

Abstract Number: 2068

110 - Latebreaker Posters
10/31/2009, 12:30-14:00
Poster Hall A

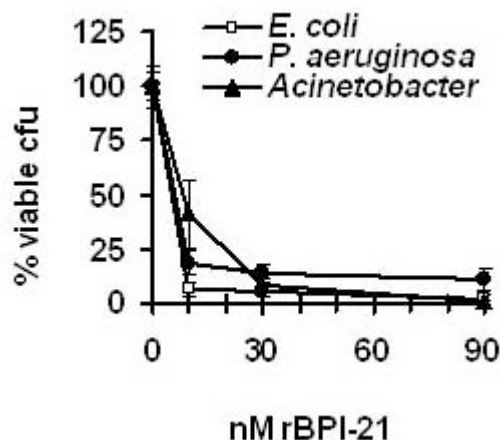
A. Antimicrobial pharmacokinetics/pharmacodynamics, drug toxicity or drug-drug interaction studies, new antimicrobial agents (i.e., pre-US IND or prior to start of clinical trials), new research technologies

Pres No: LB-19 - An Endogenous Antimicrobial Protein with Efficacy Against Multi-Drug-Resistant Gram-Negative Bacteria: The Bactericidal/Permeability-Increasing Protein

JENNIFER COLLINS, BA, STEVEN A. OVADIA, BS, NICOLE M. IOVINE, MD, PhD;
New York University, New York, NY.

Increasing antibiotic resistance in Gram-negative bacteria (GNB) has become a serious problem. Unfortunately, since 1983 there has been a steady decline in FDA approvals for new antibiotics. Consequently, clinicians have been forced to use agents such as colistin and polymixin B, drugs with significant systemic toxicities. However, our clinical labs have begun to detect isolates with elevated minimum inhibitory concentrations against polymixin B. This raises the alarming possibility that regarding multi-drug-resistant (MDR) GNB, we could be heading back to the pre-antibiotic era. The Bactericidal/Permeability-Increasing Protein (BPI) is an endogenous antimicrobial neutrophil protein. BPI exhibits potent and selective antibacterial activity against GNB via its high affinity for lipopolysaccharide (LPS), and also suppresses LPS bioactivity. These antibacterial- and LPS-neutralizing activities of BPI are entirely attributable to its 21-kDa N-terminal half (rBPI-21). This agent was studied as a clinical therapeutic for meningococemia in the 1990's, and narrowly missed FDA approval.

Given the subsequent emergence of MDR GNB, we tested the hypothesis that rBPI-21 would kill such clinical isolates. We co-incubated bacteria with BPI for 1 h and counted surviving cfu. We show that rBPI-21 effects 2-log killing of MDR *Acinetobacter* and *Pseudomonas* at a 30 nM dose; which also killed our positive control strain of *E. coli* ($p < 0.05$ v. no BPI). Similar killing of *Klebsiella* required ten-fold more BPI ($p < 0.05$); the reason for this requires additional study. We conclude that further exploration of rBPI-21 in the treatment of MDR Gram-negative infections is indicated.



Disclosures: J. Collins, None. S. A. Ovadia, None. N. M. Iovine, None.