

Compounds that Prevent Antibiotic Resistance

Wide spectrum application. Tolerability in vivo. Defined mechanism. US patent issued 2015.

Introduction

Researchers at the University of Saskatchewan have identified compounds that increase the potency and eliminate development of resistance to bactericidal antibiotics. Co-application of these compounds with antibiotics block SOS mechanisms by inhibiting RecA expression; thereby preventing the development of mutations, which contribute to antibiotic resistance in addition to increasing antibiotic efficacy.

The Target

The established paradigm suggests that antibiotic resistance emerges by selecting for pre-existing mutants in the bacterial population exposed to antibiotics. Adaptive resistance mutations however also occur in bacteria in response to antibiotic therapy through activation of the SOS DNA repair and mutagenesis pathway. The expression of RecA and LexA proteins initiate the SOS response, and regulate error-prone DNA polymerase genes. Error-prone DNA polymerases are a major factor in acquiring antibiotic resistant mutations. During the SOS response, RecA polymerizes on ssDNA in the presence of ATP and promotes LexA autoproteolysis as well as SOS gene expression.

Market

The rapid emergence of antibiotic resistance amongst pathogenic bacteria is a major clinical and public health problem. Nosocomial infections are the 6th leading cause of death in the US and are estimated to cost between \$5-10 billion/year in the US. The increasing incidence of resistance is compounded by only 2 new FDA approved antibiotics since 2008 (Telavancin and Ceftaroline). The worldwide antimicrobial market is valued at approximately \$43B with a key market driver the use of new product combinations to overcome bacterial resistance.

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