Is AST in standard bacteriologic media fully sufficient to guide management of certain highly MDR organisms or critically ill patients?

Victor Nizet, MD
Professor & Vice Chair for Basic Research, Department of Pediatrics
Chief, Division of Host-Microbe Systems & Therapeutics
Professor, Skaggs School of Pharmacy & Pharmaceutical Sciences
University of California, San Diego
Research focus on common, invasive bacterial pathogens of humans ...

- S. pyogenes (Group A Strep)
- S. agalactiae (Group B Strep)
- S. aureus (Golden Staph)
- S. pneumoniae (Pneumococcus) (e.g. Pseudomonas)

... and their interaction with host innate immunity

- Cathelicidin AMPs
- HIF and Immunity
- Neutrophil Traps
- Macrophage Signaling
- Host-Pathogen Glycobiology
Seeking alternatives to classical antibiotics, especially very broad-spectrum agents, that kill bacteria or block their growth

* Drugs to block specific pathogen immune resistance factors
  Sensitize pathogens to clearance by normal host innate defenses
  More targeted therapy, avoid “collateral damage” to microbiome

* Modulation of innate immunity to treat bacterial infections
  Can we pharmacologically boost phagocyte function?

* Explore “repurposing” existing drugs for the above properties

* Synergy between pharmaceutical and endogenous antibiotics
Quiz: Can you name these Harvard researchers?

John Howard Mueller, PhD
(1891-1954)

Jane Hinton, DVM
DVM (1919-2003)
A Protein-Free Medium for Primary Isolation of the Gonococcus and Meningococcus.

J. Howard Mueller and Jane Hinton.

From the Department of Bacteriology* and Immunology, Harvard Medical School, and School of Public Health, and the Boston Dispensary, Boston, Mass.

30.0% Beef infusion
1.75% Casein hydrosylate
0.15% Starch
1.70% Agar
pH to neutral at 25°C

Later – cation-adjusted
(for *Pseudomonas*)
Calcium 20-25 mg/L
Magnesium 10-12.5 mg/L
MIC/MBC TESTING IN BACTERIOLOGIC MEDIA (i.e. CA-MHB), STRONGLY DELIMITS PHARMACOTHERAPY OF HUMAN BACTERIAL INFECTIONS

ANTIBIOTIC DISCOVERY AND DEVELOPMENT

WHICH DRUGS CHOSEN FOR HOSPITAL FORMULARY

WHICH INFORMATION IS PROVIDED TO DOCTORS WHEN THE PATHOGEN IS CULTURED FROM THE PATIENT
Before a patient has even seen the doctor ...

... their infection is already being treated by dozens of antibiotics
Cathelicidin Peptides: Natural Antibiotics of Innate Immunity

Similar:
- encoding genes
- alpha-helical structure
- tissue distribution
- spectrum of activity

Broad-Spectrum Antimicrobial Activity

Produced on Epithelial Surfaces & By Granulocytes
- Skin
- Colon
- Salivary Gland
- Sweat Gland
- Neutrophil
- Mast Cell

Immunostain for Cathelicidin
- Normal skin
- 12 Hr Wound
- GAS infection

Dorschner et al. (2001) J Invest Derm
CRAMP-KO Mouse Has Immune Defect

Wild-type Mice

Knockout Mice

with R. Gallo Lab


Graph showing lesion size over days for different genotypes:
- ++
- +/-
- ---

Images showing mouse lesions on day 7.
METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA)

THREAT LEVEL
SERIOUS

This bacteria is a serious concern and requires prompt and sustained action to ensure the problem does not grow.

80,461 SEVERE MRSA INFECTIONS PER YEAR
11,285 DEATHS FROM MRSA PER YEAR

STAPH BACTERIA ARE A LEADING CAUSE OF HEALTHCARE-ASSOCIATED INFECTIONS

[Images of infected wounds]
“Seesaw Effect” between Daptomycin Nonsusceptibility and β-Lactam Susceptibility in *Staph. haemolyticus*

Daptomycin (S)  Daptomycin (NS)

Oxacillin
Penicillin
Imipenem

Continuation of patient therapy w/ Daptomycin

Reintroduction of β-Lactam Antibiotics in Refractory M.R.S.A. Bacteremia – With Surprising Results

Day 1

Vancomycin dosed for serum trough 15-20 mg/L

Day 12

Daptomycin 6 mg/kg

Persistent (+) blood cultures for MRSA

Day 17

Daptomycin 8 mg/kg + Gentamicin

Day 21

VAN MIC 4.0 DAP MIC 2.0 (isolate D712)

Day 22

Bacteremia Resolved

Day 23-76

Cure

Daptomycin 10 mg/kg + Nafcillin 2 g IV q 4hr

George Sakoulas, MD

Rapid MRSA Bacteremia Clearance with High-Dose Daptomycin plus a β-lactam

Exposure to Sub-MIC Nafcillin Increases Daptomycin Binding to S. aureus Cell Wall

Daptomycin-resistant VISA Clinical Isolate

Bodipy-Dapto (Green/yellow)

No nafcillin

Add nafcillin (40 µg/µl)

Daptomycin binds $\text{Ca}^{2+}$ *in vivo* as an integral part of its mechanism of action – i.e. it becomes a *de facto* cationic peptide.

Cationic antimicrobial peptides such as cathelicidin are a critical component of mammalian innate immunity ......
Sublethal Nafcillin Dramatically Sensitizes MRSA/VISA Strains to Human Cathelicidin AMP LL-37 Killing

**LL-37 Killing (128 μM)**

- **D592 VISA (DAP\(^\circ\))**
- **D712 VISA (DAP\(^{NS}\))**

**D712 VISA LL-37 Killing (128 μM)**

- Nafcillin Concentration (μg/μl)
  - 0
  - 1.5
  - 3.12
  - 6.25
  - 12.5
  - 25.0

**P < 0.0001**

**D712 VISA LL-37 Killing (128 μM)**

- **None**
- **AMP**
- **PIP**
- **CZL**
- **CTX**
- **NAF**
- **CEF**

- 2.0
- 2.0
- 2.0
- 2.0
- 2.0
- 0.063

**vs. untreated**

**LL-37 Killing (32 μM)**

- **No antibiotic**
- **Nafcillin (2 μg/μl)**

**Anti-MRSA Antibiotics (μg/μl)**

- **None**
- **DAP**
- **LIN**
- **VAN**

**Similar results with human alpha-defensin, platelet-derived AMP, and murine cathelicidin**

Nafcillin Increases Binding to MRSA by Rhodamine-Labeled Cathelicidin LL-37

MRSA + LL-37

MRSA + LL-37 + Naf 10

Sublethal Nafcillin Sensitizes MRSA/VISA Strains to Whole Blood, Neutrophil & Keratinocyte Killing

**Whole Blood Killing**

<table>
<thead>
<tr>
<th>Strain</th>
<th>No Abx</th>
<th>NAF 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>D592 VISA</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>D712 VISA</td>
<td>30</td>
<td>60</td>
</tr>
<tr>
<td>Sanger 252 MRSA</td>
<td>40</td>
<td>80</td>
</tr>
</tbody>
</table>

**Neutrophil Killing**

<table>
<thead>
<tr>
<th>Strain</th>
<th>No Abx</th>
<th>NAF 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>D592 VISA</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>D712 VISA</td>
<td>60</td>
<td>120</td>
</tr>
</tbody>
</table>

**Human Keratinocyte (HaCat) Survival at 2h**

<table>
<thead>
<tr>
<th>Condition</th>
<th>MOI 1.0</th>
<th>MOI 0.1</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Abx</td>
<td>P &lt; 0.02</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>NAF 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NAF 20</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Sublethal Nafcillin (Monotherapy) Influences MRSA Lesion Development in Mouse Skin Infection Models

Antibiotic pretreatment of Sanger 252 MRSA followed by mouse subcutaneous challenge

- No abx
- NAF
- VAN

Lesion size (mm²)

Time after infection (d)

No abx > NAF > VAN

*P < 0.05

Representative gross appearance of skin lesions at 48 h time point

Mouse s.c. challenge with Sanger 252 MRSA +/- antibiotic treatment

- No abx
- NAF

Lesion size (mm²)

Time after infection (d)

*P = 0.026

Mouse s.c. challenge with Sanger 252 MRSA +/- antibiotic treatment

Surviving MRSA cfu (cfu/g tissue x 10⁷)

No Abx > Nafcillin

P = 0.0185

Potential beneficial effects of β-Lactam antibiotics not reflected in MIC

- Reduced peptidoglycan O-acetylation
- Reduced peptidoglycan crosslinking
- Decreased shedding of membrane phospholipids
- Decreased expression of MSCRAMMs (e.g., ClfA, FnBPA)
- Increased α-toxin release
- Increased lipoteichoic acid shedding

- Increased bacterial susceptibility to lysozyme killing
- Increased cell membrane access
- Potentiation of cationic host defense peptides (e.g., daptomycin)
- Potentiation of peptide antibiotics (e.g., daptomycin)
- Reduced invasion of epithelial and endothelial cells
- Activation of the NLRP3 inflammasome
- Increased IL-1β release
- Increased TH17 response
- Increased host macrophage cytokine release
- Improved neutrophil recruitment
- Reduced neutrophil apoptosis
- Enhanced clearance of *S. aureus* bacteremia
- Augmented neutrophil antibacterial functions
CARBAPENEM-RESISTANT ENTEROBACTERIACEAE

9,000 DRUG-RESISTANT INFECTIONS PER YEAR
600 DEATHS

CRE HAVE BECOME RESISTANT TO ALL OR NEARLY ALL AVAILABLE ANTIBIOTICS

THREAT LEVEL URGENT
This bacteria is an immediate public health threat that requires urgent and aggressive action.

MULTIDRUG-RESISTANT PSEUDOMONAS AERUGINOSA

6,700 MULTIDRUG-RESISTANT PSEUDOMONAS INFECTIONS
440 DEATHS

51,000 PSEUDOMONAS INFECTIONS PER YEAR

THREAT LEVEL SERIOUS
This bacteria is a serious concern and requires prompt and sustained action to ensure the problem does not grow.

MULTIDRUG-RESISTANT ACINETOBACTER

7,300 MULTIDRUG-RESISTANT ACINETOBACTER INFECTIONS
500 DEATHS FROM MULTIDRUG-RESISTANT INFECTIONS

12,000 ACINETOBACTER INFECTIONS PER YEAR

AT LEAST THREE DIFFERENT CLASSES OF ANTIBIOTICS
NO LONGER CURE RESISTANT ACINETOBACTER INFECTIONS

THREAT LEVEL SERIOUS
This bacteria is a serious concern and requires prompt and sustained action to ensure the problem does not grow.
<table>
<thead>
<tr>
<th>ANTIBIOTIC</th>
<th><strong>Pseudomonas aeruginosa, P4 (MDR)</strong></th>
<th><strong>Klebsiella pneumoniae, K1100 (MDR, KPC)</strong></th>
<th><strong>Acinetobacter baumannii, AB5075 (MDR)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MIC</td>
<td>Interpretation</td>
<td>MIC</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>&gt; 32</td>
<td>R</td>
<td>&gt; 32</td>
</tr>
<tr>
<td>Amoxicillin/Clavulanate</td>
<td>&gt; 32</td>
<td>R</td>
<td>&gt; 32</td>
</tr>
<tr>
<td>Ampicillin/Sulbactam</td>
<td>&gt; 32</td>
<td>R</td>
<td>&gt; 32</td>
</tr>
<tr>
<td>Ticarcillin</td>
<td>&gt; 128</td>
<td>R</td>
<td>&gt; 128</td>
</tr>
<tr>
<td>Ticarcillin/Clavulanate</td>
<td>&gt; 128</td>
<td>R</td>
<td>&gt; 128</td>
</tr>
<tr>
<td>Pipericillin</td>
<td>&gt; 128</td>
<td>R</td>
<td>&gt; 128</td>
</tr>
<tr>
<td>Pipericillin/Tazobactam</td>
<td>&gt; 128</td>
<td>R</td>
<td>&gt; 128</td>
</tr>
<tr>
<td>Cefalotin</td>
<td>&gt; 64</td>
<td>R</td>
<td>&gt; 64</td>
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<tr>
<td>Cefazolin</td>
<td>&gt; 64</td>
<td>R</td>
<td>&gt; 64</td>
</tr>
<tr>
<td>Cefuroxime</td>
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<td>R</td>
<td>&gt; 64</td>
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<tr>
<td>Cefuroxime Axetil</td>
<td>&gt; 64</td>
<td>R</td>
<td>&gt; 64</td>
</tr>
<tr>
<td>Cefotetan</td>
<td>&gt; 64</td>
<td>R</td>
<td>8</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>&gt; 64</td>
<td>R</td>
<td>32</td>
</tr>
<tr>
<td>Cefpodoxime</td>
<td>&gt; 8</td>
<td>R</td>
<td>&gt; 8</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>&gt; 64</td>
<td>R</td>
<td>8</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>&gt; 64</td>
<td>R</td>
<td>&gt; 64</td>
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<td>Ceftizoxime</td>
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<td>R</td>
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<td>Ceftriaxone</td>
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<td>R</td>
<td>&gt; 64</td>
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<tr>
<td>Cefepime</td>
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<td>R</td>
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<td>Aztreonam</td>
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<td>&gt; 64</td>
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<td>Doripenem</td>
<td>&gt; 8</td>
<td>R</td>
<td>&gt; 8</td>
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<tr>
<td>Ertapenem</td>
<td>&gt; 8</td>
<td>R</td>
<td>&gt; 8</td>
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<tr>
<td>Imipenem</td>
<td>&gt; 16</td>
<td>R</td>
<td>8</td>
</tr>
<tr>
<td>Meropenem</td>
<td>&gt; 16</td>
<td>R</td>
<td>&gt; 16</td>
</tr>
<tr>
<td>Amikacin</td>
<td>32</td>
<td>I</td>
<td>&gt; 64</td>
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<tr>
<td>Gentamicin</td>
<td>8</td>
<td>I</td>
<td>&gt; 16</td>
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<td>Tobramycin</td>
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<td>S</td>
<td>&gt; 16</td>
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<td>Nalidixic Acid</td>
<td>&gt; 32</td>
<td>R</td>
<td>&gt; 32</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>&gt; 4</td>
<td>R</td>
<td>&gt; 4</td>
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<tr>
<td>Levofoxacin</td>
<td>&gt; 8</td>
<td>R</td>
<td>&gt; 8</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>&gt; 8</td>
<td>R</td>
<td>&gt; 8</td>
</tr>
<tr>
<td>Norfloxacin</td>
<td>8</td>
<td>I</td>
<td>&gt; 16</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>&gt; 16</td>
<td>R</td>
<td>4</td>
</tr>
<tr>
<td>Tigecycline</td>
<td>8</td>
<td>R</td>
<td>&gt; 4</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>&gt; 512</td>
<td>R</td>
<td>128</td>
</tr>
<tr>
<td>TMP/SFX</td>
<td>&gt; 320</td>
<td>R</td>
<td>40</td>
</tr>
</tbody>
</table>
Colistin (Polymyxin E2) from *Paenibacillus polymyxa*  
“Drug of Last Resort” for MDR Gram- Pathogens

Pentacationic polypeptide consisting of a cyclic heptapeptide, a linear tripeptide and a fatty acid tail linked to the N-terminal of the tripeptide.

The five L-diaminobutyric acid (L-Dab) molecules are positively charged.
What is the most commonly prescribed antibiotic in the United States? (> 60 million/year)
Many patients feel better in just 5 days; however, you may continue to improve for several days after taking your last dose. Zithromax keeps on working.

A full course of antibiotic therapy in just 5 doses.

AZITHROMYCIN
Dramatic Differences in Azithromycin Activity vs. Multidrug-Resistant Gram-Negative Rods in Tissue Culture Media vs. Bacteriologic Media

<table>
<thead>
<tr>
<th>Bacterial Strain</th>
<th>Azithromycin MIC in Ca-MHB (µg/ml)</th>
<th>Azithromycin MIC in 5% LB-RPMI (µg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDR Pseudomonas aeruginosa – P4</td>
<td>&gt;64</td>
<td>4</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa – PA01</td>
<td>&gt;64</td>
<td>2</td>
</tr>
<tr>
<td>Carbapenemase-Producing Klebsiella pneumoniae (KPC) – K1100</td>
<td>32</td>
<td>1</td>
</tr>
<tr>
<td>Klebsiella pneumoniae – K700603</td>
<td>64</td>
<td>2</td>
</tr>
<tr>
<td>MDR Acinetobacter baumanii – AB5075</td>
<td>32</td>
<td>0.5</td>
</tr>
<tr>
<td>Acinetobacter baumanii – AB19606</td>
<td>64</td>
<td>0.25</td>
</tr>
</tbody>
</table>

Leo Lin (UCSD MSTP)

Lin et al. eBiomedicine 2015
Subinhibitory Azithromycin Induces Marked Ultrastructural Changes in Pseudomonas

MDR *P. aeruginosa* in RPMI (5% LB)

Control

Azithromycin 1/8th MIC
Azithromycin is Cidal for MDR Gram-Negative Rods at low Concentrations in RPMI + 5% LB

**MDR K. pneumoniae**

- **Ca-MHB**
- **RPMI (5% LB)**
- **No abx**
- **AZM 1**

**MDR A. baumannii**

- **Ca-MHB**
- **RPMI (5%LB)**
- **No abx**
- **AZM 0.5**

Lin et al. eBiomedicine 2015
Synergy Between Azithromycin and Colistin in Killing MDR *Acinetobacter baumannii* (done in MHB)

Lin et al. submitted
Synergy Between Azithromycin and LL-37 in Killing MDR Gram-Negative Rods

**MDR K. pneumoniae**

- None
- LL-37 (12 μM)
- AZM 0.25
- LL-37 + AZM

**MDR A. baumannii**

- None
- LL-37 (1 μM)
- AZM 0.063
- LL-37 + AZM

Lin et al. eBiomedicine 2015
Azithromycin Synergy with LL-37: Increased Cell Wall Permeability and Azithromycin Entry

MDR Acinetobacter baumannii

Lin et al. eBiomedicine 2015
Azithromycin Monotherapy Reduces CFU, Lung Inflammation and Mortality in Mouse Model of A. baumannii Pneumonia
Azithromycin Activity vs. Carbapenem-Resistant *P. aeruginosa* & *K. pneumoniae* (Lin et al. eBiomedicine 2015)

Unrecognized Azithromycin Activity vs. MDR *Stenotrophomonas maltophilia* (Kumaraswamy et al. J Antimicrob Chemother 2016)

**MDR *K. pneumoniae* lung infection**

<table>
<thead>
<tr>
<th>Log CFU (36h)</th>
<th>PBS</th>
<th>AZM 50</th>
<th>AZM 100</th>
</tr>
</thead>
</table>

**MDR *P. aeruginosa* lung infection**

<table>
<thead>
<tr>
<th>Log CFU (36h)</th>
<th>PBS</th>
<th>AZM 50</th>
</tr>
</thead>
</table>

**Neutrophil killing**

S. *maltophilia* (2 x 10^7 CFU)

- No treatment
- AZM (0.03)

**CFU x 10^3**

- PBS
- AZM

**% bacterial survival**

- 15 min
- 45 min

- NBD-AZM (5.0)
- NBD-AZM + COL
- NBD-AZM + LL-37

**48 h**
Bacteriostatic Antibiotics INHIBIT Cathelicidin Function

**E. coli**
- No antibiotic
- Chloramphenicol (15 μM)

**S. aureus** (CRAMP 32 μM)
- No antibiotic
- Erythromycin (2.7 μM)

LL-37 binds to plane of cell division

Kristian et al., FASEB J 2007
Correcting a Fundamental Flaw in the Paradigm for Antimicrobial Susceptibility Testing

Selvi C. Ersoy a,1, Douglas M. Heithoff a,b,1, Lucien Barnes V a, Geneva K. Tripp a, John K. House c, Jamey D. Marth a,b,d, Jeffrey W. Smith d, Michael J. Mahan a,b,*

Dept. of Molecular, Cellular and Developmental Biology, University of California, Santa Barbara, CA 93106, USA

Fold change in MIC in “physiological” mammalian tissue culture media vs. Mueller-Hinton Broth (blue = MIC reduced; red = MIC increased)

Gram-positive bacteria

Gram-negative bacteria
Prediction of *in vivo* efficacy comparing MIC determine in MHB vs. that determined in “physiological” tissue culture media

**Bicarbonate addition to MHB**

Bicarbonate is absent in MHB yet an important physiological buffer required for endogenous cathelicidin antimicrobial peptide activity (Dorschner et al. 2006) Simply adding bicarbonate to MHB helped adjust MICs toward tissue culture media results and was better predictive of *in vivo* efficacy.
Bicarbonate Alters Bacterial Susceptibility to Antibiotics by Targeting the Proton Motive Force

Maya A. Farha, Shawn French, Jonathan M. Stokes, and Eric D. Brown*

Michael G. DeGroote Institute for Infectious Disease Research, Department of Biochemistry and Biomedical Sciences, McMaster University, 1200 Main Street West, Hamilton, Ontario L8N 3Z5, Canada

Figure 4. Physiological concentrations of bicarbonate enhance the antibacterial activity of various chemical factors involved in innate immunity.
Bicarbonate Alters Bacterial Susceptibility to Antibiotics by Targeting the Proton Motive Force

Maya A. Farha, Shawn French, Jonathan M. Stokes, and Eric D. Brown

Michael G. DeGroote Institute for Infectious Disease Research, Department of Biochemistry and Biomedical Sciences, McMaster University, 1200 Main Street West, Hamilton, Ontario L8N 3Z5, Canada

Figure 1. Bicarbonate affects the activity of various classes of antibiotics.
Classical β-Lactamase Inhibitors Potentiate the Activity of Daptomycin against Methicillin-Resistant
*Staphylococcus aureus* and Colistin against *Acinetobacter baumannii*

George Sakoulas, Warren Rose, Andrew Berti, Joshua Olson, Jason Munguia, Poochit Nonejui, Eleanna Sakoulas, Michael J. Rybak, Joseph Pogliano, Victor Nize

MDR *Acinetobacter baumannii*

![Diagram](image)
New Delhi metallo-beta-lactamase 1 (NDM-1) *Klebsiella pneumoniae*

AVI Enhances Killing by Antimicrobial Peptides (LL37)

NDM *K. pneumoniae* + TAMRA-LL37 (2μM)

Chulie Ulloa, MD (in prep)
Avibactam Enhances Innate Immune Clearance of (NDM-1) *Klebsiella pneumoniae*

**AVI Enhances Human Serum Killing**

![Graph showing AVI Enhances Human Serum Killing](image)

**AVI Enhances Human Neutrophil Killing**

![Graph showing AVI Enhances Human Neutrophil Killing](image)

**AVI Enhances Killing of NDM-KP Murine Pneumonia Model**

![Graph showing AVI Enhances Killing of NDM-KP Murine Pneumonia Model](image)

Chulie Ulloa, MD (in prep)
FORMER LAB (academia)

Yung-Chi Chang (National Taiwan U.)
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Kelly Doran (U. Colorado)
David Gonzalez (UC San Diego)
Deepali Kumar (U. Toronto)
Christopher LaRock (Emory Univ.)
Amanda Lewis (Wash. U. St. Louis)
George Liu (Cedars-Sinai)
Shauna McGillivray (Texas Christian U.)
Cheryl Okumura (Occidental College)
Carole Peyssonnaux (Institute Cochin)
Suzan Rooijakers (Utrecht Univ.)
Ismail Secundino (UNAM-Cuernava)
Nina van Sorge (Utrecht Univ.)
Maren von Köckritz-Blickwede (U. Hanover)
Masaya Yamaguchi (Osaka U.)
Annelies Zinkernagel (U. Zurich)

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Fred Beasley (CIBR)
John Buchanan (Aquaculture Tech)
Ericka Anderson (Human Longevity)
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Ross Corrinden (Merck Research)
Simon Döhmann (Cidara)
Andrew Hollands (InhibitRx)
Xavier Lauth (Aquaculture Tech)
Ann Lin (Crown Biosciences)
Jeff Locke (Cidara)
Sascha Kristian (Agallimmune)
Anjuli Timmer (NantKwest)

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Pieter Dorrestein, Ethan Bier,
Jamey Marth, Joe Pogliano,
Liangfang Zhang, Chris Glass,
Michael Karin, Mona Johannessen,
Bernhard Palsson

FORMER LAB (clin micro)

Morgan Pence (Cook Children’s)