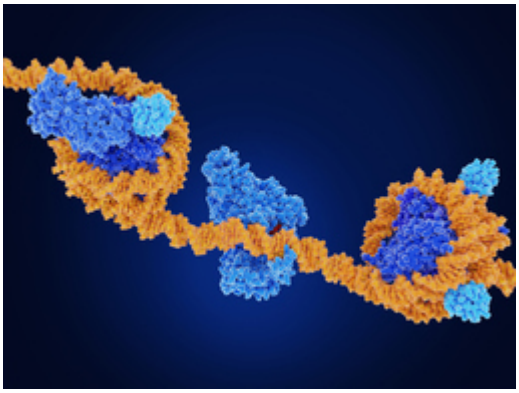
INNOVATION PARTNERSHIPS
UNIVERSITY OF MICHIGAN

PRC1 Inhibitors

TECHNOLOGY NUMBER: 2018-372



Technology ID
2018-372

Category
Therapeutics and Vaccines
Life Sciences

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OVERVIEW

Creation of small molecule inhibitors of the Polycomb Repressive Complex 1 (PCR1)

- Affects function through directly binding to the Ring1B-Bmi1 E3 lights protein
- Supports targeted destruction of leukemic stem cell populations

MODALITY

Small molecule drug; administered systemically (likely oral or intravenous)

INDICATION

Treatment of acute myelogenous leukemia (AML) and other related hematologic cancers with chemotherapy resistance

PUBLICATIONS

"Development of PRC1 Inhibitors Employing Fragment-Based Approach and NMR-Guided Optimization"

INTELLECTUAL PROPERTY

- US11319302 "PRC1 inhibitors and methods of treatment therewith"
- CN112533581B "PRC1 inhibitors and methods of treatment using the same"
- EP3813784 "Prc1 inhibitors and methods of treatment therewith"
- EP4155293 "Prc1 inhibitors and methods of treatment therewith"

BACKGROUND

Epigenetics involves the regulation of cellular genetic expression without altering its DNA code. Polycomb proteins are important epigenetic factors that operate by repressing gene expression. These proteins are vital for the normal development of blood cells and have been shown to become dysregulated in hematologic malignancies. One protein aggregation, the Polycomb Repressive Complex 1 (PCR1), normally regulates differentiation of stem cells but may fail this function in the setting of certain leukemias. Two proteins located in PCR1 are Bmi1 and Ring1B, the former of which serves as a proto-oncogene whose dysregulation correlates with leukemias that have a high resistance to chemotherapy agents. So, a need exists to improve the options for influencing the regulatory functions of PCR1.

INNOVATION

Researchers have invented small molecule inhibitors of the Polycomb Repressive Complex 1 via direct binding to the Ring1B-Bmi1 E3 ligase protein. These compounds display potent effects in cell models, specifically involving cell samples from patients with acute myelogenous leukemia (AML). The mechanism of action for this innovation supports targeted destruction of leukemic stem cell populations by inducing their differentiation. The positive effects of these small molecule inhibitors have been confirmed through study of in vivo xenograft models where significant prevention of tumor growth was noted. As ongoing elucidation for the role of PCR1 complexes in driving various malignancies becomes more apparent, this class of inhibitors holds substantial promise in improving the targeting of cancer stem cells and chemotherapy resistant cancers.