Molecular Genetics in Breast Cancer: Signaling Pathways and Tumor Biology

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ABSTRACT

Breast cancer is one of the common cancers among the women in which many factors are involved including oncogenes, tumor suppressor genes, different signaling pathways, epigenetic and environmental factors such as inflammation, immune system deficiency, genomic instability as well as Warburg effect that play an important role in the development and spread of cancer as well as cellular metabolism that intensifies the process. There are some evidence that cancer stem cells (CSCs) are responsible for tumor initiation, invasion, maintenance, heterogeneity, metastasis, and resistance to treatment. CSCs may be an important target for an effective treatment due to the fact that these cells are responsible for metastasis and resistance to treatment. Learning these various factors, we can take a great step towards better understanding of this type of cancer and help further to treatment of the disease so that, cancer cells become not resistant to chemotherapy and we can take the best possible outcome of our treatment, although breast cancer is very heterogeneous and is associated with many cases such as cell morphology, cell physiology, cell gene expression, metabolism, etc.

Keywords: Breast Cancer, Stem Cell, Signaling Pathways, Tumor Biology

Certainly, many genetic factors are involved in observing breast cancer in a woman such as Proto-oncogenes (RAS and NYC) and signaling pathways PI3K-AT-mTOR and tumor suppressors (BRCA1 and BRCA2), although each factor doesn’t have an effective role, alone (1). Also, issues such as inflammation, immune system defects, genomic instability (2) as well as Warburg effect are involved in the development and spread of cancer (3). On the other hand, cellular metabolism intensifies this process by producing bio-molecules such as pyruvate, lactate and ketone bodies (4). Proficiency in each of these sectors can be used in personalized treatment (5).

References

as Reactive oxygen species caused by Nuclear factor and NFE2L2 can be restored (6,7).

Carcinogenesis process becomes lower when the cell is subjected to poverty and energy crisis (8).

Environmental factors include cigarette smoke (9) and prolonged exposure to ethanol. Also, viral infections, obesity, allergens, radiation, toxic chemicals and other environmental factors are sometimes the microbial factors other than environmental factors (10). Most of the above cases are considered as the epigenetic changes (11). Although, breast cancer is very heterogeneous and is associated with many cellular cases such as morphology, cell physiology, cell origin, surface markers, the level of gene expression in cells, metabolism and metastasis potential (12).

According to their versatility with their environment, breast cancer cells acquire drug resistance properties, too (13,14) and that makes them resistant to chemotherapy (15,16). Although, chemotherapy and radiotherapy have been occasionally seen to cause increased ROS levels in cells (17-19). Mitochondrial accumulation causes up-regulated Wnt/β-catenin (20). that the production of mitochondria is associated with ERRα-PGC1 signaling pathway and stopping the molecular pathways is associated with sonic hedgehog TGF β – SMAD, STAT3 which are the major pathways in the

References

carcinogenic process (21). Overcoming the resistance to chemotherapy and radiotherapy in solid tumors is one of the fundamental problems in the clinical oncology. A significant percentage of resistance to the treatment as well as metastasis and recurrence processes can be attributed to cancer stem cells (CSCs) (22,23). Breast cancer stem cells (BCSCs) showed a high level of activity of Wnt, Notch, Hedgehog, JAK/STAT and Nuclear factor-kappa B (NF-κB) and these pathways set the process of differentiation and self-renewal (24). CSCs may be an important target for an effective treatment due to the fact that these cells are responsible for metastasis and resistance to treatment (25).

Figure 1: This model shown to us metabolic coupling in tumor metabolism, such as: Warburg effect, ROS-mediated pseudo hypoxia/survival mechanism, Lactate efflux/uptake, Anabolism/Catabolism, Autophagy, high mitochondrial mass.

References


Conclusion

In this study, we explain the various factors involved in breast cancer; although, breast cancer is a heterogeneous disease in which many factors are involved but certainly, being mastered in any above-mentioned factors can help us in the future individual treatment.