

## **PNA-Neamine Conjugates for use as Therapeutic agents and Research Tools**

### **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 is 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. For example, PNAs conjugated to diethylenetriamine and neocuproine Zn (II) derivatives hydrolyze RNA targets.

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 HIV-Rev 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. However, these derivatives do not exhibit strong antigenic properties. **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.

### **Advantages**

- Conjugation of PNA to the neamine improved PNA solubility
- PNA conjugates disclosed herein target the non-mutable region of TAR element

### **Applications**

- Therapeutics: PNA-aminoglycoside conjugates can be used as antiviral and anticancer agents.
- Research: to study structures and functions of nucleic acids.

### **Patent Status**

- PCT Patent Application filed.

## **Licensing Opportunity**

- This technology is available for licensing non-exclusively for research or exclusively for therapeutic applications.

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