



In Silico Identification of Dysregulated miRNAs, Target Genes, and Pathways in Breast Cancer with Network-Based Analysis



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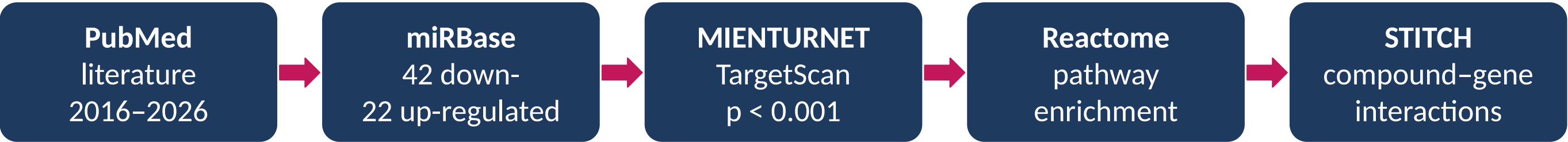
Introduction

- Breast cancer is the second leading cause of cancer death in women worldwide.
- miRNAs regulate gene expression; their dysregulation drives progression.
- Linking miRNAs to genes and pathways reveals therapeutic targets.

Objective

- Curate down- and up-regulated miRNAs in breast cancer (2016–2026).
- Identify target genes and enriched pathways, then natural compounds that interact with them.

Methodology



Results: Downregulated miRNA Targets (120 genes)

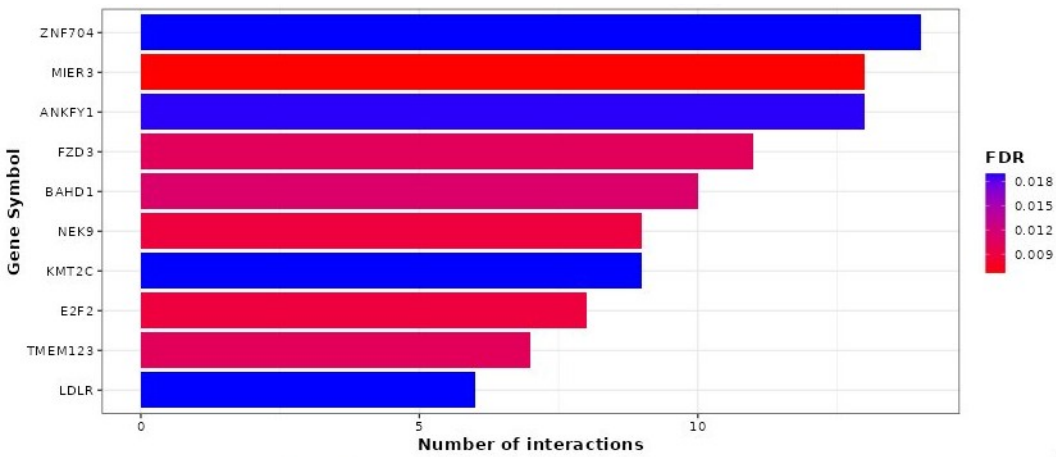


Fig 1. Top targets by interactions

Gene	Interactions	FDR
MIER3	13	0.0067
E2F2	8	0.0089
CCND2	12	0.0226
ZNF704	14	0.0189

Table 1. Top targets ($p < 0.001$)

Pathway Enrichment (Reactome)

Overrepresentation analysis results for TOTAL Data submitted with no name							
Pathway name	Entities found	Entities Total	Entities ratio	Entities pValue	Entities FDR	Reactions found	Reactions total
Defective binding of RB1 mutants to E2F1,(E2F2, E2F3)	3	17	0.001	4.46E-4	1.12E-1	1	1
Aberrant regulation of mitotic G1/S transition in cancer due to RB1 defects	3	17	0.001	4.46E-4	1.12E-1	1	2
MECP2 regulates transcription factors	2	10	0.001	3.41E-3	3.69E-1	2	8
Aberrant regulation of mitotic cell cycle due to RB1 defects	3	36	0.002	3.77E-3	3.69E-1	1	3
Diseases of mitotic cell cycle	3	39	0.002	4.39E-3	3.69E-1	1	5

- Fig 2: Reactome, downregulated set
- 452 pathways identified
- Top: RB1–E2F defects ($p = 4.5 \times 10^{-4}$)
- E2F2 hit by 8 miRNAs; CCND2 by 12

Results: Upregulated miRNA Targets (29 genes)

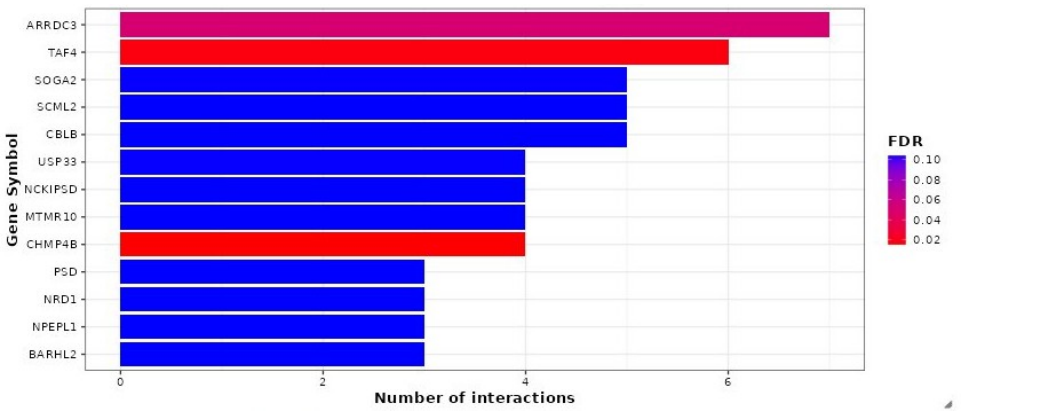


Fig 3. Top upregulated-miRNA targets

Gene	Interactions	FDR
CHMP4B	4	0.0151
TAF4	6	0.0174
ARRDC3	7	0.0504
PSAP	3	0.1040

Enriched: surfactant metabolism, Pol II transcription

Bioactive Compounds Interacting with Hub Genes (STITCH)

Network	Hub genes	Bioactive compounds
Downregulated	E2F2, CCND2	Curcumin, resveratrol, quercetin, EGCG
Upregulated	CHMP4B, TAF4, PSAP, GTF2H1	Sulforaphane, andrographolide, berberine, ginsenosides

Conclusion

- Loss of tumor-suppressive miRNAs deregulates the RB1–E2F / cyclin D axis (E2F2, CCND2).
- STITCH links hub genes to natural compounds; experimental validation is needed.



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