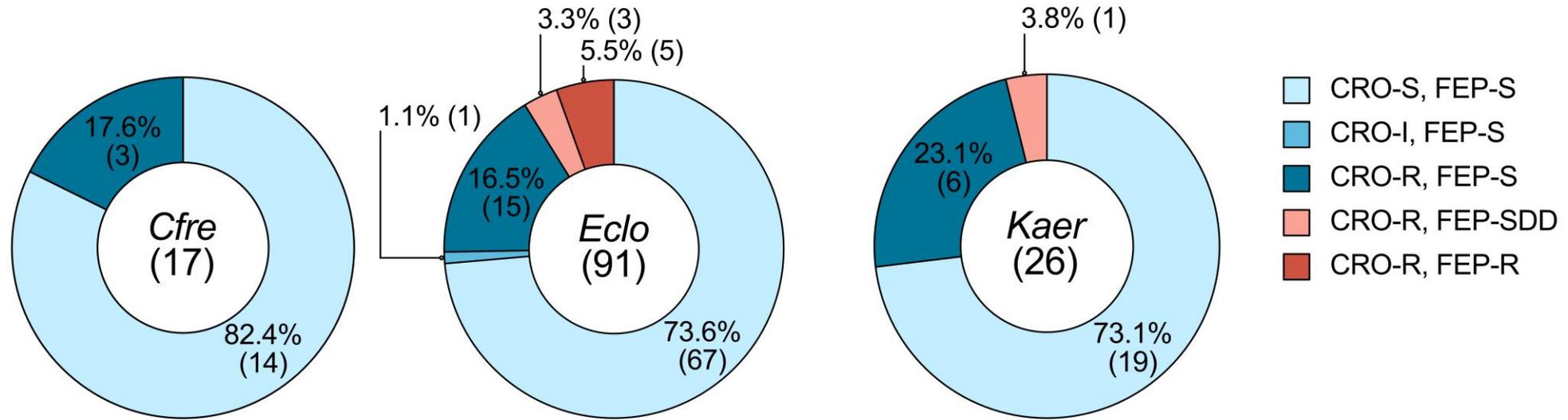
<i>Cfre</i>	17
<i>Eclo</i>	91
<i>Kaer</i>	26



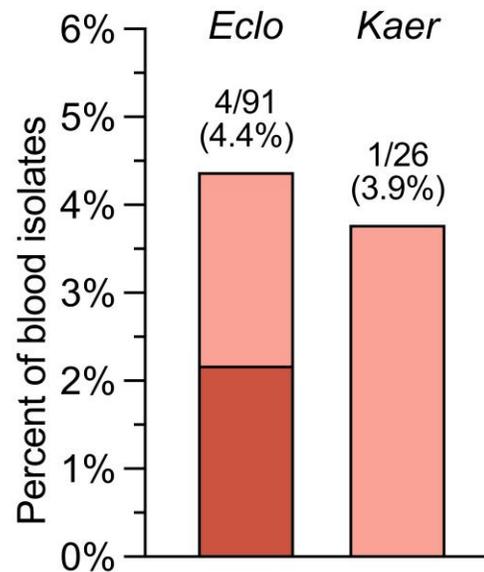
Cefepime susceptibility and *bla* target detection in isolates detected on BCID2



Cefepime susceptibility and *bla* target detection in isolates detected on BCID2



BCID2 *bla* target **NOT** detected:



BCID2 *bla* TARGETS

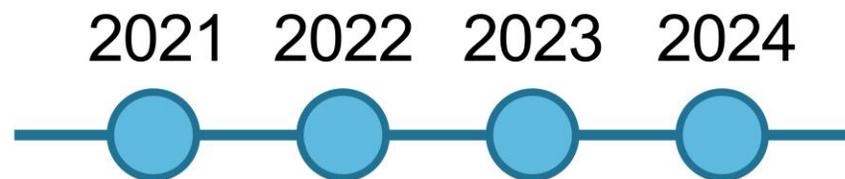
ESBL:

- *bla*CTX-M

Carbapenemase:

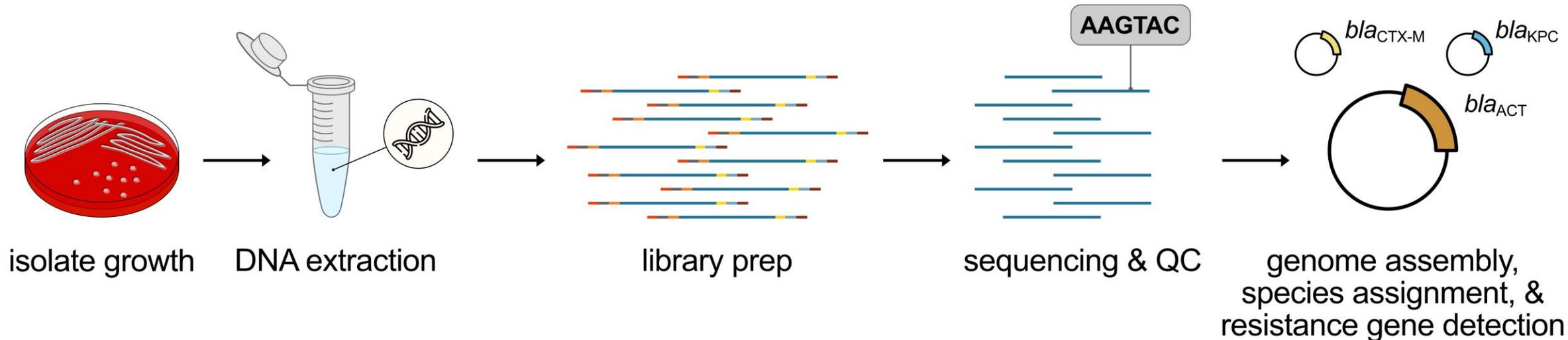
- *bla*KPC
- *bla*NDM
- *bla*IMP
- *bla*VIM
- *bla*OXA-48-like

Study design, part 3: whole-genome sequencing analysis

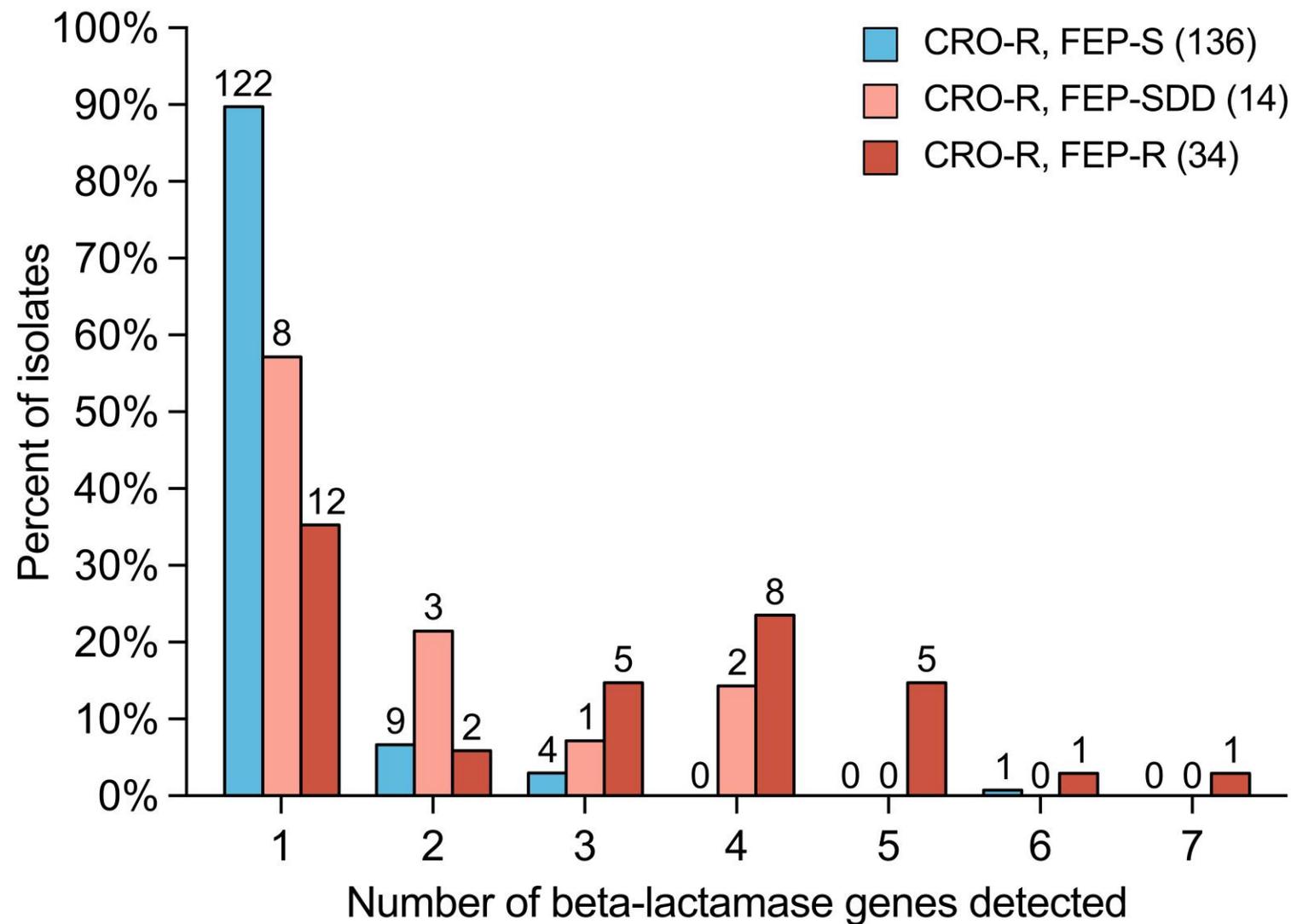


184 CRO-R ISOLATES

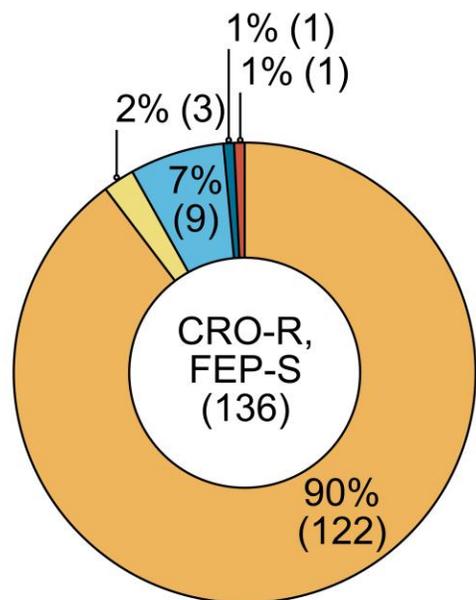
FEP-S	136	(37 <i>Cfre</i> , 67 <i>Eclo</i> , 32 <i>Kaer</i>)
FEP-SDD	14	(2 <i>Cfre</i> , 12 <i>Eclo</i> , 0 <i>Kaer</i>)
FEP-R	34	(5 <i>Cfre</i> , 22 <i>Eclo</i> , 7 <i>Kaer</i>)



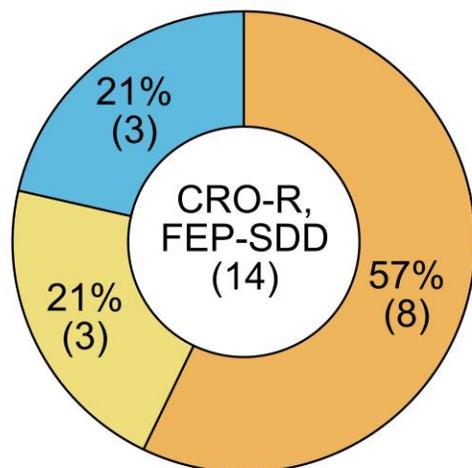
Number of beta-lactamase genes by cefepime susceptibility category



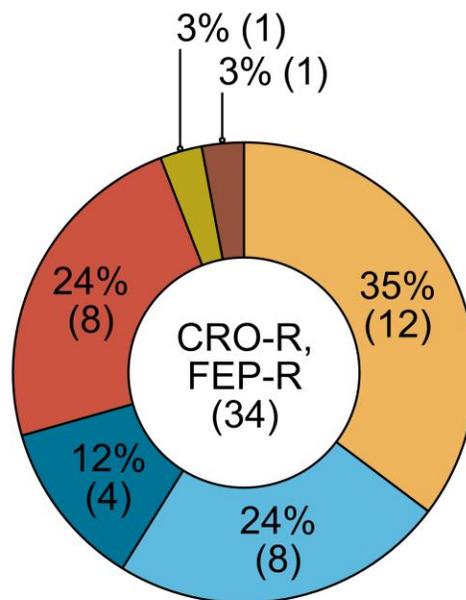
Beta-lactamase profiles by cefepime susceptibility category



	T	■
<i>Cfre</i>	37	31
<i>Eclo</i>	67	60
<i>Kaer</i>	32	32



	T	■
<i>Cfre</i>	2	1
<i>Eclo</i>	12	7
<i>Kaer</i>	0	0



	T	■
<i>Cfre</i>	5	1
<i>Eclo</i>	22	6
<i>Kaer</i>	7	5

Beta-lactamase genes in addition to chromosomal *ampC*:

- None
- Non-ESBL, non-CP, non-PAC *bla*
- ESBL
- CP
- ESBL + CP
- PAC + CP
- ESBL + PAC + CP

CP: carbapenemase

PAC: plasmid-borne *ampC*

Substantial variability in FEP-SDD/R among AmpC producers by organism, patient setting, and body site

- Overall prevalence **3.2%** → empiric FEP therapy generally safe
- Caution warranted in certain settings
 - *Eclo*: 5% overall, 7% in inpatients, 8% in respiratory isolates

Absence of *bla* target on BCID2 does NOT rule out a FEP-SDD/R phenotype

- **4.3%** of *Eclo* and *Kaer* detected on BCID2

Applied CLSI breakpoints only

- EUCAST breakpoints: likely higher FEP resistance rates

WGS data might not reflect general patterns of beta-lactamase carriage

- Small sample size
- Convenience sample of CRO-R isolates

Investigation of non-*bla* resistance determinants outside scope

- Mutations in components of *ampC* regulatory pathway (*ampD*, *ampR*)
- Porin mutations

Analysis of patient outcomes and metadata outside scope

Acknowledgements

Project mentors

Nicole Pecora, MD, PhD



Brigham and Women's Hospital
Teaching Center, Harvard Medical School

Sanjat Kanjilal, MD, MPH



Amsterdam UMC

Pecora lab

Zachary Pearson, MLT(ASCP)

Samantha Taffner, MS

MGB clinical microbiology laboratory staff



Mass
General
Brigham

Funding

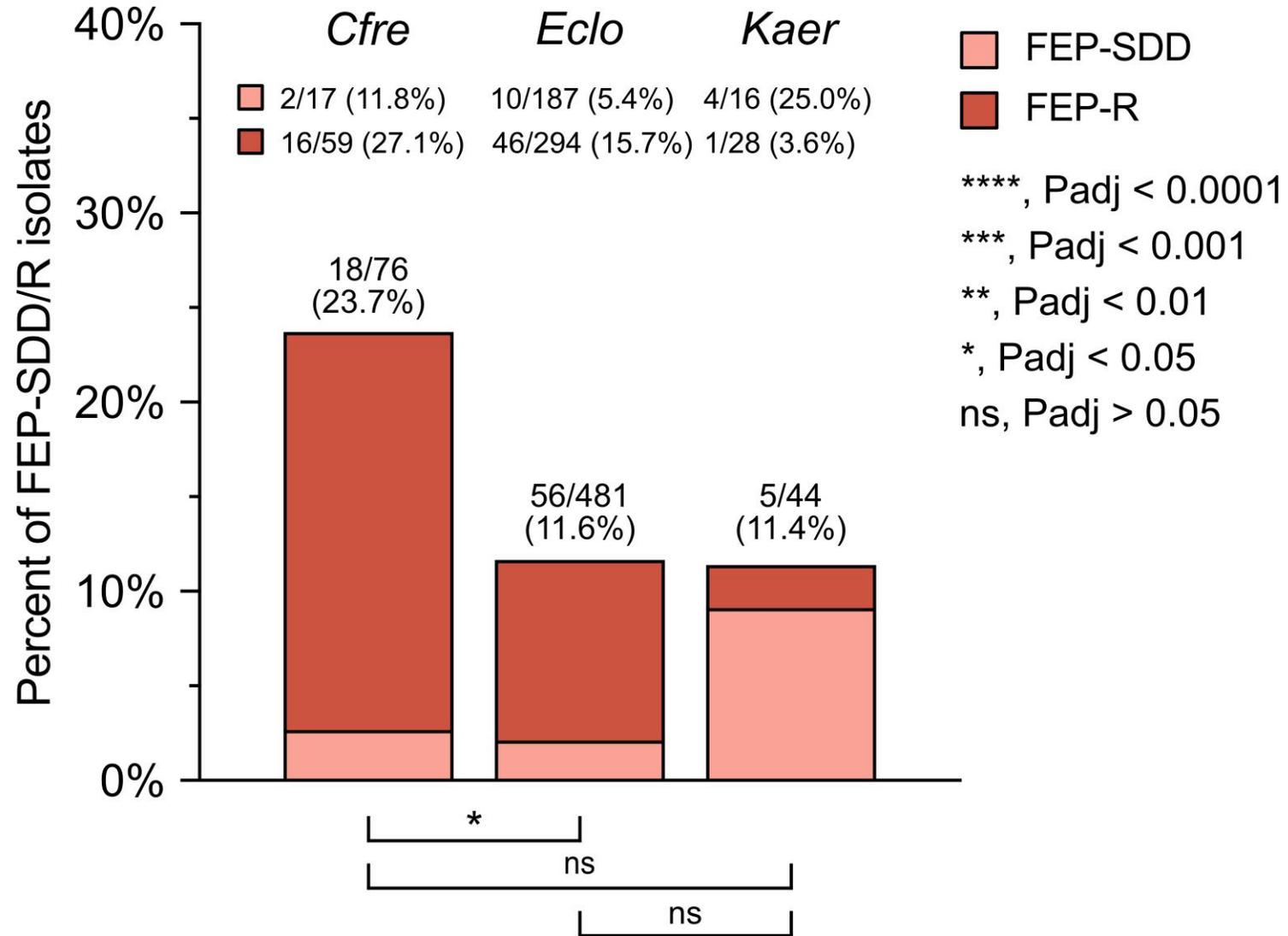
BWH Pathology Department



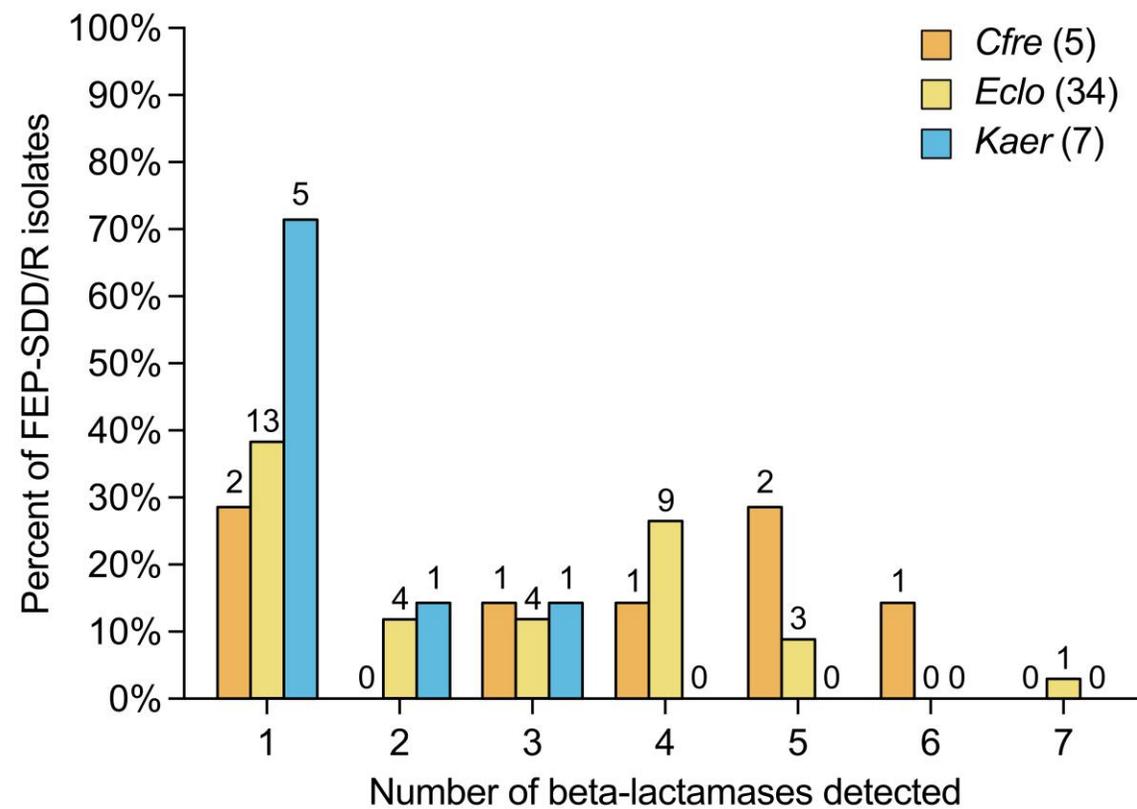
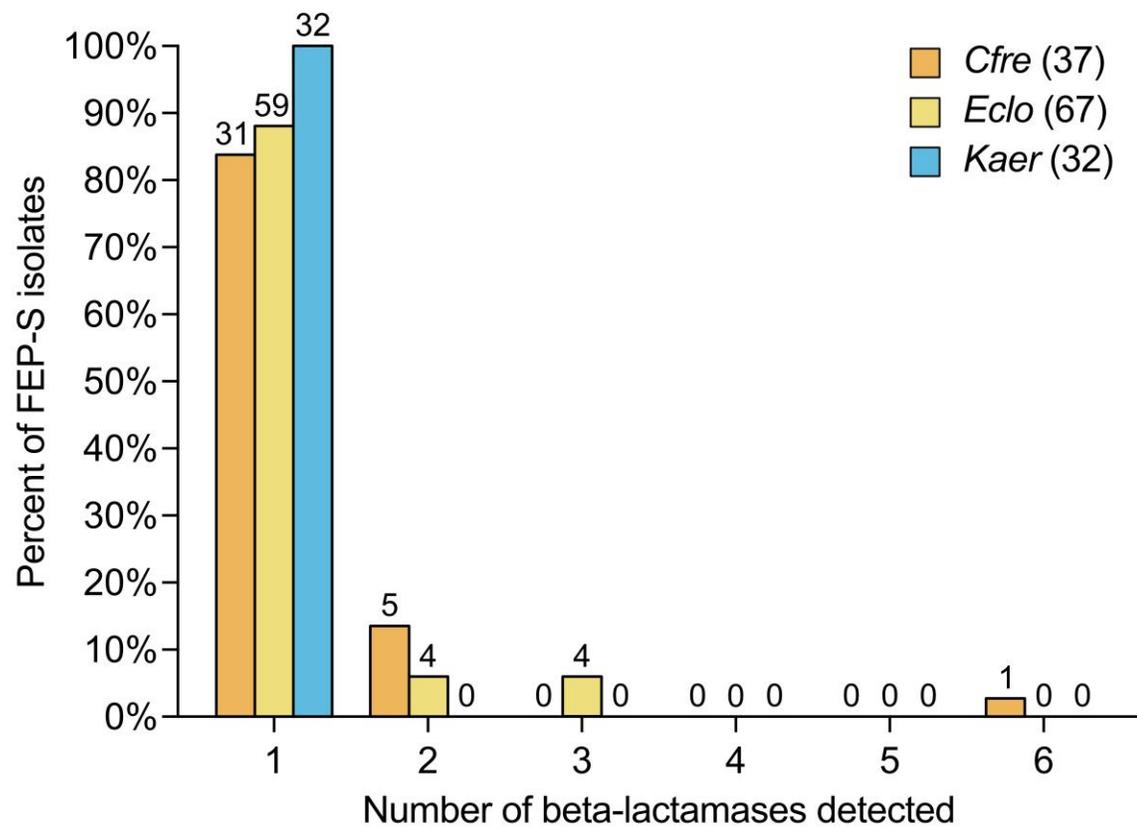
Supplementary slides

1. Meropenem resistance rates among FEP-SDD/R isolates
2. Number of *bla* genes by species and FEP phenotype
3. *bla*_{ACT} alleles in *Eclo* by FEP phenotype
4. Prevalence of beta-lactamase genes by cefepime susceptibility category
5. Presence of molecular panel *bla* targets in cefepime SDD/R isolates

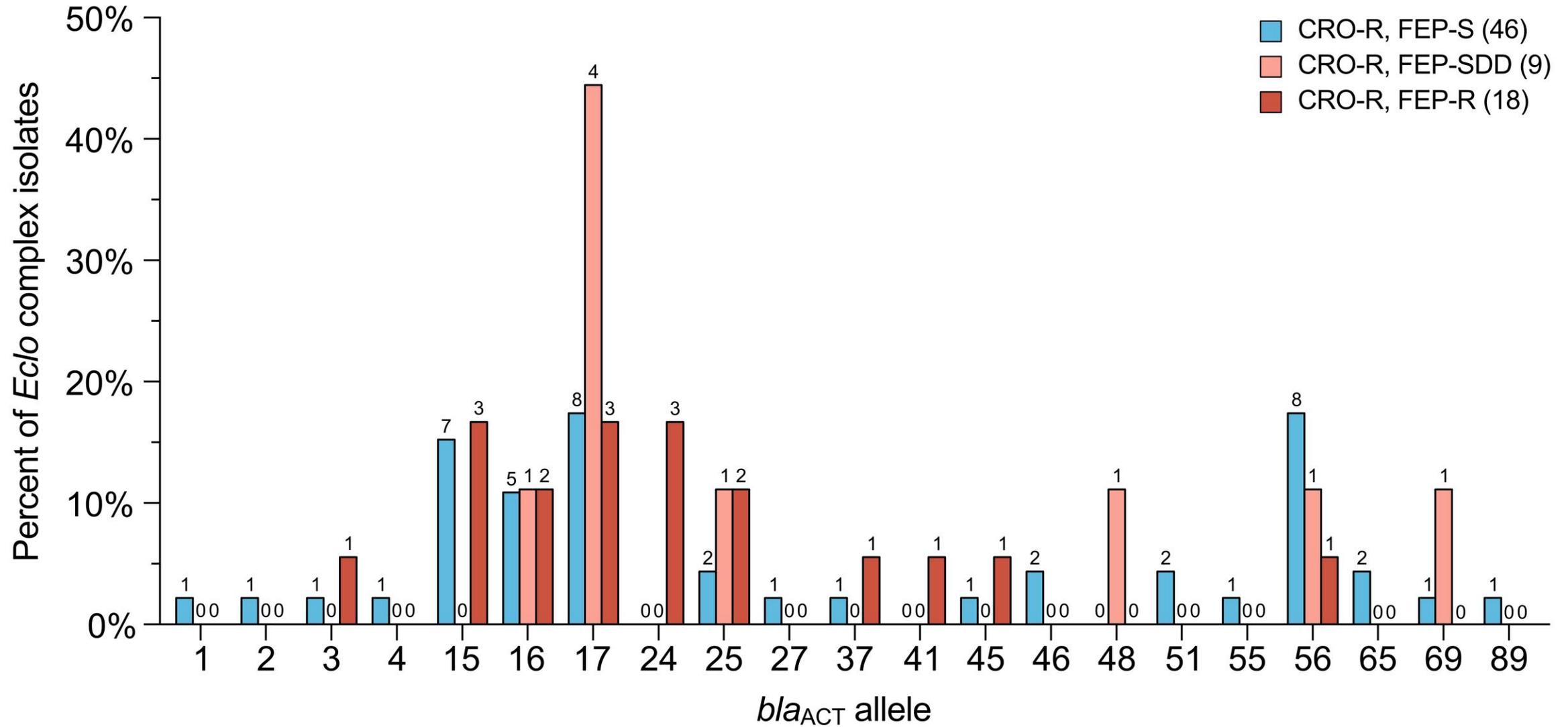
Meropenem resistance rates among FEP-SDD/R isolates



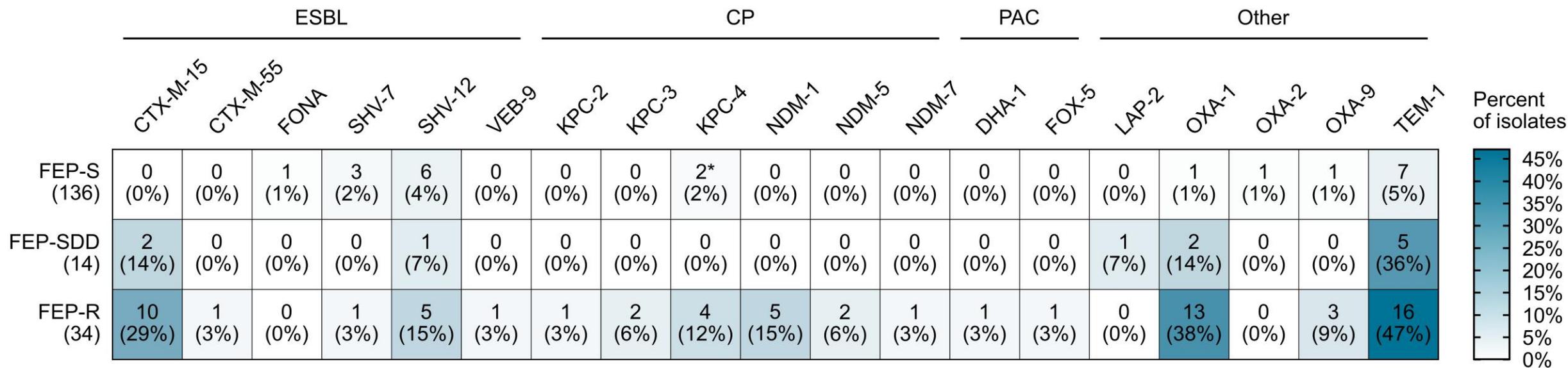
Number of beta-lactamase genes by species



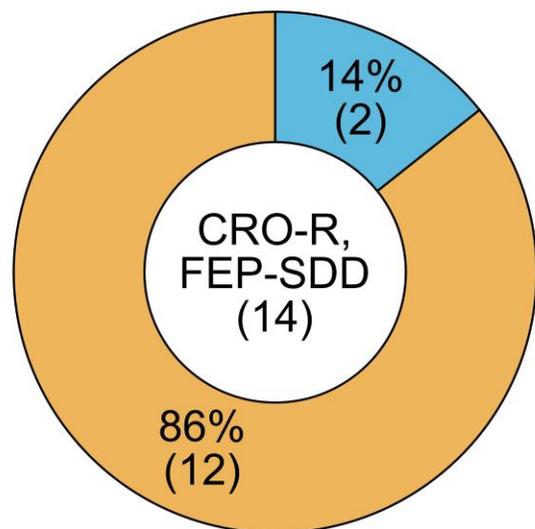
bla_{ACT} alleles in *Eclo* isolates by cefepime susceptibility



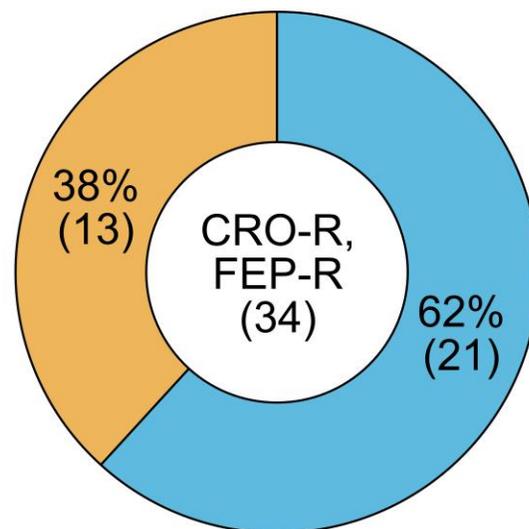
Prevalence of beta-lactamase genes by cefepime susceptibility category



Presence of molecular panel *bla* targets in cefepime SDD/R isolates



	T	■	■
<i>C. fre.</i>	2	0	0
<i>E. clo.</i>	12	2	10
<i>K. aer.</i>	0	0	0



	T	■	■
<i>C. fre.</i>	5	4	1
<i>E. clo.</i>	22	15	7
<i>K. aer.</i>	7	2	5

- Multiplex PCR panel *bla* target present
- Multiplex PCR panel *bla* target absent

MULTIPLEX PCR PANEL *bla* TARGETS

ESBL:

- *bla*CTX-M

Carbapenemase:

- *bla*KPC
- *bla*NDM
- *bla*IMP
- *bla*VIM
- *bla*OXA-48-like