The STING Agonist SB 11285 is a Broad-spectrum Antiviral Agent


Background

Cyclic guanylate adenylate synthase (cGAS), an important pattern recognition receptor (PRR) for viral genomes, uses Stimulator of Interferon Genes (STING) as the key adapter protein in the IRF3-IFN signaling axis to trigger innate and adaptive immune response for antiviral defense. We report here the antiviral evaluation of a novel nucleotide compound SB 11285, a potent STING agonist, that is being developed for immuno-oncology.

Methods

In vitro antiviral evaluations of SB 11285 were conducted as follows:

1. RSV: We used RSV2A-infected (0.5 MOI) A549 cells (human lung epithelial cells) and viral titer was estimated by plaque assays.

2. Norovirus: A replication of Norovirus strain GI NoV in HG23 (hepatoma) cell line was used and activity assessed by RNA hybridization and quantitative PCR.

3. HCV: Activity against HCV genotype 3 was assessed using the capture fusion assay. Briefly, THP-1 cells were exposed to donor serum, fused with HuH7 derivative cells and qPCR was used to assess HCV replication.

4. Hemorrhagic fever viruses: Activity against JUNV strain 4454 and Dengue-2 strain NGC, was conducted respectively in A549 cells and extracellular yields were determined in Vero cells by plaque assays.

Cytotoxicity assays were done in parallel by neutral red, MTT or MTS methods.

Results

Antiviral assays against Norovirus were conducted at Georgetown University under contract from NIAID (Brent Korb, PI).

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SB 11285 elicited potent antiviral activity against all tested RNA viruses with EC50 ranging from 0.002 to 25 μM, and with high selectivity index.

Consistent with its mechanism of action, the STING agonist SB 11285 showed potent antiviral activity against several RNA viruses including hemorrhagic fever viruses. Additional preclinical studies are ongoing.

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