PDE Stable Endo-phosphorothioate Substituted 2'3'-cGAMP Analogues as STING Agonist

Selective small molecules effective against multi-drug-resistant malaria strains.

Researchers at Purdue University have developed novel 2,3'cGAMP analogs as a STING antagonist. Targeting the c-GAS-STING pathway has been associated with multiple immune responses. The pathway is responsible for the synthesis of 2,3'cGAMP. 2,3'cGAMP promotes antitumor immune memory and antitumor immunity. The degradation of cGAS via ENNP1 advances cancer cell metastasis. Research has demonstrated that targeting the cGAS-STING pathway by synthesizing 2,3'cGAMP analogs leads to rapid tumor regression. Further joint ENPP1 and 2,3'cGAMP agonists are believed to further retain STING agonism.

Purdue researchers have identified molecules that associates with hSTING. These molecules have EC50 values as low as 4.3 ÂµM in-cellulo. Furthermore, it is important that these compounds are stable against ENNP1 degradation. Studies demonstrated that after 24 hours the molecule is still intact. This technology can be used to for immunogenic tumor clearance, vaccine adjunctive, and antiviral therapy.

Technology Validation: Docking was initially utilized to identify the top analogs to be synthesized and tested for STING agonism. The binding affinity to STING was demonstrated using a fluorescent polarization assay. ENNP1 degradation assay was performed to demonstrate the stability of the analogs.

Advantages:

-Active in cells

-Stable against ENNP1

-Low micromolar affinity

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Category

Chemicals & Advanced Materials/Specialty & Performance Chemicals

Chemicals & Advanced Materials/Materials Processing & Manufacturing Technologies

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Applications:

-Immunogenic tumor clearance

-Vaccine adjunctive

-Antiviral therapy

TRL: Pharmaceuticals

Intellectual Property:

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