

NOVEL COMPOUNDS FOR IMMUNOMODULATORY ACTIVITY

A novel anti-Mpro inhibitor derived from Chloropyridyl ester derivatives offers effective, Remdesivir-comparable antiviral potency against SARS-COV-2, with applications in COVID-19 treatment and vaccine development.

Purdue University researchers have developed a potent small molecule for use in cancer immunotherapy which acts by inhibiting the Programmable Cell Death Protein 1/Programmable Death-Ligand 1 (PD-1/PD-L1) interaction. Cancer cells express PD-L1, a cell surface protein that binds to PD-1 on T-cells, debilitating anti-cancer immunity. Antibodies targeting the PD-1/PD-L1 interaction have proven to be a viable therapeutic strategy toward mitigating cancer growth but suffer from high production costs, limited administration techniques, and low therapeutic indices. To address these limitations, Purdue University researchers created a small molecule inhibitor of the PD-1/PD-L1 interaction that specifically target PD-1 dimerization. The researchers developed the new molecule through robust computational modeling of publicly available PD-1/PD-L1 inhibitory data. In homogenous time-resolved fluorescence binding assays the Purdue compound exhibited about 1.6 fold increased potency in inhibiting the PD-1/PD-L1 interaction compared to a positive control molecule known from the patent literature (IC₅₀ = 339.9 nM and 521.5 nM, respectively). Further medicinal chemistry optimization promises to increase potency and yield an excellent preclinical candidate for use in small molecule immune checkpoint blockade therapy.

Advantages:

-Increased Potency to PD-1/PD-L1 Interaction

-Combined Scaffolds of BMS Compounds

Potential Applications:

-Immune Checkpoint Blockade

-Cancer Therapeutics

Technology ID

2020-CHOP-68949

Category

Biotechnology & Life
Sciences/Biomarker Discovery &
Diagnostics
Biotechnology & Life
Sciences/Bioinformatics &
Computational Biology
Biotechnology & Life
Sciences/Analytical & Diagnostic
Instrumentation
Pharmaceuticals/Computational
& Software Tools

Authors

Gaurav Chopra
Jonathan Fine
Krupal Jethava
Prageeth Wijewardhane

Further information

Joe Kasper
JKKasper@prf.org

Nathan Smith
nesmith@prf.org

View online



Related Publication:

Combined Molecular Graph Neural Network and Structural Docking Selects Potent Programmable Cell Death Protein 1/Programmable Death-Ligand 1 (PD-1/PD-L1) Small Molecule Inhibitors

Preprint available at chemrxiv.org

DOI: 10.26434/chemrxiv.12083907.v1

TRL: 3

Intellectual Property:

Provisional-Gov. Funding, 2020-03-11, United States | NATL-Patent, 2021-03-05, Japan | NATL-Patent, 2021-03-05, Mexico | PCT-Gov. Funding, 2021-03-05, WO | NATL-Patent, 2021-03-05, Canada | NATL-Patent, 2021-03-05, China | NATL-Patent, 2021-03-05, Europe | NATL-Patent, 2021-03-05, India | NATL-Patent, 2022-08-31, United States | CON-Patent, 2025-09-26, United States

Keywords: Small molecule inhibitor, cancer immunotherapy, PD-1/PD-L1 interaction, immune checkpoint blockade, cancer therapeutics, PD-1 dimerization, BMS compounds, preclinical candidate, potent, molecular graph neural network