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Review Paper

An overview of new therapeutic approaches for the treatment of metastatic breast cancer

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ABSTRACT

Metastatic cancer, also known as stage-IV cancer, is the process by which cancer cells move to different areas of the body, contributing to the majority of cancer deaths. Immunotherapy, a novel treatment for breast cancer, has emerged as a new option due to the discovery of immune checkpoint inhibitors and a better understanding of how cancer cells evade the immune system. However, single-drug treatments using monoclonal antibodies against programmed death-1 and PD-L1 have not shown much success in treating metastatic breast cancer patients. The development of immunotherapy and molecularly targeted treatment combinations for metastatic breast cancer is gaining attention. This Personal View examines the safety and effectiveness of immunotherapeutic approaches when used in conjunction with chemotherapy, radiotherapy, angiogenesis inhibitors, inhibitors of cyclin-dependent kinases 4 and 6, HER2-targeted therapy, poly (ADP-ribose) polymerase inhibitors, and other treatments. Gene therapy, a new scientific revolution, has been heralded as the next great revolution in biomedicine, but its therapeutic efficacy is severely compromised by extracellular and intracellular hurdles during gene transport.

INTRODUCTION

Metastatic cancer is also referred to as stage- IV cancer, it is the process by which cancer cells move to different areas of the body. Metastasis is the main factor contributing to deaths from cancer.

⁽¹⁾ A novel kind of treatment for breast cancer is immunotherapy. Following the long-standing use of targeted biological therapy and endocrine

therapy, new treatment options have been made possible by the discovery of immune checkpoint inhibitors and a better understanding of how cancer cells evade the immune system. Because most breast cancers have a limited number of lymphocytes that infiltrate the tumour, single-drug treatments using monoclonal antibodies against programmed death-1 (PD-1) and programmed

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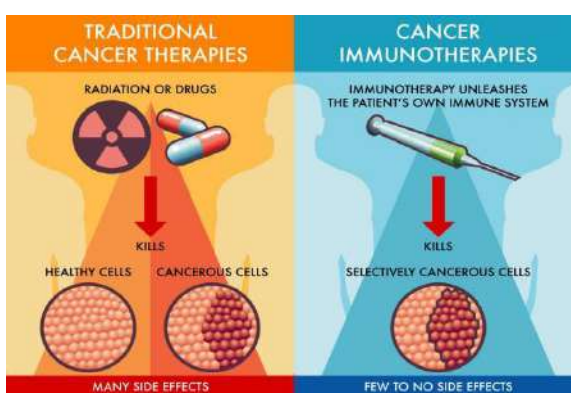
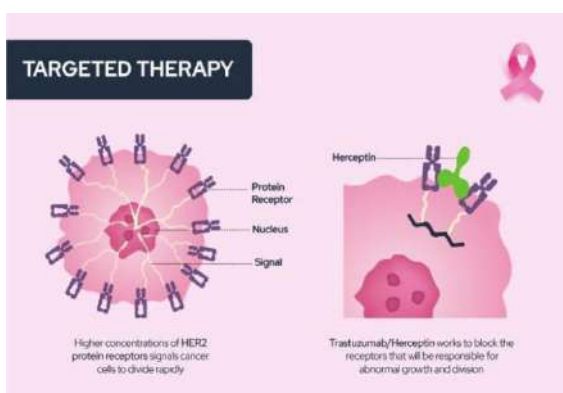


death ligand-1 (PD-L1) have not demonstrated much success in treating patients with metastatic breast cancer. The development of immunotherapy and molecularly targeted treatment combinations for metastatic breast cancer is gaining attention.⁽²⁾ In this Personal View, we examine the information that is currently available and the ongoing research being done to determine the safety and effectiveness of immunotherapeutic approaches when used in conjunction with chemotherapy, radiotherapy, angiogenesis inhibitors, inhibitors of cyclin-dependent kinases 4 and 6, HER2-targeted therapy, poly(ADP-ribose) polymerase inhibitors, and other treatments.⁽²⁾ Gene therapy has been hailed as a new scientific revolution since it offers the advantage of treating diseases at the genetic level. However, the therapeutic efficacy is severely compromised by the extracellular and intracellular hurdles that occur during gene transport, such as enzymatic degradation and endo-/lysosomal sequestration. The translocation of internalized molecules into the cytosol through photochemical internalization (PCI) has emerged as a promising method for inducing endo-/lysosomal leakage; nevertheless, the effect of PCI is currently inadequate because of the shallow light penetration depth.⁽³⁾ A novel kind of treatment for breast cancer is immunotherapy. Following the long-standing use of targeted biological therapy and endocrine therapy, new treatment options have been made possible by the discovery of immune checkpoint inhibitors and a better understanding of how cancer cells evade the immune system. Because most breast cancers have a limited number of lymphocytes that infiltrate the

tumor, single-drug treatments using monoclonal antibodies against programmed death-1 (PD-1) In the world of biomedicine, gene therapy has been heralded as the next great revolution. However, the therapeutic efficacy is severely compromised by the extracellular and intracellular hurdles that occur during gene transport, such as enzymatic degradation and endo-/lysosomal sequestration. The translocation of internalised molecules into the cytosol through photochemical internalisation (PCI) has emerged as a promising method for inducing endo-/lysosomal leakage; nevertheless, the effect of PCI is currently inadequate because of the shallow light penetration depth. Here, we use ROS produced by in situ cascaded catalytic events in tumours using Mn²⁺-mediated Fenton-like reaction and GOx-mediated redox reaction to establish tumour microenvironment-specific improved gene delivery. Cargo gene complexes have showed effective enzymatic protection and successful endo-/lysosomal escape.⁽²⁾

Combination of immunotherapy and targeted therapy for breast cancer:

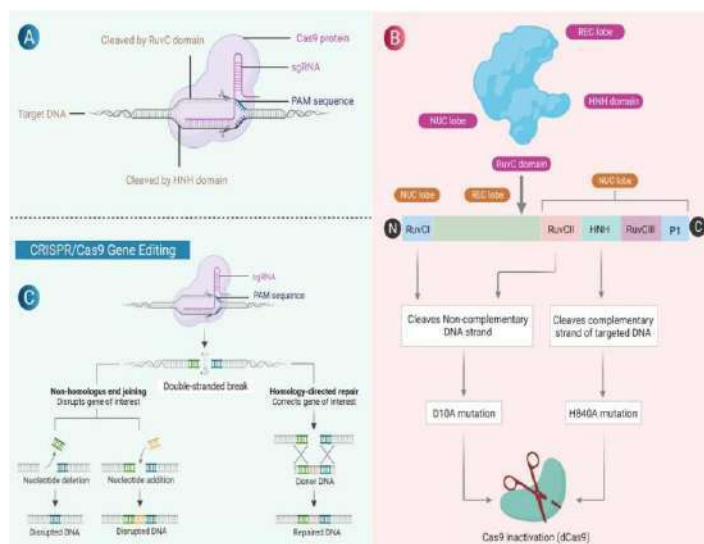
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Gene Therapy:

In the world of biomedicine, gene therapy has been heralded as the next great revolution. However, the therapeutic efficacy is severely compromised by the extracellular and intracellular hurdles that occur during gene transport, such as enzymatic degradation and endo-/lysosomal sequestration. The translocation of internalised molecules into the cytosol through photochemical internalisation (PCI) has emerged as a promising method for

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DISCUSSION:

Immunotherapy targets malignant cells with one's immune response, gaining popularity as a safe and fewer side effect cancer treatment due to numerous methods to activate or strengthen the immune system.⁽⁴⁾ Targeted medication therapy aims to target proteins on breast cancer cells for development, metastasis and proliferation.

Successful treatment targets ER and HER2 receptors, with new treatments for TNBC and HER2+ carcinomas, including aromatase antagonists, endocrine therapy and selective estrogen downregulators.⁽⁵⁾ Gene therapy offers a promising future for cancer treatment by enhancing immune responses, using oncolytic viruses and inhibiting cancer survival and supportive activities.⁽⁴⁾

CONCLUSION:

Immunotherapy, gene therapy, and targeted therapy are examples of anticancer strategies that are quickly developing in an effort to overcome the shortcomings of traditional treatments. The capacity of coley toxins to activate immune cell tolllike receptors and elicit an immunological response against tumours gave rise to the idea of immunotherapy. A thorough understanding of the molecular mechanisms of carcinogenesis and how they relate to the prognosis of the disease has made molecular targeted therapy approaches promising. These approaches work by either stimulating or inhibiting specific molecules that either promote or inhibit cancer.⁽⁴⁾ Treatments for breast cancer have included a range of gene therapy approaches. While some of these strategies concentrate on the tumor cells, others try to alter how immune cell behave. Gene therapy targets have included molecular alterations in breast cancer cells, such as oncogene activation or suppressor gene mutation. Numerous researchers have employed gene transfer to disrupt oncogene products or reinstate the functions of suppressor genes.⁽⁵⁾

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