PURDUE INNOVATES | Office of Technology Commercialization

NOVEL COMPOUNDS FOR IMMUNOMODULATORY ACTIVITY

A novel, potent small molecule inhibitor targeting the PD-1/PD-L1 interaction offers a cost-effective alternative to antibody therapies for use in immune checkpoint blockade and cancer therapeutics.

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

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Category

Biotechnology & Life Sciences/Biomarker Discovery & Diagnostics
Biotechnology & Life Sciences/Bioinformatics & Computational Biology
Pharmaceuticals/Drug Discovery & Development
Biotechnology & Life Sciences/Analytical & Diagnostic Instrumentation
Pharmaceuticals/Small Molecule Therapeutics

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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

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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

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