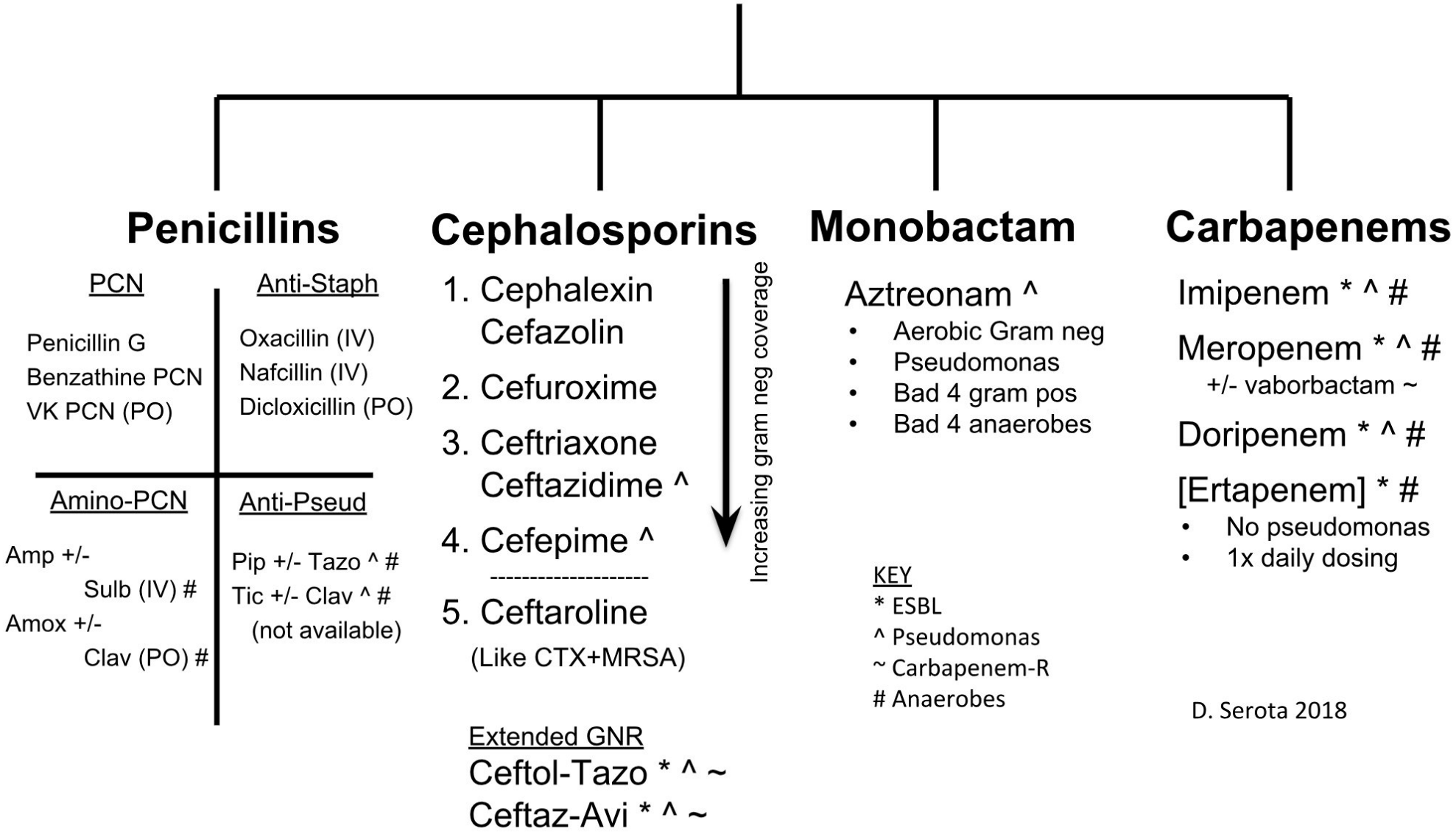
# CRE/CPE

## WHAT IS THE DIFFERENCE?

POPPY SMITH

# Beta Lactams

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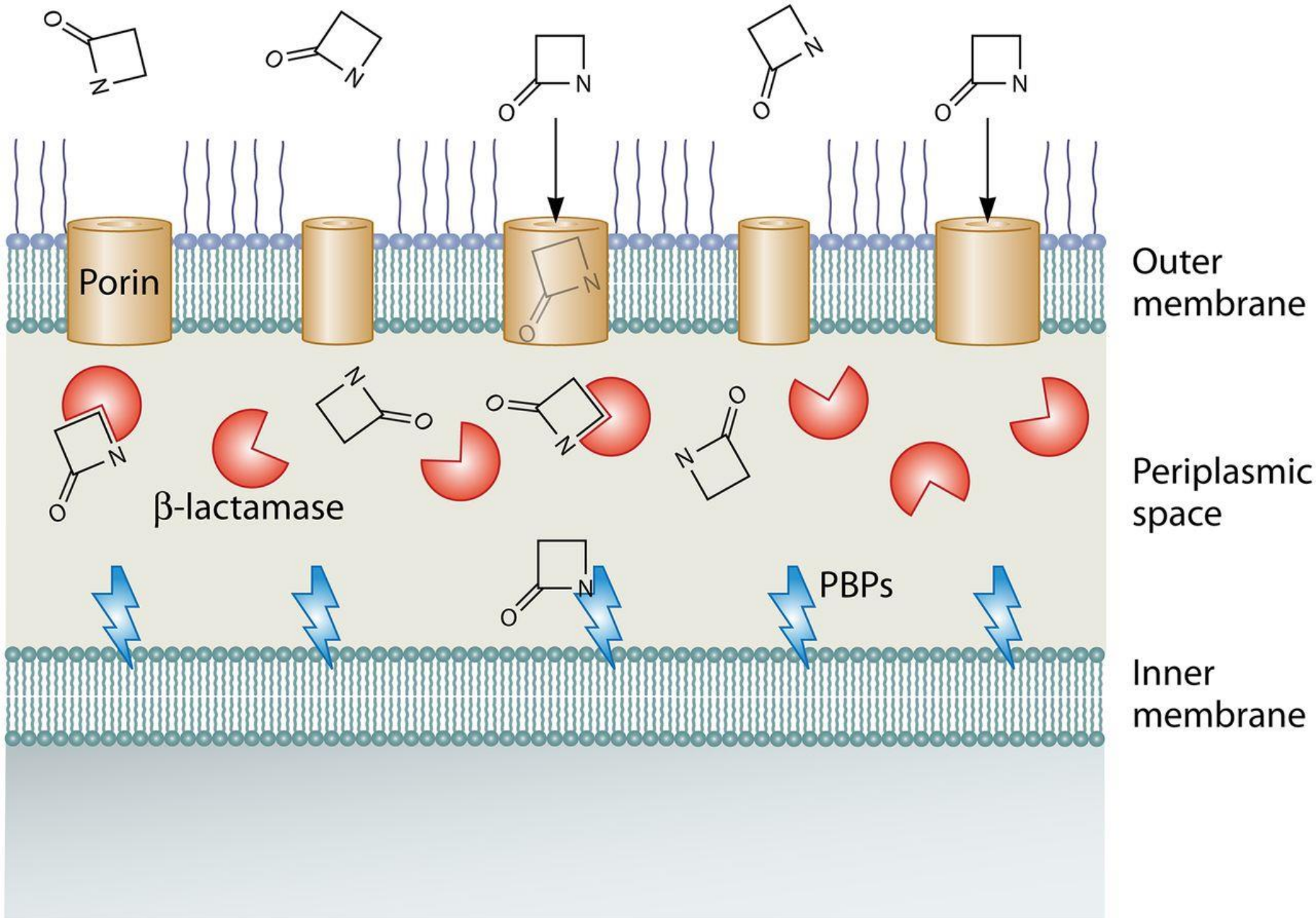

Porin
β-lactamase
PBPs
Outer membrane
Periplasmic space
Inner membrane

# WHAT ARE CRE/CPE ORGANISMS

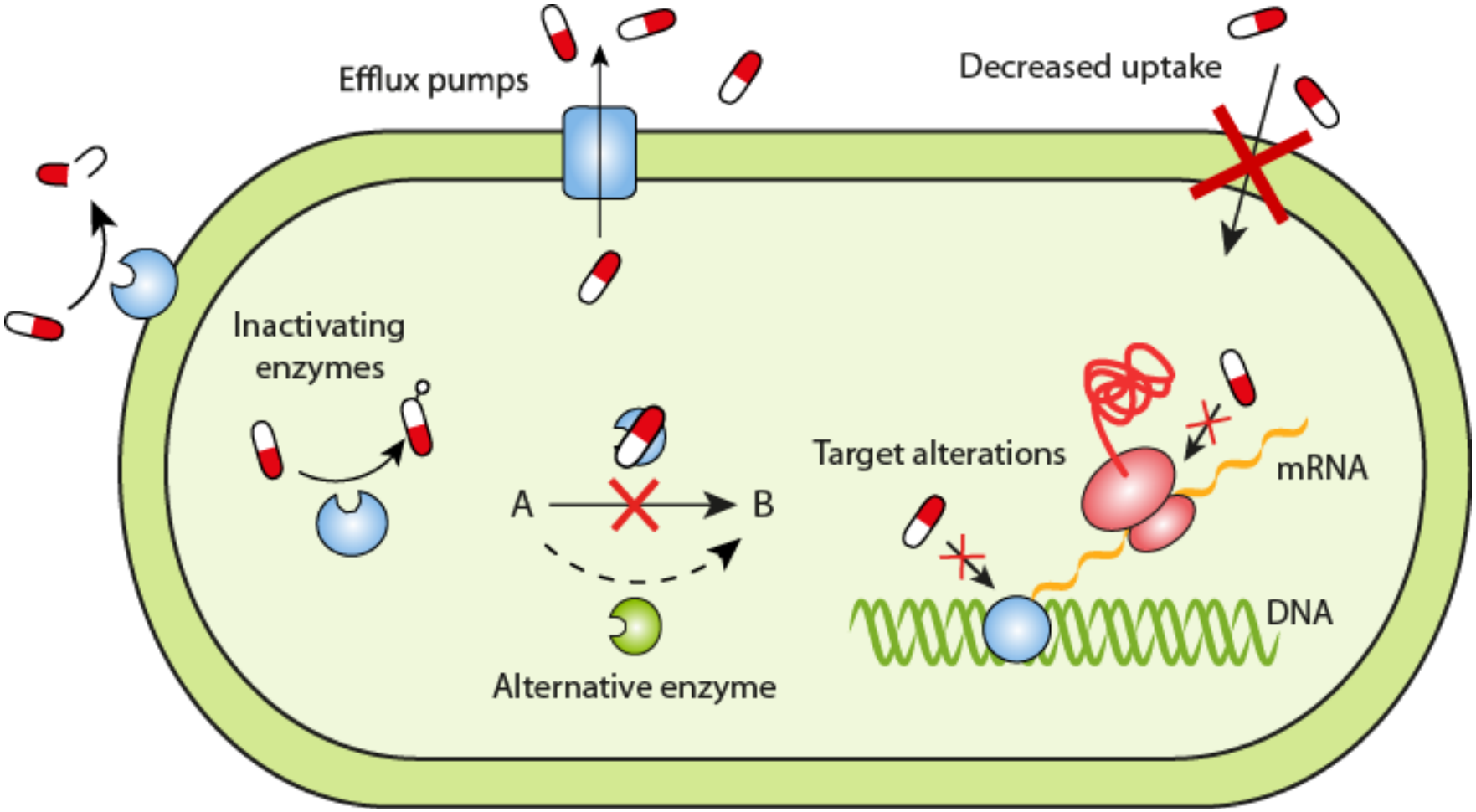
- CRE is the term most commonly used in our laboratory
- “Carbapenem Resistant Enterobacterales”
- CPE is an alternate and perhaps more accurate term for the organisms we are trying to isolate
- “Carbapenamase Producing Enterobacterales”
- Notice that this DOES NOT include Pseudomonads within this term
- CREs can be defined as been carbapenem-nonsusceptible whilst also being extended-spectrum cephalosporin-resistant

# A BREAKDOWN OF TERMS

- Carbapenem Resistant Enterobacterales

- Carbapenem – the group of antibiotics that the organisms is resistant to (Meropenem, Ertapenem, Imipenem)
- Resistant – this group of antibiotics is neither bacteriostatic or bactericidal i.e no affect on the organism
- Enterobacterales – the group of organisms (Coliforms)

- This term DOES NOT define by which mechanism these organisms are resistant and is therefore a broader term to encompass all Enterobacterales that are resistant to carbapenem antibiotics.
- Mechanisms can include porin loss and upregulated efflux of carbapenems


Efflux pumps
Decreased uptake
Inactivating
enzymes
A
B
Alternative enzyme
Target alterations
mRNA
DNA

# A BREAKDOWN OF TERMS

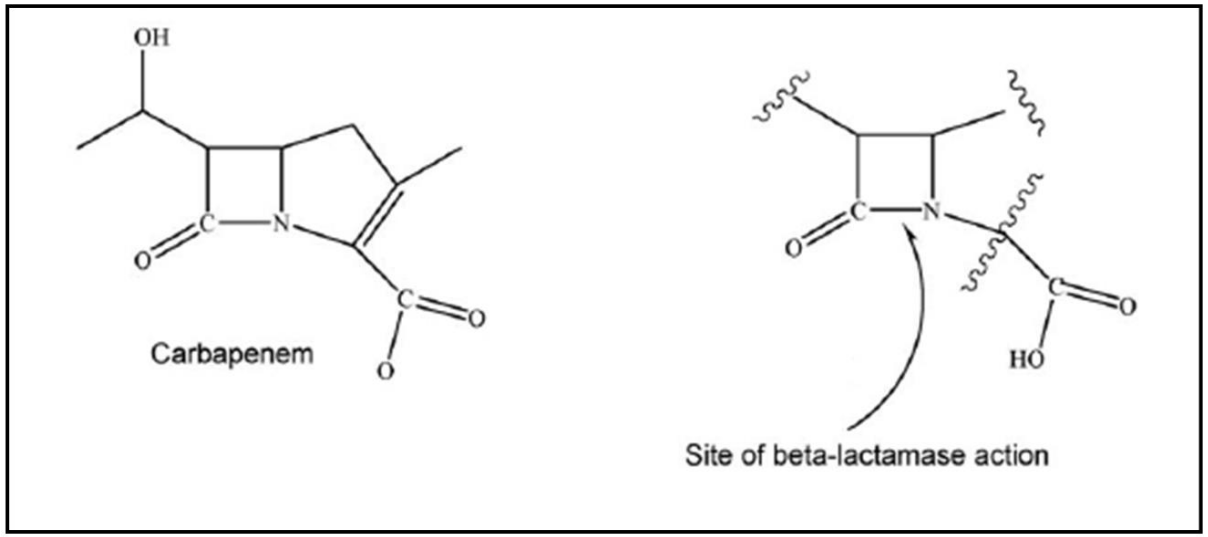
- Carbapenamase Producing Enterobacterales

- Carbapenemase –An enzyme (beta-lactamase) designed to hydrolyse carbapenem antibiotics
- Producing – The enzyme is produced by the organism
- Enterobacterales – the group of organisms (Coliforms)

- This term is used for organisms which have a defined Carbapenamase mechanism and the genes for such have been confirmed.

# CARBAPENAMASES – HOW DO THEY WORK

- Carbapenems work by hydrolysing the carbapenem and therefore inactivating them through the cleavage of their beta-lactam ring
- Carbapenamases are enzymes and are classified into 4 groups based on several criteria, one of which being the molecular composition of their active site.
- Most carbapenemases will have a serine active site
- Metallo-betalactamases have require zinc ions in their active site and therefore differ from other carbapenemases.



# SO, WHY THE CONCERN?

- Carbapenem antibiotics are typically seen as a last resort for treating infections, so resistance to these may lead medical staff to be out of options in terms of treatments.
- Carbapenemase genes are highly transmissible. This can be through horizontal gene transfer, integrons or finally via plasmid mediated transfer.
- Because transfer of genes can occur it is important for infection control teams to be notified of any potential CPE carrier as soon as possible in order to isolate the individual and prevent outbreaks particularly in areas where patients are immunocompromised.

- Agar contains a “modified carbapenem antibiotic formula” in order to detect the presence of CREs along with indicators to allow colour detection of organisms.
- E.coli grow pink, KESC group organisms grow blue and non-CRE organisms such as Acinetobacter and Stenotrophomonas grow white.

# FOLLOW UP WORK

- Any isolate grown on the CRE media must be identified using MALDI-TOF
- E.coli and KESC group organisms must all be followed up with VITEK sensitivities
- Pseudomonas sp. require follow up work
- Stenotrophomonas isolates that are intrinsically resistant to carbapenems do not require follow up and the results can go out as CRE negative.
- Acinetobacter species are intrinsically resistant to Ertapenem and it is not recommended in the SMI to carry out any further work on these isolates.

# SENSITIVITIES

- Meropenem is recommended as the marker for CRE activity for all laboratories as part of the SMI.
- Meropenem is the midway point between sensitivity and selectivity out of all the carbapenem antibiotics (Ertapenem is more sensitive, Imipenem is more selective) hence we why use a meropenem e-test to confirm resistance before sending an isolate away for further testing.
- Within a VITEK report, we are looking for several things when deciding if an isolate is a true CRE or not: High MIC resistance to carbapenem (particularly meropenem and imipenem), cephalosporin resistance and potential resistance to Aztreonam.

Organism Quantity:

**Selected Organism: Klebsiella pneumoniae ssp pneumoniae**

| | |
|---|---|
| **Comments:** | ***AMP C POSITIVE***<br>? Carbapenemase producer- follow cpe flowchart |

| | | | | | |
|---|---|---|---|---|---|
| **Identification Information** | **Card:** | GN | **Lot Number:** | 2411758203 | **Expires:** Sep 19, 2022 13:00 BST |
| | **Status:** | Final | **Analysis Time:** | 7.98 hours | **Completed:** Jul 14, 2022 21:25 BST |
| **Organism Origin** | VITEK 2 | | | | |
| **Selected Organism** | 98% Probability **Klebsiella pneumoniae ssp pneumoniae** | | | | |
| | Bionumber: 6607735573565152 Confidence: Excellent identification | | | | |
| **Analysis Organisms and Tests to Separate:** | | | | | |
| **Analysis Messages:** | | | | | |
| **Contraindicating Typical Biopattern(s)** | | | | | |
| Klebsiella pneumoniae ssp pneumoniae URE(76), | | | | | |

| | | | | | |
|---|---|---|---|---|---|
| **Susceptibility Information** | **Card:** | AST-N350 | **Lot Number:** | 7901855503 | **Expires:** Dec 25, 2022 12:00 GMT |
| | **Status:** | Final | **Analysis Time:** | 9.45 hours | **Completed:** Jul 14, 2022 23:00 BST |

| Antimicrobial | MIC | Interpretation | Antimicrobial | MIC | Interpretation |
|---|---|---|---|---|---|
| Ampicillin | >= 32 | R | Aztreonam | 16 | R |
| Amoxicillin/Clavulanic Acid | >= 32 | R | Ertapenem | 2 | R |
| Piperacillin/Tazobactam | >= 128 | R | Meropenem | >= 16 | R |
| Cefuroxime | >= 64 | R | Amikacin | <= 2 | S |
| Cefuroxime Axetil | >= 64 | R | Gentamicin | 4 | *R |
| Cefoxitin | >= 64 | R | Tobramycin | 8 | R |
| Cefotaxime | >= 64 | R | Ciprofloxacin | <= 0.25 | S |
| Ceftazidime | >= 64 | R | Tigecycline | <= 0.5 | S |
| Cefepime | >= 32 | R | Trimethoprim/ Sulfamethoxazole | <= 20 | S |

*= AES modified **= User modified

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# CEPHEID GENE XPERT CARBA-R


- Rapid “big 5” gene detection within one hour
- KPC, NDM, IMP, VIM, OXA-48
- Can test both the isolate and directly from a dry swab
- Can be useful in the event of an outbreak
- Downside is that if the organism does not have a “big 5” carbapenemase it will still need sending to the reference laboratory
- It is still important to culture the specimen to confirm the result is correct and if the bacteria is still present
- Similar testing can be done on other PCR platforms

# THANK YOU ☺