Turning A Phage
Partnering with multiple institutions, UC San Diego launches North America’s first bacteriophage therapy center to use viruses as new weapon against multidrug-resistant bacteria; clinical trials planned

With microbial resistance to antibiotics growing into a major global health crisis, researchers at University of California San Diego School of Medicine, in collaboration with national research institutions and private industry, are leveraging hard-won expertise to exploit a natural viral enemy of pathogenic bacteria, creating North America’s first Center for Innovative Phage Applications and Therapeutics (IPATH).

Bacteriophages, or phages, are viruses that specifically target and consume bacteria. They are ubiquitous, found wherever bacteria exist and were once considered a promising therapeutic tool. The advent of modern antibiotics in the 1930s redirected research interests, but with 10 million people estimated to die from “superbug” infections by 2050, they are getting a second look.

In 2016, UC San Diego School of Medicine physicians and scientists conducted a dramatic, last-ditch effort to save the life of Tom Patterson, PhD, then a 69-year-old professor in the Department of Psychiatry at UC San Diego School of Medicine who had become systemically infected by a multidrug-resistant bacterium during a vacation in the Middle East.

Comatose and dying, a team that included experts from UC San Diego, the U.S. Navy, Texas A&M University, San Diego State University and private industry developed experimental cocktails of bacteriophages to treat Patterson. The approach worked; Patterson awoke within days and fully recovered. He was the first U.S. patient with a systemic multidrug-resistant bacterial infection to be successfully treated intravenously with bacteriophages. In the two years since, physicians at UC San Diego Health have treated five other patients with phages for bacterial infections under emergency investigational new drug approval from the Food and Drug Administration (FDA).

“All of the patients tolerated phage therapy well without adverse effects,” said Saima Aslam, MD, associate professor of medicine and medical director of the solid organ transplant infectious diseases service at UC San Diego Health. “Phage combinations were given by direct instillation into the infected site, intravenously and/or by inhaled routes. This led to resolution of infection in three cases. In two others, it helped ameliorate the infection. In one case, treatment came too late in the course of infection and the patient was transitioned to hospice.”

Encouraged by the broadly positive results observed in these first patients, UC San Diego Chancellor Pradeep Khosla has announced a three-year, $1.2 million grant to help launch the center.

“The story of how phages saved Tom’s life and have helped others, the tremendous depth of scientific knowledge and medical practice, combined with intuition, innovation and just sheer guts, is what UC San Diego is all about,” said Khosla. “IPATH captures many of our most cherished ambitions: a robust, interdisciplinary research that advances science, but also delivers tangible benefits to patients and society. Phage therapy has the potential to save millions of lives.”

Steffanie Strathdee, PhD, associate dean of global health sciences and Harold Simon Professor in the Department of Medicine, and Robert Schooley, MD, professor of medicine and an infectious disease expert at UC San Diego School of Medicine, will be co-directors of IPATH. It was Strathdee, who is married to Patterson, who collaborated with Schooley and others to seek an emergency compassionate-use exemption to experimentally treat her husband with phages after all standard antibiotic treatments failed.

“IPATH builds upon what we’ve learned and will apply rigorous principles that span from bench to bedside to better understand the potential role for phage therapeutics in the treatment of patients with infections that cannot successfully be treated with currently available antibiotics,” said Strathdee.

“It taps into and enhances a wide range of existing clinical and translational research programs — there are few places in the world with similar resources to treat multidrug-resistant bacterial infections — and
fosters emerging collaborations with the U.S. Navy Medical Research Center, industry partners and the strengths of the UC San Diego Health system."

The center will begin with multiple key personnel:
- Strathdee
- Schooley
- Aslam
- Davey Smith, MD, chief, Division of Infectious Diseases and Global Public Health
- Constance Benson, MD, professor of medicine
- Michelle Ritter, MD, assistant professor of medicine
- Randy Taplitz, MD, professor of medicine and Clinical Director of the Division of Infectious Diseases
- Sharon Reed, MD, professor of pathology and medicine
- David Pride, MD, PhD, assistant professor of pathology and medicine
- Darcy Wooten, MD, assistant professor of medicine
- Jenifer Dan, MD, PhD, senior fellow, division of infectious diseases
- Doug Conrad, MD, professor of medicine
- Rob Knight, PhD, director, Center for Microbiome Innovation; professor of pediatrics, computer science and engineering
- Bernd Schnabl, PhD, associate professor of gastroenterology
- Victor Nizet, MD, professor, Skaggs School of Pharmacy and Pharmaceutical Sciences and Department of Pediatrics
- Pieter Dorrestein, PhD, professor, Skaggs School of Pharmacy and Pharmaceutical Sciences and department of Pediatrics and Pharmacology

Strathdee and Schooley said IPATH will use existing resources at UC San Diego Antiviral Research Center to build the infrastructure needed to validate phage therapy for treating multidrug-resistant bacterial infections in clinical settings.

It will also partner with other like-minded institutions, including the Center for Phage Technology (CPT) at Texas A&M University, San Diego State University and two biotechnology companies specializing in the development of therapeutic bacteriophages: Ampliphi Biosciences, based in San Diego, and Adaptive Phage Therapeutics, Inc. or APT, based in Maryland.

“The CPT has been developing phages as agents for combating bacterial infections in plants, animals and humans since 2010, and promoting best practices for the ethical and sustainable use of this technology,” said Ryland F. Young III, CPT director and Regents Professor at Texas A&M. “The CPT fully supports the establishment of IPATH at UC San Diego, and based on our past collaboration that resulted in successful application of phage therapeutics, we look forward to fruitful interactions in the future.”

Schooley said a primary goal of IPATH is to conduct rigorous clinical trials of phage therapies, thus advancing their potential to practical application: “The clinical research will be integrated with leading-edge translational and basic research that will provide critical insights into the mechanisms by which phage selectively kill their bacterial targets, and that will accelerate the development of more advanced clinical research that we hope will lead the FDA to make phage therapeutics more widely available.

“That requires a lot of things: clinical trial infrastructure and design expertise, microbiome expertise, a patient population needing novel interventions like phage therapy who wish to join us in this journey. Although all of these elements are here, we plan to work with a wide range of partners around the world to advance phage therapeutics from anecdote to a globally available tool to combat the rising tide of multidrug resistant infections.”

Initial research will focus on patients with multidrug-resistant chronic infections associated with cystic fibrosis, organ transplantation and implantable hardware, such as pacemakers or joint replacements.
“The launch of IPATH is a momentous and gratifying step,” said Hubert Mazure, the great-grandson of Félix d'Herelle, the French-Canadian microbiologist who discovered bacteriophages in 1917 at the Pasteur Institute and was the first to experiment with them in treating human diseases caused by pathogenic bacteria. “This is the kind of effort needed to truly and fully explore the healing potential of bacteriophages in the modern era.”

For more on bacteriophage therapy and the story of Tom Patterson, visit health.ucsd.edu/phage

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**Caption:** Scanning electron micrograph of two bacteriophages. Image courtesy of Wikimedia/AFADadcADSasd.

**Caption:** A chronic bacterial infection kept 65-year-old Joel Grimwood from getting the heart transplant he desperately needed. UC San Diego Health doctors used an experimental bacteriophage therapy – viruses that eat bacteria – to eliminate the infection. Grimwood got his new heart.