THE HARTWELL FOUNDATION

2016 Individual Biomedical Research Award

Heather W. Pinkett, Ph.D.

Associate Professor
Department of Molecular Biosciences

Northwestern University

Blocking the Antimicrobial Transport Pathway to Eradicate Multidrug-Resistant Bacteria in Otitis Media

Middle ear infection or otitis media (OM) is the most common respiratory tract infection of infancy and early childhood. The bacteria that typically cause the infection are gram-negative non-typeable Haemophilius influenzae (NTHi), which moves from the throat behind the nose to the middle ear. Colonization by NTHi leads to inflammation and fluid accumulation in the ear and may result in tearing or perforation of the eardrum. Children under the age of five are more susceptible and often endure severe earache and frequent doctor visits. Alarmingly, repeated infections can reduce hearing and in some cases, cause developmental delays in language. With an estimated 2.2 million episodes of OM occurring annually in the U.S., it is the single greatest reason children receive antibiotics. Unfortunately, NTHi are becoming increasingly resistant to antibiotics, making NTHi virulence a pressing biomedical issue. This often occurs because children carrying undiagnosed antibiotic-resistant NTHi are treated with increased doses of antibiotics, risking the further spread of resistant pathogens to other children in daycare, at home and in the community. Regrettably, even though bacterial responsiveness to antibiotic treatment has declined markedly in the last 15 years, only modest progress has been achieved in developing new antibacterial drugs; in part because over time such drugs cannot overcome antibiotic resistance. Therefore, finding an effective way to treat this very common upper respiratory tract infection is essential. To address the unmet need, Heather hypothesizes that the best way to treat antimicrobial resistant bacterial infections with drug inhibitors is to target the nutrient uptake system in bacteria but not in the host. Using a strain of NTHi colonized from a patient with acute OM, she will design inhibitors that will target and destroy the bacteria through its own nutrient uptake system. She will take advantage of the fact that bacteria support their continued growth through specific bacterial membrane proteins used import a variety of nutrients from their environment. Because these importer proteins are present in all bacteria but not in humans, they represent a feasible and unique druggable target during host infection. If the approach contemplated by Heather is successful, it will inform translation to novel drug therapies that will provide a powerful new therapeutic intervention for OM in children, as well as a wide range of other bacterial infections. The effective use of drugs that specifically target the vulnerable nutrient transport system of bacteria has the potential to enable the clearance of bacterial infections by the natural human immune response, which would reduce antibiotic resistant infections in children while also contributing generally to the reduction of antibiotic-resistant bacteria.