Novel Small Molecules that Inhibit Hepatitis B Virus Replication by Targeting Packaging of Pre-genomic RNA

Summary (1024-character limit)

Researchers at the National Cancer Institute (NCI) have developed an invention describing novel small molecule agonists of a previously unidentified hepatitis B virus (HBV) RNA packaging signal (pgRNA) as promising therapeutic strategies for HBV infections, either alone or in combination with other antiviral agents. The NCI seeks licensing and/or co-development research collaborations for these novel small molecules that inhibit hepatitis B virus replication by targeting pre-genomic RNA.

NIH Reference Number

E-062-2018

Product Type

- Therapeutics

Keywords

- Hepatitis B Virus, HBV, Small Molecule Agonists, RNA Packaging Signal, pgRNA, RNA Binding Small Molecule, Le Grice

Collaboration Opportunity

This invention is available for licensing and co-development.

Contact

- John D. Hewes
  NCI - National Cancer Institute

  240-276-5515

  John.Hewes@nih.gov

Description of Technology

Hepatitis B virus (HBV) is the smallest animal-infecting DNA virus with a compact 3.2 kDa genome that encodes seven proteins contained in four overlapped genes. Its small genome size and limited coding capacity make finding effective anti-HBV therapies difficult. Current treatment strategies for chronic HBV include liver transplantation or broad-spectrum nucleos(t)ide analogs including Lamivudine and Tenofovir, which are used to achieve viral suppression. Unfortunately, long-term administration of these nucleos(t)ide analogs is costly and can lead to the development of resistance mutations. While vaccines exist for HBV, there is a risk of vaccine escape mutations occurring due to complete overlap of the surface antigen proteins inside the gene for the HBV polymerase protein. The threat of a vaccine-

immune virus entering the general population warrants continued studies to uncover novel targets for viral suppression.

Researchers at the National Cancer Institute (NCI), in collaboration with the University of Leeds and the University of York, have investigated a novel, previously unidentified HBV RNA packaging signal (PS1). Furthermore, the researchers have identified small molecules capable of specifically recognizing PS1 in HBV pre-genomic RNA (pgRNA). These small molecules have proven effective at suppressing HBV replication with little to no toxicity. Compared to some clinically approved anti-HBV drugs, these molecules are significantly more inhibitory. This discovery provides, for the first time, small molecules that can be used to inhibit HBV replication by targeting an important packaging signal of its pgRNA. These can be used either alone or in combination with nucleoside/nucleotide analogs currently being used to treat HBV infections.

Potential Commercial Applications

- Hepatitis B virus (HBV) therapy

Competitive Advantages

- Small molecules effective at suppressing HBV virus replication with little to no toxicity
- Only known small molecules that inhibit HBV replication by targeting pre-genomic RNA

Inventor(s)

Stuart Le Grice (NCI), Fardokht Abulwerdi (NCI), Peter Stockley (University of Leeds), Reidun Twarock (University of York)

Development Stage

- Discovery (Lead Identification)

Patent Status

- **U.S. Provisional:** U.S. Provisional Patent Application Number 62/685,145 , Filed 14 Jun 2018

Therapeutic Area

- Infectious Diseases