Designer Aminoglycosides: The Race to Develop Improved Antibiotics and Compounds for the Treatment of Human Genetic Diseases

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Aminoglycosides are highly potent, broad-spectrum antibiotics that exert their bactericidal therapeutic effect by selectively binding to the decoding aminoacyl site (A-site) of the bacterial 16S rRNA, thereby interfering with translational fidelity during protein synthesis. The appearance of bacterial strains resistant to these drugs, as well as their relative toxicity, have inspired extensive searches towards the goal of obtaining novel molecular designs with improved antibacterial activity and reduced toxicity [1-5]. In the last several years, a new, aminoglycoside dependent therapeutic approach for the treatment of certain human genetic diseases has been identified. These treatments rely on the ability of certain aminoglycosides to induce mammalian ribosomes to readthrough premature stop codon mutations. This new and challenging task has introduced fresh research avenues in the field of aminoglycosides research [6-10]. Recent observations and current challenges in the design of aminoglycosides with improved antibacterial activity and the treatment of human genetic diseases will be discussed.
