Cell-potent and Selective Inhibitors of Nicotinamide N-methyltransferase for Disease Treatment

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Categories:
- Biotechnology

Keywords:
- Biotechnology
- Cell-potent Inhibitor
- Nicotinamide N-methyltransferase
- Selective

NCS: Researchers at Purdue University have synthesized a series of cell-potent and selective inhibitors of nicotinamide N-methyltransferase (NNMT) that can be used to treat cancer, metabolic and neurodegenerative diseases. NNMT plays an important role in regulating both epigenetics and metabolism by methylating nicotinamide. Elevated levels of NNMT have been associated with diseases like cancer, liver disease, diabetes, and obesity. The most potent compound (IC50 =3.4 nM) synthesized by the Purdue researchers had an IC50 value of 100 nanomolar for inhibiting N-methylated Nicotinamide in cells, over 1000-fold selectivity for NNMT compared to related methyltransferases. Moreover, cell-potent NNMT inhibitors exhibit a favorable pharmacokinetics profile.

Related Publications: Chen D, Li L, Diaz K, Iyamu ID, Yadav R, Noinaj N, Huang R. (2019) Novel propargyl-linked bisubstrate analogs as tight-binding Inhibitors for nicotinamide N-methyltransferase. Journal of Medicinal Chemistry. 62 (23), 10783-10797. PMID: 31724854; PMCID: PMC7296983. www.ncbi.nlm.nih.gov/pubmed/31724854

Iyamu ID, Vilseck JZ, Yadav R, Noinaj N, Huang R. (2022) Exploring unconventional SAM analogues to build cell-potent bisubstrate inhibitors for nicotinamide /N-methyltransferase. Angewandte Chemie International Edition. https://doi.org/10.1002/anie.202114813

Advantages

- Selective

- Low concentration

Applications

-Metabolic disorders

-Cancers

-Neurodegenerative diseases

People:

- Huang, Rong (Project leader)
- Iyamu, Iredia David

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