Novel Small GTPase Inhibition Platform: Chemical Genetic Switch II Pocket Inhibitors Targeting Ras, Rho, Rab, and Roc GTPases for Therapeutic Applications in Cancer, CNS Disorders, and Beyond

Tech ID: 34568 / UC Case 2024-007-0

TECHNOLOGY DESCRIPTION

UCSF inventors have developed a novel platform for the chemical inhibition of small GTPases, including members of the Ras, Rho, Rab, and Roc families, using Switch II Pocket inhibitors. Small GTPases, often considered “undruggable” due to their high affinity for GTP and lack of accessible regulatory sites, play critical roles in diseases like cancer, neurological disorders, vascular disease, and Parkinson’s disease. This groundbreaking technology introduces a first-in-class approach by exploiting a cryptic allosteric pocket in the Switch II region of GTPases and incorporating non-natural cysteine residues to enable selective and durable inhibition. Currently in the development stage, the platform provides a medium-throughput assay for identifying small molecule inhibitors, offering transformative capabilities for drug development, particularly for CNS and oncology indications. By overcoming traditional challenges in targeting small GTPases, this innovation unlocks opportunities for novel therapeutic strategies and research tools to address significant unmet medical needs.

RELATED MATERIALS

- Targeting Ras-, Rho-, and Rab-family GTPases via a conserved cryptic pocket, PMCID: PMC11531380

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DATA AVAILABILITY

PATENT STATUS

Patent Pending

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OTHER INFORMATION

KEYWORDS

Undruggable proteins, Cancer treatments, Protein engineering, Parkinson’s disease, Chemical inhibition of GTPases, Small molecule drug discovery, Allosteric inhibition, Ras-like GTPases, Switch II Pocket inhibitors

CATEGORIZED AS

- **Medical**
  - Disease: Central Nervous System
  - New Chemical Entities, Drug Leads
  - Research Tools
  - Screening
  - Therapeutics
- **Research Tools**
  - Screening Assays

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