Chapter 18
Breast Cancer Etiopathogenesis Through Different Molecular Signatures (Biomarkers) Serving as a Chemical Mediators/Modulators (Pharmaco-Therapeutics): Gemcitabine Nanoparticles and Cisplatin Nanoliposome of Pharmaceutical Drug Delivery Targeting

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ABSTRACT

Chemotherapy is still mainstay treatment for various cancers. However, it has run into problems like low tumor selectivity and MDR (multidrug resistance). One creative solution to these problems is the use of nanotechnology materials for targeted drug delivery. This study's goals included improving cisplatin nanoliposomes and Gemcitabine Nanoparticles(NPs) and determining how toxic they were to breast cancer cell lines. The results of the study showed that cisplatin's and Gemcitabine NPs cytotoxic effects were increased in liposomes/NPs as opposed to in its free form. In conclusion, nanoliposome and Nanoparticle synthesis methods have proven to be an invaluable asset in improving therapeutic drugs, particularly in the area of chemotherapy. Nevertheless, it is essential to carefully assess the toxicity and fate of nanoliposomes before using them for pharmaceutical applications. These research aims to provide the numerous studies that have investigated the Anticancer effects of different medications formulated in nanoliposomes/NPs in various cell lines.

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INTRODUCTION TO BREAST CANCER ETIOPATHOGENESIS

Recently, in the field of cancer treatment, the paradigm has changed to immunotherapy that activates the immune system to induce cancer attacks. Among them, immune checkpoint inhibitors (ICI) are attracting attention as excellent and continuous clinical results. However, it shows not only limitations such as efficacy only in some patients or some indications, but also side-effects and resistance occur. Therefore, it is necessary to understand the factors of the tumor microenvironment (TME) that affect the efficacy of immunotherapy, that is, the mechanism by which cancer grows while evading or suppressing attacks from the immune system within the TME. Tumors can evade attacks from the immune system through various mechanisms such as restricting antigen recognition, inhibiting the immune system, and inducing T cell exhaustion. In addition, tumors inhibit or evade the immune system by accumulating specific metabolites and signal factors within the TME or limiting the nutrients available to immune cells. In order to overcome the limitations of immunotherapy and develop effective cancer treatments and therapeutic strategies, an approach is needed to understand the functions of cancer and immune cells in an integrated manner based on the TME. In this review, we will examine the effects of the TME on cancer cells and immune cells, especially how cancer cells evade the immune system, and examine anti-cancer strategies based on TME.(*Agemy, L., 2010)*

Breast Cancer Immunity and Tumor Immunosurveillance: The Immune System in Cancer: The immune system maintains its defense against infected antigens and self-antigens through an appropriate balance between activation and inhibition of immune response. At its core, this process involves receptor-ligand binding between T cells activated by antigens and various cells within the immune system, and the immune response is known to play an important role in carcinogenesis and anti-tumor immunity. The immune response is the intraorganism defense mechanism that responds to threats to self. This defensive reaction takes place in three stages: recognition, processing, and reaction. Non-self elements are recognized as foreign substances by cells or active molecules involved in the immune response. Cells or active molecules involved in innate immunity recognize molecular patterns of non-self antigens. Innate immunity includes cells such as natural killer (NK) cells, macrophages, dendritic cells (DC), and neutrophils, as well as active molecules such as complement system in serum. The lymphocytes and antibodies involved in adaptive immunity have the ability to recognize the structure of non-self antigens or amino acid sequences in detail with high accuracy. In order to induce an effective immune response that can fight infectious diseases or cancer, cells or active molecules in the innate immune system and the adaptive immune system must interact in a coordinated manner. When cells from both systems respond properly at the early stage of cancer, cancer cells can be removed and the tissue returns to its normal state. However, cancer cells grow and spontaneously proliferate faster than the immune system can handle through strategies that deceive the immune system and prevent attacks from immune cells. To do this, cancer cells begin to build a microenvironment starting at the time of cancer occurrence, and in most cases, when a cancer mass is found, a tumor microenvironment (TME) is present, making it difficult for the immune system to efficiently eliminate cancer cells.(*Ahlers J. D., 2010)*

Angiogenesis involves the development of new blood vessels from pre-existing vessels and plays an important role in tumor growth, maintenance, and metastasis. Free Gemcitabine Nanoparticles has been described presenting anti-angiogenesis effects by inhibiting or modulating many pro-angiogenesis factors such as vascular endothelial growth factor (VEGF), matrix metalloproteinases (MMPs), and basic fibroblast growth factor (bFGF) in *in vitro* and *in vivo* studies. Similar effects were reported in