14-3-3 COVALENT MOLECULAR GLUE STABILIZERS

Tech ID: 32638 / UC Case 2022-070-0

PATENT STATUS

Patent Pending

BRIEF DESCRIPTION

This drug discovery platform focuses on identifying and developing covalent molecular glue stabilizers specifically designed to target 14-3-3 proteins. Researchers at UC Berkeley have engineered this system to discover small molecules that create a permanent, covalent bond between 14-3-3 adapter proteins and various disease-relevant targets. By stabilizing these protein-protein interactions (PPIs), the platform enables the sequestration and functional inhibition of proteins that are typically considered "undruggable" due to a lack of traditional binding pockets. This approach exploits the extensive regulatory network of 14-3-3 proteins, which interact with hundreds of signaling partners, to provide a modular strategy for therapeutic intervention across a wide range of human diseases.

SUGGESTED USES

» Oncology Therapeutics: Developing glues to sequester oncogenic signaling proteins that depend on 14-3-3 for stability or cellular localization.

» Neurodegenerative Disease Treatment: Targeting proteins involved in pathological signaling or misfolding pathways within the central nervous system.

» Modulation of Scaffolding Proteins: Providing a mechanism to inhibit the activity of adapter proteins that lack enzymatic domains and are therefore difficult to target with conventional inhibitors.

» High-Throughput Lead Discovery: Serving as a specialized screening system to rapidly identify novel covalent ligands for challenging protein-protein interfaces.

» Biological Research Tools: Utilizing specific molecular glues to acutely sequester proteins in cell models to validate their roles in complex biological pathways.

ADVANTAGES

» Irreversible Stabilization: The covalent nature of these molecular glues ensures long-lasting sequestration of the target protein, providing more robust inhibition than reversible binders.

» Targeting "Undruggable" Space: Effectively modulates protein-protein interfaces that are traditionally inaccessible to standard occupancy-based small molecules.

» Enhanced Selectivity: The mechanism requires the specific cooperative binding of 14-3-3 and the target protein, minimizing off-target interactions with other cellular proteins.

» Versatile Platform: Capable of being adapted to a wide variety of targets within the vast 14-3-3 interactome.

» Accelerated Development: The platform streamlines the transition from initial screening to the identification of therapeutic lead compounds.

RELATED MATERIALS

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Covalent Degrader of the Oncogenic Transcription Factor CTNNB1
- Stereoselective Covalent Destabilizing Degradation of the Oncogenic Transcription Factor MYC

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OTHER INFORMATION

CATEGORIZED AS

» Biotechnology
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» Screening Assays

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