

Supplementary Material

Supplementary Table 1: AI approaches for drug repurposing in BC. Representative studies applying AI/ML methods to drug repurposing, with BC context and validation level defined as follows.

Study	Title	BC focus	Data used	AI/ML method	Repurposing output / key result	Validation level	Ref
Cui et al., 2021	Drug repurposing for cancer by integrating drug-disease expression profiles and drug-drug similarity networks (GraphRepur)	Pan-breast cancer	Disease differentially expressed genes, LINCS L1000, drug-drug links	Graph neural networks (GraphSAGE)	Prioritized drug candidates via disease-drug proximity	Cross-validation, case studies	[76]
Lin et al., 2023	Identifying candidate drugs based on transcriptional landscape associated with TNBC	TNBC	TNBC transcriptomes; LINCS/CMap	Connectivity mapping + enrichment	Drugs reversing TNBC oncogenic programs	In-silico prioritization	[77]
Ouyang et al., 2024	AI-powered omics-based drug pair discovery for pyroptosis therapy targeting TNBC	TNBC	TNBC multi-omics + drug databases	Biofactor-regulated neural network	Screened drug pairs (e.g., mitoxantrone+gambogic acid)	In-vitro validation (nanocrystal delivery)	[64]
Di Cosimo et al., 2024	A gene expression-based classifier for HER2-low BC	HER2-low	Multicohort RNA-seq / expression	Gene-expression classifier	Stratified HER2-0 vs HER2-low to guide ADC selection	Retrospective multicohort validation	[78]
He et al., 2023	ASGARD: Single-cell guided pipeline for drug repurposing	Breast cancer among cancers	scRNA-seq + LINCS	scRNA-guided repurposing	Predicted drugs targeting resistant cell subclones	Benchmark on scRNA-seq datasets	[79]
Hamed & Fandy, 2024	Accelerating complex disease treatment through network medicine and generative AI: a case study on drug repurposing for BC	Breast cancer	Pathway networks + LLM text-mining	Network medicine + GenAI	Repositioned drugs mapped to BC pathways	Computational demonstration	[80]
Karampuri et al., 2024	ResisenseNet: a hybrid neural network for drug repositioning and resistance prediction in cancer	Breast cancer context	LINCS + omics	Hybrid neural networks	Repurposed DDR-targeting candidates	Simulation study	[81]

Supplementary Table 1: AI approaches for drug repurposing in BC. (continued).

Study	Title	Breast cancer focus	Data used	AI/ML method	Repurposing output / key result	Validation level	Ref
Fauteux et al., 2015	Computational selection of antibody-drug conjugate targets for BC	Luminal, HER2+, TNBC	Subtype-stratified expression	Computational target prioritization	ADC targets overexpressed by subtype	In-silico; literature corroboration	[82]
Mundi et al., 2023	A transcriptome-based precision oncology platform for patient-therapy alignment in a diverse set of treatment resistant malignancies	Mixed tumors including BC	Patient transcriptomes; drug perturbation atlas	Network-inference + inversion logic	Patient-specific repurposed drug lists	Prospective single-patient N-of-1 trials	[65]
Jurj et al., 2025	Redefining BC Care by Harnessing Computational Drug Repurposing	Breast cancer	Multi-omics + AI literature	Systematic review	Evaluated computational repositioning methods	State-of-the-art synthesis	[83]
Subramanian et al., 2017	A next generation connectivity map: L1000 platform and the Drug Repurposing Hub	Core platform, used across BC	1M perturbational profiles (L1000)	Signature matching	Provided basis for drug-repurposing studies	Benchmark platform paper	[25]
Corsello et al., 2017	The Drug Repurposing Hub: a next-generation drug library and information resource	Resource for BC studies	Approved + investigational drugs	Curated database	Standardized reference library	Widely used resource	[6]
Firoozbakht et al., 2022	Subtype-specific drug repurposing in BC using network-based repurposability scoring	BC subtypes	TCGA + LINCS	Network-based scoring	Subtype-aware drug repurposing predictions	In-silico validation	[58]
Ocasio et al., 2024	Pre-clinical pan-cancer drug repurposing via deep learning	Pan-cancer incl. BC	Mutation + drug data	ML framework	Predicted drug matches across cancers	Clinical retrospective analysis	[84]

Breast cancer focus, *Breast cancer*: primary study population was breast cancer patients or BC-derived models; *Pan-cancer including BC*: multiple tumour types with BC as one application; *Among cancers*: BC was one of several cancers without primary focus.

Validation level, *In-vitro*: experimental testing in cancer cell lines or patient-derived cells; *Organoid*: testing in patient-derived organoid systems; *In-vivo*: animal models (xenograft or syngeneic); *In-silico validation*: computational benchmarking against known drug–disease associations with quantitative metrics (e.g., AUC, enrichment score); *Computational demonstration*: proof-of-concept analysis without quantitative benchmarking; *Retrospective clinical analysis*: analysis of patient outcomes data; *Benchmark platform*: primary publication establishing a computational resource rather than a repurposing study.