DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

The Role of the National Institute of Allergy and Infectious Diseases Research in Combating Antibiotic Resistance

Testimony before the

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Mr. Chairman, Ranking Member DeGette, and members of the Committee, thank you for the opportunity to discuss antibiotic resistance, a serious and growing global health threat. The National Institute of Allergy and Infectious Diseases (NIAID) is the lead institute at the National Institutes of Health (NIH) for conducting and supporting research on infectious diseases, including research on antibiotic resistance.

NIAID has a dual mandate to balance a robust research portfolio in established infectious and immunologic diseases with the capacity to respond quickly to newly emerging and re-emerging infectious diseases. Infections resistant to currently available antibiotics are among the most urgent of these emerging threats.

Antibiotic resistance is a multifaceted problem, and multiple approaches are being undertaken to work toward a comprehensive solution. These include bolstering surveillance, diagnostic capacity, hospital infection control, and the prudent use of antibiotics in both humans and animals. Biomedical research also is essential to address the problem. NIAID's longstanding research efforts in this area aim to understand the molecular basis of antibiotic resistance, to develop specific and sensitive diagnostics, to develop vaccines to prevent infections prone to resistance to antibiotics, and, importantly, to partner with the pharmaceutical industry to develop novel and improved interventions.

Antibiotic Resistance

The development and use of antibiotics to treat bacterial infections are among of tht51 0 f0iI42a7st

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High-throughput genome sequencing efforts also are leading to a better understanding of bacterial pathogenesis and how antibiotic resistance develops. NIAID supports genome sequencing for a national genome sequence database of antibiotic-resistant bacteria as part of the CARB initiative. This database, being developed by NIH in collaboration with FDA and CDC, will provide a comprehensive resource for surveillance, epidemiology, and basic research into the mechanisms of antibiotic resistance. NIAID also funds a large-scale sequencing project to understand the genetics of drug resistance in TB. In addition, NIAID scientists and their colleagues have sequenced the complete genome of a drug-resistant strain of *Klebsiella pneumoniae*, which is a significant cause

associated funding, will increase the capacity to evaluate new antibacterial products and strategies and move needed countermeasures along the research and development pipeline.

Diagnostics

Rapid, point-of-care diagnostic tests can be important in determining precisely which drugs will be effective against a given infection, thereby reducing the inappropriate use of broad-spectrum antibiotics. Currently, broad-spectrum antibiotics that target a wide range of bacteria are often prescribed when a diagnosis , pteoin[(-)]TJETBT1 0 0 1 1345.4T115.9broapectruma-a3

NIAID also has supported the development and validation of a test that can rapidly identify TB and simultaneously detect resistance to rifampicin, an antibiotic commonly used to treat TB. This test, and next-generation versions of the test, currently are being implemented in developing countries to diagnose TB, including drug-resistant TB.

Therapeutics

NIAID is screening new compounds and repurposing existing drugs to provide better options to treat antibiotic-resistant infections. In addition, many novel approaches are being explored, including monoclonal antibodies, bacteriophages, and strategies targeting the microbiome or the host immune system. NIAID recently awarded approximately $5 million in funding for 24 research projects seeking to develop non-traditional therapeutics for bacterial infections. These awards are investigating novel therapies such as bacteriophages, probiotics, and nanoparticles to treat or prevent infections. NIAID intramural researchers also are exploring a novel treatment for TB called host-directed immunotherapy. Rather than targeting the bacteria directly, this approach involves manipulating the body's response to TB, using a regimen that includes zileuton, a clinically approved drug for asthma, to target components of the immune response. In addition, NIAID-supported scientists recently identified the drug teixobactin using an innovative iChip platform that allows researchers to screen natural products from bacteria that live in soil. This drug has a novel mechanism of action and has shown promise against several antibiotic-resistant microbes. Although teixobactin is still under development, potentially it could be a new tool to treat drug-resistant bacteria.

Optimizing the use of existing drugs also can help limit the development of antibiotic resistance. To this end, NIAID funds clinical studies testing new formulations, dosing regimens, or combination therapies of currently approved drugs such as colistin. NIAID-supported

researchers recently found evidence that two off-patent antibiotics, clindamycin and trimethoprim/sulfamethoxazole, work equally well against bacterial skin infections caused by MRSA, indicating that these infections can be treated successfully and inexpensively with either therapy. In addition, an ongoing NIAID-supported Phase IV clinical trial is comparing different combinations of existing antibiotics for treatment of gonorrhea, a disease for which drug resistance is a growing concern.

Vaccines

Developing vaccines to prevent infectious diseases can help prevent the inappropriate use of antibiotics and the development of antibiotic resistance.

government. NIAID will continue to support promising research to develop and test new antibiotics as well as methods to help prevent the further spread of antibiotic resistance.