PURDUE INNOVATES | Office of Technology Commercialization

Inhibitors of Solvent Front Mutated RET Kinase

Highly soluble, potent small molecule inhibitors effectively target common RET mutations, providing a needed treatment option for multiple forms of RET-altered cancers.

Researchers at Purdue University have developed novel RET protein tyrosine kinase inhibitors (TKIs). RET is a transmembrane receptor protein-tyrosine kinase that activates multiple downstream pathways involved in cell proliferation and survival. Several small molecule TKIs that are specific to RET have been recently approved to treat RET-altered cancers. However, these compounds are inactive against RET mutations. Viable treatment options for treating mutated RET is direly needed.

Purdue researchers have identified molecules that potently inhibit a common RET mutation better than previously reported molecules. Aside from the increased activity, these molecules also exhibit better drug-like properties, such as solubility. The half maximal inhibitory concentration with mutated RET is as low as 1.5 nanomolar. Furthermore, the solubility of these molecules is 100 times greater than current treatments. This technology can be used to treat multiple forms of RET-altered cancers.

Technology Validation: This technology has been validated using in-vitro kinase assay. This method demonstrated the half maximal inhibitory concentration of the synthesized molecules.

Advantages:

-Potent

-Active against common RET mutation

-Highly soluble

Applications:

-RET-altered cancers

Technology ID

2023-SINT-70021

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

Authors

Neetu Dayal
Elizabeth Larocque
Herman O Sintim
Jie Wu

Further information

Joe Kasper
JRKasper@prf.org

Nathan Smith
nesmith@prf.org

View online

-Cancers with RET mutation

Publication:

Targeting RET Solvent-Front Mutants with Alkynyl Nicotinamide-Based Inhibitors

Khatri, Ujjwol ; Dayal, Neetu ; Hu, Xueqing ; Larocque, Elizabeth ; Naganna, Nimishetti ; Shen, Tao ; Liu, Xuan ; Holtsberg, Frederick W. ; Aman, M. Javad ; Sintim, Herman O. ; Wu, Jie

Molecular cancer therapeutics, 2023-06, Vol.22 (6), p.717-725

https://doi.org/10.1158/1535-7163.MCT-22-0629

TRL: 3

Intellectual Property:

Provisional-Gov. Funding, 2023-01-23, United States | PCT-Gov. Funding, 2024-01-23, WO | NATL-Patent, 2025-07-23, United States

Keywords: RET protein tyrosine kinase inhibitors, TKIs, RET-altered cancers, mutated RET treatment, highly soluble RET inhibitors, potent TKI, RET mutation inhibitor, alkynyl nicotinamide-based inhibitors, cell proliferation, cancer therapy