Novel Cyclic Dinucleotide Analogues as STING Agonists

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BACKGROUND

Stimulator of interferon genes (STING) is known to be a central mediator of innate immunity. It is a 379 amino acid protein expressed in various endothelial and epithelial cell types as well as in hematopoietic cells such as T cells, macrophages and dendritic cells. STING is naturally activated by aberrant DNA species via formation of native cyclic dinulcleotides (CDNs) in cytosol of the cell. When stimulated STING induces the expression of type I interferon (IFN), cytokines and T cell recruitment factors that result in the activation of macrophages and dendritic cells, innate effector cells such as natural killer (NK) cells and priming of tumor specific T cells.

Recent studies have shown that the STING pathway is essential for radiation induced and spontaneous natural antitumor T cell responses. Tumor cells often induce an immunosuppressive microenvironment favoring cancer development. Targeting STING pathway by using TING agonists to produce IFNs for enhancing antitumor immune response may provide an alternative strategy for the improvement of cancer immunotherapy.

TECHNOLOGY DESCRIPTION

Researchers at UC San Diego have developed novel series of c-diGMP analogues that were able to activate the innate immune response through the STING pathway in mammalian cells. Unlike Aduro's ADU-S100 where phosphate group is modified into S analogue, these analogues incorporate novel nitrogenous bases with regular phosphates.

APPLICATIONS

Combination with check-point inhibitors and as adjuvants in anticancer vaccines

ADVANTAGES

- Novel CDN analogues yield 10-fold higher IFN production than that of the native CDN
- These analogues have longer half-life than native CDN that would enable less frequent dosing
- CDN analogues are generated through enzymatic synthesis that is extremely efficient and cost effective. The enzymatic synthesis allows incorporating synthetic nitrogenous bases in CDN molecules
- These molecules could yield improved cancer immunotherapies

STATE OF DEVELOPMENT

Lead optimization and biological profiling

INTELLECTUAL PROPERTY INFO

This technology is patent pending and available for licensing and/or research sponsorship.

PATENT STATUS

Patent Pending

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OTHER INFORMATION

KEYWORDS

Cancer, Immunotherapy, Innate immunity, STING, cyclic dinucleotides, Interferon

CATEGORIZED AS

- **Medical**
  - Disease: Cancer
  - Therapeutics

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