PURDUE INNOVATES | Office of Technology Commercialization

4-substituted-3-isoquinoline Amides and Amidines as Anticancer Agents

Novel, metabolically stable compounds that simultaneously inhibit key protein kinases and bind to G-quadruplexes show potent activity against AML and offer broad potential as cancer therapeutics.

Acute myeloid leukemia (AML) has a five-year survival rate of 25 percent. Patients develop resistance to the current standard AML drug, ara-C, both alone and in combination with other cancer drugs. In AML as well as a number of other cancers, the disease is driven by protein kinases like FLT-3 and TrkC. Another structure implicated in cancer is the G-quadruplex formed through DNA interactions. This biology can be taken advantage of to design a more effective treatment for AML.

A Purdue University researcher has developed a series of new compounds that inhibit the FLT-3 and TrkC protein kinases and bind to G-quadruplexes. These compounds display activity in AML cell lines with nanomolar IC50 values. In addition to their effectiveness against cancer cell lines, these compounds have been designed to be metabolically stable. It is anticipated that these compounds will have superior performance against AML compared to the standard treatment. The mechanisms that drive AML also drive many cancers, so these dual protein kinase inhibitors/G-quadruplex binders have broad potential as cancer therapeutics.

Advantages:

-Potent anticancer agents

-Designed to be metabolically stable

Potential Applications:

-AML therapeutic

-Treatment for multiple cancers

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Identification of new FLT3 inhibitors that potently inhibit AML cell lines, via an azo cllick-it/staple-it approach. ACS Medicinal Chemistry Letters.

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Intellectual Property:

Provisional-Patent, 2016-08-15, United States | NATL-Patent, 2017-08-15, Canada | NATL-Patent, 2017-08-15, China | DIV-Patent, 2017-08-15, Canada | PCT-Patent, 2017-08-15, WO | NATL-Patent, 2017-08-15, India | NATL-Patent, 2017-08-15, Japan | NATL-Patent, 2017-08-15, European Patent | NATL-Patent, 2019-02-12, United States | DIV-Patent, 2021-03-01, United States | DIV-Patent, 2022-01-10, Europe | Foreign, Non-PCT, 2022-12-13, Hong Kong | CON-Patent, 2024-09-17, United States | EP-Patent, N/A, United Kingdom | EP-Patent, N/A, France | EP-Patent, N/A, Germany

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