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Maria Filsinger Interrante, Christian Choe, Zachary Rosenthal
Stanford University (Stanford, Calif.)
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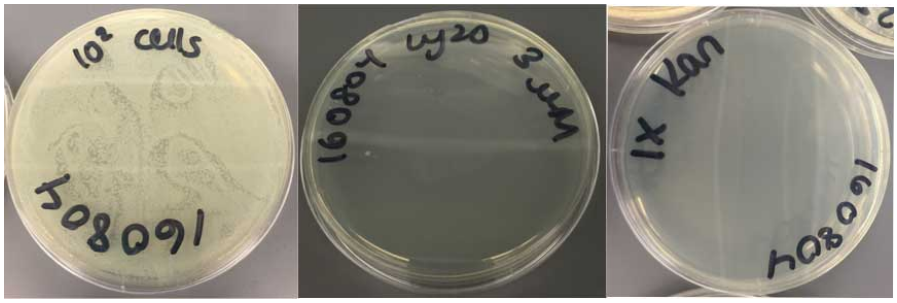
Novel Proteins to Fight Superbug Bacterial Infections

The Challenge: Antibiotic-resistant bacteria caused 2 million illnesses that killed 23,000 patients globally in 2013. The toll is projected to rise to 10 million deaths, surpassing cancer mortality, by 2050. Despite the threat's magnitude, the pharmaceutical industry has mostly shut down antibiotic research. Antibiotics aren't as profitable as drugs developed to treat chronic conditions because they're usually taken only briefly, until they cure the disease.



Although prices can run into thousands of dollars for certain courses of antibiotic treatment, that's still considerably less expensive than the cost for cancer chemotherapy. In addition, resistance can emerge to render new antibiotics all but useless after just a few years on the market.
Meanwhile, only seven new antibiotics are in advanced clinical trials and the number of new candidates being submitted to the FDA has declined steadily since 1980.

The Solution: Team Lyseia's invention gives naturally-occurring bacteriophages ("bacteria eaters") the power to attack multidrug-resistant, Gram-negative bacteria by endowing their therapeutic protein with cell-penetrating capabilities.

Team Lyseia's invention utilizes a novel protein therapeutic that has been specifically engineered to attack the cell walls of multidrug-resistant, Gram-negative bacteria. "Gram-negative" bacteria (so-named because they don't retain the crystal violet stain used in the Gram-staining laboratory technique) are found everywhere on Earth and include the model *Escherichia coli* as well as such pathogens as carbapenem-resistant Enterobacteriaceas (CRE), *Pseudomonas aeruginosa* and *Acinetobacter baumanii*. The U.S. Centers for Disease Control and Protection classifies CRE as an "urgent" threat that kills nearly half of the patients who contract it, while the other two organisms are "serious" threats that could become widespread if no treatment is found.[1] Gram-negative bacteria all have a thin peptidoglycan cell wall sandwiched between an inner cell membrane and a bacterial outer membrane. Unfortunately, this makes targeting them especially difficult –

[1] https://www.cdc.gov/drugresistance/biggest_threats.html#urgent-threats

traditional small-molecule antibiotics frequently fail to penetrate the outer membrane, rendering them obsolete. Team Lyseia has thus found a way to utilize a protein therapeutic to reach and break down the peptidoglycan layer, killing the bacterium in the process.

Commercialization: While other people are already utilizing protein therapeutics against Gram-positive bacteria, Gram-negative pathogens haven't yet gotten the same attention. Lyseia's engineered proteins could be the first to enter clinical trials against these organisms. There's an urgent need for an effective weapon against CRE, *A. baumanii* and *P. aeruginosa*, and Lyseia could be the first to deliver it. The students received a $10,000 grant from the Undergraduate Entrepreneurship Program at Stanford's Chemistry, Engineering, & Medicine for Human Health (ChEM-H) institute to prove the concept against *E. coli* and are now working with a contract research organization to test against *A. baumannii* and *P. aeruginosa*. Team members determined that they can file patents on their new, engineered proteins and are preparing to do so. With that in hand, they will hire a scientific advisory board, incorporate, and seek funding for further trials. They expect to spend two years and $5 million on pre-clinical trials.