

PROTAC-Based Therapy for BRCA-Mutant Cancers

Technology Domain: Pharmaceuticals

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Status (Patent/TRL): Patent Pending / TRL 3

Technology Summary:

This invention introduces novel PROTAC (PROteolysis TArgeting Chimera) compounds designed for the selective and irreversible degradation of the PARP1 protein, a crucial DNA repair enzyme overexpressed in various cancers. The key technical solution involves bifunctional molecules that hijack the ubiquitin-proteasome system (UPS) to eliminate PARP1, a significant advancement over traditional, reversible PARP inhibitors. The key inventive feature lies in the rational design of these PROTACs, integrating a novel PARP1-binding ligand, an E3 ligase recruiter (e.g., pomalidomide), and an optimized chemical linker to form a stable ternary complex.

Results from *in vitro* assays in triple-negative breast cancer cells (MDA-MB-231) demonstrate enhanced cytotoxic activity (e.g., P1C1 IC₅₀ ~70.13 μM), confirming effective PARP1 degradation. Its primary use is as a promising therapeutic strategy for cancers, particularly those with BRCA1/2 mutations and acquired resistance, offering improved target specificity, lower dosages, and potential to overcome drug resistance.

