PURDUE INNOVATES | Office of Technology Commercialization

PROTEIN:PROTEIN INTERACTION INHIBITORS

A novel therapeutic strategy targets the PRMT5:MEP50 protein interaction to disrupt cancer proliferation pathways, leading to the development of selective, targeted cancer treatments with fewer side effects.

Researchers at Purdue have developed a therapeutic strategy for cancer treatment by targeting the protein-protein interaction between PRMT5 and MEP50. PRMT5 is a protein that has been found to be frequently overexpressed in cancers and associated with poor clinical outcomes. By analyzing the crystallographic structure of the PRMT5:MEP50 complex and utilizing Bimolecular Fluorescence Complementation to study their interactions, researchers were able to identify key residues in the proteins that are crucial for their interaction. To prove the efficacy of in-vitro use of this technology, researchers developed various compounds for the inhibition of the protein-protein interaction. These compounds showed remarkable inhibition of PRMT5:MEP50 complex formation, as evidenced by its ability to inhibit multiple PRMT5-regulated pathways critical to the survival and proliferation of lung and prostate cancer cells

This discovery can be used to develop small molecules that specifically target the binding interface between PRMT5 and MEP50, thereby disrupting their interaction and potentially inhibiting the progression of cancer. This approach offers a specific method to target PRMT5 in a context-specific manner. By focusing on the protein-protein interaction rather than the catalytic function of PRMT5, this technology can lead to the development of more selective and specific therapeutic compounds for cancer treatment.

Technology Validation:

- Specific mutations into the PRMT5 and MEP50 proteins led to a significant reduction in their interaction.

- The reduction in protein-protein interaction discussed above, suggests that targeting the electrostatic interactions at the interface of the PRMT5:MEP50 protein-protein interaction could be a promising therapeutic approach.

- 65.4% decrease in amount of MEP50 co-immunoprecipitated with PRMT5 bait across three independent biological replicates

Technology ID
2022-HU-69918

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

Authors
Xuehong Deng
Changdeng Hu (DECEASED)

Further information
Joe Kasper
JRKasper@prf.org

Nathan Smith
nesmith@prf.org

View online

Advantages:

- Selective targeting of PRMT5:MEP50 interaction for cancer treatment

- Reduced off-target effects compared to pan-methyltransferase inhibitors

- Potential for tailored treatment based on cancer type or stage

- Enhanced efficacy through combination therapies

- May overcome resistance to current therapies

Applications:

- Personalized medicine for cancer patients based on PRMT5:MEP50 dependency

- Development of targeted cancer therapies with fewer side effects

- Treatment of various cancer types, including solid and blood cancers

TRL: 2

Intellectual Property:

Provisional-Gov. Funding, 2022-08-19, United States | NATL-Patent, 2023-08-18, Europe | PCT-Gov. Funding, 2023-08-18, WO | NATL-Patent, 2025-02-19, United States

Keywords: cancer treatment, protein-protein interaction, PRMT5, MEP50, targeted cancer therapies, small molecules, selective inhibitors, lung cancer, prostate cancer, personalized medicine