Design of selective Erm inhibitors to thwart antibiotic resistance

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The use on antibiotics to treat bacterial infections has been highly beneficial to human health. The effectiveness of antibiotic has been on a large decline. This is due to the emergence of resistant strains of bacteria. The resistance factor normally comes in the form of a plasmid and is therefore easily transported between organisms, allowing for a quick rise of resistance to particular antibiotics. The Erm (erythromycin resistant methyltranferases) family of methyltransferases provides resistance to the macrolide-lincosamide-streptogramin B (MLS-B) group of antibiotics. This includes erythromycin. These antibiotics could again become useful through the design of a drug to inhibit Erm. However, there are proteins similar to Erm, both in structure and in function. Dim1 is a human enzyme that is one of these proteins. KsgA is another similar enzyme that exists in bacteria. The goal is to design an Erm inhibitor that is therapeutically useful and selective for Erm. Specificity for Erm is essential. It has been found that inhibition of KsgA in bacteria has negative effects. Inhibition of Dim1 has shown to be lethal. In order to obtain leads in inhibitors binding assays are being carried out on these proteins through equilibrium dialysis.