Breast Cancer Metastasis Metabolic Mechanisms

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Description

Breast cancer is one of the most common cancers in women around the world. Treatment failure is mostly caused by metastasis, which is also the cause of the majority of breast cancer deaths. The importance of metabolism in breast cancer progression and metastasis is increasingly being recognized. However, the regulatory mechanisms that lead to cancer metastasis in breast cancer by metabolic reprogramming have not been explored. Depending on their molecular subtypes and metastatic sites, breast cancer cells have different metabolic phenotypes. Extrinsic factors such as hypoxia, oxidative stress, and acidosis, as well as intrinsic factors such as MYC amplification, PIK3CA, and TP53 mutations, all lead to various metabolic reprogramming phenotypes in metastatic breast cancers. The metabolic processes underlying breast cancer metastasis can provide valuable clues for developing novel therapeutic methods for metastatic breast cancer treatment [1].

Breast cancer is the most common malignant tumour in women and the second leading cause of cancer death. More than 90% of cancer-related deaths are caused by metastatic breast cancer rather than the primary tumor. According to a SEER-based analysis, 30-60 percent of metastatic breast cancer patients have metastases in the bone, 21-32 percent has metastases in the lung, 15-32 percent has metastases in the liver, and 4-10 percent has metastases in the brain. Furthermore, it appears that the chosen metastatic sites are dependent on the pathological subtypes of primary breast cancers. Oncogenic signaling pathways participate in energy control and anabolism to help rapidly growing tumors, according to new evidence. Cancer is not only a hereditary disorder, but also a metabolic disease, according to new evidence. Metabolic reprogramming is thus regarded as a hallmark of cancer [2]. Notably, metabolic reprogramming and its intricate regulatory networks have an effect on breast cancer tumorigenesis and progression. Breast cancer is classified as a highly heterogeneous disease with four major intrinsic molecular subtypes: luminal a, luminal B, HER2-positive, and triple-negative breast cancer (TNBC). Each subtype has distinct capabilities for proliferation and metastasis, as well as metabolic genotypes and phenotypes. TNBC cells, in particular, have metabolic characteristics that include high glycolysis and low mitochondrial respiration. Some subtypes of tumors have lower glutamine metabolic activity and higher lipid metabolism than HER2-positive tumors. Nonetheless, metabolic changes can vary not only between breast cancer subtypes, but also depending on how cancer cells interact with their complex microenvironment. Normal cells in a rapidly proliferating state activate various signaling pathways in response to external growth signals, suppressing oxidative phosphorylation (OXPHOS) and advancing glycolysis and anabolic metabolism for cell growth. Even if there are no external signals, cancer cells will hijack this process to meet developmental needs. In contrast to normal cells, where glycolysis and OXPHOS are often antagonistic, cancer cells have both modes coexisting to varying degrees. Furthermore, unlike normal cells, which produce adenosine triphosphate (ATP) primarily via OXPHOS through the TCA cycle from glucose-derived pyruvate, most cancer cells rely on glycolysis to generate energy even under aerobic conditions. Tumor cells were discovered to have dual metabolic natures, with tumor cells switching from aerobic glycolysis to OXPHOS phenotype in response to lactic acidosis. Furthermore, certain tumors have two-compartment tumor metabolism, also known as the reverse Warburg effect or metabolic coupling, in which glycolytic metabolism in the cancer-related stroma keeps the neighboring cancer cells alive. This metabolic phenotype will lead to chemotherapy resistance, as well as explain why certain tumor cells have high mitochondrial respiration but low glycolysis rates. Furthermore, a large sample data analysis found that luminal subtype correlated with metabolically inactive reverse-Warburg/null phenotypes, while TNBC correlated with metabolically active Warburg/mixed phenotypes [3]. Furthermore, the hypoxic environment in breast tumors increases the synthesis of reactive oxygen species (ROS), while induced hypoxia-inducible factor 1 (HIF-1) boosts glucose metabolism to maintain redox homeostasis.

Several stages of active breast cancer metastasis are assisted by metabolic programming. In different metastasis sites, breast cancer cells have different metabolic phenotypes. Extrinsic factors, such as metabolic stresses imposed by the microenvironment, such as hypoxia, oxidative stress, and acidosis, as well as intrinsic factors, such as MYC amplification, PIK3CA, and TP53 mutations, lead to various metabolic programming phenotypes in metastatic breast cancer. More specifically, interfering with tumor metabolism to slow tumor growth is a successful cancer treatment strategy, but one fraught with difficulties. More research is needed to learn more about the associated genes and molecular mechanisms involved in metabolism reprograming during cancer progression, so that they can be used in clinical practice in the future. We also anticipate advancements in methods for judging and quantifying metabolic phenotypes in human breast cancers in vivo, such as metabolomics, metabolic imaging, and isotope tracing studies, so that clinical oncologists can establish treatment strategies based on the patient's unique tumor metabolic characteristics.

References

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