Novel Molecular Glues Targeting 14-3-3/ER for Treatment-Resistant ER+ Breast Cancer

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TECHNOLOGY DESCRIPTION

UCSF researchers have developed small molecule glues designed to stabilize the 14-3-3/ERα protein-protein interaction (PPI), offering a groundbreaking approach to treating metastatic ER+ breast cancer resistant to current therapies. This technology addresses the unmet need for effective treatments post-CDK4/6 inhibitor progression by targeting a unique site on ER, distinct from existing inhibitors, enabling combination therapies and overcoming resistance. Using advanced computational scaffold-hopping, biophysical screening, and structural biology, the team has identified hit tool compounds at the early development stage with orthogonal mechanisms of action. These molecular glues hold promise for improving outcomes in later lines of therapy and expanding therapeutic options for patients with limited treatment efficacy.

RELATED MATERIALS

- Stabilization of Native Protein-Protein Interactions with Molecular Glues: A 14-3-3 Case Study, PMCID: PMC12444995, DOI: 10.1021/acs.accounts.5c00441 - 09/05/2025
- Modulation of the 14-3-3s/C-RAF "auto" inhibited complex by molecular glues, PMCID: PMC12324506, DOI: 10.1101/2025.07.30.667769 - 07/31/2025
- Scaffold-hopping for molecular glues targeting the 14-3-3/ERa complex PMCID: PMC12260087, DOI: 10.1038/s41467-025-61176-4 - 07/14/2025

PATENT STATUS

Patent Pending

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OTHER INFORMATION

KEYWORDS

Molecular glues, 14-3-3/ER interaction, ER+ breast cancer, Drug resistance, Scaffold-hopping, Oncology therapeutics, Metastatic breast cancer

CATEGORIZED AS

- Medical
  - Disease: Cancer
  - Therapeutics

RELATED CASES

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