STING PATHWAY

STING AGONISTS: ANTICANCER REGIMENS, WHICH KILL MAUSIGNANT CELLS AND SIMULTANEOUSLY CONVERT THEM INTO A CANCER-SPECIFIC THERAPEUTIC VACCINE

Activation of the STING signaling pathway in tumor-resident antigen-presenting cells (APC, e.g. dendritic cells) leads to MyD88/Trif-dependent production of type I IFN and promotes antigen-presenting cell-tumor cell printing.

STING agonists modulate immune system promoting cancer cell lysis by dendritic cells. CD8+ T cells activation and sensitization resistant tumors to therapy.

CONCLUSIONS

SELVITA DISCOVERED NON-MACROCYCLIC, NON-NUCLEOTIDE SMALL MOLECULE STING AGONISTS WITH POTENTIAL FOR SYSTEMIC ADMINISTRATION

STING AGONISTS PROPERTIES

CHEMICAL SERIES OF SELVITA STING AGONISTS HAS FINE TUNABLE IN VITRO ADME AND PHARMACOCHEMICAL PROPERTIES

Cmpd 1 and Cmpd 2 are stable in both human and mouse plasma.

Cmpd 1 and Cmpd 2 are potent inducers of cytokine release in mouse bone narrow-derived macrophages (MDM).

Cmpd 1 and Cmpd 2 efficiently promotes in vitro maturation of human monocytic-derived dendritic cells (mDC).

Cmpd 1 and Cmpd 2 have efficacy superior to cyclic dinucleotides (CDN) in cytokine release in human mononuclear cells (mDC).

Cmpd 1 and Cmpd 2 induce in vitro expression of surface activation markers on human monocyte-derived macrophages (MDM) and cytokine release across different STING haplotypes.

Cmpd 1 and Cmpd 2 bind to Listing binding of selvita STING agonists promotes arrangement of STING close conformation similar to cyclic dinucleotides.