PURDUE INNOVATES | Office of Technology Commercialization

PRMT Inhibitors

Low-cost, self-collection tools for EV diagnostics and remote biobanking.

Researchers at Purdue University have developed a novel potent and selective protein arginine methyltransferase (PRMT) inhibitor. Cancer, cardiovascular diseases, inflammatory diseases, and diabetes have been linked to abnormal expression or activity of PRMTs. PRMTs share a highly conserved active, imposing challenges on developing potent and selective inhibitors. S-adenosyl-L-homocysteine (SAH) has a high affinity to PRMTs making SAH mimics an attractive strategy for developing therapeutic agents.

Purdue researchers have developed a focused library of SAH surrogate and profiled the active site of PRMTs. SAH Analog Library Unveils Ligand Preferences for each PRMT, serving as a rational guide to develop isoform-selective inhibitors. Additionally, a unique and novel binding pocket was discovered by a noncanonical but less polar SAH surrogate. This discovery leads to an opportunity for a new class of PRMT inhibitors to be developed.

Notably, there are a few exciting discoveries. 1. New, potent and selective inhibitors of type I PRMTs exhibit inhibitory activity less than 5 nanomolar. 2. Selective and potent inhibitor for PRMT1 exhibits over 7-fold selectivity over other type I PRMTs, which is the most selective inhibitor to date. 3. Potent and selective PRMT4 inhibitors demonstrate picomolar inhibitory activity and over 1,000-fold selectivity to other PRMTs. The prodrug also displayed efficacy in cellular, organoid, and animal models.

Technology Validation: This technology has been validated using SAHH-coupled assay, thermal shift assay, and co-crystallization. These methods demonstrated that these novel compounds selectively inhibit PRMT and do so in a unique and novel binding pocket.

Advantages:

-Novel mechanism of action

-Potent

Technology ID

2023-HUAN-70160

Category

Chemicals & Advanced Materials/Specialty & Performance Chemicals

Pharmaceuticals/Drug Discovery & Development

Chemicals & Advanced Materials/Materials Processing & Manufacturing Technologies

Authors

Youchao Deng

Rong Huang

Further information

Joe Kasper

JRKasper@prf.org

Nathan Smith

nesmith@prf.org

View online

-Selective

Applications:

-Cancer

-Inflammatory Diseases

-Diabetes

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TRL: Pharmaceuticals

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