

Adipocyte–Tumor Cell Metabolic Communication in the Advancement of Cancer

Faseeha Nadeem, Asima Tayyeb

School of Biological Sciences, University of the Punjab, Lahore, Pakistan

Abstract

The tumor-microenvironment (TME) can be defined as an ecosystem comprising various factors including predominantly immunosuppressive cytokines, Tumor-Associated Adipocytes (TAAs) and infiltrating immune cell population (dendritic cells, macrophages, B and T lymphocytes) surrounding a tumor. TME has emerged as a key player in cancer progression, mainly the molecular interaction between tumor cells and its neighboring adipocytes. Adipocyte-derived extracellular vesicles play a pivotal role in cancer invasion by enhancing fatty acid oxidation through the delivery of both fatty acid substrates and essential protein machinery. Interestingly, tumor cells actively induce lipolysis in TAAs promoting the lipolysis that serves as an energy source to fuel tumor growth. Furthermore, the heightened mitochondrial activity in tumor cells leads to the redistribution of mitochondria toward membrane protrusions facilitating cell migration in the presence of adipocyte-derived extracellular vesicles. Collectively, these complex interactions promote cancer cells invasion. Current review provides a comprehensive understanding of the contribution of adipocyte-derived extracellular vesicles in mediating physiological interaction between tumor cells and neighboring adipocytes with a specific emphasis on the tumor advancement.

Key Words: Adipocytes, Tumor-microenvironment, Tumor-associated adipocytes, Cancer

Adipocytes and Adipogenesis

White adipose tissue (WAT) is majorly composed of adipocytes. They function as endocrine and paracrine organs in addition to storing and metabolizing triglycerides to maintain energy balance. They secrete different factors that regulate angiogenesis, appetite, regulation of blood pressure, reproductive function, glucose metabolism, aging, immunological responses and inflammatory responses [1-3]. In mature adipocytes, cytoplasm is compressed to form a thin layer due to a large internal fat droplet and moving of nucleus to other edge of the cell [4]. Adipose tissues are formed due to accumulation of large number of adipocytes and form an insulting layer under the skin which regulates the body temperature. After reaching maturity, adipocytes become functional by highly controlled process known as adipogenesis [5]. Adipogenesis seems to be affected by Age, gender, and lifestyle in one way or another [6-8].

Adipogenesis has been complemented with in depth research to understand characteristics of adipocytes. Adipogenesis is defined as the mechanism of cellular differentiation of fibroblast like pre-adipocytes into functional lipid containing adipocytes [Figure 1]. There are six roughly defined stages of adipogenesis including formation of mesenchymal precursors, commitment of pre-adipocytes, growth-arrest of pre-adipocytes, expansion of mitotic colonies, differentiation and maturation of adipocytes [1, 9]. Distinct morphological and molecular alterations occur in the pre-adipocytes to successfully transform into adipocytes.

Molecular Mechanism of Adipogenesis

The process of adipogenesis is extremely intricate mainly depends on interaction with surrounding tissue. Despite identification of several factors playing vital role in the process of adipogenesis, the detailed molecular mechanism is still unknown. Some of the key modulators of adipogenesis include fatty acids, growth hormone, prostaglandins, glucocorticoids, PPAR, STATs, SREBP1, C/EBP α , C/EBP β , C/EBP δ , IGF-I, and macrophage colony stimulating factor [10-13]. Some additional regulators that affect the adipogenesis pathway have been reported by recent studies such as Krupel-like factors (KLFs), Wingless proteins (Wnts), B-cell factor 1 and GATA-binding

Corresponding Author: Asima Tayyeb

Email: asima.sbs@pu.edu.pk

Received: 05.12.2025

Revised: 30.12.2025

Accepted: 30.12.2025

Published: 02.01.2026

protein-2 and 3. Various cell cycle proteins, clock proteins and a number of interferon regulatory factors (IRFs) including IRF3 and IRF4 are also reported to impact abiogenesis [1, 14-18]. In addition, extracellular signaling proteins such as bone morphogenesis proteins, transforming growth factors,

fibroblast growth factor, insulin like growth factor, notch ligands, pro-inflammatory cytokines and hypoxia discovered to have a significant impact on the adipogenesis process [6]. The series of events involving several of these molecules have been shown in Figure 2.

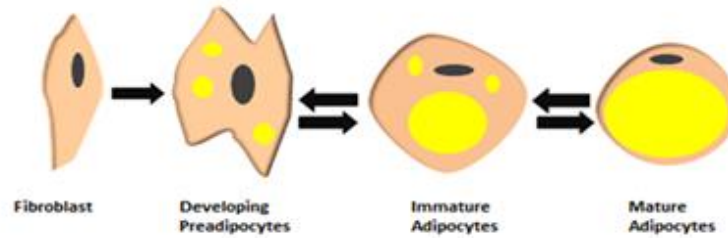


Figure 1: Stages of adipocytes differentiation. Reverse arrows showing shrinking of mature adipocytes in case of energy decrease.

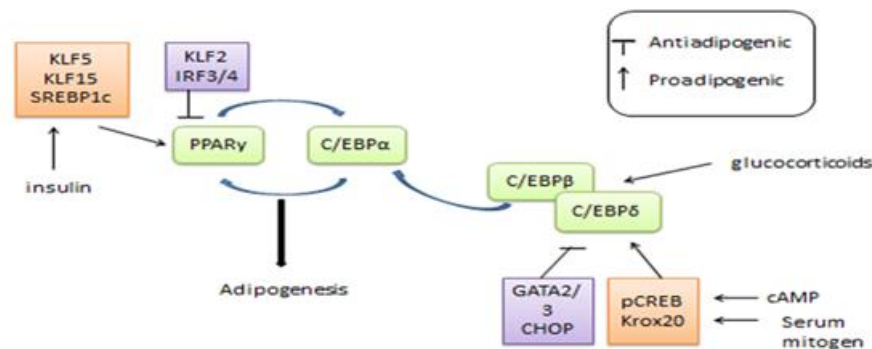


Figure 2: Transcription cascade of adipogenesis. Insulin and glucocorticoids are the factors that induce abiogenesis. These factors stimulate the regulation of various vital transcription factors that merge on PPAR γ . PPAR then positively regulate the transcription of C/EBP α gene, and these factors collectively maintain differentiation of adipocytes.

Tumor-Microenvironment and Cancer

Tumorigenesis implicates continuous communication between Tumor-microenvironment (TME), immediate neighboring environment of a tumor and tumor cells. It has recently been suggested that TME through communication with the cancer cells supports the development of the hallmark characteristics which are required for tumor growth [19-22]. Without the complete explanation of TME, understanding of cancer is not possible. TME studies focus on the cancer-associated fibroblasts (CAF), their tumor promoting role [23] and the transformation of normal fibroblasts to CAFs through complex signaling pathways [24-25]. As pre-adipocytes are similar to fibroblasts and both originate from the same adipose stem cells (ASCs), therefore, functions of CAFs may explain adipocyte function as well [26]. Different studies have indicated that through adipokines or direct contact putative cancer associated adipocytes (CAA) near to cancer cell stimulates tumor growth. In benign adipose tissue, predominant cell type is adipocytes, other cell types such as vascular cells, fibroblasts, macrophages and

precursor adipose cells are also present. Transition of benign fibroblast to a CAF speculates that all the cancer cells can recruit various elements of adipose tissue to enhance tumor growth and invasion. A number of studies suggest that in TME mature, differentiated adipocytes degenerate into pre-adipocytes to remove their large lipid droplet [27-28].

Tumor-Associated Adipocytes and Tumor Microenvironment

Tumor-Associated Adipocytes (TAAs) are the main residents of cancer microenvironments and are contributors of tumor growth by soluble factors like interleukin 6 or leptin. There is a strong crosstalk between tumor cells and TAA that plays an important role in tumor invasion [29-31]. Fatty acids occupy over 90% of adipocytes and their primary role is to provide energy for tumors. Tumor cells themselves promote lipolysis in the neighboring TAAs. The fatty acids release in this process triggers fatty acid oxidation in tumor cells that enhances the tumor aggressiveness [32]. It is predicted that the main

contributors in this process are TAAs associated extracellular vesicles allowing transport of nutrients to the distant cells. In obesity, more extracellular vesicles are secreted by adipocytes that transport proteins taking part in lipid metabolism such as fatty acid oxidation enzymes. It is not only protein machinery that is transported by these adipocytes derived extracellular vesicles but fatty acid substrates necessary for oxidation are also carried by extracellular vesicles [33-35].

Signaling Pathways Driving Adipocyte Lipolysis

Adipocytes maintain tissue homeostasis by releasing multiple endocrine factors such as adipokines, lipids mediators and extracellular vesicles. Studies showed that the interaction between the tumor cells and adipocytes secrete cytokines and adipokines. Interleukin-6 (IL-6) interacts with its IL-6R. This complex binds with gp130 on adipocytes which leads to the activation of Janus kinases (JAKs) and ultimately recruitment of transcription factors STAT1 and STAT3. The activation of STAT proteins moves to the nucleus which regulates the transcription of target genes such as *SOCS3* in adipose tissues. SOCS3 impedes the insulin signaling pathway which drives lipolysis.

Tumor necrosis factor (TNF- α) also induces lipolysis by interacting with its receptors on adipocytes. The binding of TNF- α with its receptors also causes the activation of JNK signaling pathway through TRADD, RIP1, and TRAF2 proteins. TNF- α downregulate the expression of phosphodiesterase-3B which increases the level of cAMP. cAMP activates the hormone sensitive lipase that causes the breakdown of lipids. The level of cAMP also increases by binding of β -adrenergic receptor with G-proteins

Tumor Cell Metabolic Adaptations for Fatty Acid Utilization

Tumor cells use fatty acid as alternative source of energy by remodeling their metabolic pathways. CD36 is a lipid translocator protein that also activates STAT pathway. Tumor cells express high level of CD36 and FABPs proteins that enhance the cellular intake of fatty acids from adipocytes. Overexpression of CD36 protein causes the accumulation of lipid inside the cells that induce metastasis. Once fatty acids move into the cytosol, they are converted into the fatty acyl-CoA and undergo β -oxidation inside the mitochondria. Moreover, tumor cells also express high level of CPT1 (Carnitine Palmitoyl transferase 1) that increases the oxidation of fatty acid to meet the high energy demand for cell division. Low level of ATP also activates AMPK (AMP-activated protein kinase) pathway which increases PGC-1 α gene expression. PGC-1 α induces mitochondrial biogenesis and also increases the production of enzymes involved in fatty

acid oxidation and oxidative phosphorylation. This enhances tumor survival and therapy resistance.

Crosstalk Between Mitochondrial Dynamics and Cell Migration

Mitochondria are organelle whose number and morphology depends on the metabolic state of cells. Tumor cells which are in contact with adipocytes undergo change in mitochondrial dynamics. Migration of tumor cells require mitochondrial fission which is achieved by Drp1 to supply the ATP and reactive oxygen species at leading edge. These ROS activate the ERK and FAK signaling pathways which are required for cell division and migration.

Tumor-Associated Adipocytes and Cancer Progression

TAAs together with extra cellular matrix constituents have emerged to contribute to tumor progression and invasion by producing a more supportive TME. Traditionally, adipose tissues act as energy reservoir in the form of triglyceride (TGs). These TGs release fatty acid when surplus amounts of energy are required. These TAAs not only produce energy but also provide protection for organs. However, in 1994, after discovery of leptin, adipose tissues were regarded as fully functional endocrine organ, having ability to regulate systemic energy and metabolic homeostasis [36]. A correlation between obesity and certain malignancies as endometrial and esophageal which have been demonstrated by epidemiological studies have further supported the notion of TAAs role in cancer progression.

Adipocytes are directly associated with tumor cells in many solid tumors during tumor proliferation, cancer cell infiltration and in hematological malignancies due to prevalence of adipose tissue in several organs. Over the last decade, studies relating adipocytes to tumorigenesis have increased with more focus on breast, ovarian, colon and prostate cancer. Adipocytes show profound functional and phenotypic alteration in stromal environment. In solid tumors histological images showed decrease in both cell size and cell number of adipocytes present at the invasive front as compared to adipocytes distant from the tumor [37-39]. In the tumor protruding region, the ratio of fibroblast-like cells becomes high due to de-differentiation of adipocytes because cancer cells release various signaling molecules [40].

Breast Cancer

TAAs have been reported to show their significant impact in breast cancer. Cell culture studies suggested that in serum restricted conditions, the co-culture differentiated murine 3T3-L pre-adipocyte cell line increases the tumor growth, metastasis, and survival of human breast cancer cell lines [41]. Conditioned-medium from differentiated 3T3-L1 cells supported

AP-1 transcription factors mediated invasion of cancer cells and NF κ B and cyclin D1 mediated proliferation. Both adipocytes and fibroblasts contribute to proliferation of breast cancer cell lines, however adipocytes have significant impact on the division of cancer cells as compared to those of fibroblasts, lasting only a few days. Conditioned media release by adipocytes and fibroblasts induce similar survival transcriptional program but adipocytes influence the large number of genes and induce remarkable modifications as compared to fibroblast [42-43]. Studies conducted that conditioned-medium derived from primary human breast pre-adipocytes differentiated in culture promote the survival and proliferation of both normal and breast cancer cell lines [44]. However, the elements in the conditioned media that moderate this impact (growth factors, fatty acids, or reactive oxygen species) are unknown. A study reported that using differentiated murine 3T3-F442A pre-adipocytes increased invasiveness of the cancer cells in vitro providing evidence of establishing a crosstalk between adipocytes and breast cancer cells [45].

Prostate Cancer

Adipocytes have also a remarkable influence on the progression of prostate cancer. An adverse prognostic factor of prostate cancer is extra-capsular extension into peri-prostatic adipose tissue [46]. Adipocytes support tumorigenesis in highly differentiated, androgen-sensitive prostate cancer cell lines. Through the secretion of the MMPs peri-prostatic and visceral adipose tissue have a significant influence in progression and motility of prostate cancer cells [47-48]. Studies using FTIR spectroscopy reveal the transfer of lipid from adipocytes to prostate cancer cells that indicated adipocytes support prostate tumorigenesis [49-52].

Colon Cancer

Adipocytes also have a remarkable influence on the progression of colon cancer. Adipose tissue, mature adipocytes, or pre-adipocytes from leptin-deprived or wild-type induce the division of colon cancer cell lines in collagen three-dimensional collagen culture matrix. In every situation, the division of colon cancer cells was encouraged. Colon cancer cell proliferation was supported in all conditions. However, adipocytes provided leptin dependent proliferative effect. Mature adipocytes could not promote the growth of cancer cells in the absence of leptin, but this effect could be rescued by exogenous leptin treatment [53-56].

Ovarian Cancer

Ovarian cancer spread to omentum as primary human omental adipocytes induce the growth and metastasis of colon, breast, and ovarian cancer both in vitro and in vivo. Cytokines (IL-8 and IL-6) released by

adipocytes cause the flow of ovarian cancer cells to the omentum. When ovarian cancer cells interact with adipocytes they induce hormone-sensitive lipase mediated lipolysis. These fatty acids release energy which are utilized by ovarian cancer cells. This was reported that ovarian cancer increases the β -oxidation of TGA which was suppressed by inhibitor, etomoxir. Etomoxir blocked the activity of enzyme carnitine-palmitoyl transferase 1 which inhibits the transportation of fatty acids into mitochondria and stops the growth of ovarian cancer cells. These high energy lipids from adipocytes support fast tumor growth by activating mitochondria metabolism. Lipid accumulation was also observed in colon and breast cancer cells which are cultured with adipocytes and metastatic human ovarian cancer tissue sections [57-59].

Clinical Significance and Therapeutic Implications of Adipocytes in TME

Tumor cells reprogram adipocytes into cancer associated adipocytes (CAAs) in TME. These CAAs secrete adipokines such as TNF- α and IL-6 that are correlated with tumor growth and metastasis. Therefore, these signaling molecules act as biomarkers for disease progression and increase metastasis. Moreover, high levels of lipolytic enzymes, lipid transporters and lipid binding proteins such as (CD36 and FABP4) also show the high lipid intake and tumor progression within adipocytes. Tumor metabolic state and treatment response can be detected by monitoring these changes in patients. Targeting the metabolic interaction between adipocytes and tumor cells can improve the chemotherapy induced apoptosis treatment. Tumor progression and invasion can also be reduced by targeting the adipokines, their receptors and lipid uptake pathways.

Conclusion

The current review highlights the role of TAAs in cancer mainly through regulation of TME by releasing several cytokines and lipids favoring cancer cells. These results suggest that by targeting TAAs and associated lipid metabolism, they may provide a potential paradigm to treat and prevent cancer progression. Moreover, the enzymes involved in regulation of lipolysis could be inhibited to stop cancer growth. Lifestyle interventions such as exercise and weight loss may be suggested to prevent cancer and enhance survival rates. The understanding of adipocytes effect in promoting cancer has greatly in past years, but some questions still need to be answered by further research. Despite these insights, the detailed mechanism of therapeutic exploitation of metabolic interaction between parasitic cancerous cells and host supportive TAAs will be required.

REFERENCES

1. Lefterova MI, Lazar MA. New developments in adipogenesis. *Trends in Endocrinology & Metabolism*. 2009 Apr 1;20(3):107-14.
2. Hemat Jouy S, Mohan S, Scichilone G, Mostafa A, Mahmoud AM. Adipokines in the crosstalk between adipose tissues and other organs: implications in cardiometabolic diseases. *Biomedicines*. 2024 Sep 19;12(9):2129.
3. Park S, Shimokawa I. Influence of adipokines on metabolic dysfunction and aging. *Biomedicines*. 2024 Apr 15;12(4):873.
4. Di Rocco G, Trivisonno A, Trivisonno G, Toietta G. Dissecting human adipose tissue heterogeneity using single-cell omics technologies. *Stem Cell Research & Therapy*. 2024 Sep 27;15(1):322.
5. Liu Y, Qian SW, Tang Y, Tang QQ. The secretory function of adipose tissues in metabolic regulation. *Life Metabolism*. 2024 Apr 1;3(2):loae003.
6. Rosen ED, MacDougald OA. Adipocyte differentiation from the inside out. *Nature reviews Molecular cell biology*. 2006 Dec 1;7(12):885-96.
7. MacDougald OA, Mandrup S. Adipogenesis: forces that tip the scales. *Trends in Endocrinology & Metabolism*. 2002 Jan 1;13(1):5-11.
8. Rehman A, Lathief S, Charoenngam N, Pal L. Aging and adiposity—focus on Biological females at midlife and Beyond. *International Journal of Molecular Sciences*. 2024 Mar 4;25(5):2972.
9. Liu SS, Fang X, Wen X, Liu JS, Alip M, Sun T, Wang YY, Chen HW. How mesenchymal stem cells transform into adipocytes: Overview of the current understanding of adipogenic differentiation. *World Journal of Stem Cells*. 2024 Mar 26;16(3):245.
10. Xu D, Zhuang S, Chen H, Jiang M, Jiang P, Wang Q, Wang X, Chen R, Tang H, Tang L. IL-33 regulates adipogenesis via Wnt/ β -catenin/PPAR- γ signaling pathway in preadipocytes. *Journal of Translational Medicine*. 2024 Apr 17;22(1):363.
11. Kim HY, Jang HJ, Muthamil S, Shin UC, Lyu JH, Kim SW, Go Y, Park SH, Lee HG, Park JH. Novel insights into regulators and functional modulators of adipogenesis. *Biomedicine & Pharmacotherapy*. 2024 Aug 1;177:117073.
12. Richard AJ, Stephens JM. Emerging roles of JAK–STAT signaling pathways in adipocytes. *Trends in Endocrinology & Metabolism*. 2011 Aug 1;22(8):325-32.
13. Payne VA, Au WS, Lowe CE, Rahman SM, Friedman JE, O'Rahilly S, Rochford JJ. C/EBP transcription factors regulate SREBP1c gene expression during adipogenesis. *Biochemical Journal*. 2010 Jan 1;425(1):215-24.
14. Muhi DJ, Murad MM, Panahi G, Zabihi-Mahmoudabadi H, Emamgholipour S, Nowrouzi A. Gene expression profiling of KLF4 and KLF5 in visceral adipose tissue of obese women: insights into adipogenic and metabolic regulation. *Lipids in Health and Disease*. 2025 Oct 16;24(1):331.
15. Liu M, Hemba-Waduge RU, Li X, Huang X, Liu TH, Han X, Wang Y, Ji JY. Wnt/Wingless signaling promotes lipid mobilization through signal-induced transcriptional repression. *Proceedings of the National Academy of Sciences*. 2024 Jul 9;121(28):e2322066121.
16. Griffin MJ, Zhou Y, Kang S, Zhang X, Mikkelsen TS, Rosen ED. Early B-cell factor-1 (EBF1) is a key regulator of metabolic and inflammatory signaling pathways in mature adipocytes. *Journal of Biological Chemistry*. 2013 Dec 13;288(50):35925-39.
17. Bacha R, Alwisi N, Ismail R, Pedersen S, Al-Mansoori L. Unveiling GATA3 signaling pathways in health and disease: Mechanisms, implications, and therapeutic potential. *Cells*. 2024 Dec 22;13(24):2127.
18. Ahmad Z, Kahloan W, Rosen ED. Transcriptional control of metabolism by interferon regulatory factors. *Nature Reviews Endocrinology*. 2024 Oct;20(10):573-87.
19. Taubes G. Epidemiology faces its limits: the search for subtle links between diet, lifestyle, or environmental factors and disease is an unending source of fear—but often yields little certainty. *Science*. 1995 Jul 14;269(5221):164-9.
20. Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. *cell*. 2011 Mar 4;144(5):646-74.
21. Pavlides S, Whitaker-Menezes D, Castello-Cros R, Flomenberg N, Witkiewicz AK, Frank PG, Casimiro MC, Wang C, Fortina P, Addya S, Pestell RG. The reverse Warburg effect: aerobic glycolysis in cancer associated fibroblasts and the tumor stroma. *Cell cycle*. 2009 Dec 1;8(23):3984-4001.
22. Martinez-Outschoorn UE, Sotgia F, Lisanti MP. Power surge: supporting cells “fuel” cancer cell mitochondria. *Cell metabolism*. 2012 Jan 4;15(1):4-5.
23. Hanahan D, Coussens LM. Accessories to the crime: functions of cells recruited to the tumor microenvironment. *Cancer cell*. 2012 Mar 20;21(3):309-22.
24. Mitra AK, Zillhardt M, Hua Y, Tiwari P, Murmann AE, Peter ME, Lengyel E. MicroRNAs reprogram normal fibroblasts into cancer-associated fibroblasts in ovarian cancer. *Cancer discovery*. 2012 Dec 1;2(12):1100-8.
25. El Alaa RS, Al-Mannai W, Darwish N, Al-Mansoori L. Adipose-derived stromal cells and cancer-associated fibroblasts: interactions and implications in tumor progression. *International Journal of Molecular Sciences*. 2024 Oct 28;25(21):11558.

26. Uhrbom M, Muhl L, Genové G, Liu J, Palmgren H, Alexandersson I, Karlsson F, Zhou AX, Lunnardal S, Gustafsson S, Buyandelger B. Adipose stem cells are sexually dimorphic cells with dual roles as preadipocytes and resident fibroblasts. *Nature Communications*. 2024 Sep 2;15(1):7643.
27. Andarawewa KL, Motrescu ER, Chenard MP, Gansmuller A, Stoll I, Tomasetto C, Rio MC. Stromelysin-3 is a potent negative regulator of adipogenesis participating to cancer cell-adipocyte interaction/crosstalk at the tumor invasive front. *Cancer research*. 2005 Dec 1;65(23):10862-71.
28. Zhu Q, Zhu Y, Hepler C, Zhang Q, Park J, Gliniak C, Henry GH, Crewe C, Bu D, Zhang Z, Zhao S. Adipocyte mesenchymal transition contributes to mammary tumor progression. *Cell reports*. 2022 Sep 13;40(11).
29. Frühbeck G, Gómez-Ambrosi J, Muruzábal FJ, Burrell MA. The adipocyte: a model for integration of endocrine and metabolic signaling in energy metabolism regulation. *American Journal of Physiology-Endocrinology and Metabolism*. 2001 Jun 1;280(6):E827-47.
30. Duong MN, Geneste A, Fallone F, Li X, Dumontet C, Muller C. The fat and the bad: Mature adipocytes, key actors in tumor progression and resistance. *Oncotarget*. 2017 May 20;8(34):57622.
31. Grunt TW, Wagner R, Ries A, Berghoff AS, Preusser M, Grusch M, Valent P. Targeting endogenous fatty acid synthesis stimulates the migration of ovarian cancer cells to adipocytes and promotes the transport of fatty acids from adipocytes to cancer cells. *International Journal of Oncology*. 2024 Jan 11;64(3):24.
32. Yao H, He S. Multi-faceted role of cancer-associated adipocytes in the tumor microenvironment. *Molecular medicine reports*. 2021 Dec;24(6):866.
33. Liu S, Benito-Martin A, Pelissier Vatter FA, Hanif SZ, Liu C, Bhardwaj P, Sethupathy P, Farghli AR, Piloco P, Paik P, Mushannen M. Breast adipose tissue-derived extracellular vesicles from obese women alter tumor cell metabolism. *EMBO reports*. 2023 Dec 6;24(12):e57339.
34. Kuo CY, Ann DK. When fats commit crimes: fatty acid metabolism, cancer stemness and therapeutic resistance. *Cancer Communications*. 2018 Jul 11;38(1):47.
35. Clement E, Lazar I, Attané C, Carrié L, Dauvillier S, Ducoux-Petit M, Esteve D, Menneteau T, Moutahir M, Le Gonidec S, Dalle S. Adipocyte extracellular vesicles carry enzymes and fatty acids that stimulate mitochondrial metabolism and remodeling in tumor cells. *The EMBO journal*. 2020 Feb 3;39(3):e102525.
36. Yum C, Andolino C, Layosa MA, Coleman M, Hursting SD, Teegarden D. Differential effects of leptin on energy metabolism in murine cell models of metastatic triple negative breast cancer. *Diabetology & Metabolic Syndrome*. 2024 Nov 28;16(1):288.
37. Wolf M, Brochhausen C, Ramakrishnan V, Iberl S, Roth J, Seitz S, Burkhardt R, Stadler SC. Histologic characterization of tumor-adjacent mammary adipose tissue in normal-weight and overweight/obese patients with triple-negative breast cancer. *Cancers*. 2024 Oct 17;16(20):3515.
38. Nieman KM, Kenny HA, Penicka CV, Ladanyi A, Buell-Gutbrod R, Zillhardt MR, Romero IL, Carey MS, Mills GB, Hotamisligil GS, Yamada SD. Adipocytes promote ovarian cancer metastasis and provide energy for rapid tumor growth. *Nature medicine*. 2011 Nov;17(11):1498-503.
39. Dirat B, Bochet L, Dabek M, Daviaud D, Dauvillier S, Majed B, Wang YY, Meulle A, Salles B, Le Gonidec S, Garrido I. Cancer-associated adipocytes exhibit an activated phenotype and contribute to breast cancer invasion. *Cancer research*. 2011 Apr 1;71(7):2455-65.
40. Tan J, Buache E, Chenard MP, Dali-Youcef N, Rio MC. Adipocyte is a non-trivial, dynamic partner of breast cancer cells. *International Journal of Developmental Biology*. 2011 Sep 2;55(7-8-9):851-9.
41. Bellanger D, Dziagwa C, Guimaraes C, Pinault M, Dumas JF, Brisson L. Adipocytes promote breast cancer cell survival and migration through autophagy activation. *Cancers*. 2021 Aug 3;13(15):3917.
42. Balaban S, Shearer RF, Lee LS, van Geldermalsen M, Schreuder M, Shtein HC, Cairns R, Thomas KC, Fazakerley DJ, Grewal T, Holst J. Adipocyte lipolysis links obesity to breast cancer growth: adipocyte-derived fatty acids drive breast cancer cell proliferation and migration. *Cancer & metabolism*. 2017 Jan 13;5(1):1.
43. Nickel A, Blücher C, Kadri O, Schwagarus N, Müller S, Schaab M, Thiery J, Burkhardt R, Stadler SC. Adipocytes induce distinct gene expression profiles in mammary tumor cells and enhance inflammatory signaling in invasive breast cancer cells. *Scientific reports*. 2018 Jun 21;8(1):9482.
44. Carter JC, Church FC. Mature breast adipocytes promote breast cancer cell motility. *Experimental and molecular pathology*. 2012 Jun 1;92(3):312-7.
45. Castro-Muñozledo F, Beltrán-Langarica A, Kuri-Harcuch W. Commitment of 3T3-F442A cells to adipocyte differentiation takes place during the first 24–36 h after adipogenic stimulation: TNF- α inhibits commitment. *Experimental cell research*. 2003 Apr 1;284(2):161-70.
46. Drewa J, Lazar-Juszczak K, Adamowicz J, Juszczak K. Periprostatic Adipose Tissue as a Contributor to Prostate Cancer Pathogenesis: A Narrative Review. *Cancers*. 2025 Jan 23;17(3):372.

47. Lin CY, Tsai PH, Kandaswami CC, Lee PP, Huang CJ, Hwang JJ, Lee MT. Matrix metalloproteinase-9 cooperates with transcription factor Snail to induce epithelial–mesenchymal transition. *Cancer science*. 2011 Apr;102(4):815-27.
48. Li W, Wei X, Yu Y, Tian Y, Yu Q, Qiao J, Tao Y, Li Y, Li T. Landscape analysis of matrix metalloproteinases reveals key prognostic markers for prostate cancer. *Frontiers in Immunology*. 2025 Jun 18;16:1582992.
49. Ribeiro R, Monteiro C, Cunha V, Oliveira MJ, Freitas M, Fraga A, Príncipe P, Lobato C, Lobo F, Morais A, Silva V. Human periprostatic adipose tissue promotes prostate cancer aggressiveness in vitro. *Journal of Experimental & Clinical Cancer Research*. 2012 Apr 2;31(1):32.
50. Gazi E, Gardner P, Lockyer NP, Hart CA, Brown MD, Clarke NW. Direct evidence of lipid translocation between adipocytes and prostate cancer cells with imaging FTIR microspectroscopy. *Journal of lipid research*. 2007 Aug 1;48(8):1846-56.
51. Fontana F, Anselmi M, Carollo E, Sartori P, Procacci P, Carter D, Limonta P. Adipocyte-derived extracellular vesicles promote prostate cancer cell aggressiveness by enabling multiple phenotypic and metabolic changes. *Cells*. 2022 Aug 3;11(15):2388.
52. Altuna-Coy A, Ruiz-Plazas X, Sánchez-Martin S, Ascaso-Til H, Prados-Saavedra M, Alves-Santiago M, Bernal-Escoté X, Segarra-Tomás J, R. Chacón M. The lipidomic profile of the tumoral periprostatic adipose tissue reveals alterations in tumor cell's metabolic crosstalk. *BMC medicine*. 2022 Aug 18;20(1):255.
53. Amemori S, Ootani A, Aoki S, Fujise T, Shimoda R, Kakimoto T, Shiraishi R, Sakata Y, fTsunada S, Iwakiri R, Fujimoto K. Adipocytes and preadipocytes promote the proliferation of colon cancer cells in vitro. *American Journal of Physiology-Gastrointestinal and Liver Physiology*. 2007 Mar;292(3):G923-9.
54. Socol CT, Chira A, Martinez-Sanchez MA, Nunez-Sanchez MA, Maerescu CM, Mierlita D, Rusu AV, Ruiz-Alcaraz AJ, Trif M, Ramos-Molina B. Leptin signaling in obesity and colorectal cancer. *International journal of molecular sciences*. 2022 Apr 24;23(9):4713.
55. Ma Y, Nenkov M, Chen Y, Gaßler N. The role of adipocytes recruited as part of tumor microenvironment in promoting colorectal cancer metastases. *International journal of molecular sciences*. 2024 Jul 30;25(15):8352.
56. Singh S, Mayengbam SS, Chouhan S, Deshmukh B, Ramteke P, Athavale D, Bhat MK. Role of TNF α and leptin signaling in colon cancer incidence and tumor growth under obese phenotype. *Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease*. 2020 May 1;1866(5):165660.
57. Nieman KM, Kenny HA, Penicka CV, Ladanyi A, Buell-Gutbrod R, Zillhardt MR, Romero IL, Carey MS, Mills GB, Hotamisligil GS, Yamada SD. Adipocytes promote ovarian cancer metastasis and provide energy for rapid tumor growth. *Nature medicine*. 2011 Nov;17(11):1498-503.
58. Pakhira S, Roy SS. Altered fatty acid oxidation via CPT1A promotes epithelial-to-mesenchymal transition in ovarian cancer. *The FEBS Journal*. 2025 Jul 24.
59. Lin H, Wang L, Chen H, Shen Y, Wang C, Xue Y, Zheng Z, Zhang Y, Xia D, Wu Y, Wang F. Mitochondrial fatty acid oxidation as the target for blocking therapy-resistance and inhibiting tumor recurrence: The proof-of-principle model demonstrated for ovarian cancer cells. *Journal of Advanced Research*. 2025 Mar 17:S2090-1232

Open Access

This article is licensed under a Creative Commons Attribution 4.0 International License. The license permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source provides a link to the Creative Commons license, and indicates if changes were made. <https://creativecommons.org/licenses/by/4.0/>.

