

Compounds inhibiting STING mediated cytokine production



Three-dimensional structure of human STING.

Description

Stimulator of Interferon Genes protein (STING) gain of function mutations, or its dysregulated continuous activation, is involved in the aberrant activation of innate immune pathways, including a broad range of auto-inflammatory conditions. Hence, specifically targeting STING function by means of small molecule pharmacological intervention is a promising way to treat and/or prevent STING-associated diseases, such as auto-inflammatory diseases.

The identified compounds are highly potent and selective small-molecule antagonists, suppressing STING-dependent type I interferon (IFN) induction in both human and mouse cells, and proved able to attenuate pathological features of auto-inflammatory diseases in mice. The compounds have been selected by high-throughput on the binding to STING and the modification of the transmembrane-located cysteine C91, blocking the palmitoylation of STING.

Ref. Nr

6.1857

Keywords

AGS
IFN I
Interferonopathies
STING

Intellectual Property

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Publications

Simone M Haag et al.
"Targeting STING With
Covalent Small-Molecule
Inhibitors"
Nature. 2018
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0287-8.

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Advantages

Selective inhibition of STING-dependent signaling, without interference with RIG-I or TBK1-mediated IFN I induction.

Applications

- Treatment of STING-associated diseases: type I interferonopathies (e.g. STING-associated vasculopathy with onset in the infancy (SAVI), Aicardi-Goutières Syndrome (AGS)), inflammation-associated disorders (e.g. systemic lupus erythematosus)
- Prevention of STING-associated diseases