NIH NATIONAL CANCER INSTITUTE

Anti-Viral Compounds that Inhibit HIV Activity

Summary (1024-character limit)

The National Cancer Institute (NCI) Molecular Targets Laboratory is seeking parties interested in collaborative research to co-develop antiviral tropolone derivatives developed by systematic medicinal chemistry on the lead series.

NIH Reference Number

E-081-2011

Product Type

- Therapeutics

Keywords

- HIV
- AIDS, RNase H
- tropolone derivative
- ribonuclease H
- viral replication

Collaboration Opportunity

This invention is available for licensing and co-development.

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Description of Technology

Several novel tropolone derivatives have been identified that inhibit HIV-1 RNase H function and have potential for anti-viral activity due to reduced cellular toxicity. Inhibiting RNase H function is a potential treatment for many viral infections, since RNase H function is essential for viral replication for many pathogenic retroviruses such as HIV-1 and HIV-2. Although many hydroxytropolone compounds are potent RNase H inhibitors biding at the enzymatic active site, they are limited as therapeutic candidates by their toxicity in mammalian cells. The toxicity thought to be a result of inhibition of multiple essential mammalian metalloenzymes. We reasoned that the potential beneficial application of tropolone RNase H inhibition might be of therapeutic use if the toxic effects in mammalian cell were eliminated. By

selectively adding steric bulk to add new drug-enzyme contacts for the RNase H active site, a number of novel compounds, that have initially demonstrated reduced cytotoxicity, have been produced. Importantly, these novel compounds appear to retain antiviral activity essential for use as therapeutics.

Potential Commercial Applications

- As an HIV-1 therapeutic

Competitive Advantages

- Potentially reduced toxicity
- Availability of x-ray crystallographic information to guide analog design

Inventor(s)

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Development Stage

- Discovery (Lead Identification)

Publications

Chung S, et al. Synthesis, activity and structural analysis of novel alpha-hydroxytropolone inhibitors of human immunodeficiency virus reverse transcriptase-associated ribonuclease H. [PMID 21568335]

Patent Status

- **U.S. Patent Issued:** U.S. Patent Number , Filed 08 Nov 2013, Issued 31 Mar 2015
- **Foreign Issued:** Foreign Filed - Patent Number

Related Technologies

- E-183-2009 - Schweinfurthins and Uses Thereof

Therapeutic Area

- Infectious Diseases