Small Molecule Inhibitors of HIV-1 Tat that Block Interaction with Protein Phosphatase-1

Howard University researchers have identified a family of small molecule inhibitors that prevent HIV-1 Tat protein from binding to Protein Phosphatase-1 in infected cells, an essential step in HIV-1 replication.

Contact

Hamid A. Bhatti
TreMonti Consulting, LLC.
2944 Hunters Mill Rd., Suite 204
Oakton, Va. 22124
(305)467-5942
hbhatti@tremonticonsulting.com

Dan McCabe
Associate General Counsel
Howard University
(202)806-2650
contracts@howard.edu

Inventors

Dr. Sergei Nekhai et al.

Potential Commercial Applications

New class of HIV-1 therapeutics
Potentially useful when administered alone or in combination with existing therapeutics
Potentially useful against strains resistant to other therapies

Stage of Development

In vitro toxicity testing and HIV transcription IC50 studies completed; limited *in vivo* toxicity testing performed

Status

Seeking development & licensing partners

Background

HIV-1 replication is dependent on numerous steps including entry of the virus into cells, crossing into the nucleus, transcription of HIV DNA, and budding of new viral particles. These steps are regulated by several HIV-specific proteins which present targets for therapeutic inhibition. HIV protease, integrase, reverse transcriptase, and host cell CCR5 have all been targeted with pharmaceuticals. Unfortunately existing therapies lose efficacy as HIV becomes resistant, and new targets for pharmaceutical inhibition are desirable. HIV-1 Tat protein, which is essential to transcription of HIV in infected cells, may offer an unexploited, druggable target. Tat's ability to initiate HIV transcription is dependent on recruiting the host cell's Protein Phosphatase 1 (PP1).

Description of Technology

Dr. Nekhai has identified a family of small molecules that inhibit HIV replication by interfering with its interaction with host cell Protein Phosphatase-1. This interaction is essential to Tat's translocation to the nucleus, where it initiates transcription of HIV-specific genes. These inhibitors have been selected from a library that in general possesses good ADME properties and drug-like characteristics. Several in the family have been tested and show inhibition of Tat transcription *in vitro* between 2 and 10µM concentration, without toxicity to 293T or reporter CEM GFP cells. These inhibitors have undergone limited testing in a mouse model but full toxicity studies remain to be performed. The Tat transcription inhibitors of the current invention could be administered alone or in combination with existing therapies.

Opportunity

This family of small molecules and methods of using them to treat HIV infection are the subject of a patent application. Howard University is seeking development partners to further characterize the compound family, to complete toxicity testing and to explore novel drug delivery systems. Dr. Nekhai is available to talk about the invention under a NDA.