



# DRUG-RESISTANT *ACINETOBACTER BAUMANNII* – A GROWING SUPERBUG POPULATION

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Technical Writer

March 13<sup>th</sup> 2014



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# ATCC

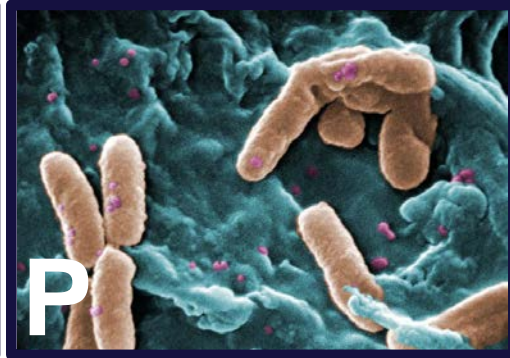
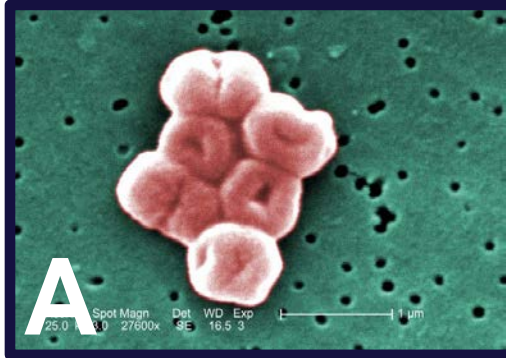
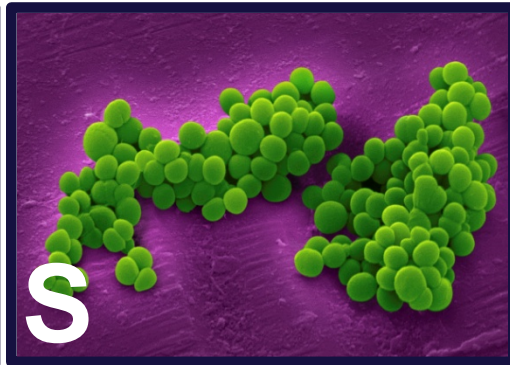
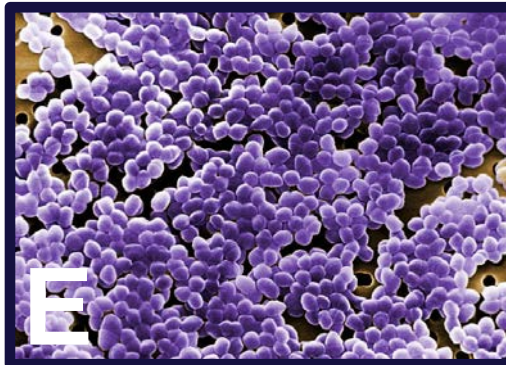
- Founded in 1925, ATCC is a non-profit organization with headquarters in Manassas, VA
- ATCC serves and supports the scientific community with industry-standard products and innovative solutions
- World's leading biological resource center and provider of biological standards
- Broad range of biological materials
  - Microorganisms
  - Cell lines
  - Derivatives
  - Bioproducts





# Drug-resistance

- Drug-resistant bacteria are an emerging threat.
- Bad Bugs, No Drugs = No “ESKAPE”



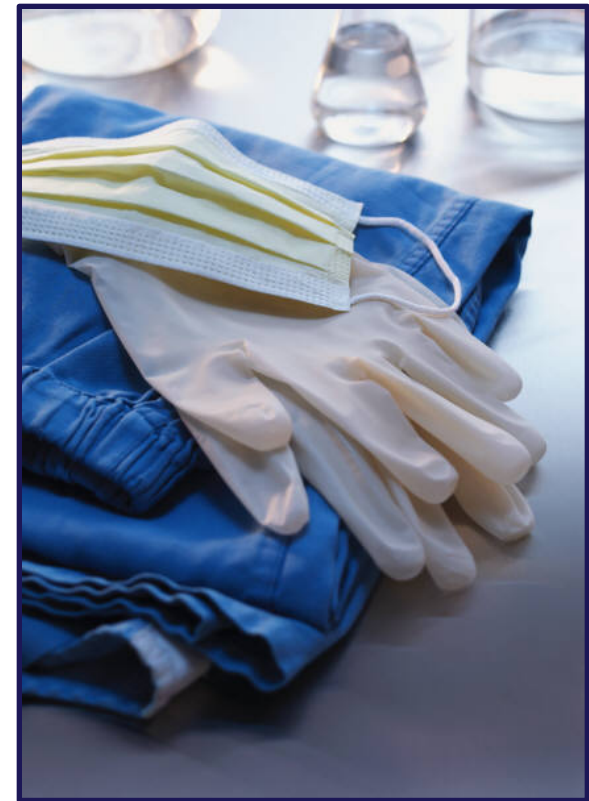
# Antibiotic resistance – Evolution & spread

## Evolution of MDR strains

- Inadequate infection control practices
- Overuse of antibiotics
- Misuse of antibiotics

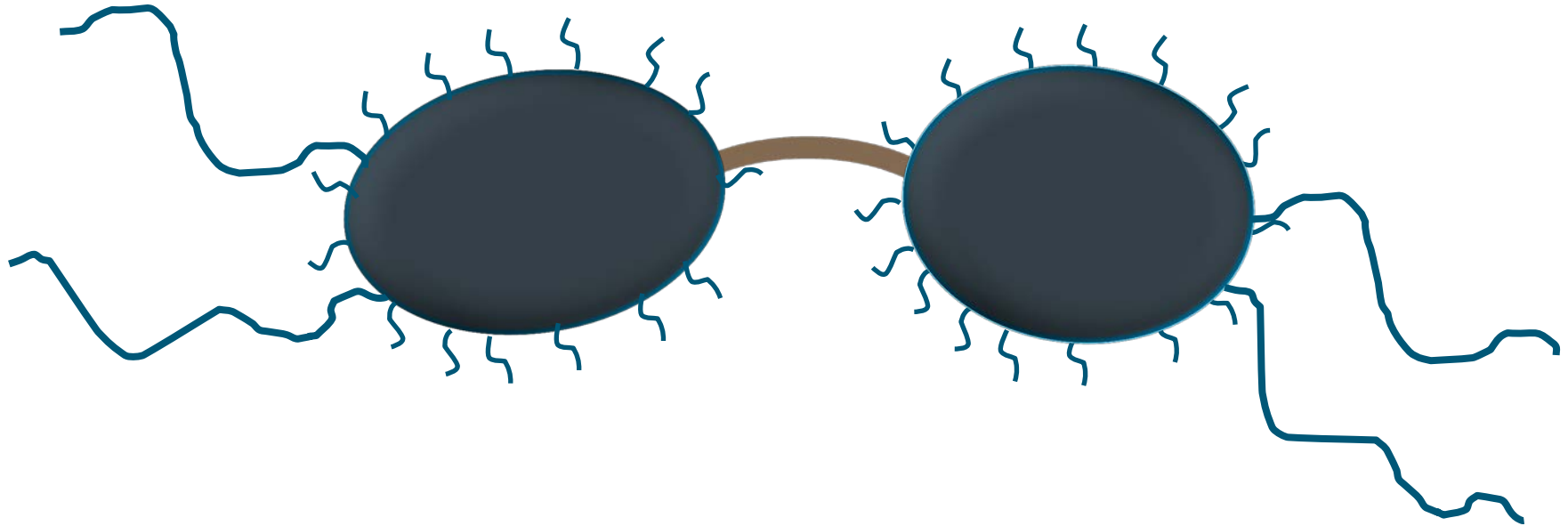
## Dissemination within and between patients

- Invasive medical devices and procedures
- Inadvertent transmission
- Patient transfer between healthcare facilities
- Global travel and medical tourism



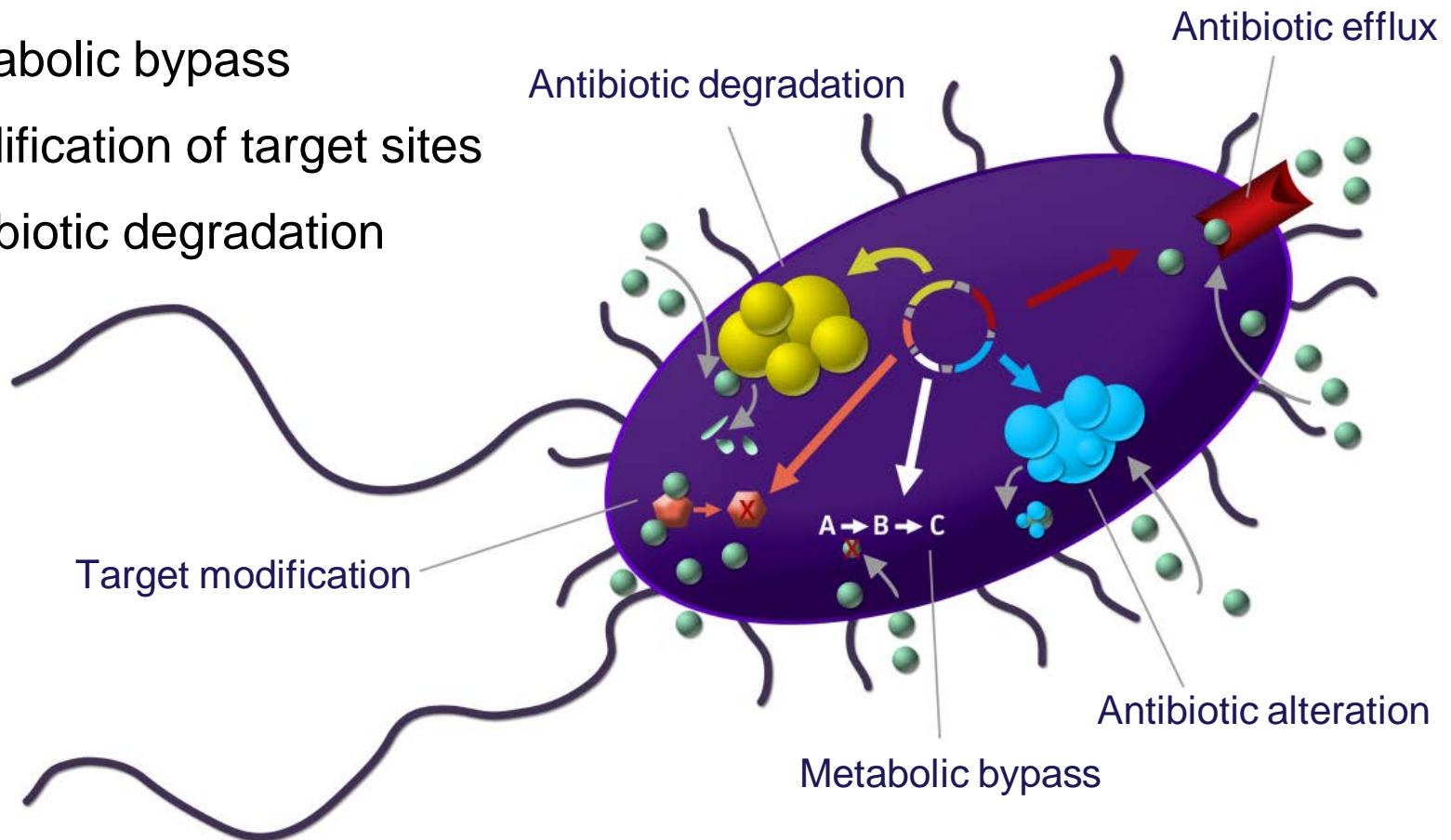
# Antibiotic resistance – Evolution & spread

- Inherent resistance
- Genetic mutation
- Horizontal gene transfer



# Antibiotic resistance – Mechanisms

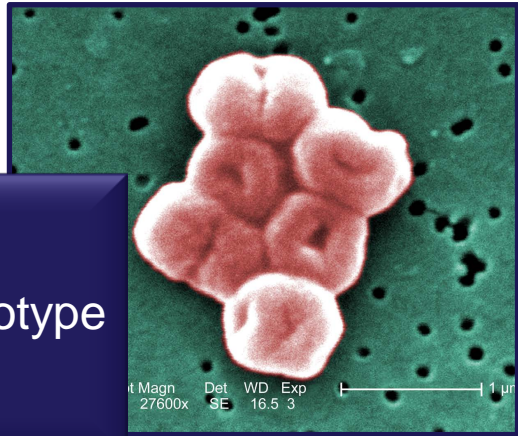
- Reduced drug accumulation
- Antibiotic alteration
- Metabolic bypass
- Modification of target sites
- Antibiotic degradation





# *Acinetobacter baumannii*

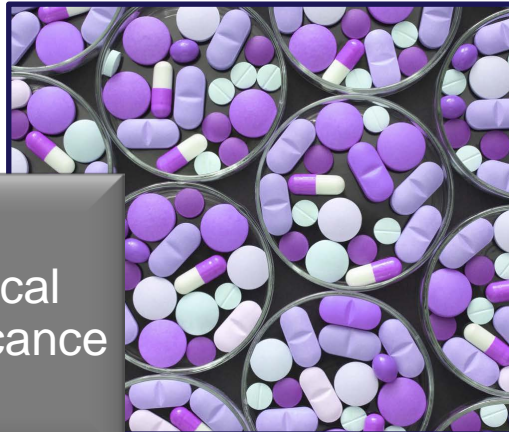
Phenotype



Natural habitat



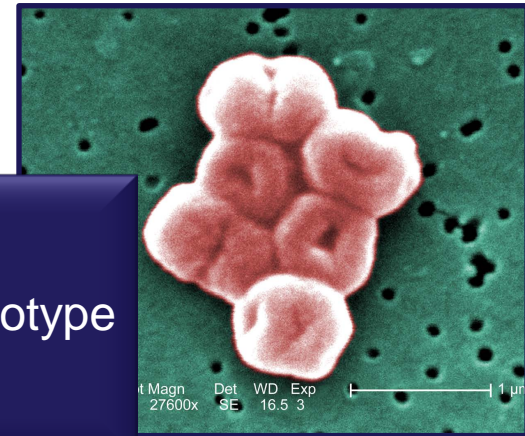
Clinical significance



# *Acinetobacter baumannii*

- Grows at various temperatures
- Resistant to low humidity
- Survives on a variety of surfaces

Phenotype





# *Acinetobacter baumannii*

- Grows at various temperatures
- Resistant to low humidity
- Survives on a variety of surfaces

- Aquatic environments
- Soil
- Moist tissues

Natural  
habitat



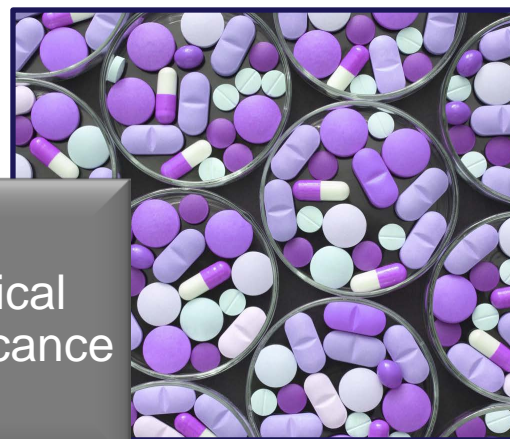
# *Acinetobacter baumannii*

- Grows at various temperatures
- Resistant to low humidity
- Survives on a variety of surfaces

- Aquatic environments
- Soil
- Moist tissues

- Opportunistic pathogen
- Nosocomial infections
- Drug-resistance

Clinical  
significance

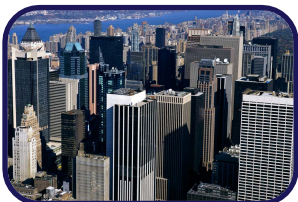


# *Acinetobacter baumannii* – Infections



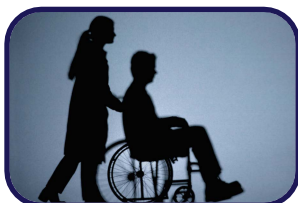
## Manifestation

- Pneumonia, bacteremia, meningitis, urinary tract infection, central venous catheter-related infection, and wound infection



## Community-acquired infections

- May be related to underlying conditions such as alcoholism, diabetes, or cancer



## Hospital-acquired infections

- Acquired by healthy or immunologically compromised patients
- Associated with wounds and invasive procedures



## Wartime-acquired infections

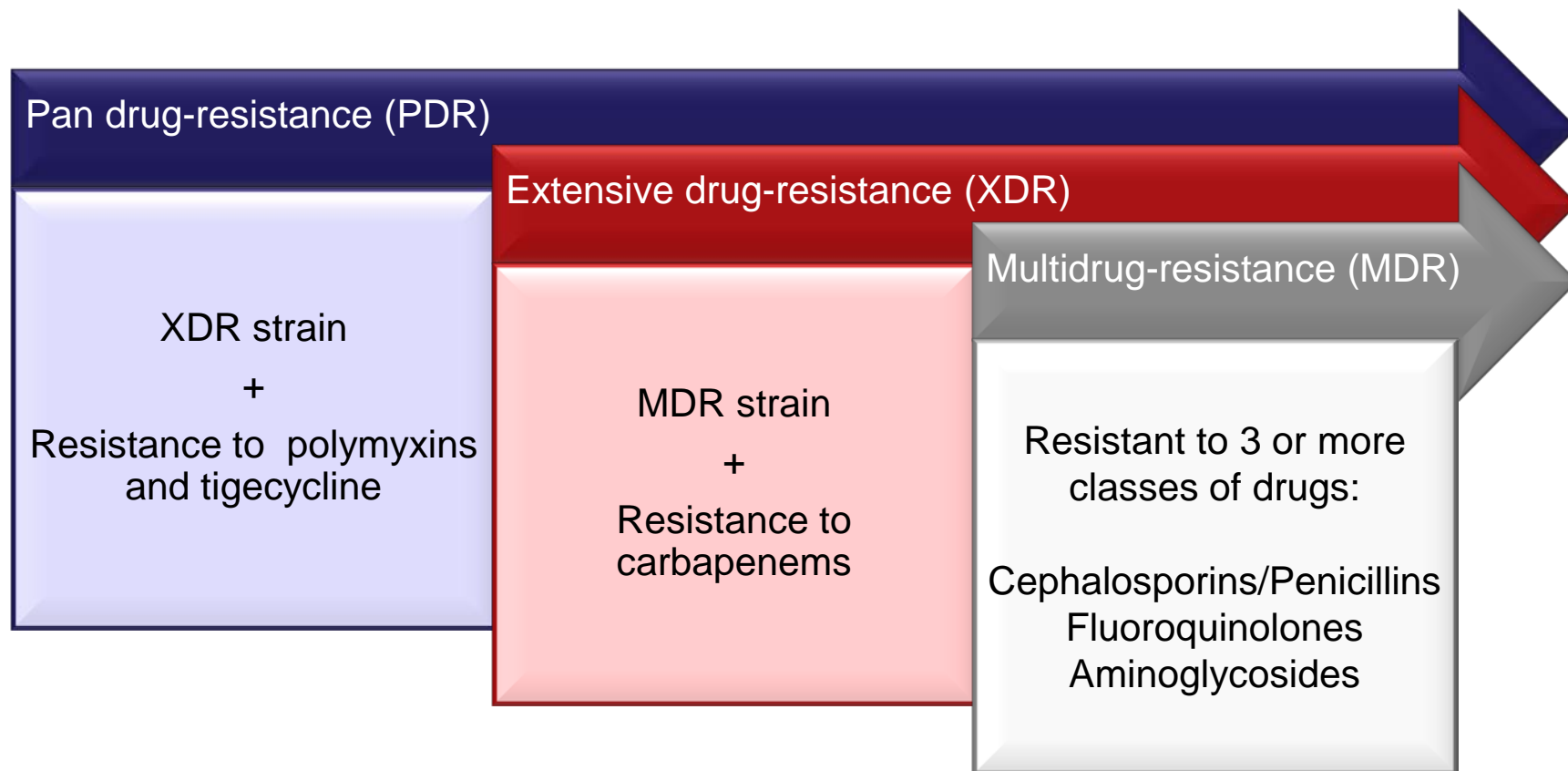
- Associated with wounded soldiers in non-native conflict zones



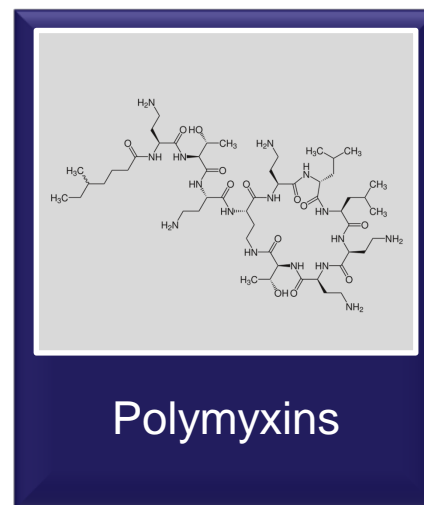
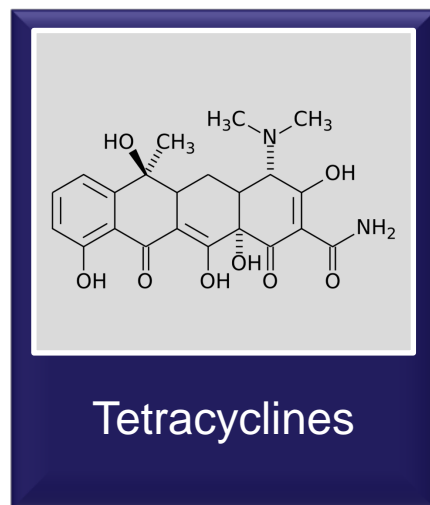
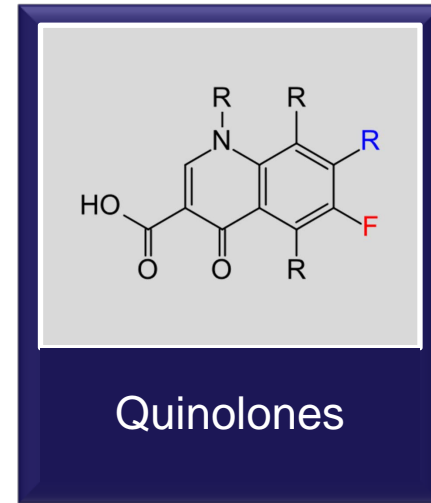
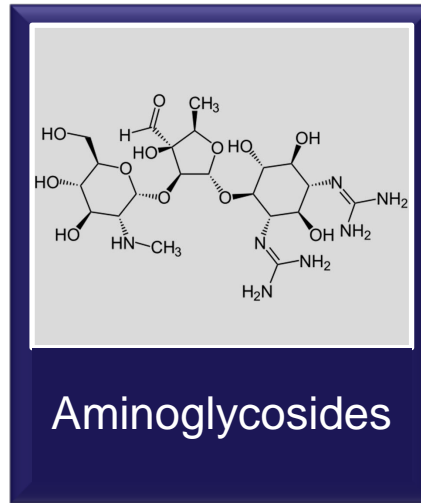
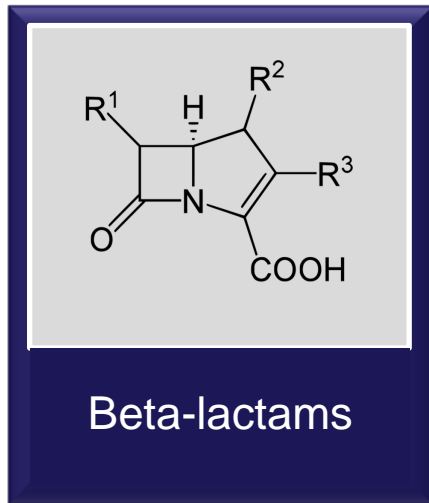
# Antibiotic resistance – Definitions



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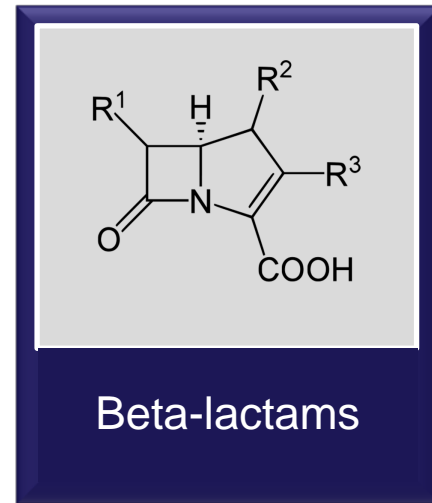
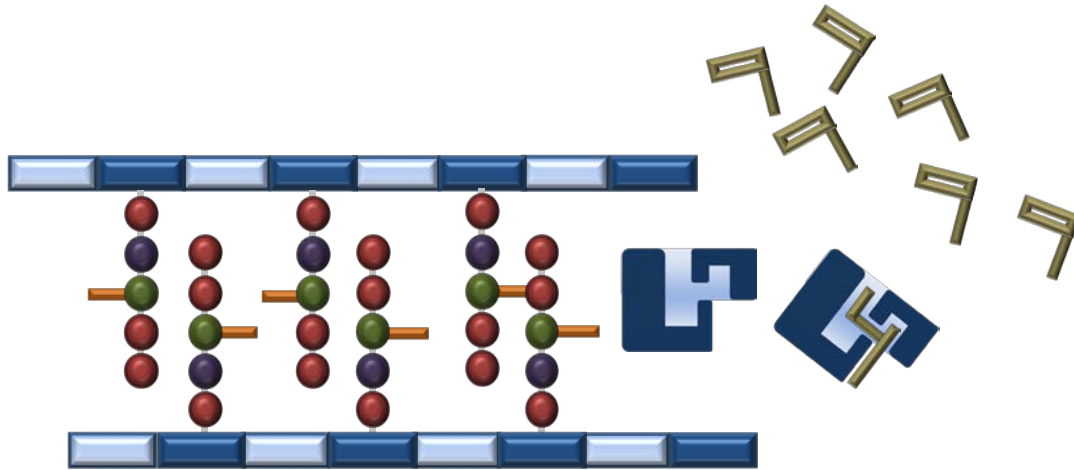


# Antibiotic resistance in *A. baumannii*





# Antibiotic resistance in *A. baumannii*



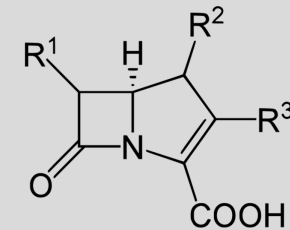
# Antibiotic resistance in *A. baumannii*

AdeABC efflux pump

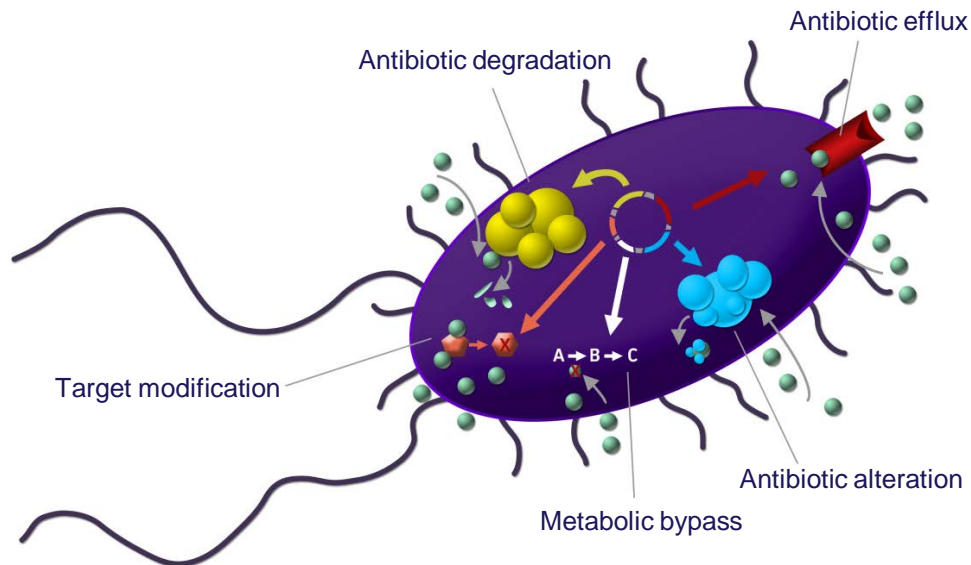
Reduction in porin number

Reduced penicillin binding protein expression

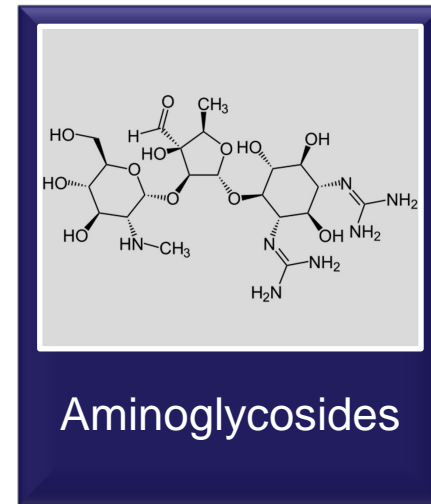
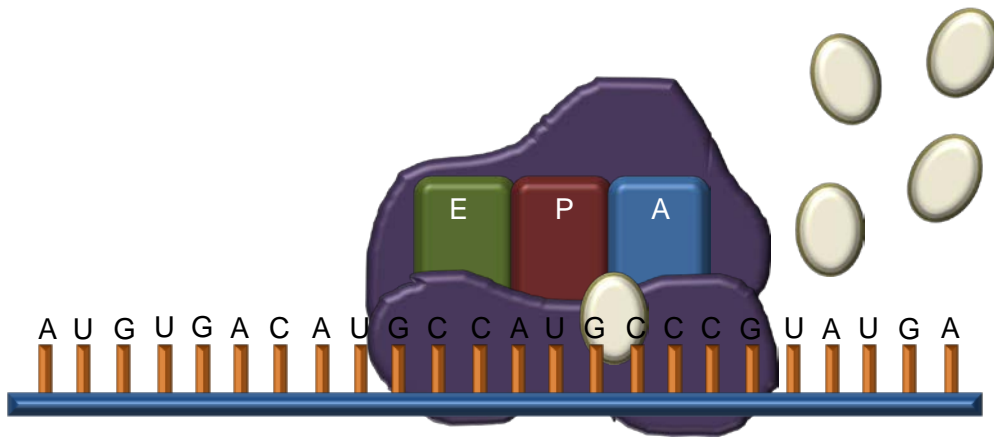
Beta-lactamases



Beta-lactams



# Antibiotic resistance in *A. baumannii*

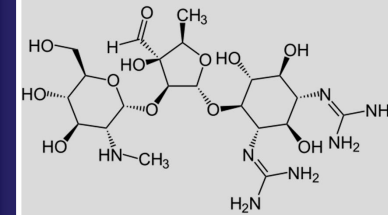




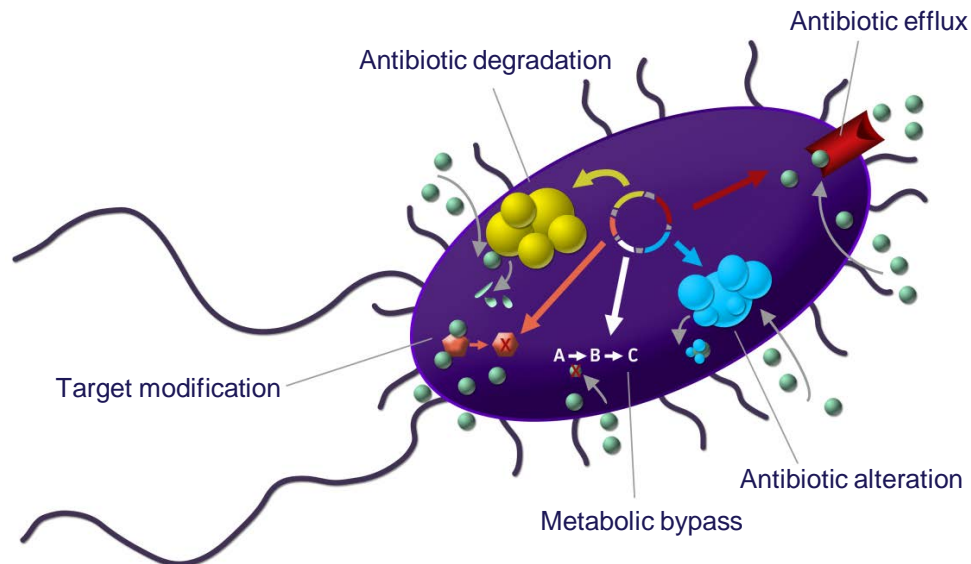
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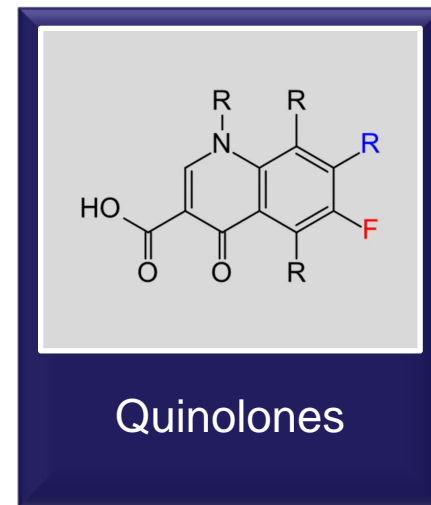
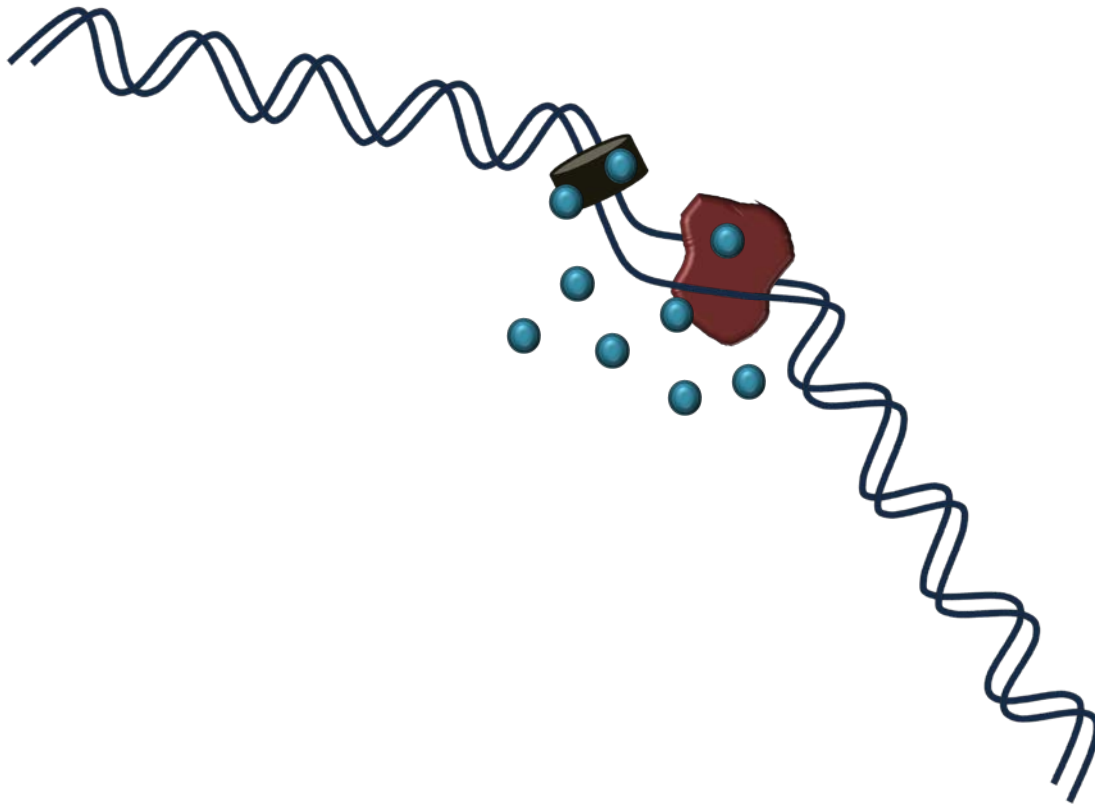
Aminoglycoside modifying enzymes



Aminoglycosides

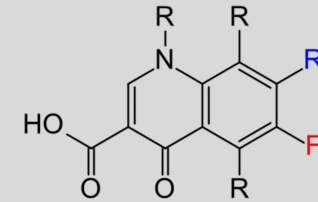


# Antibiotic resistance in *A. baumannii*



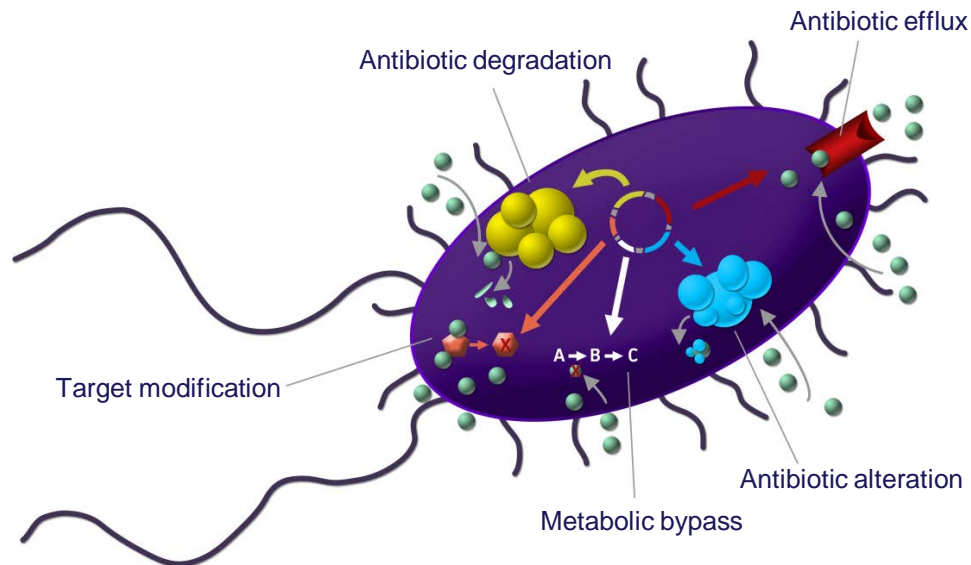
# Antibiotic resistance in *A. baumannii*

AdeABC efflux pump



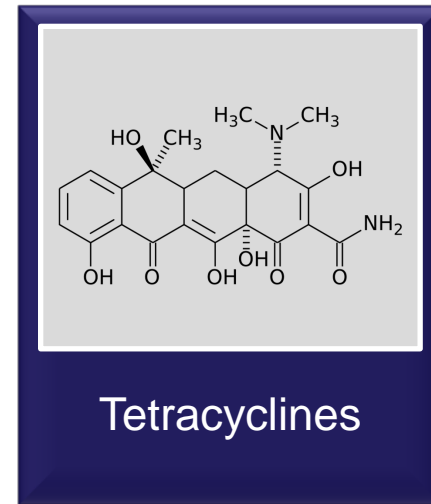
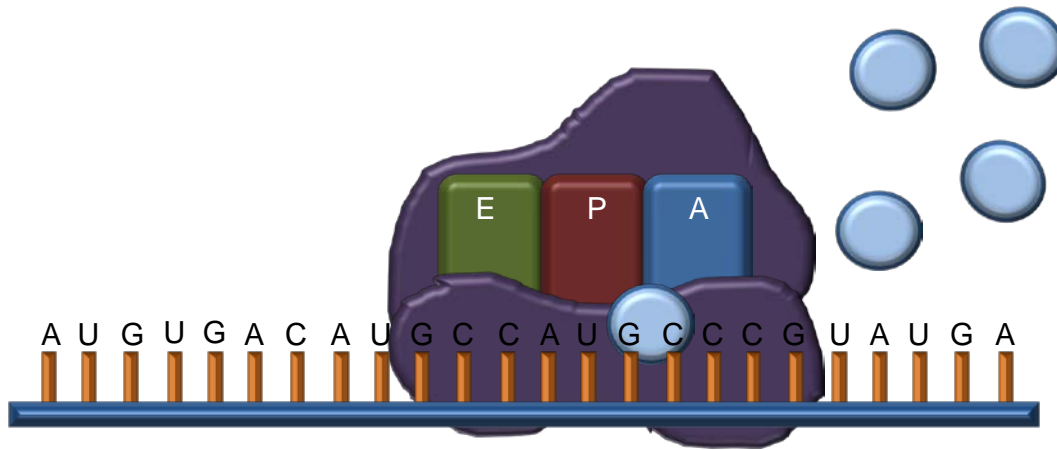
Quinolones

Modification of the genes encoding the DNA gyrase or topoisomerase IV





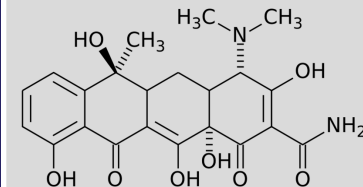
# Antibiotic resistance in *A. baumannii*



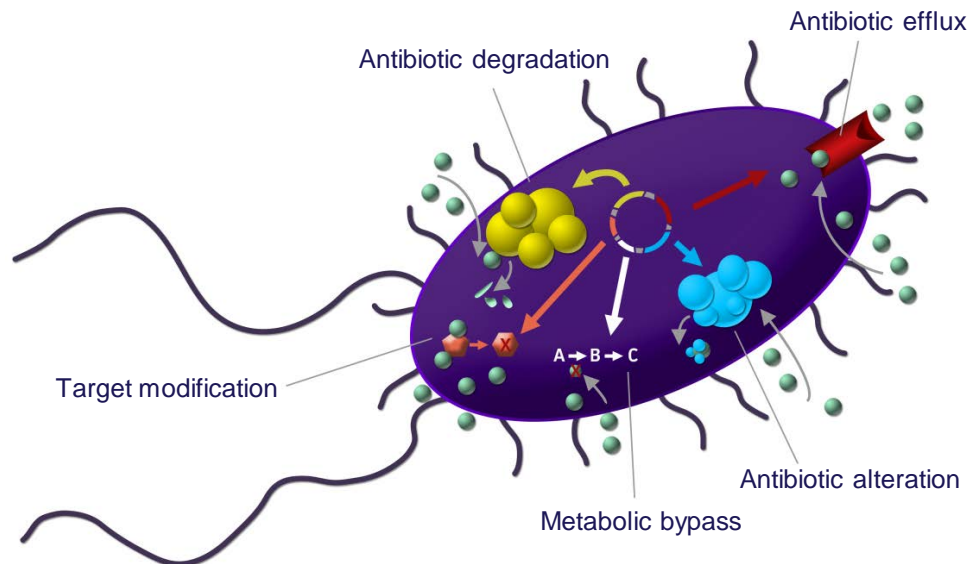
# Antibiotic resistance in *A. baumannii*

TetA and TetB efflux pumps

Ribosomal protection protein



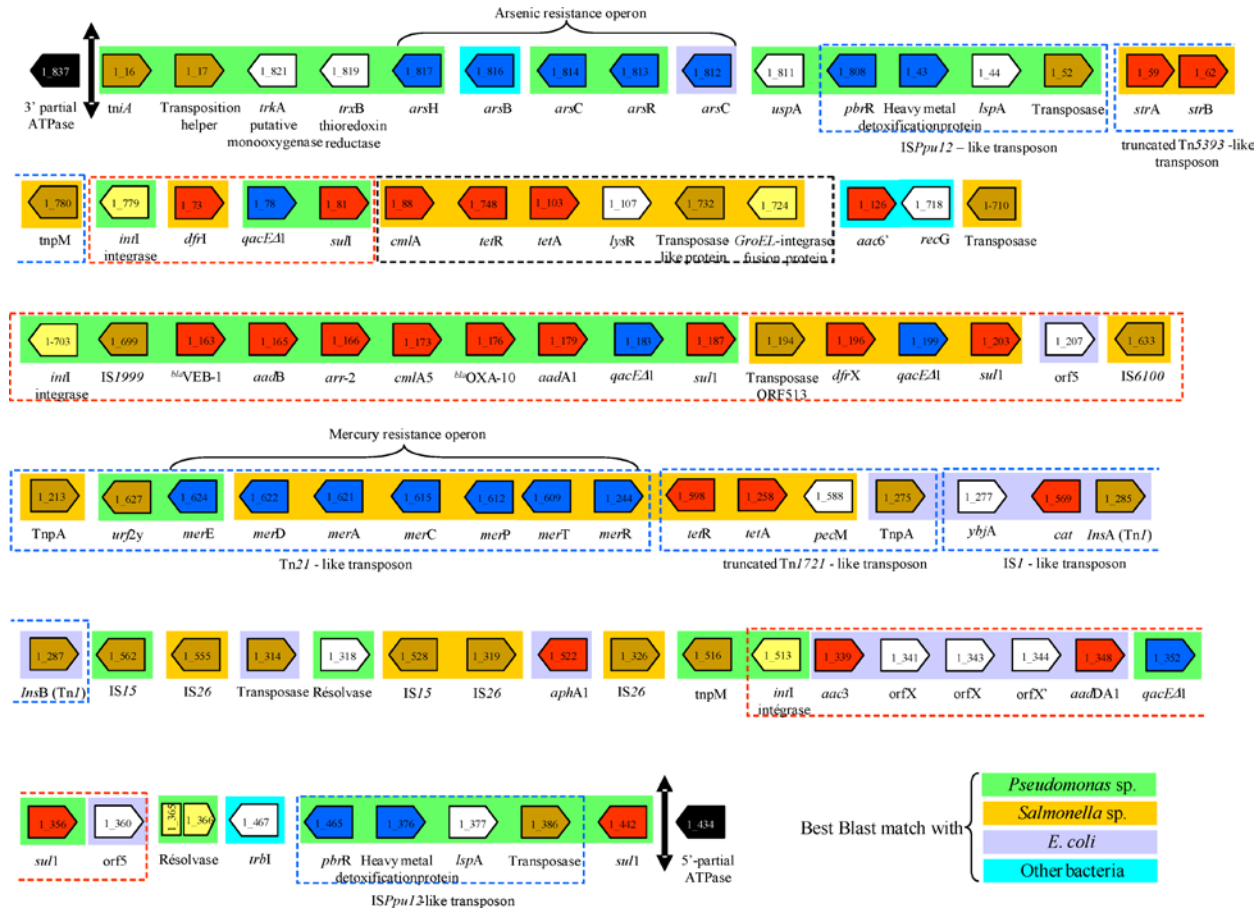
Tetracyclines







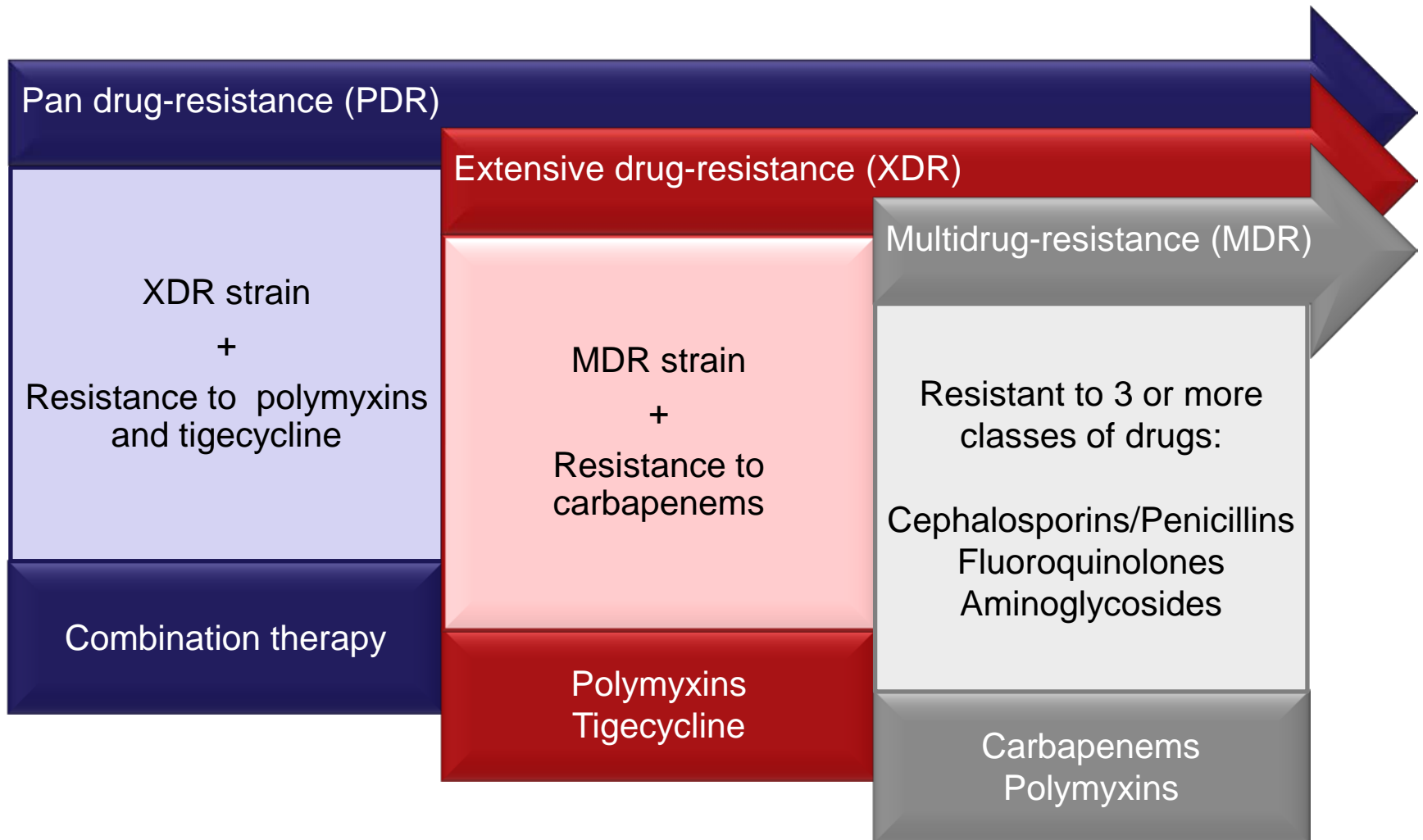
# Antibiotic resistance in *A. baumannii*



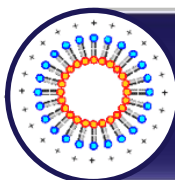
**Figure 2.** Layout of the Complete AbaR1 Inserted into the AYE strain ATPase-Encoding Gene



# Therapeutics



# Emerging therapeutic approaches



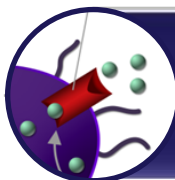
## Vancomycin encapsulated in fusogenic liposomes

Nicolosi D, *et al.* *Int. J. Antimicrob. Agent* 35(6): 553-558, 2010.



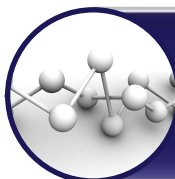
## Antimicrobial peptides

Routsias JG, *et al.* *Peptides* 31(9): 1654-1660, 2010.



## Efflux pump inhibitors

Pannek S, *et al.* *J. Antimicrob. Chemother.* 57(5): 970-974, 2006.



## Antisense agents (e.g. RNAi)

Woodford N, Wareham DW. *J. Antimicrob. Chemother.* 63(2): 225-229, 2009.

# Prevention and control

Determine  
organism-  
specific  
risks



Determine  
patient-  
specific  
risks



Develop a  
plan



# Prevention and control

- Geographical location of bacteria
- Hospital-specific localization

Determine  
organism-  
specific  
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# Prevention and control

- Geographical location of bacteria
- Hospital-specific localization

- Length of stay
- Procedure performed
- Treatment

Determine  
patient-  
specific  
risks





# Prevention and control

- Geographical location of bacteria
- Hospital-specific localization

- Length of stay
- Procedure performed
- Treatment

- Implementation of new practices to reduce the occurrence of infection

Develop a plan



# Prevention and control



Improve sanitation procedures and barrier precautions



Reduce patient-to-patient contact



Use disposable equipment



Limit indwelling devices



Establish a surveillance plan



Practice antimicrobial stewardship

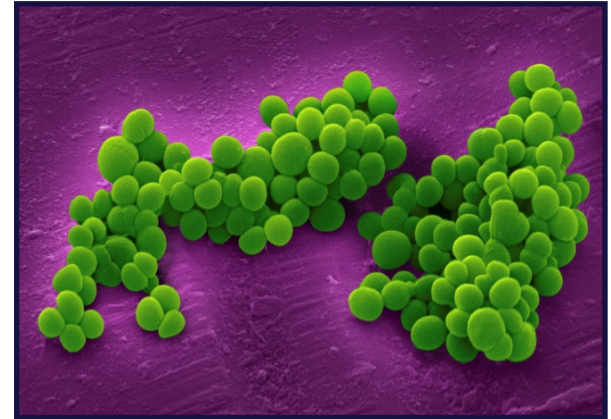
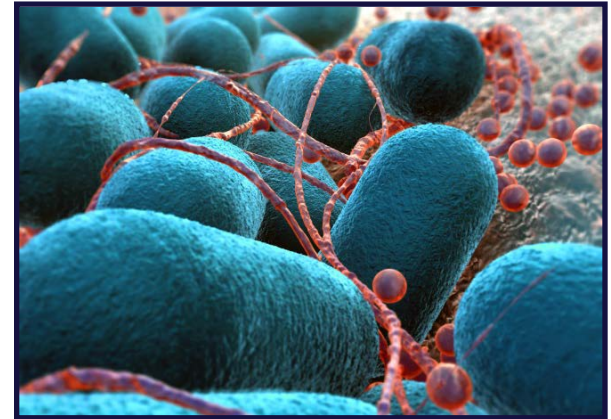
# ATCC – Aiding the scientific community

ATCC provides top-quality, authenticated reference strains and associated molecular materials

Enhance diagnostics

Analyze novel therapeutics

Improve sterility protocols



# ATCC – *Acinetobacter baumannii*

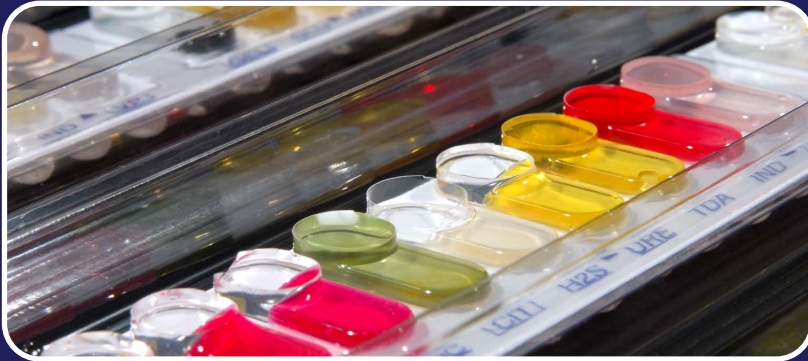
## Drug-Resistant *Acinetobacter baumannii* Research Materials

ATCC® No.	Species	Designation	Isolation
BAA-1605™	<i>Acinetobacter baumannii</i>	–	Human sputum
BAA-1789™	<i>Acinetobacter baumannii</i>	–	Tracheal aspirate
BAA-1790™	<i>Acinetobacter baumannii</i>	–	Sputum
BAA-1791™	<i>Acinetobacter baumannii</i>	–	Induced sputum
BAA-1792™	<i>Acinetobacter baumannii</i>	–	Sputum
BAA-1793™	<i>Acinetobacter baumannii</i>	–	Sputum
BAA-1794™	<i>Acinetobacter baumannii</i>	–	Sputum
BAA-1795™	<i>Acinetobacter baumannii</i>	–	Nasotracheal aspirate
BAA-1796™	<i>Acinetobacter baumannii</i>	–	Sputum
BAA-1797™	<i>Acinetobacter baumannii</i>	–	Human blood
BAA-1798™	<i>Acinetobacter baumannii</i>	–	Sputum
BAA-1799™	<i>Acinetobacter baumannii</i>	–	Sputum
BAA-1800™	<i>Acinetobacter baumannii</i>	–	Deep trachea

Drug-resistant clinical isolates

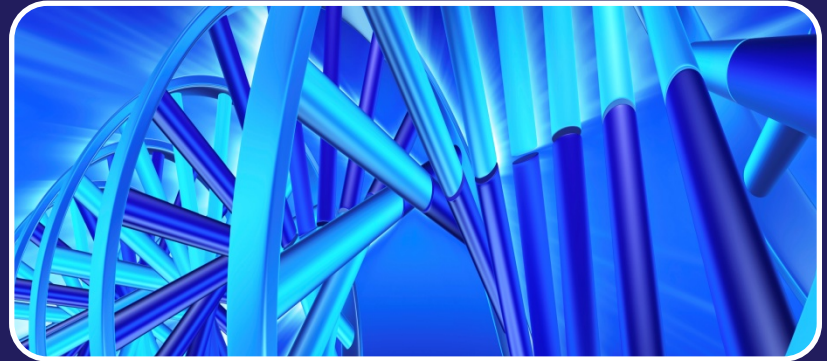


# ATCC – Strain authentication



## Phenotypic analysis

Colony morphology  
Bacterial morphology  
Biochemical analysis



## Genotypic analysis

16S rRNA sequencing  
Ribotyping



# ATCC – Verification of drug-resistance



## Antibiotic profiling using VITEK

Penicillins

Aminoglycosides

Cephalosporins

Tetracycline

Carbapenems

Tigecycline

Quinolones

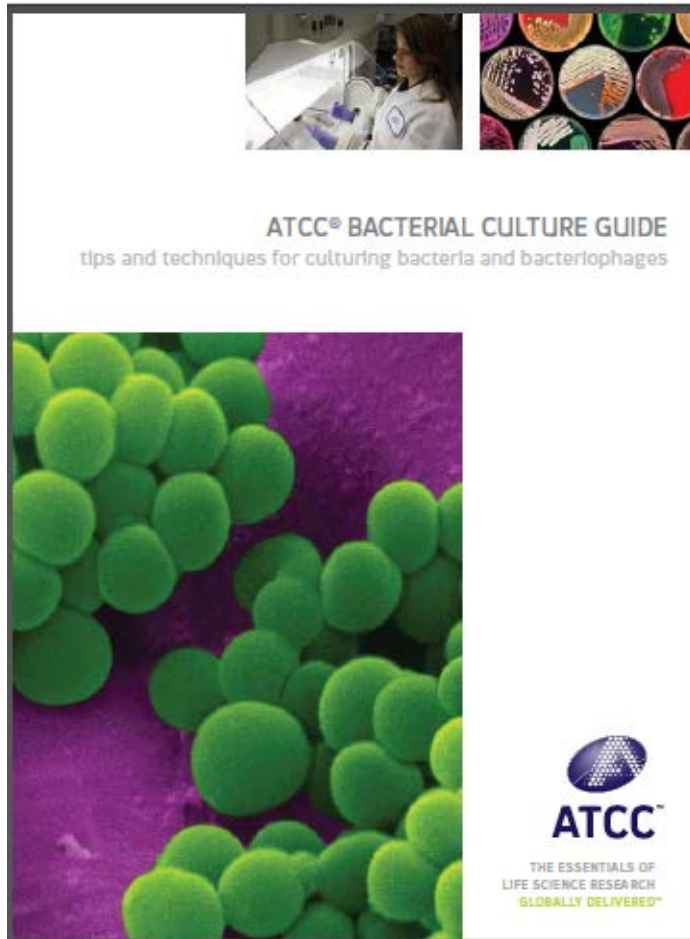
# ATCC – *Acinetobacter baumannii*

ATCC® Drug-Resistant *Acinetobacter baumannii* - Antibiotic Profiles

	BAA-1605™	BAA-1789™	BAA-1790™	BAA-1791™	BAA-1792™	BAA-1793™	BAA-1794™	BAA-1795™	BAA-1796™	BAA-1797™	BAA-1798™	BAA-1799™	BAA-1800™
Penicillins	Amoxicillin/Clavulanic Acid	NT	R	R	R	R	R	R	R	R	R	R	R
	Ticarcillin	R	I	R	R	R	R	R	R	R	R	R	R
	Ticarcillin/Clavulanic acid	NT	I	R	R	R	R	R	R	R	R	R	R
	Piperacillin	R	R	R	R	R	R	R	R	R	R	R	R
	Piperacillin/Tazobactam	NT	R	R	R	R	R	R	R	R	R	R	R
	Ampicillin	NT	R	R	R	R	R	R	R	R	R	R	R
	Ampicillin/Sulbactam	NT	S	I	S	R	S	S	R	S	S	S	R
Cephalosporins	Cefalotin	NT	R	R	R	R	R	R	R	R	R	R	R
	Cefuroxime	NT	R	R	R	R	R	R	R	R	R	R	R
	Cefuroxime Axetil	NT	R	R	R	R	R	R	R	R	R	R	R
	Cefotetan	NT	R	R	R	R	R	R	R	R	R	R	R
	Cefpodoxime	NT	R	R	R	R	R	R	R	R	R	R	R
	Cefotaxime	NT	R	R	R	R	R	R	R	R	R	R	R
	Ceftizoxime	NT	R	R	R	R	R	R	R	R	R	R	R
	Cefazolin	NT	R	R	R	R	R	R	R	R	R	R	R
	Cefoxitin	NT	R	R	R	R	R	R	R	R	R	R	R
	Ceftazidime	R	R	R	R	R	R	R	R	R	R	R	R
	Ceftriaxone	NT	R	R	R	R	R	R	R	R	R	R	R
	Cefepime	R	R	R	R	R	R	R	I	R	R	R	R
	Carbapenems	Meropenem	NT	R	R	R	R	R	R	R	R	R	R
Imipenem		R	I	R	R	R	R	R	S	R	R	R	R
Quinolones	Nalidixic acid	NT	R	R	R	R	R	R	R	R	R	R	R
	Moxifloxacin	NT	R	R	R	R	R	R	R	R	R	R	R
	Norfloxacin	NT	R	R	R	R	R	R	R	R	R	R	R
	Ciprofloxacin	R	R	R	R	R	R	R	R	R	R	R	R
	Levofloxacin	NT	R	R	R	R	I	I	R	I	I	R	I

R = Resistant, S = Susceptible, I = Intermediate susceptibility, NT = Not tested

# Bacteriology guide



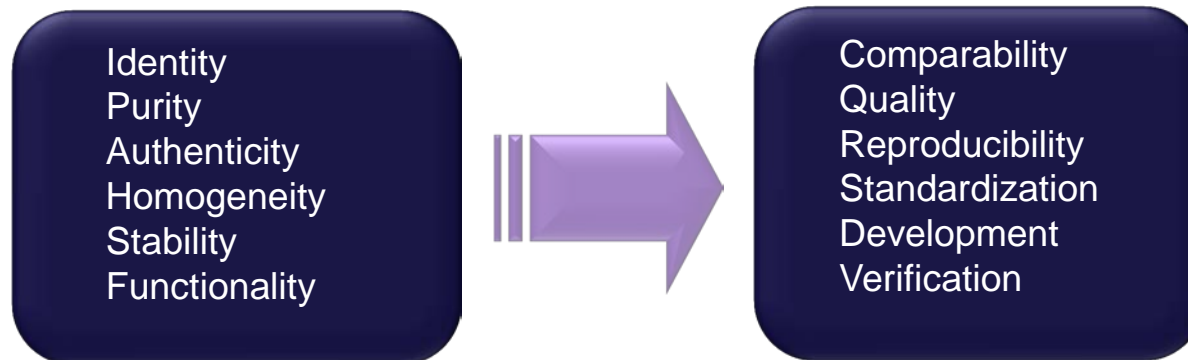
## Chapters included:

- Getting started with an ATCC bacterial strain
- Bacterial growth and propagation
- Growth media
- Preservation
- Biosafety and disposal
- Bacterial authentication
- Bacterial applications

Available on the ATCC website  
[www.atcc.org](http://www.atcc.org)

# Conclusion

- Multidrug-resistant, extensive drug-resistant, and pan drug-resistant *A. baumannii* strains are an emerging problem throughout the world
- ATCC acquires, authenticates, and distributes clinically-relevant strains that are essential to the scientific community
  - Phenotypic, genotypic, functional testing
- Drug-resistant strains of *A. baumannii* are now available at ATCC
  - Clinical strains
  - Antibiotic susceptibility profiles available





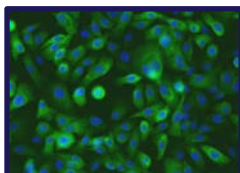
# Sources

- Durante-Mangoni E, Zarrilli R. Global Spread of Drug-resistant *Acinetobacter baumannii*. *Future Microbiol.* 6(4): 407-422, 2011.
- Manchanda V, Sanchaita S, Singh NP. Multidrug Resistant *Acinetobacter*. *J Glob Infect Dis.* 2(3): 291-304, 2010.
- Howard A, O'Donoghue M, Feeney A, Sleator RD. *Acinetobacter baumannii* – An emerging opportunistic pathogen. *Virulence* 3(3): 243-250, 2012.
- Maragakis LL, Perl TM. *Acinetobacter baumannii*: Epidemiology, Antimicrobial Resistance, and Treatment Options. *Antimicrobial Resistance*, Invited Article. April 2008.
- APIC. Guide to the elimination of multidrug-resistant *Acinetobacter baumannii* transmission in healthcare settings. 2010.
- Perez F, *et al.* Global Challenge of Multidrug-Resistant *Acinetobacter baumannii*. *Antimicrobial Agents and Chemotherapy* 51(10): 3471-3484, 2007.
- Fournier PE, *et al.* Comparative Genomics of Multidrug Resistance in *Acinetobacter baumannii*. *PLoS Genet* 2(1): e7, 2006.



# Thank you!

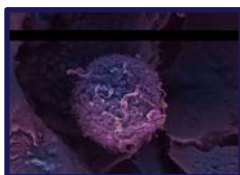
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**March 27, 2014**

**10:00 AM, 3:00 PM EST**

Dr. Chengkang Zhang will discuss hTERT immortalized cell lines and their use as relevant models for cancer research.



**April 24, 2014**

**10:00 AM, 3:00 PM EST**

Dr. Fang Tian will highlight cell lines that can be used to address recently identified genomic and clinical features of breast cancer subtypes.



**May 8, 2014**

**10:00 AM, 3:00 PM EST**

Liz Kerrigan will discuss the importance of molecular standards, and how their use can contribute to improvements in assay reproducibility and reliability.

**Thank you for joining today!**  
**Please send additional questions to [tech@atcc.org](mailto:tech@atcc.org)**