PURDUE INNOVATES | Office of Technology Commercialization

5-6-5/6 Scaffold as Selective Kinase Inhibitor Moiety with Low Activity Against Immune and Cardiovascular Anti-targets

A novel, potent, and selective FLT3 inhibitor with nanomolar activity shows promise for treating acute myeloid leukemia and acute lymphoblastic leukemia by combating drug resistance.

Researchers at Purdue University have developed a novel FLT3 inhibitor for multiple myeloma. FMS-like tyrosine kinase 3 (FLT3) is normally expressed in hematopoietic cells, lymphohematopoietic organs, and the brain. Overexpression of phosphorylated FLT3 results in cell maturation and proliferation in acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL). Furthermore, FLT3 overexpression is correlated with a poor prognosis. There are currently three FDA approved FLT3 inhibitors, unfortunately these compounds struggle with on-target drug resistance and selectivity. There is a dire need to develop novel selective compounds to combat resistance.

Purdue researchers have identified a selective and potent molecule which inhibits FLT3. The synthesized molecules had a maximal inhibitory concentration against FLT3 at 1 nanomolar. After screening the compound against an array of common off target proteins, the molecule selectively inhibits FLT3. Furthermore, the compounds were active in Molm-14 cells with a concentration that reduces total cell growth by 50% at 2 nanomolar. As phosphorylated FLT3 overexpressed in AML and ALL, researchers demonstrated that there is a significant reduction of phosphorylated FLT3 at 5 nanomolar. This technology can be used to treat AML and ALL.

Technology Validation: This technology has been validated with ADP Glo kinase assay, CellTiter-Blue cell viability assay, and western blot. These methods demonstrated that these compounds can inhibit phosphorylation of FLT3 and inhibit growth of Molm-14 cells.

Advantages:

Technology ID
2024-SINT-70378

Category
Biotechnology & Life Sciences/Biomarker Discovery & Diagnostics
Pharmaceuticals/Drug Discovery & Development
Biotechnology & Life Sciences/Analytical & Diagnostic Instrumentation
Pharmaceuticals/Small Molecule Therapeutics
Pharmaceuticals/Research Tools & Assays

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View online

-Nanomolar activity

-Selective

-In cellulo activity in Molm-14 cells

-Reduces FLT3 phosphorylation

Applications:

-Acute myeloid leukemia

-Acute lymphoblastic leukemia

Publication:

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