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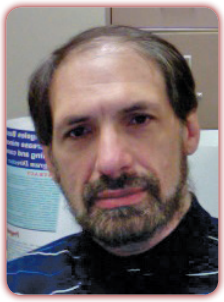

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Multidrug resistant bacterial pathogens: The need for action

There is currently an epidemic of antibiotic resistant bacterial infections that has been identified as one of the greatest threats to human health. Within this epidemic, a group of pathogens responsible for most deaths in hospital infections has been individualized and named ESKAPE (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa*, and *Enterobacter*). Numerous strains resistant to most antibiotics, including aminogylcosides and carbapenems, are becoming increasingly hard to treat. The major need for new antibiotic therapies is for severe infections caused by multidrug resistant Gram-negatives. The resistance to aminoglycosides is mainly caused by enzymatic modification. The aminoglycoside 6'-N-acetyltransferase type Ib [AAC(6')-Ib] is one of the most clinically relevant resistance enzymes and it was found in isolates of all four Gram-negatives included in the ESKAPE group. We have characterized mechanisms of dissemination of aac(6')-Ib at the molecular and cellular level and explored strategies to counter the resistance conferred by AAC(6')-Ib. We identified a locked nucleic acid/oligodeoxynucleotide hybrid oligomer that reduced the levels of resistance to amikacin by eliciting RNase P-mediated degradation of the mRNA. Furthermore, using *in silico* molecular docking and other screening methods we identified inhibitors of the AAC(6')-Ib enzymatic activity. One of them, Zn^{2+} in complex with the ionophore pyrithione was able to reverse resistance to amikacin of *aac(6')*-Ib-harboring Gram-negatives in culture. Our results indicate that inhibition of expression of aminoglycoside modifying enzymes or inhibition of their activity could contribute to alleviate the current antibiotic resistance crisis.

Biography

Marcelo E Tolmasky has completed his PhD at University of Buenos Aires and did his Postdoctoral studies at the Oregon Health & Sciences University. He is currently a Professor at California State University Fullerton and is the Director of the Center for Applied Biotechnology studies. He has published over 85 papers in peer-reviewed journals and co-edited the book "*Enzyme-Mediated Resistance to Antibiotics*". Among other awards he received are the Biotechnology Research Faculty Award 2002 (CSUPERB) and the Outstanding Professor CSUF (the highest honor the university confers) 2009-2010.

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