Share

Back to Search Results

Vaccines to counter emerging antibiotic resistance

Project Number	Contact PI/Project Leader	Awardee Organization
5R01AI138970-02	PICKING, WENDY L	UNIVERSITY OF KANSAS LAWRENCE

Description

Abstract Text

Vaccination may be the greatest public health achievement of our time. With an explosion of antibiotic resistance, developing vaccines against multi-drug resistant (MDR) bacterial pathogens is more important than ever, but most current vaccine strategies fail to target conserved structures that would allow them to protect across serotype, strain and species boundaries. We have developed a protective antigen strategy that targets the type III secretion system (T3SS) of important Gram-negative bacteria and which should be efficacious regardless of serotype, thereby working across genus (e.g. Shigella) or species (e.g. Salmonella enterica) boundaries. With this antigen strategy, we have elicited broad serotype-independent protection against infections by bacteria that are becoming increasingly antibiotic resistant. This strategy employs an adjuvant and provides 70-90% protection in mice against lethal challenge by multiple Shigella species and it protected five of six monkeys from developing severe dysentery after challenge with Shigella sonnei. This same platform has elicits serotype-independent protection against Salmonella enterica challenge (70% protection) as well as other Gram-negative bacteria. To reach complete (100%) protection, we have developed a novel adjuvant carrier platform to create next generation vaccine candidates. With the adjuvant carrier platform, the protective antigen simultaneously enters into antigen presenting cells. This protective antigen will be combined with a carrier to form a multi-protein antigen delivery vehicle to drive uptake by dendritic cells and transport to regional lymph nodes for extended antigen presentation. We hypothesize that the antigen-carrier platform will provide broad serotype-independent protection against all strains of the pathogen including MDR species/strains. The specific aims being proposed are to: 1) Validate cross-strain protection for clinical MDR strains; 2) Optimize the three candidate vaccines using the new particle; 3) Complete the proof-of-concept efficacy studies, including immune response assessment, in appropriate animal models; 4) Assess vaccine efficacy following subclinical pre-exposure to the pathogen as often occurs; 5) Complete biophysical characterization of the top vaccine candidates for subsequent formulation. By the completion of this project, we will have demonstrated that our antigen-carrier platform will prevent infections by MDR Gram negative pathogens.

Public Health Relevance Statement

Vaccination may be the greatest public health achievement of our time. As antibiotic resistance becomes more prevalent among pathogenic bacteria, vaccines will become even more important, however, many vaccines being developed only work against a narrow range of bacteria, even within a single genus or species, due to being “serotype-specific.” To overcome this limitation, we have developed a new vaccine strategy that provides protection across serotype, strain and species boundaries. This nanoparticle-antigen platform will provide broad protection against pathogenic Shigella, Salmonella and Pseudomonas. Furthermore, it will provide preventative measure that overcomes the increasing development of antibiotic resistance in these important pathogens.

NIH Spending Category

Thank you for your feedback!

Antimicrobial Resistance Biodefense Bioengineering Biotechnology Cystic Fibrosis Digestive Diseases Emerging Infectious Diseases Foodborne Illness Immunization Infectious Diseases Lung Nanotechnology Orphan Drug Prevention Rare Diseases Vaccine Related

Project Terms

Achievement Adjuvant Animal Model Animals Antibiotic Resistance Antibiotics Antigen Presentation Antigen-Presenting Cells Antigens Bacteria Bacterial Infections Bordetella Bordetella bronchiseptica Burkholderia Burkholderia pseudomallei Chimeric Proteins Clinical Complex Cystic Fibrosis Dendritic Cells Development Dose Dysentery Effectiveness Ensure Explosion Exposure to Family suidae Formulation Gram-Negative Bacteria Hyaluronan Hyaluronic Acid Immune response Infection Infection prevention Lipopolysaccharides Lung Lymphoid Tissue Mediating Microbiology Modeling Monkeys Multi-Drug Resistance Mus

Details

No information available for 5R01AI138970-02

Sub Projects

No Sub Projects information available for 5R01AI138970-02

Publications

No Publications available for 5R01AI138970-02

Patents

No Patents information available for 5R01AI138970-02

Outcomes

The Project Outcomes shown here are displayed verbatim as submitted by the Principal Investigator (PI) for this award. Any opinions, findings, and conclusions or recommendations expressed are those of the PI and do not necessarily reflect the views of the National Institutes of Health. NIH has not endorsed the content below.

No Outcomes available for 5R01AI138970-02

Thank you for your feedback!

Clinical Studies

No Clinical Studies information available for 5R01AI138970-02

News and More

Related News Releases

No news release information available for 5R01AI138970-02

History

No Historical information available for 5R01AI138970-02

Similar Projects

No Similar Projects information available for 5R01AI138970-02

Thank you for your feedback!