DRUG-RESISTANT ACINETOBACTER BAUMANNII – A GROWING SUPERBUG POPULATION

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Technical Writer
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• 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”

Photo credit: Janice Haney Carr
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

![Diagram of antibiotic resistance mechanisms](image-url)
Acinetobacter baumannii

Phenotype

Natural habitat

Clinical significance
**Acinetobacter baumannii**

- Grows at various temperatures
- Resistant to low humidity
- Survives on a variety of surfaces
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- 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
Antibiotic resistance – Definitions

Pan drug-resistance (PDR)

XDR strain
+ Resistance to polymyxins and tigecycline

Extensive drug-resistance (XDR)

MDR strain
+ Resistance to carbapenems

Multidrug-resistance (MDR)

Resistant to 3 or more classes of drugs:
Cephalosporins/Penicillins
Fluoroquinolones
Aminoglycosides

Antibiotic resistance in *A. baumannii*

- Beta-lactams
- Aminoglycosides
- Quinolones
- Tetracyclines
- Polymyxins
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](image)
Antibiotic resistance in *A. baumannii*
Antibiotic resistance in *A. baumannii*

- AdeABC efflux pump
- Aminoglycoside modifying enzymes
- Aminoglycosides

Antibiotic degradation
Antibiotic efflux
Target modification
Antibiotic alteration
Metabolic bypass
Antibiotic resistance in *A. baumannii*

Quinolones
Antibiotic resistance in *A. baumannii*

- **AdeABC efflux pump**
- **Modification of the genes encoding the DNA gyrase or topoisomerase IV**
- **Quinolones**

![Diagram showing the mechanisms of antibiotic resistance](image-url)
Antibiotic resistance in *A. baumannii*

**Tetracyclines**
Antibiotic resistance in *A. baumannii*

- TetA and TetB efflux pumps
- Ribosomal protection protein
- Tetracyclines

![Diagram showing antibiotic resistance mechanisms](image)
Antibiotic resistance in *A. baumannii*
Antibiotic resistance in *A. baumannii*

Lipopolysaccharide modification through acidification, acylation, or the presence of antigens that interfere with antibiotic binding.
Antibiotic resistance in *A. baumannii*

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

Therapeutics

Pan drug-resistance (PDR)

Extensive drug-resistance (XDR)

Multidrug-resistance (MDR)

XDR strain
+ Resistance to polymyxins
and tigecycline

MDR strain
+ Resistance to carbapenems

Resistant to 3 or more classes of drugs:
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Fluoroquinolones
Aminoglycosides

Polymyxins
Tigecycline

Carbapenems
Polymyxins

Combination therapy

Emerging therapeutic approaches

**Vancomycin encapsulated in fusogenic liposomes**

**Antimicrobial peptides**

**Efflux pump inhibitors**

**Antisense agents (e.g. RNAi)**
Prevention and control

Determine patient-specific risks

Determine organism-specific risks

Develop a plan
Prevention and control

- Geographical location of bacteria
- Hospital-specific localization

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- Geographical location of bacteria
- Hospital-specific localization

- Length of stay
- Procedure performed
- Treatment

Determine patient-specific risks
Prevention and control

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- 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

<table>
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<tr>
<th>ATCC® No.</th>
<th>Species</th>
<th>Designation</th>
<th>Isolation</th>
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<td>BAA-1605™</td>
<td><em>Acinetobacter baumannii</em></td>
<td>—</td>
<td>Human sputum</td>
</tr>
<tr>
<td>BAA-1789™</td>
<td><em>Acinetobacter baumannii</em></td>
<td>—</td>
<td>Tracheal aspirate</td>
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<td><em>Acinetobacter baumannii</em></td>
<td>—</td>
<td>Sputum</td>
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<td>—</td>
<td>Induced sputum</td>
</tr>
<tr>
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<td><em>Acinetobacter baumannii</em></td>
<td>—</td>
<td>Sputum</td>
</tr>
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<td><em>Acinetobacter baumannii</em></td>
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<tr>
<td>BAA-1800™</td>
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<td>—</td>
<td>Deep trachea</td>
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</tbody>
</table>
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
- Cephalosporins
- Carbapenems
- Quinolones
- Aminoglycosides
- Tetracycline
- Tigecycline
# ATCC – Acinetobacter baumannii

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

| ATCC® Strain Code | Amoxicillin/Clavulanic Acid | Ticarcillin | Ticarcillin/Clavulanic Acid | Piperacillin | Piperacillin/Tazobactam | Ampicillin | Ampicillin/Sulbactam | Cefalotin | Cefuroxime | Cefuroxime Axetil | Cefotetan | Cefpodoxime | Cefotaxime | Ceftizoxime | Cefazolin | Cefoxitin | Ceftazidime | Ceftriaxone | Cefepime | Meropenem | Imipenem | Nalidixic acid | Moxifloxacin | Norfloxacin | Ciprofloxacin | Levofloxacin |
|-------------------|-----------------------------|------------|-----------------------------|-------------|-------------------------|------------|----------------------|----------|-------------|----------------|---------|-------------|-----------|------------|-----------|----------|------------|----------|-------------|-----------|-----------|-------------|-------------|
| BAA-1605*         | NT                          | R          | R                            | R           | R                       | R          | NT                   | NT       | NT          | NT             | NT      | NT          | NT          | NT         | NT        | NT        | NT         | NT        | NT         | NT         | NT         |
| BAA-1790*         | R                           | I          | R                            | R           | R                       | R          | NT                   | NT       | NT          | NT             | NT      | NT          | NT          | NT         | NT        | NT        | NT         | NT        | NT         | NT         | NT         |
| BAA-1791*         | NT                          | I          | R                            | R           | R                       | R          | R                    | NT       | NT          | NT             | NT      | NT          | NT          | NT         | NT        | NT        | NT         | NT        | NT         | NT         | NT         |
| BAA-1792*         | NT                          | R          | R                            | R           | R                       | R          | R                    | NT       | NT          | NT             | NT      | NT          | NT          | NT         | NT        | NT        | NT         | NT        | NT         | NT         | NT         |
| BAA-1793*         | NT                          | R          | R                            | R           | R                       | R          | R                    | NT       | NT          | NT             | NT      | NT          | NT          | NT         | NT        | NT        | NT         | NT        | NT         | NT         | NT         |
| BAA-1794*         | NT                          | R          | R                            | R           | R                       | R          | R                    | NT       | NT          | NT             | NT      | NT          | NT          | NT         | NT        | NT        | NT         | NT        | NT         | NT         | NT         |
| BAA-1795*         | NT                          | R          | R                            | R           | R                       | R          | R                    | NT       | NT          | NT             | NT      | NT          | NT          | NT         | NT        | NT        | NT         | NT        | NT         | NT         | NT         |
| BAA-1796*         | NT                          | R          | R                            | R           | R                       | R          | R                    | NT       | NT          | NT             | NT      | NT          | NT          | NT         | NT        | NT        | NT         | NT        | NT         | NT         | NT         |
| BAA-1929*         | NT                          | R          | R                            | R           | R                       | R          | R                    | NT       | NT          | NT             | NT      | NT          | NT          | NT         | NT        | NT        | NT         | NT        | NT         | NT         | NT         |
| BAA-1800*         | R                           | I          | R                            | R           | R                       | R          | R                    | NT       | NT          | NT             | NT      | NT          | NT          | NT         | NT        | NT        | NT         | NT        | NT         | NT         | NT         |

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

ATCC Multidrug Resistant & Antimicrobial Reference Strains brochure available at www.atcc.org
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
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


• APIC. Guide to the elimination of multidrug-resistant *Acinetobacter baumannii* transmission in healthcare settings. 2010.


Thank you!

Register for more webinars in the ATCC “Excellence in Research” webinar series at www.atcc.org/webinars.

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