

**BACTERIAL AND FUNGAL RIBOSOME
SELECTIVE ANTIMICROBIALS**Arya Dev P.*Clemson University, Department of Chemistry, Clemson, SC 29634*

Aminoglycosides inhibit bacterial growth by binding to the A-site decoding region of the bacterial 16s ribosomal RNA (rRNA) within the 30S ribosomal subunit. Previous work has shown that there is approximately a five-fold difference in the affinity of aminoglycosides (neomycin) for the human A-site model and the *E. coli* model (Figure 1).¹ Herein, we describe an approach to develop compounds that are selective for bacterial rRNA and include motifs such as aminosugars, amino acids and nucleobases. To accomplish such a task, we have first developed a screening assay that rapidly identifies compounds that discriminate between the two model rRNA structures. This approach, coupled with a rapid solid phase methodology for aminoglycoside variants, has identified active antimicrobials (against wild type and mutant strains) that show large differences in binding affinity for the *E. coli* A-site and the human A-site than that of neomycin (~30 fold).² The methodology for synthesizing, screening for both ribosomal binding/selectivity and bacterial growth inhibition, and rapid analysis of the data provides a systematic method for identification of bacterial ribosome specific antibacterial that can evade bacterial resistance pathways.^{3,4}

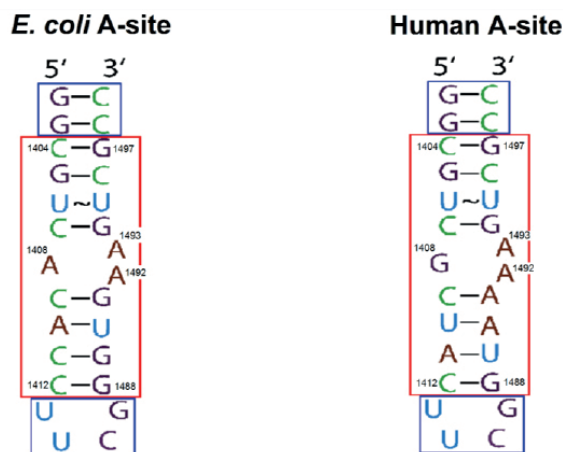


Figure 1. Secondary Structures of Bacterial and mammalian rRNA A-sites.

References:

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