3H-pyrazolo[4,3-f]quinoline-based Compounds as STING Antagonists

Highly selective N-terminal methylation inhibitors for cancer and stem cell research.

Researchers at Purdue University have developed a class of novel stimulator of IFN gene (STING) inhibitors for inflammatory related diseases and diseased states. Persistent activation of STING is known to be the cause of STING-associated vasculopathy with onset infancy (SAVI) and activated STING is believed to play important roles in worsening various diseased states, such as traumatic brain injury, diabetic kidney disease, and colitis. Further, chronic activation of STING has been associated with autoimmune disorders, pulmonary inflammation, diabetes, fibrosis, and many other conditions.

The Purdue researchers have identified a STING inhibitor that suppresses STING mediated cytokine production in macrophages at low nanomolar concentrations. These compounds are orally bioavailable and have the potential to be translated in vivo. The researchers were able to identify the mechanism of which the molecules were able to inhibit STING activation. These compounds inhibit STING by attenuating type 1 interferon. This technology can be utilized to further understand the role of STING or be developed into a therapy for inflammatory diseases.

Technology Validation: This technology has been validated using a fluorescence polarization assay and western blot. These methods demonstrated that this novel class of proteins has a high affinity to STING and identified the mode of action.

Advantages:

-Activity in multiple cell lines

-Minimal cytotoxicity

-Known mechanism of action

Applications:

Technology ID

2023-SINT-70181

Category

Pharmaceuticals/Pharmaceutical Packaging & Delivery Systems
Pharmaceuticals/Computational Drug Delivery & Nanomedicine
Chemicals & Advanced Materials/Materials Processing & Manufacturing Technologies

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-Inflammatory diseases

-Diabetes

-Traumatic brain injuries

-Fibrosis

Related Publication:

STING antagonists, synthesized via Povarovâ€"Doebner type multicomponent reaction

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Tags: Inflammatory diseases, diabetes, STING, neurological

TRL: Pharmaceuticals

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NATL-Patent, N/A, Canada

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NATL-Patent, N/A, Japan

NATL-Patent, N/A, United States

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