NOVEL COMBINATION OF CHEMICAL ENTITIES FOR LYTIC ACTIVATION AND THERAPEUTIC TARGETING OF KAPOSI'S SARCOMA-ASSOCIATED HERPESVIRUS (KSHV)

SUMMARY (1024-CHARACTER LIMIT)

The National Cancer Institute (NCI) seeks co-development and licensing interest in novel methods for treating Kaposi's sarcoma-associated herpesvirus (KSHV).

NIH REFERENCE NUMBER

E-223-2017

PRODUCT TYPE

- Therapeutics

KEYWORDS

- Kaposi's Sarcoma-associated Herpesvirus, KSHV, -hydroxytropolones, RNA Triple Helix Target, Human Immunodeficiency Virus, HSV-1, Le Grice

COLLABORATION OPPORTUNITY

This invention is available for licensing.

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STATUS

Active

DESCRIPTION OF TECHNOLOGY

Kaposi's sarcoma-associated herpesvirus (KSHV) is classified as an oncogenic human herpesvirus and is one of the most frequent causes of cancer in human immunodeficiency virus (HIV)-infected patients and the most common cause of cancer in Sub-Saharan Africa. Unfortunately, the mechanism of KSHV replication and pathogenesis is not fully understood. Like HIV, a major problem in the treatment of KSHV is viral latency which allows the virus to subvert host immunity.

Researchers at the National Cancer Institute (NCI) have developed an invention describing a novel "kick-and-kill" strategy for KSHV infections that mimics a strategy already employed for treating HIV in which

the latent viruses are “kicked” into an activated state and then “killed” by a second compound targeting critical viral proteins/enzymes.

The strategy proposed here for KSHV uses two classes of compounds that, when used in combination, could result in a more potent KSHV therapy with fewer unwanted side effects. The “kick” compound activates the virus, bringing it out of latency. Other agents currently used as viral activators often target cellular proteins, such as histone deacetylase inhibitors, leading to extensive stress and damage to the host cell. The “kick” compound described in this invention is unique in that it targets an RNA triple helix encoded by a viral long noncoding RNA (lncRNA) and, therefore, shows no, or fewer, cytotoxic effects towards the host cell. The second “kill” compound of the invention are select □-hydroxytropolones that target a previously uncharacterized KSHV nuclease enzyme, ORF29 in vitro, and inhibit KSHV replication in culture following lytic activation.

Together, these two compounds provide a unique and promising treatment strategy for KSHV that is likely to be more effective than currently available anti-KSHV therapies.

POTENTIAL COMMERCIAL APPLICATIONS

- Novel method of treating and eradicating KSHV

COMPETITIVE ADVANTAGES

- “Kick” compound is the only known viral activator that targets a RNA triple helix of the virus instead of host cell proteins like currently available viral activators
- “Kick” compound shows no cytotoxic effects toward the host cell
- The proposed strategy uses two compounds in combination that, together, provide a more potent KSHV therapy with fewer unwanted side effects

INVENTOR(S)

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DEVELOPMENT STAGE

- Basic (Target Identification)

PUBLICATIONS

Miller JT, et al. Sensitivity of the C-terminal nuclease domain of Kaposi's sarcoma-associated herpesvirus ORF29 to two classes of active site ligands. [PMID 30061278]

PATENT STATUS

- **U.S. Provisional:** U.S. Provisional Patent Application Number 62/598,807 , Filed 15 Dec 2017

THERAPEUTIC AREA

- Infectious Diseases