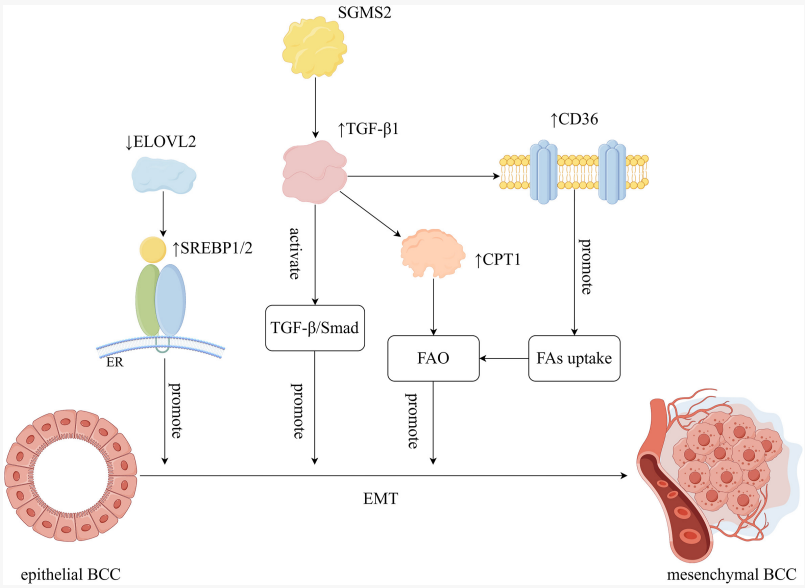
The Role of Lipid Metabolism in Breast Cancer Progression and Treatment Resistance

SHANNON, CLARE, IRELAND, April 20, 2025 /EINPresswire.com/ --
Lipid metabolism has emerged as a central player in the progression and therapy resistance of breast cancer, particularly the aggressive subtype known as triple-negative breast cancer (TNBC). This review article highlights how disruptions in lipid regulation can significantly influence the behavior of breast cancer cells, impacting their growth, metastasis, and response to treatment.



Dysregulation of lipid metabolism promotes EMT (by Figdraw). Down-regulation of ELOVL2 promotes EMT in breast cancer by up-regulating expression of SREBP1/2.

Alterations in the metabolism of fatty acids, cholesterol, sphingolipids, and glycolipids are profoundly intertwined with breast cancer cell survival and invasiveness. The uptake and biosynthesis of fatty acids are notably upregulated in tumor cells, which not only fuels cellular energy demands but also supports membrane synthesis and intracellular signaling. Key enzymes and transporters, such as CD36, FASN, and FABP4, are instrumental in facilitating this metabolic shift, thereby enhancing tumor proliferation and metastatic potential.

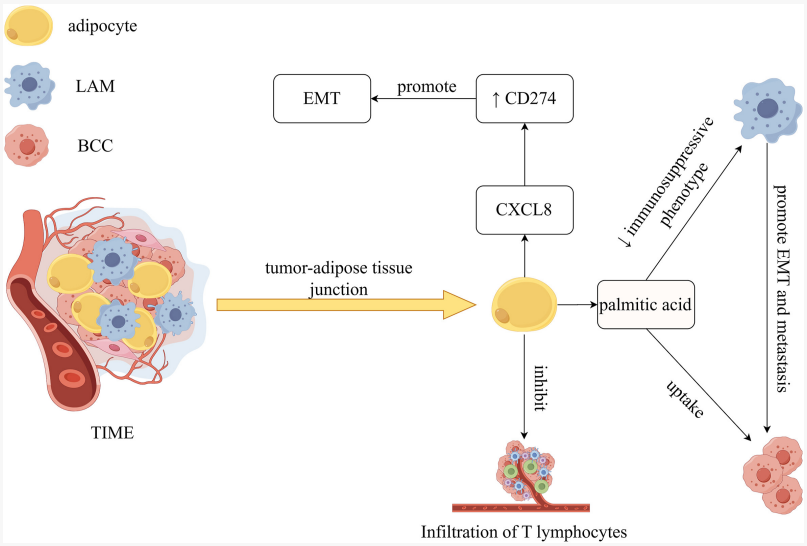
In cholesterol metabolism, the focus falls on how elevated cholesterol synthesis and its potent metabolite 27-hydroxycholesterol (27HC) accelerate tumor progression and interfere with immune responses. Proteins such as SREBP2, NSDHL, and STARD4 further contribute to this dysregulation, reinforcing cancer cell survival and dissemination. The interplay of 27HC with estrogen receptors and immune-modulatory pathways further complicates therapeutic strategies, particularly in hormone-sensitive and resistant tumors.

The dual nature of sphingolipid metabolism, especially the contrasting roles of ceramide and its glycosylated derivatives, underscores a complex metabolic paradox. While ceramide accumulation exhibits tumor-suppressive effects, including enhanced apoptosis and

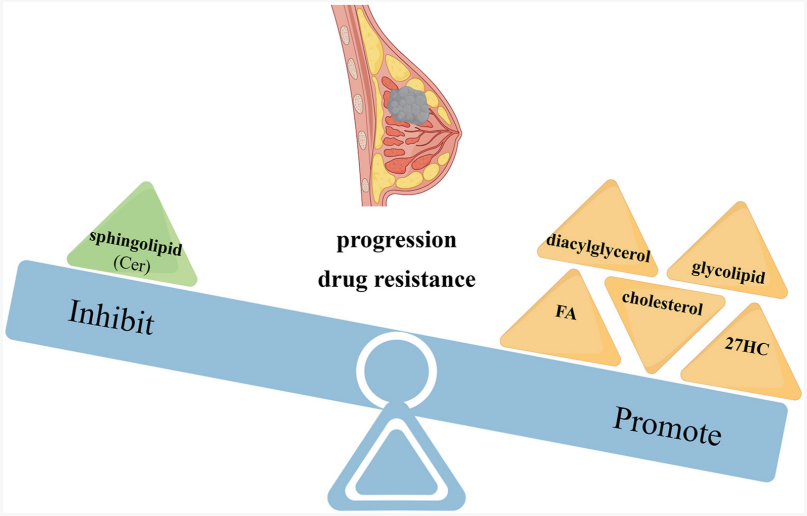
chemotherapy sensitization, glycosylated forms such as Globo-H ceramide and GD2 are linked to tumorigenesis, angiogenesis, and cancer stem cell maintenance.

A crucial outcome of lipid reprogramming is its role in promoting epithelial-mesenchymal transition (EMT), a process associated with enhanced migratory ability and drug resistance. Factors like ELOVL2, SGMS2, and CXCL8 modulate EMT through intricate signaling cascades, including TGF-β, PI3K/AKT, and SREBP1/2 axes.

Beyond intrinsic cancer cell metabolism, the surrounding tumor immune microenvironment (TIME) also adapts in response to lipid cues. M2 macrophages, cancer-associated fibroblasts, and CD8+ T cells exhibit lipid-driven phenotypic shifts that support tumor evasion and therapy failure.



TIME associated with lipids in breast cancer (by Figdraw). Tumor-associated adipocytes secrete palmitic acid; BCCs uptake palmitic acid; LAM is mainly distributed in the tumor-fat junction; M2 macrophages promote EMT and migration of BCCs; palmitic acid r



Lipid metabolism involved in progression and drug resistance of breast cancer.

Resistance to standard treatments—including chemotherapy, endocrine therapy, HER2-targeted therapy, and immune checkpoint inhibitors—is intimately linked to lipid metabolic rewiring. Upregulation of CD36, FASN, CPT1, and GPR120 exemplifies how tumor cells exploit lipid pathways to avoid apoptosis, reduce drug accumulation, and sustain stemness.

# # # # #

Genes & Diseases publishes rigorously peer-reviewed and high quality original articles and authoritative reviews that focus on the molecular bases of human diseases. Emphasis is placed on hypothesis-driven, mechanistic studies relevant to pathogenesis and/or experimental therapeutics of human diseases. The journal has worldwide authorship, and a broad scope in basic and translational biomedical research of molecular biology, molecular genetics, and cell biology, including but not limited to cell proliferation and apoptosis, signal transduction, stem

cell biology, developmental biology, gene regulation and epigenetics, cancer biology, immunity and infection, neuroscience, disease-specific animal models, gene and cell-based therapies, and regenerative medicine.
Scopus CiteScore: 7.3
Impact Factor: 6.9

# # # # # #

More information: https://www.keaipublishing.com/en/journals/genes-and-diseases/
Editorial Board: https://www.keaipublishing.com/en/journals/genes-and-diseases/editorial-board/
All issues and articles in press are available online in ScienceDirect (https://www.sciencedirect.com/journal/genes-and-diseases).
Submissions to Genes & Disease may be made using Editorial Manager (https://www.editorialmanager.com/gendis/default.aspx).
Print ISSN: 2352-4820
eISSN: 2352-3042
CN: 50-1221/R
Contact Us: editor@genesndiseases.com
X (formerly Twitter): @GenesNDiseases (https://x.com/GenesNDiseases)

# # # # # #
Reference
Wenxiang Fu, Aijun Sun, Huijuan Dai, Lipid metabolism involved in progression and drug resistance of breast cancer, Genes & Diseases, Volume 12, Issue 4, 2025, 101376, https://doi.org/10.1016/j.gendis.2024.101376

Funding Information:
National Natural Science Foundation of China 82303865
Science and Technology Commission of Huaian Municipality, Jiangsu, China HAB202209

Genes & Diseases Editorial Office
Genes & Diseases
+86 23 6571 4691
editor@genesndiseases.com
