Saccharides, Pseudosaccharides, and their Mimetics

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The aminoglycoside antibiotics (AGAs) are listed by the WHO as one of the critically important classes of antimicrobials for human therapy. They continue to be of critical importance for the treatment of MRSA, Gram-negative pathogens, multidrug-resistant *Mycobacterium tuberculosis*, and complex infectious diseases including exacerbated cystic fibrosis, complicated urinary tract infections, sepsis, and chronic obstructive pulmonary disease. High efficacy, antibacterial potency, lack of drug-related allergy, little interaction with other pharmacological substances and predominantly unchanged excretion in the urine are well known attributes.

However, the clinical use of AGAs and their development into more effective drugs unaffected by resistance factors have been limited by their toxicity, in particular reversible kidney damage (nephrotoxicity) and especially irreversible hearing damage (ototoxicity). AGA ototoxicity affects as much as 20% of the patient population, with estimates as high as 37% in patients with mycobacterial diseases taking AGAs for long durations.

The lecture will cover the design, synthesis and evaluation of next generation AGAs intended to retain high antibacterial potency while minimizing ototoxicity. The ability of the novel AGAs to circumvent common mechanisms of resistance will also be discussed.