Collaborating with the Innate Immune System to Treat Antibiotic-Resistant Superbugs

Victor Nizet, MD
Professor & Vice Chair for Basic Research, Pediatrics
Professor of Pharmacy & Pharmaceutical Sciences
Chief, Division of Host-Microbe Systems & Therapeutics
Collaborative to Halt Antibiotic-Resistant Microbes (CHARM)
University of California, San Diego
First, a Quiz …..

Who are these notable clinical microbiologists?

J. Howard Mueller (1891-1954)
Jane Hinton (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.


RECIPE:

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

Later – cation-adjusted (for Pseudomonas)
Ca2+ 20-25 mg/L
Mg2+ 10-12.5 mg/L
Moreover, before a patient has even seen the doctor ...

... their infection is already being treated by dozens of (natural) antibiotics
Antibiotic Susceptibility Testing
Vis-à-vis Innate Immunity

Prof. dr. Jos van Strijp
Microbiologist and Artist
UMC Utrecht
Cathelicidins: Antibiotics of Mammalian Innate Immunity

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

Produced on Epithelial Surfaces & By Granulocytes

Skin
Colon
Neutrophil
Mast Cell
CRAMP-KO Mouse Has Immune Defect

Wild-type Mice

Knockout Mice

Richard Gallo, MD, PhD

with R. Gallo Lab

Part One - Reconsidering

Do we underestimate the therapeutic potential of current FDA-approved antibiotics by evaluating them agnostic to host innate immunity?

Part Two - Repurposing

Can drugs from other fields of medicine possess beneficial activity at the host-pathogen interface?
Daptomycin binds Ca$^{2+}$ \textit{in vivo} in its mechanism – i.e. it becomes a \textit{de facto} cationic peptide.

“Seesaw Effect” between Daptomycin Nonsusceptibility and β-Lactam Susceptibility in \textit{Staph. haemolyticus}.

Continuation of patient therapy w/ Daptomycin.

Reintroduction of β-Lactam Antibiotics in Refractory MRSA/VISA Bacteremia – With Surprising Results

Day 1
- Vancomycin dosed for serum trough 15-20 mg/L

Day 12
- Daptomycin 6 mg/kg

Day 17
- Persistent (+) blood cultures for MRSA
- Daptomycin 8 mg/kg + Gentamicin
- Daptomycin 10 mg/kg + Nafcillin 2 g IV q 4hr

Day 22
- Vancomycin MIC 4.0
- Daptomycin MIC 2.0
- Bacteremia Resolved

Day 23-76
- Cure

Vancomycin dose: 15-20 mg/L
Daptomycin 6 mg/kg
Daptomycin 8 mg/kg + Gentamicin
Daptomycin 10 mg/kg + Nafcillin 2 g IV q 4hr

George Sakoulas
J Mol Med 2014

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

Dhand et al.
Clin Infect Dis 2011

ESCMID eLibrary
© by author
Exposure to Sub-MIC Nafcillin Increases Daptomycin Binding to the *Staphylococcus aureus* Cell Wall

Daptomycin-resistant VISA Clinical Isolate

**No nafcillin**

**Add nafcillin (40 µg/µl)**

Can this principle be extended to natural cationic peptides of our innate immune system?

Human cathelicidin LL-37

---

Sublethal Nafcillin Markedly Sensitizes MRSA/VISA Strains to LL-37 Killing

Similar results with human α-defensin, platelet-derived AMPs, and CRAMP

Sublethal Nafcillin Sensitizes MRSA/VISA Strains to LL-37

Whole Blood Killing

% survival (1 h)

No Abx | NAF 2
---|---
D592 VISA | ![Graph](image1)
D712 VISA | ![Graph](image2)
Sanger 252 MRSA | ![Graph](image3)

Neutrophil Killing

% survival (90 min)

No Abx | NAF 2
---|---
D592 VISA | ![Graph](image4)
D712 VISA | ![Graph](image5)

Keratinocyte Killing

Relative survival % vs. cell free control

No Abx | NAF 5 | NAF 20
---|---|---
P < 0.02

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

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

Surviving MRSA, cfu (cfu/g tissue x 10^3)

No Abx | Nafcillin
---|---
P = 0.0185

George Liu: β-lactam antibiotics promote IL-1β responses to S. aureus infections

Müller et al. Cell Host Microbe 2015
Wolf et al. J Leuk Biol 2017

Warren Rose, PharmD, MPH
U. Wisconsin Pharmacy

Volk et al. (submitted)

Day 1
- Glyco peptide
- β-lactam
- $P = 0.090$

Day 3
- Glyco peptide
- β-lactam
- $P = 0.007$

Day 7
- Glyco peptide
- β-lactam
- $P = 0.016$

Low serum IL-1β on admission predicts protracted bacteremia

Bacteremia ≤ 4 days (tree falling)
Bacteremia > 4 days ($n = 5$)
Ceftaroline: A Newer Anti-MRSA Cephalosporin

Antimicrobial Salvage Therapy for Persistent Staphylococcal Bacteremia Using Daptomycin Plus Ceftaroline

George Sakoulas, MD1; Pamela A. Moise, PharmD2; Anthony M. Casapao, PharmD3; Poochini Nongjius, PhD4; Joshua Olson, BS5; Cheryl Y.M. Okumura, PhD3; Michael J. Rybak, PharmD2; Ravina Kular, PharmD1,4; Abhijit Dhand, MD1; Warren E. Rose, PharmD6; Debra A. Goff, PharmD7; Adam M. Bresler, MD3; Yuman Lee, PharmD8; Joseph Pogliano, PharmD9; Scott Johns, PharmD10; Glenn W. Kaatz, MD11; John R. Ebright, MD1; and Victor Nizet, MD1

CFT+DAP Mono

Loss of equipoise

Geriak et al. AAC 2019
Ampicillin Enhances Daptomycin- and Cationic Host Defense Peptide-Mediated Killing of Ampicillin- and Vancomycin-Resistant *Enterococcus faecium*

Ceftaroline Restores Daptomycin Activity against Daptomycin-Nonsusceptible Vancomycin-Resistant *Enterococcus faecium*

Sir Alexander Fleming
(Penicillin discovered 1928)

Sakoulas et al. 2018
## Extreme MDR GNRs: A Doctor's Nightmare

### Carbapenem-Resistant Enterobacteriaceae
- **Threat Level:** Urgent
- **Cases:** 9,000
- **Deaths:** 1,400
- **Antibiotics Resistant:** Carbapenem

### Multidrug-Resistant Pseudomonas Aeruginosa
- **Threat Level:** Serious
- **Cases:** 6,700
- **Deaths:** 440
- **Antibiotics:** Aminoglycosides, Carbapenems

### Multidrug-Resistant Acinetobacter
- **Threat Level:** Serious
- **Cases:** 7,300
- **Deaths:** 500
- **Antibiotics:** Carbapenems, Aminoglycosides

### Antibiotic Resistance Table

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Pseudomonas aeruginosa, P4 (MDR)</th>
<th>Klebsiella pneumoniae, K1100 (MDR, KPC)</th>
<th>Acinetobacter baumannii, ABS075 (MDR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin</td>
<td>MIC &gt; 32</td>
<td>MIC &gt; 32</td>
<td>MIC &gt; 32</td>
</tr>
<tr>
<td>Amoxicillin/Clavulanate</td>
<td>MIC &gt; 32</td>
<td>MIC &gt; 32</td>
<td>MIC &gt; 32</td>
</tr>
<tr>
<td>Ampicillin/Subactam</td>
<td>MIC &gt; 32</td>
<td>MIC &gt; 32</td>
<td>MIC &gt; 32</td>
</tr>
<tr>
<td>Ticarcillin</td>
<td>MIC &gt; 128</td>
<td>MIC &gt; 128</td>
<td>MIC &gt; 128</td>
</tr>
<tr>
<td>Ticarcillin/Clavulanate</td>
<td>MIC &gt; 128</td>
<td>MIC &gt; 128</td>
<td>MIC &gt; 128</td>
</tr>
<tr>
<td>Piperacillin</td>
<td>MIC &gt; 128</td>
<td>MIC &gt; 128</td>
<td>MIC &gt; 128</td>
</tr>
<tr>
<td>Piperacillin/Tazobactam</td>
<td>MIC &gt; 128</td>
<td>MIC &gt; 128</td>
<td>MIC &gt; 128</td>
</tr>
<tr>
<td>Cefalotin</td>
<td>MIC 64</td>
<td>MIC 64</td>
<td>MIC 64</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>MIC 64</td>
<td>MIC 64</td>
<td>MIC 64</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>MIC 64</td>
<td>MIC 64</td>
<td>MIC 64</td>
</tr>
<tr>
<td>Cefuroxime/Axetil</td>
<td>MIC 64</td>
<td>MIC 64</td>
<td>MIC 64</td>
</tr>
<tr>
<td>Cefotetan</td>
<td>MIC 64</td>
<td>MIC 8</td>
<td>MIC *R</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>MIC 64</td>
<td>MIC 32</td>
<td>MIC 64</td>
</tr>
<tr>
<td>Cefepime</td>
<td>MIC 64</td>
<td>MIC 4</td>
<td>MIC *R</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>MIC 64</td>
<td>MIC 64</td>
<td>MIC 64</td>
</tr>
<tr>
<td>Doripenem</td>
<td>MIC 8</td>
<td>MIC 8</td>
<td>MIC 8</td>
</tr>
<tr>
<td>Eradipenem</td>
<td>MIC 16</td>
<td>MIC 8</td>
<td>MIC 16</td>
</tr>
<tr>
<td>Imipenem</td>
<td>MIC 16</td>
<td>MIC 8</td>
<td>MIC 16</td>
</tr>
<tr>
<td>Meropenem</td>
<td>MIC 16</td>
<td>MIC 16</td>
<td>MIC 16</td>
</tr>
<tr>
<td>Amikacin</td>
<td>MIC 32</td>
<td>MIC 64</td>
<td>MIC 64</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>MIC 8</td>
<td>MIC 16</td>
<td>MIC 16</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>MIC &lt; 1</td>
<td>MIC 16</td>
<td>MIC 8</td>
</tr>
<tr>
<td>Colistin</td>
<td>MIC &lt; 1</td>
<td>MIC 16</td>
<td>MIC 8</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>MIC 4</td>
<td>MIC 4</td>
<td>MIC 4</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>MIC 8</td>
<td>MIC 8</td>
<td>MIC 8</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>MIC 8</td>
<td>MIC 8</td>
<td>MIC 8</td>
</tr>
<tr>
<td>Norfloxacin</td>
<td>MIC 8</td>
<td>MIC 16</td>
<td>MIC 16</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>MIC 16</td>
<td>MIC 4</td>
<td>MIC 1</td>
</tr>
<tr>
<td>Tigecycline</td>
<td>MIC 8</td>
<td>MIC 4</td>
<td>MIC &lt; 0.5</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>MIC 512</td>
<td>MIC 128</td>
<td>MIC 512</td>
</tr>
</tbody>
</table>

**Interpretation:**
- **S**: Susceptible
- **I**: Intermediate
- **R**: Resistant
- **U**: Uninterpretable
Colistin (Polymyxin E2) from *Paenibacillus polymyxa* “Drug of Last Resort” for MDR Gram- Pathogens

Cyclic pentacationic polypeptide

Dose-limited renal toxicity

L-diaminobutyric acid (L-Dab) residues + charge

Eadon et al. Physiol Genom 2013
What is the most commonly prescribed antibiotic in the U.S.? (~60 million/year)

Azithromycin
AZM is Cidal for MDR GNRs at low Concentrations in RPMI + 5% LB

<table>
<thead>
<tr>
<th>Pathogen (all MDR strains)</th>
<th>Ca-MHB</th>
<th>RPMI+5% LB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>MIC &gt; 64</td>
<td>MIC = 4</td>
</tr>
<tr>
<td>Klebsiella pneumoniae (CRE)</td>
<td>MIC = 32</td>
<td>MIC = 1</td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
<td>MIC = 32</td>
<td>MIC = 0.5</td>
</tr>
</tbody>
</table>

Lin et al. eBiomedicine 2015
Subinhibitory AZM induces marked structural changes in *Pseudomonas* (rod --> coccus)

AZM signature of protein synthesis inhibition (toroid nuclei) only in tissue culture media
Synergy Between AZM and Cationic Peptides vs. MDR GNRs

Lin et al. eBiomedicine 2015
Azithromycin Monotherapy Reduces CFU, Lung Inflammation and Mortality in Mouse Model of *A. baumannii* Pneumonia

**Figure 1:**

- **Graph 1:** Log CFU (24h) vs. Treatment Groups (PBS, AZM 50, AZM 100).
- **Graph 2:** BAL Cells x 10^5 vs. Treatment Groups (PBS, AZM 100).
- **Graph 3:** IL-1β, IL-6, MIP-2 ng/ml in BAL vs. Treatment Groups (PBS, AZM 100).
- **Graph 4:** % survival vs. Treatment Groups (PBS control, AZM 100 q 24h x 2).

**Legend:**
- *A. baumannii*
- PMN
- Mac
- MDR *A. baumannii*
- BAL Fluid
- 100μm

Lin et al. eBiomedicine 2015
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)
New Delhi metallo-beta-lactamase 1 (NDM-1) *Klebsiella pneumoniae*

AVI Enhances Killing by Antimicrobial Peptides (LL37)

AVIBACTAM (a non-β-lactam BLI)

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

**Ulloa et al. J Infect Dis 2019**
Avibactam Enhances Immune Clearance of (NDM-1) K. pneumoniae

Ulloa et al. J Infect Dis 2019
Neutrophil “NETs”: DNA-Based Extracellular Traps for Killing Pathogenic Bacteria
Statins: Inhibitors of HMG-CoA reductase

Mainstay of hyperlipidemia treatment ~ 55 million users in the U.S. Lower LDL, raise HDL

Clinical Data: Decreased Risk or Improved Outcomes of Infection in Patients Receiving Statins

<table>
<thead>
<tr>
<th>Disease</th>
<th>Effect of Statins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteremia</td>
<td>Reduced Mortality</td>
</tr>
<tr>
<td>Sepsis</td>
<td>Reduced Incidence, Reduced Mortality</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>Reduced Incidence, Reduced Mortality</td>
</tr>
</tbody>
</table>

Prevailing Hypothesis: Statin downregulates inflammatory mediatory release deleterious in sepsis (TNF, INOS, IL-1, IL-6)

We sought to test an Alternative Hypothesis: Could statins improve the innate immune function of phagocytes?
Statin treated neutrophils and macrophages kill *S. aureus* more efficiently

*with*  
*C. Glass Lab*

Effect is observed with multiple bacterial species
Statins actually REDUCED phagocytosis & oxidative burst; rather, they boosted NET production & killing.

Chow et al. Cell Host Microbe (2010)
Mice Treated With Statin Have Increased ET Production and Killing of *S. aureus* Ex Vivo and In vivo

![Graph](image1)

*Figure 1: NET Production and *S. aureus* CFU Recovery in Murine Peritoneal Exudate Cells with and without Simvastatin.

![Image](image2)

*Figure 2: CRAMP-NET in Alveolar Space in S. aureus Pneumonia Model with and without Statin.*

*Figure 3: CFU per gm lung tissue in *S. aureus* Pneumonia model with and without Simvastatin.*

Chow et al. Cell Host Microbe (2010)

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Tamoxifen Induces NETs By Increasing Intracellular Ceramide Levels

Corriden et al. Nat Commun 2015
Tamoxifen Boosts Host Defense Against Staphylococcal Infection in vivo

Corriden et al. Nat Commun 2015
Hypoxia-Inducible Factor (HIF): Master Regulator of the Metabolic Adaptation to Hypoxic Stress

Genes for:
- Glycolysis
- VEGF
- EPO

**PHD inhibitors**
- Roxadustat (AZ)
- Vadadustat (Akebia)
- Darbropustat (GSK)

Advanced Phase III for chronic anemia
Myeloid-Cell Specific Knockout of HIF-1α in Mice
cre/flox Deletion Driven by LysM promoter (Neutrophils and Macrophages)

Normal Phagocytosis

Defect in Bacterial Killing

Cramer et al., Cell 2003
HIF-1α Activated in Response to Bacteria (Even at Normoxia) and Contributes to Innate Immunity

**Cathelicidin AMP**

<table>
<thead>
<tr>
<th></th>
<th>WT</th>
<th>HIF-/-</th>
<th>VHL-/-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-CRAMP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-β-actin</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**GAS Skin Infection Model**

**WT Mice**

Wild-type mice

HIF-1α KO

**Peyssonnaux et al., J Clin Invest 2005**
Genetic Augmentation of HIF (vHL-/-) Boosts Bactericidal Capacity
HIF Agonists (PHD Inhibitors) Boost Phagocyte and Keratinocyte Killing of MRSA *in vitro* and *in vivo*  

Okumura et al.  
*J Mol Med* 2012
HIF Boosting Drug AKB-4924 in Delayed Treatment of Vancomycin-Intermediate S. aureus (VISA) Infection

Infect with VISA strain HIP5836 (MIC = 8)

Begin treatment Vanco IP b.i.d. 4294 orally q.d.

Sacrifice

Fred Beasley, PhD

Weight Loss

Kidney CFU

% body mass change

log CFU/g

No Rx  VAN  4924  VAN + 4924

Day 4 baseline None  VAN  4924  VAN + 4924

NS

*
Immune Boosting with HIF Agonist AKB-4924 Efficacy in UPEC Urinary Tract Infection

HTB-9 Bladder Epithelial Cells

HIF-1 (nucleus)

In vivo UPEC Infection

Invasion

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Bacteria Recovery (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMSO</td>
<td>[Bar graph showing bacteria recovery]</td>
</tr>
<tr>
<td>4924</td>
<td>[Bar graph showing bacteria recovery]</td>
</tr>
</tbody>
</table>

**P < 0.0001

In vivo UPEC Infection

ESCMID eLibrary

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Anthrax Lethal Factor Suppresses HIF, but Pharmacological Boosting Saves the Host

Macrophage Killing of B. anthracis (Sterne)

Systemic Mouse Infection B. anthracis (Sterne)

Raza Ali, unpublished
Platelets produce cationic host defense peptides
Low Platelet Count (Thrombocytopenia) is Associated with Higher Mortality *Staphylococcus aureus* Bacteremia Patients

Sun et al. (invited revision)
Platelets Kill *Staphylococcus aureus* Better than Neutrophils

Sun et al. (in review)
**Staphylococcus aureus** Infection Drives Down the Count of Antibacterial Platelets in the Blood

Sun et al. (invited revision)
Staphylococcus aureus α-Toxin is Responsible for Knocking Down Antibacterial Platelet Counts/Function
FDA-approved P2Y12 inhibitor Ticagrelor (Brillinta®) Blocks *Staphylococcus aureus* α-Toxin Mediated Platelet Cytotoxicity

Sun et al. (invited revision)
FDA-Approved P2Y12 Inhibitor Ticagrelor (Brillinta®) Protects Against *Staphylococcus aureus* Bacteremia

Sun et al. (invited revision)
FDA-Approved P2Y12 Inhibitor Ticagrelor (Brillinta®) Protects Against *Staphylococcus aureus* Mortality

Sun et al. (in review)
Aging (Desialylated) Platelets are Removed from Circulation by the Hepatic Ashwell-Morell Receptor

Loss of terminal sialic acids
Staphylococcus aureus $\alpha$-Toxin Activates Endogenous Platelet Sialidase Activity (Neu1)
Genetic Deletion of the Hepatic AMR Supports Platelet-Mediated Defense vs. MRSA Bacteremia

Sun et al. (in review)
FDA-approved sialidase inhibitor oseltamivir blocks AMR-mediated platelet clearance to protect vs. MRSA bacteremia.
Pharmacological Targeting of the “Toxin-Platelet-AMR” Pathway During *Staphylococcus aureus* bacteremia

Sun et al. (in review)
Cell Membrane-Coated Nanoparticle Technology

Red blood cells  Platelets  White blood cells  Cancer cells  Bacteria

Natural cell membrane  Coating  Cell membrane-coated nanoparticle

ACS Nano, 2016  Adv Mater, 2017(a)  ACS Nano, 2017(a)
Adv Mater, 2017(b)  ACS Nano, 2017(b)  Nature Commun, 2017
Angew Chem, 2017  Angew Chem, 2018  ACS Nano, 2018
Adv Mater, 2018  Science Robot, 2018  Nature Nanotech, 2018

w/ Liangfang Zhang, UCSD
RBC-Derived Nanosponges Neutralize Pore-Forming Toxins

Macrophage-Derived “Nanosponges” for Sepsis Treatment

Thamphiwatana et al. PNAS 2017
Appropriate Antibiotics Chosen

Antibiotic Sensitive

Antibiotic Resistant

RIP

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Concluding Thoughts

Novel Therapeutics Targeting the Host-Pathogen Interface

- Immune Boosters
- Immune Sensitizers
- Innate Immunity
- Virulence Mechanisms
- Cytoprotective Agents
- Toxin Inhibitors

Classical Antibiotics

Munguia & Nizet Trends Pharm Sci 2017
FORMER LAB (academia)

Aaron Carlin (UC San Diego)
Yung-Chi Chang (National Taiwan U.)
Laura Crotty Alexander (UC San Diego)
Kelly Doran (Univ. Colorado)
David Gonzalez (UC San Diego)
Jacqueline Kimney (UC Santa Cruz)
Christopher LaRock (Emory Univ.)
Amanda Lewis (Wash. U. St. Louis)
George Liu (Cedars-Sinai)
Shauna McGillivray (Texas Christian U.)
Cheryl Okumura (Occidental College)
Carole Peyssonaux (Institut Cochin)
Suzan Rooljakkers (Utrecht Univ.)
Ismael Secundino (Univ. De La Salle Bajio)
Nina van Sorge (Utrecht Univ.)
Maren von Köckritz-Blickwede (U. Hanover)
Masaya Yamaguchi (Osaka U.)
Annelies Zinkernagel (U. Zurich)

FORMER LAB (biotech)

S. Raza Ali (NantKwest)
Ericka Anderson (Human Longevity)
Fred Beasley (Jecure Therapeutics)
Stephanie Brandt (General Atomics)
John Buchanan (Aquaculture Tech)
Jason Cole (Cidara Therapeutics)
Ingrid Cornax (Johnson & Johnson)
Ross Corriden (Merck Research)
Simon Döhrmann (Cidara Therapeutics)

COLLABORATORS


http://nizetlab.ucsd.edu
The **Collaborative to Halt Antibiotic-Resistant Microbes** @UC San Diego

Neutralizing virulence
Boosting immunity
Marine chemical discovery
Microbiome innovation
Chemical genomics
Bacteriophage therapy

Novel vaccines
OMICs – systems biology
Nanotherapeutics
Rapid diagnostics
CRISPR active genetics
Drug repurposing

Debuting Fall 2019, we are seeking like-minded academic, government & industry partners