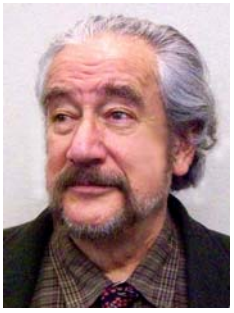
THE HARTWELL FOUNDATION

2009 Individual Biomedical Research Award

Review of Proposed Research



Investigator: **Richard Goldstein, Ph.D.**
Professor
Department of Pediatrics

Institution: **Boston University**

Proposal: **A Vaccine Against Streptococcus pneumoniae Based on Bacterial Surface Proteins Phylogenically Certified as Highly Conserved**

Given the known natural diversity of pneumococcus bacteria and its ability to circumvent current vaccines, Dr. Goldstein proposes a promising alternative that would provide universal protection against all known pneumococcal strains. Streptococcus pneumoniae (S. pneumoniae or pneumococcus) is a bacterium commonly found in the nasopharynx (back of the nose) of healthy individuals. It is the most common cause of acute ear infection, sinusitis, and pneumonia. In immunocompromised children, it is the leading cause of bacterial meningitis (infection of the fluid surrounding the spinal cord and brain) and sepsis (general infection of the bloodstream). More than 90 pneumococcus serotypes (defined by the antibodies that an individual possesses, based on sampling from blood serum or saliva) have been identified and traced to differences in the polysaccharides (sugars) in the capsule coating the outside of the bacteria. The variants differ in virulence, prevalence, and extent of drug resistance. The currently available pediatric vaccine consists of at least seven of the most common capsular polysaccharides responsible for disease, but there is growing concern that a highly variable pathogen like S. pneumoniae that is not adequately targeted may become more prevalent and possibly, drug resistant. Dr. Goldstein intends to identify those quiescent regions in targeted genes of S. pneumoniae, which are highly resistant to the recombination-based mutations responsible for the antigenic differences and that have been conserved by natural selection. To achieve this, he will leverage his extraordinary personal collection of more than 900 phylogenically organized clinical isolates of S. pneumoniae collected from around the world over the last decade (the largest known collection in any single laboratory) that effectively represent the evolutionary diversity of the pneumococcus bacteria. Dr. Goldstein seeks to identify a unique, untapped reservoir of genes that code for highly conserved, proteins exposed on the surface of the bacterium. By this approach, he has already identified in the flank regions of the 16S structural RNA molecule a critical and highly conserved component of the indispensable protein synthesizing machinery of S. pneumoniae. Dr. Goldstein believes such essentially constant regions are likely to be sites that code for the most important surface proteins, which will be essential for an effective and universal pneumococcal vaccine.