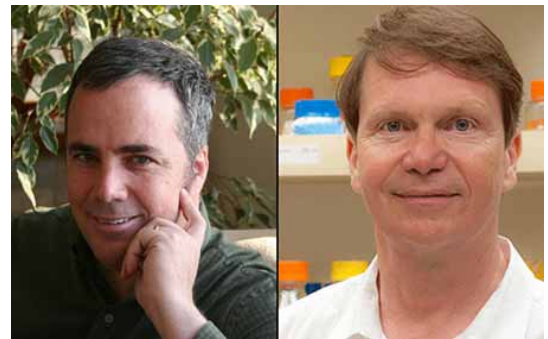


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UC San Diego Scientists Receive \$9.5 Million NIH Grant to Combat Antibiotic Resistance

Interdisciplinary program will use systems biology approaches to understand how antibiotics work in concert with patient's immun

Researchers at University of California, San Diego School of Medicine have received a five-year, \$9.5-million award from the National Institute of Allergy and Infectious Diseases at the National Institutes of Health (NIH) to establish an interdisciplinary center to define the systems biology of antibiotic resistance. The program will be led by Bernhard Palsson, PhD, Distinguished Professor of Bioengineering and Pediatrics, and Victor Nizet, MD, professor of pediatrics and pharmacy.



(From left to right) Victor Nizet, MD, is a professor of pediatrics and pharmacy, and Bernhard Palsson, PhD, is a Distinguished Professor of Bioengineering and Pediatrics.

Bacteria that no longer reliably respond to antibiotic therapy, so-called “superbugs,” pose one of the greatest threats in modern medicine. Superbugs, such as methicillin-resistant *Staphylococcus aureus* (MRSA), *Clostridium difficile* (*C. diff*), and carbapenem-resistant *Enterobacteriaceae* (CRE), often strike hospitalized patients, the elderly or those with weakened immune systems or chronic medical conditions. The U.S. Centers for Disease Control and Prevention estimate that at least 2 million Americans become infected with antibiotic-resistant bacteria and at least 23,000 people die each year as a direct result of these infections.

“I worry that approaches currently used in the clinic to evaluate antibiotic activity are antiquated and simplistic, and address the drug’s action only on bacteria growing in artificial laboratory media without attention to the human immune system,” Nizet said. “Our research has shown that certain antibiotics can synergize with the natural defenses of our immune system to clear infections in a way that wouldn’t have been predicted by current testing paradigms.”

Palsson is a leader in the emerging field of systems biology, which explores the complexity of living systems — from the genome to the entire organism — using experimental and computational methods. Concerned by the exploding problem of drug-resistant bacterial pathogens, Palsson reached out to Nizet, a physician-scientist, to explore whether systems-level approaches could be coupled with experimental models of antibiotic drugs, living bacterial pathogens, human immune cells and animal models of infection to benefit patients with antibiotic-resistant infections.

“Dr. Nizet’s work demonstrates how unexpected environmental factors influence the efficacy of antibiotics. Thus, improving treatment outcomes in serious or antibiotic-resistant bacterial infection will require systems-level analyses at the molecular level,” said Palsson. “We could paraphrase and honor geneticist and evolutionary biologist Theodosius Dobzhansky’s famous quote by saying: ‘Nothing in biology makes sense, except in the light of systems thinking.’”

“By bringing together researchers from our School of Medicine, Skaggs School of Pharmacy and Pharmaceutical Sciences and Jacobs School of Engineering, this new center embodies the collaborative, interdisciplinary spirit for which UC San Diego is known,” said David Brenner, MD, vice chancellor of UC San Diego Health Sciences and dean of UC San Diego School of Medicine. “We’re grateful to the NIH for recognizing our leading-edge capabilities in medicine, engineering and computer science, and for supporting researchers ambitious and talented enough to take on one of the greatest global medical challenges of our time.”

The new research program will be headquartered in the UC San Diego School of Medicine, Department of Pediatrics, Division of Host-Microbe Systems and Therapeutics. Other faculty leaders in the team are:

- **Joseph Pogliano, PhD**, professor of biological sciences, who uses advanced microscopy techniques for real-time analysis of bacterial antibiotic responses
- **Rob Knight, PhD**, professor of pediatrics and computer sciences and engineering and director of the UC San Diego Center for Microbiome Innovation, who will oversee microbial genome analysis and antibiotic effects on the normal human microbiome
- **George Sakoulas, MD**, associate professor of pediatrics, an infectious disease clinician-scientist who provides bedside-to-bench analysis of novel antibiotic combinations
- **Pieter Dorrestein, PhD**, professor of pediatrics and pharmacy, who uses advanced mass spectrometry techniques to study metabolic responses of bacteria to antibiotic exposure
- **Adam Feist, PhD**, associate project scientist in bioengineering, who has pioneered advanced laboratory systems to understand the adaptive evolution of bacterial genomes

and metabolic circuits

In addition to this new systems biology and antibiotic resistance center, funded by NIH grant 1-U01-AI124316-01, the UC San Diego School of Medicine's Division of Host-Microbe Systems and Therapeutics played a key leadership role launching the UC San Diego Center for Microbiome Innovation in October 2015. In late 2016, the division will launch another campus-wide research and educational initiative known as Collaborative to Halt Antibiotic-Resistant Microbes (CHARM), which will support a wide range of innovative scientific and outreach strategies to address this pressing challenge to clinical medicine and public health.

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