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PTP1B/TC-PTP Dual Protein Degraders

A highly potent and selective dual small-molecule drug degrades specific protein tyrosine phosphatases (PTPs) implicated in cancer and diabetes, effectively halting tumor growth in mouse models.

Researchers at Purdue have developed a dual degrader that is highly specific to two protein tyrosine phosphatases (PTPs) implicated in cancer, diabetes, and obesity. These PTPs - PTP1B and TC-PTP- have synergistic roles in negatively regulating insulin and T-cell activation, making them desirable targets for the design of small molecule inhibitors. While different small molecule inhibitors could be developed for each PTP, generally, there is an increased risk and unpredictability with multi-drug therapeutics compared with single drug systems.

Purdue researchers have designed a small-molecule drug that is multi-specific to PTP1B and TC-PTP. This small molecule drug is effective in the low nanomolar range. Further, the dual PTP drug includes a motif that activates the ubiquitin-proteasome pathway, which can selectively degrade the target proteins instead of only inhibiting them. The drug reversibly binds to proteins of interest, allowing the same drug molecule to bind to and activate the degradation of many PTP1B/TC-PTP's catalytically.

Technology Validation:

- Ability to degrade PTP1B and TC-PTP in vivo tested in MC38 syngeneic mice. The mice were split into three experimental groups, daily injection of saline, daily injection of 25 mg/kg of duel PTP degrader, and daily injection of 50 mg/kg of duel PTP degrader. Tumor growth was effectively halted for all mice treated with dual PTP degrader as compared to those injected with saline only.

- High selectivity of dual PTP degrader verified by administering the drug to HEK293 cells and measuring the level of other PTP's in cell lysate. Post treatment, PTP1B and TC-PTP were completely degraded and none of the other PTP's were affected.

Advantages:

Technology ID
2023-ZHAN-70087

Category
Chemicals & Advanced Materials/Specialty & Performance Chemicals
Pharmaceuticals/Drug Discovery & Development
Chemicals & Advanced Materials/Materials Processing & Manufacturing Technologies
Pharmaceuticals/Small Molecule Therapeutics

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- Potent degrader of target PTP's, effective in low nanomolar range

- Highly selective to two target PTP's

- Halts tumor growth in mouse model

Applications:

- Cancer treatment

- Diabetes treatment

Related Publication:

Small Molecule Degraders of Protein Tyrosine Phosphatase 1B and T-Cell Protein Tyrosine Phosphatase for Cancer Immunotherapy

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Intellectual Property:

Provisional-Gov. Funding, 2023-02-06, United States | NATL-Patent, 2023-12-08, Europe | NATL-Patent, 2023-12-08, Australia | NATL-Patent, 2023-12-08, Canada | NATL-Patent, 2023-12-08, Japan | NATL-Patent, 2023-12-08, China | PCT-Gov. Funding, 2023-12-08, WO | NATL-Patent, 2025-08-06, United States

Keywords: Dual degrader, Protein tyrosine phosphatases, PTP1B, TC-PTP, ubiquitin-proteasome pathway, small-molecule drug, cancer treatment, diabetes treatment, tumor growth inhibitor, selective protein degradation