



## **PNA-Neamine Conjugates for use as Therapeutic agents and Research Tools** (Virendra N. Pandey, NJMS 03-37) Therapeutic

### **Background**

Peptide nucleic acids (PNAs) are analogs of nucleic acid with peptide backbone replacing sugar phosphate backbone in a nucleic acid. These analogs bind to both single stranded and double stranded RNA or DNA in sequence specific manner to inhibit translation and replication. They are gene-specific, nontoxic, and non-immunogenic. However, their therapeutic potential has been limited because of their poor uptake into mammalian cells. Thus, new methods for efficient transfer of therapeutic agents and artificial nucleases with improved cell permeation properties have been extensively investigated.

Aminoglycoside antibiotics such as neomycin B, which are specific to 16S bacterial rRNA, also bind HIV RNA recognition elements, RRE (Rev Responsive Element) and TAR and block HIVRev and HIV-Tat RNA-protein interactions. However, the toxicity of neomycin B and the risk of developing antibiotic resistance due to modification by aminoglycoside-modifying enzyme limits its use as a therapeutic agent. Neamine derivatives with increased affinity to RNA targets or resistance to aminoglycoside modifying enzymes have been prepared by mimetics. **The present invention discloses new methods and compositions for the synthesis of improved PNA-aminoglycoside derivatives.**

### **Description of the Technology**

The aminoglycoside neamine was conjugated to a PNA sequence specific to the TAR region of HIV-1 RNA genome. The TAR specific PNA-neamine conjugate had improved cellular uptake and enhanced binding with the target sequence resulting in robust inhibition of viral replication. Furthermore, the conjugate was also able to block the production of HIV-1 in lymphocyte CEM cells infected with pseudotyped HIV-1 virions. One of the conjugates disclosed in the present invention showed RNA cleavage activity in the absence of magnesium ions. Taken together, these results indicate that aminoglycoside-PNA conjugates could be used as antiviral agents.

### **Applications**

Therapeutics: PNA-aminoglycoside conjugates can be used as antiviral and anticancer agents.

### **Patent Status**

PCT Patent Application filed

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