Jeffrey H Miller, J Drug Metab Toxicol 2015, 6:4
http://dx.doi.org/10.4172/2157-7609.C1.001

OMICS International
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World Congress and Exhibition on
Antibiotics

September 14-16, 2015 Las Vegas, USA

Jeffrey H Miller
University of California, USA

Using synergies to potentiate drugs such as vancomycin in gram negative bacteria

Vancomycin (VAN) is an effective antibiotic against certain multi-drug resistant Gram-positive pathogens, such as MRSA (methicillin-resistant *Staphylococcus aureus*). The large size of this glycopeptide precludes it from penetrating the outer membrane of Gram-negative cells, rendering it ineffective against Gram-negative infections. However, a very small amount of VAN does enter Gram-negative cells. We sought to exploit this small concentration by finding synergies with approved drugs. We have detected strong synergies in the Gram-negative *Escherichia coli* between VAN and nitrofurantoin (NIT), and also trimethoprim (TMP). Concentrations of VAN as low as 12.5 µg/ml can display an effect with NIT and concentrations of VAN of 6.25 µg/ml can show effects with TMP. Combinations of approved drugs that are already in use offer important advantages over screening for new drugs, as the former can be applied in a clinical setting with far less delays. We have also used synergy in pair-wise drug interactions to examine models of antibiotic mechanism of action and to understand the mechanism of synergy itself.

Biography

Jeffrey H Miller is a distinguished Professor in Microbiology, Immunology, & Molecular Genetics in the University of California, Los Angeles. He completed his Postdoc in the Harvard Medical School, Boston, MA. In 2011 he is elected as a member of the American Academy of Arts and Sciences.

jhmiller@microbio.ucla.edu

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