Review

Cancer Biology

A Perspective Review of Cancer Therapy (Part I)
Immunotherapy, Gene Therapy, and Nanotechnology

Alberto Pajuelo*
University of Valencia, Av. de Blasco Ibáñez, 13, El Pla del Real, 46010 València, Valencia, Spain
*: All correspondence should be sent to: Dr. Alberto Pajuelo.
Author's Contact: Alberto Pajuelo, Ph.D., E-mail: alberto.pajuelo@hotmail.com
DOI: https://doi.org/10.15354/si.23.re833
Funding: No funding source declared.
COI: The author declares no competing interest.

The application of genomic profiling approaches has propelled the advancement of precision medicine, enabling the development of personalized treatment programs that are specifically customized for each particular patient. This method considers the distinct genetic composition of each tumor, allowing for the detection of crucial driver mutations and possible weaknesses that might be targeted for therapeutic purposes. Furthermore, immunotherapy has emerged as a promising approach in cancer treatment, utilizing the potential of the immune system to identify and eradicate cancerous cells. Medical breakthroughs like CAR-T cell therapy have already demonstrated exceptional efficacy in treating hematologic malignancies. Moreover, state-of-the-art technologies such as CRISPR-Cas9 gene editing offer potential for directly altering tumor cells or augmenting the efficacy of current treatments. The future of cancer therapy is focused on developing more precise and targeted techniques to enhance patient outcomes and ultimately overcome this destructive illness. This involves continual research and cooperation among scientists, physicians, and pharmaceutical corporations on a worldwide level.

Keywords: Cancer; Personalized Therapy; Immunotherapy; Gene Therapy; Outcomes

Science Insights, 2023 December 31; Vol. 43, No. 6, pp.1155-1165.

THE FIELD of cancer treatment is advancing quickly and includes a range of cutting-edge medicines that focus on specific biochemical changes in cancer cells. Conventional treatment methods like surgery, chemotherapy, and radiation therapy remain commonly employed, yet they are frequently supplemented by more recent approaches. Immunotherapy has transformed cancer treatment by utilizing the patient's immune system to identify and eliminate cancer cells (1). This includes immune checkpoint inhibitors that hinder proteins such as PD-1 or CTLA-4, amplifying T-cell activity, and fostering the body's immunological response against tumors. Moreover, targeted medicines have arisen as precision medicine strategies for tumors characterized by specific genetic abnormalities (2). These medications specifically block the communication routes in cancer cells, decreasing the growth and dissemination of cancer while preserving the integrity of healthy tissues. Moreover, gene

therapy has potential in the treatment of specific forms of tumors through the introduction of novel genes or the alteration of preexisting ones to augment the body's capacity to combat the illness (3). Personalized medicine approaches utilizing genomic profiling have also gained popularity for customizing treatments specifically for individual patients, resulting in improved overall outcomes (4). Advancements in research are enhancing our comprehension of the fundamental molecular pathways that propel the advancement of cancer. Consequently, new therapeutic strategies will continue to arise, providing optimism for the development of more efficient treatments and enhanced patient outcomes.

It is crucial to make progress in cancer therapy in order to enhance patient outcomes and elevate survival rates. Although notable advancements have been achieved in the treatment of specific cancer types, such as breast and prostate cancer, numerous other forms of the illness continue to pose challenges in terms of successful treatment. Progress in cancer therapy can offer more precise treatments that selectively target cancer cells while preserving healthy cells, minimizing adverse effects, and enhancing the overall quality of life for patients (5). In addition, it is imperative to prioritize research and development endeavors towards the creation of individualized medicines that are specifically designed according to a patient's genetic composition and biomarkers. This approach will enable the implementation of customized treatment strategies that optimize effectiveness. In addition, the advancement of newer medications with unique modes of action can effectively address the issue of drug resistance commonly encountered in the later stages of the disease. Hence, it is crucial for researchers, healthcare experts, and pharmaceutical companies to cooperate in order to enhance cancer treatment by employing cutting-edge methods including immunotherapies, gene therapies, and combination medicines (6). Through the allocation of resources towards these technological developments, we can aspire to transform the field of cancer therapy and ultimately enhance the preservation of human lives.

Immunotherapy

Checkpoint Inhibitors

Checkpoint inhibitors in cancer immunotherapy are a class of medications that have significantly transformed the management of several forms of cancer (7). These inhibitors function by selectively targeting certain proteins on immune cells that serve as inhibitory mechanisms or checkpoints, hence impeding the immune system's ability to effectively attack cancer cells. Checkpoint inhibitors can unleash the complete potential of the immune system to identify and eliminate cancer cells by obstructing these proteins.

PD-1 inhibitors are a prevalent form of checkpoint inhibitor employed in cancer immunotherapy. PD-1 is an immunoregulatory protein present on immune cells that aids in the control of immunological reactions (8). Cancer cells could exploit this checkpoint in order to avoid being detected and eliminated by the immune system. PD-1 inhibitors, including pembrolizumab and nivolumab, attach to the PD-1 protein, effectively deactivating it and enabling immune cells to identify and eradicate cancer cells (9).

Ipilimumab is a frequently utilized CTLA-4 inhibitor, which is a type of checkpoint inhibitor. CTLA-4 is an additional protein found in immune cells that controls and manages immune responses (10). By obstructing CTLA-4, these inhibitors amplify the stimulation and reproduction of immune cells, resulting in a robust anti-tumor immunological reaction.

Checkpoint inhibitors have demonstrated exceptional effectiveness in various cancer forms, such as melanoma, lung cancer, and bladder cancer (11). These inhibitors have, in certain instances, resulted in enduring remission, even in individuals with advanced or metastatic illnesses. Checkpoint inhibitors have revolutionized cancer treatment, providing renewed optimism for patients with restricted therapeutic alternatives.

Nevertheless, similar to all medical interventions, checkpoint inhibitors possess inherent risks of adverse consequences. These may encompass immune-related side effects, such as hepatotoxicity, pneumonitis, or colitis (12). These adverse effects can be controlled with the use of immunosuppressive medications or by temporarily discontinuing the delivery of checkpoint inhibitors. Generally, the advantages of treatment surpass the drawbacks, and vigilant supervision can assist in reducing potential unfavorable occurrences.

Although checkpoint inhibitors have achieved remarkable success, they are not universally effective for all individuals (13). Certain individuals may possess malignancies that lack the expression of specific proteins that are targeted by checkpoint inhibitors, while others may have acquired resistance to these medications. Scientists are currently engaged in the active pursuit of devising novel approaches and combinations of checkpoint inhibitors with other therapies to surmount these obstacles and attain superior results for patients.

Checkpoint inhibitors have significantly transformed cancer immunotherapy by harnessing the potential of the immune system to target and destroy cancerous cells. PD-1 and CTLA-4 inhibitors have demonstrated efficacy across several cancer types, providing renewed optimism for patients with advanced disease. Although some medications may have possible adverse effects, diligent treatment and monitoring can help alleviate these risks. Nevertheless, additional investigation and advancement are necessary to tackle the constraints and difficulties linked to checkpoint inhibitors in order to provide optimal therapeutic alternatives for all cancer patients.

CAR-T Cell Therapy

Chimeric Antigen Receptor T-Cell Therapy (CAR-T cell therapy) is an innovative and highly promising type of immunotherapy that has significantly transformed the field of cancer treatment (14). This treatment entails genetically altering a patient's own T cells, which are a type of immune cell, to identify and eradicate cancer cells. CAR-T cell therapy has demonstrated exceptional efficacy in the treatment of some cancer types, specifically relapsed or refractory B-cell malignancies.

CAR-T cell therapy is based on genetically modifying T cells to express a chimeric antigen receptor (CAR). CARs are artificial receptors that merge the antigen-binding region of an antibody with the signaling region of a T cell receptor (15). This enables the altered T cells to selectively identify and attach to a

specific antigen that is present on cancer cells. Upon being bound, the CAR-T cells undergo activation, resulting in their rapid multiplication and release of cytotoxic substances, ultimately causing the destruction of the cancer cells.

CAR-T cell therapy has demonstrated exceptional efficacy in treating B-cell acute lymphoblastic leukemia (B-ALL). For patients suffering from relapsed or refractory B-ALL who have not responded to standard treatments, CAR-T cell therapy has demonstrated complete remission rates surpassing 80% (16). Comparable achievements have been observed in the treatment of various B-cell cancers, including non-Hodgkin lymphoma and chronic lymphocytic leukemia.

Nevertheless, the execution of CAR-T cell treatment is not devoid of obstacles. An important obstacle lies in the toxicities linked to the treatment, including cytokine release syndrome (CRS) (17). CRS occurs due to the secretion of inflammatory cytokines by the activated CAR-T cells, leading to symptoms such as fever, low blood pressure, and, in extreme instances, malfunction of several organs. Continued endeavors are being made to enhance comprehension and control of CRS, wherever the utilization of immunosuppressive medications like tocilizumab exhibits potential in alleviating its impacts.

An additional obstacle lies in the production of CAR-T cells. The manufacturing process of CAR-T cells encompasses several stages, which include the collection of T cells, genetic alteration, expansion, and purification (18). The process is intricate, laborious, and expensive. Moreover, the fluctuation in the quality and functioning of T cells presents additional difficulties in guaranteeing consistent therapeutic effectiveness (19). Continual research is being conducted to enhance and simplify the manufacturing process of CAR-T cell therapy, with the aim of increasing its accessibility and cost-efficiency.

Notwithstanding these obstacles, the outlook for CAR-T cell treatment is encouraging. Current research is dedicated to broadening the utilization of CAR-T cell therapy to encompass additional categories of cancer, including solid tumors. The existence of an immunosuppressive tumor microenvironment poses distinct difficulties when dealing with solid tumors (20). Efforts are underway to investigate the potential of augmenting the efficacy of treatment by combining CAR-T cell therapy with other immunomodulatory treatments, such as checkpoint inhibitors.

Furthermore, there are ongoing endeavors to create readily available CAR-T cell products. Presently, CAR-T cell therapy is dependent on the utilization of the patient's own T cells, which must be gathered, genetically altered, and multiplied before being reintroduced into the body (21). The implementation of this individualized strategy presents practical difficulties and constraints in relation to availability. The advancement of allogeneic CAR-T cell products, which involve modifying T cells from healthy donors for universal application, has the potential to overcome these challenges and provide broader accessibility to this groundbreaking therapy.

Cancer Vaccines

Cancer has always been regarded as one of the most formidable and destructive diseases in human history. Throughout time, scientists and researchers have achieved noteworthy advancements in comprehending the intricate characteristics of cancer cells and formulating diverse therapeutic alternatives. An encouraging area of investigation involves the utilization of cancer vaccines in the field of cancer immunotherapy. Vaccines, typically linked with the prevention of infectious diseases, are currently being investigated as a means to stimulate the innate capacity of the immune system to identify and eliminate cancerous cells.

To grasp the potential of cancer vaccines, it is crucial to have a thorough understanding of the fundamentals of immunotherapy. Immunotherapy is a therapeutic approach that harnesses the patient's immune system to specifically target and eliminate cancerous cells (22). It distinguishes itself from conventional treatment methods like chemotherapy and radiation, which specifically focus on cancer cells. Immunotherapy, on the other hand, fortifies and amplifies the immune system, enabling it to identify and combat cancerous cells more efficiently.

Cancer vaccines, within the realm of immunotherapy, function by regulating the immune response towards cancerous cells (23). These vaccinations can be broadly classified into two categories: preventative vaccines and therapeutic vaccines. Preventive cancer vaccinations are designed to hinder the occurrence of particular cancer types by focusing on viral infections that are recognized to heighten the likelihood of cancer development (24). An exemplary instance of a prophylactic cancer vaccination is the human papillomavirus (HPV) vaccine, which efficiently averts HPV infection, a notable predisposing factor for cervical cancer.

Conversely, therapeutic cancer vaccinations are specifically created to activate the immune system's ability to identify and combat preexisting cancer cells. These vaccines generally contain certain antigens present on cancer cells, which elicit an immunological response upon detection by the immune system (25). Therapeutic cancer vaccines seek to enhance the immune system's capacity to identify and eliminate cancer cells by specifically targeting these antigens.

Sipuleucel-T, a widely recognized therapeutic cancer vaccine, received FDA approval in 2010 specifically for the treatment of advanced prostate cancer (26). Sipuleucel-T functions by harvesting a patient's immune cells and subjecting them to a protein present in prostate cancer cells (27). Upon reintroduction into the patient, these activated immune cells elicit an immunological reaction against prostate cancer, ultimately leading to a decrease in tumor size and a prolonged lifespan.

Personalized vaccinations are a promising field of research in the fight against cancer. These vaccinations are customized to target the unique tumor antigens of each individual patient, rendering them highly specific and perhaps more efficacious (28). They employ genetic data obtained from a patient's tumor to pinpoint distinct targets for the immune system to target. Despite being in the nascent phase of advancement, tailored cancer vaccines exhibit significant potential for enhancing patient outcomes.

It is crucial to acknowledge that cancer vaccines, similar to other immunotherapies, may not be effective for all forms of cancer or all patients (29). Cancer cells possess a remarkable ability to adapt and have devised strategies to elude immune recognition. Hence, current research endeavors to ascertain tac-

tics to surmount these obstacles and enhance the effectiveness of cancer vaccinations.

In addition, cancer vaccines are frequently integrated with other immunotherapies or conventional therapy modalities to optimize their efficacy. Combination therapy can address many elements of cancer biology, bolster the immune response, and overcome mechanisms of resistance. An instance of this is the combination of a cancer vaccine with immune checkpoint inhibitors, which has exhibited encouraging outcomes in clinical trials. This is because the checkpoint inhibitors augment the immune system's reaction to the vaccination.

Precision Medicine and Targeted Therapies

Genomic Profiling

The discovery of genetic changes in tumor cells is a crucial factor in the efficacy of immunotherapy. Genomic profiling, commonly referred to as genetic profiling, involves a thorough examination of the genomic changes found in cancer cells. It has a vital function in directing treatment choices, forecasting the response to therapy, and establishing possible objectives for immunotherapy.

Genomic profiling entails examining genetic changes that stimulate the development and advancement of cancer (30). These modifications can manifest as somatic mutations, gene fusions, copy number alterations, or alterations in DNA methylation. Through the identification of these modifications, researchers can ascertain the patients who are most inclined to derive advantages from immunotherapy. For example, cancers that have particular mutations in genes like PD-L1 or BRAF might be more vulnerable to specific immune checkpoint inhibitors (31).

Moreover, genetic profiling can assist in forecasting the reaction to immunotherapies. Occasionally, tumors with a substantial mutational burden, which signifies a greater number of mutations in the tumor genome, have demonstrated superior response rates to immunotherapy (32). These findings indicate that cancers containing a higher quantity of neoantigens, which are specific molecules recognized by the immune system, are more likely to exhibit positive responses to immunotherapeutic treatments.

Moreover, genetic profiling enables researchers to pinpoint potential targets for novel immunotherapies. By examining genomic modifications, scientists can detect genes that are expressed or altered in an abnormal manner, thereby identifying them as prospective candidates for targeted immunotherapies (33). This strategy has already resulted in the creation of precise immunotherapies, such as immune cell treatments that focus on CAR or certain tumor-associated antigens.

Genomic profiling is particularly useful in identifying causes of resistance to immunotherapies. Although immunotherapy has demonstrated great efficacy in numerous patients, it is susceptible to the development of resistance over time. Immunotherapy resistance can be caused by mechanisms such as changes in the interferon pathway or immunological checkpoint proteins (34). Genomic profiling can identify these changes, allowing researchers to devise strategies to overcome resistance and enhance patient outcomes.

Although genetic profiling in cancer immunotherapy has great potential, there are obstacles that must be overcome during implementation. The expense and intricacy of genomic sequencing can restrict its extensive utilization. Moreover, the process of understanding and incorporating genetic data into clinical practice can present difficulties (35). Nevertheless, the progress in sequencing technologies and bioinformatics tools is consistently enhancing the precision, efficiency, and cost-efficiency of genomic profiling.

Targeted Therapies against Specific Genetic Mutations

Targeted therapies aim to combat specific genetic abnormalities that stimulate the progression and advancement of certain diseases, resulting in enhanced outcomes and heightened rates of survival.

An instance of targeted therapy involves the utilization of tyrosine kinase inhibitors (TKIs) for the management of specific forms of cancer (36). TKIs function by inhibiting the aberrant or hyperactive activity of proteins called tyrosine kinases, which are present in cancer cells. TKIs can disrupt the signaling pathways that facilitate cancer development and survival by targeting these proteins, resulting in tumor reduction and disease reversal (37).

A compelling demonstration of the efficacy of targeted therapy is exemplified by the utilization of the pharmaceutical imatinib in the management of chronic myeloid leukemia (CML). CML is attributed to a genetic anomaly referred to as the Philadelphia chromosome, which leads to the amalgamation of two genes and the synthesis of a hybrid protein named BCR-ABL (38). Imatinib selectively targets and suppresses the activity of the BCR-ABL protein, resulting in notable clinical responses and extended survival in patients with CML.

Targeted therapies are being researched for the treatment of genetic abnormalities, in addition to cancer. An illustrative instance is the use of gene therapy to rectify particular gene mutations that result in infrequent and incapacitating illnesses. Gene therapy entails the introduction of intact, functioning replicas of a mutant gene into the cells of a patient, enabling them to generate the absent or faulty protein (39). This method has demonstrated encouraging outcomes in disorders such as spinal muscular atrophy and hemophilia, providing enduring therapeutic advantages and potentially achieving a cure for these ailments.

Another noteworthy instance of targeted therapy in genetic disorders involves the utilization of tiny molecules or antisense oligonucleotides to regulate the function of RNA molecules (40). RNA-based therapeutics demonstrate high efficacy in disorders resulting from aberrant RNA processing, namely in some forms of muscular dystrophy. Through the specific identification and rectification of the deviant RNA, these treatments have the capability to reinstate regular protein synthesis and enhance the overall medical results for those who are impacted (41).

Targeted therapies directed at target genetic alterations not only provide the possibility of more efficient therapy but also result in fewer adverse effects in comparison to traditional therapies (42). As these medicines primarily focus on the altered

proteins or genes, they avoid harming normal cells, which helps to minimize toxicity and decrease the negative effects associated with treatment. This tailored therapeutic strategy has significant potential for patients, enabling enhanced accuracy and customized medical attention.

Nevertheless, targeted therapy poses certain problems. An important obstacle is the process of identifying and confirming pertinent genetic alterations. Accurate detection of certain mutations necessitates the utilization of sophisticated genetic testing methods (43). Additionally, progress in creating tailored treatments may be hindered by an insufficient understanding of the genetic processes that underlie specific diseases.

Furthermore, the development of resistance to targeted therapies might occur gradually, thereby restricting the long-term efficacy of these treatments. Tumors can acquire novel mutations or activate alternative signaling pathways, which can reduce the effectiveness of the first successful treatment (44). This requires the ongoing surveillance of patients' genetic profiles and the formulation of various therapeutic approaches to overcome resistance.

Notwithstanding these difficulties, targeted treatments targeting certain genetic abnormalities have undeniably revolutionized the field of medicine. These treatments have greatly enhanced patient outcomes and increased survival rates for several forms of cancer and genetic diseases. As our comprehension of the genetic foundation of diseases expands, focused medicines will persistently advance and provide optimism for patients who once had restricted therapy alternatives.

Nanotechnology in Cancer Therapy

Nanoparticle Drug Delivery Systems

Conventional treatment approaches, including surgery, chemotherapy, and radiation therapy, have demonstrated partial effectiveness. However, they frequently lead to significant adverse effects and have limited therapeutic efficiency. Nanoparticle Drug Delivery Systems (NDDS) have emerged as a viable approach to tackle these issues in cancer therapy.

NDDS refers to the method of administering therapeutic medications by utilizing nanoparticles as carriers (45). Nanoparticles can be manipulated to possess different dimensions, configurations, and surface compositions, enabling the precise administration of therapeutic agents to cancerous cells (46). Enclosing medications within nanoparticles enhances their stability, avoiding breakdown in the bloodstream and facilitating regulated release at the tumor location.

An important benefit of NDDS is the heightened penetration and retention effect (EPR). Nanoparticles could selectively gather in tumor tissues because of the tumor's permeable blood vessels and decreased lymphatic outflow (47). This accumulation enables the attainment of elevated drug concentrations in cancer cells while simultaneously minimizing the impact on healthy tissues, hence reducing off-target side effects. In addition, NDDS can surpass many biological obstacles that restrict the efficacy of traditional cancer treatments. Nanoparticles have the ability to circumvent the multidrug resistance mechanisms frequently acquired by cancer cells, thereby preventing therapy ineffectiveness (48). Moreover, NDDS can safeguard medications against enzymatic degradation and prolong their circulation duration, hence enhancing their therapeutic capacity.

Nevertheless, there are obstacles that must be confronted in the process of creating NDDS for cancer treatment. Extensive research and optimization are necessary due to the intricate nature of nanoparticle design, production, and characterization. Furthermore, it is crucial to thoroughly assess the possible toxicity of nanoparticles to guarantee the safety of patients.

Another obstacle lies in the heterogeneity of malignancies. Tumor cells could acquire resistance to specific medications, which reduces the effectiveness of NDDS. To address this issue, scientists are investigating the utilization of various medications encapsulated in nanoparticles to optimize the therapeutic effect and reduce the development of drug resistance.

Notwithstanding these difficulties, the outlook for NDDS in cancer treatment appears encouraging. The ongoing progress in nanotechnology and drug delivery systems will continue to improve the therapeutic capabilities and safety of NDDS (49). The advancement of multifunctional nanoparticles, capable of concurrently administering various medications and imaging agents, exhibits significant potential for customized medicine and targeted cancer treatment. Moreover, the incorporation of NDDS with additional therapeutic approaches, such as immunotherapy or gene therapy, can significantly augment their effectiveness. By using nanoparticles to transport immune-stimulating chemicals or gene editing tools, it is possible to increase the body's immune response against cancer cells in a synergistic manner, resulting in superior outcomes.

Theranostics: Simultaneous Therapy and Diagnosis

Theranostics is an emerging discipline in medicine that integrates therapy and diagnosis into a unified entity, offering a groundbreaking approach to healthcare (50). Conventional medical treatments frequently require distinct diagnostic tests to detect an illness and subsequent medications for therapy. Nevertheless, theranostics combines the diagnostic and therapeutic elements, providing numerous advantages for patient care.

Theranostics utilizes nanoparticles, biomarkers, and imaging techniques to detect and treat diseases simultaneously (51). The nanoparticles, capable of being infused with curative substances, are engineered to selectively target tissues or cells within the organism. Furthermore, these nanoparticles can transport imaging agents, enabling real-time observation, and monitoring of the therapy. This technique not only improves the precision of diagnosis but also allows for individualized and focused therapy.

An important benefit of theranostics is the ability to diagnose and intervene at an early stage. Through the integration of diagnostic and therapeutic methodologies, clinicians are able to detect diseases in their early phases, enabling prompt and enhanced treatment. For example, in the field of cancer treatment, theranostics can assist in identifying the minimum residual disease, facilitating prompt intervention, and mitigating the risk of relapse (52).

Moreover, theranostics can enhance patient outcomes and decrease healthcare expenses. Integrating diagnosis and therapy can prevent unnecessary treatment procedures and redundant

diagnostic testing, resulting in quicker recovery periods and substantial financial savings (53). In addition, the utilization of nanoparticles enables precise drug delivery, minimizing the risk of adverse effects by specifically targeting affected areas while preserving healthy cells.

Theranostics offers a notable advantage in the realm of individualized medicine. Theranostics enables the customization of treatment programs by adapting therapies to individual patients, taking into account their distinct disease characteristics, genetic makeup, and response to therapy (54). This strategy enhances the effectiveness of treatment and reduces the likelihood of unpleasant responses or treatment failures that are frequently observed in therapies that are designed to fit everyone.

Nevertheless, theranostics also poses many obstacles. First and foremost, the advancement and refinement of theranostic agents necessitate a thorough investigation and substantial financial commitment. The successful execution of this innovation process necessitates the cooperation of interdisciplinary teams comprising chemists, biologists, engineers, and doctors. Hence, the availability of funds and the allocation of resources are obstacles to the extensive adoption of theranostics. An additional obstacle exists in the regulatory framework and the procedures for obtaining approval. Given the integrated characteristics of theranostics, regulatory authorities may need supplementary validation and substantiation to ensure its safety and effectiveness. This elongates the process of transferring scientific discoveries from the laboratory to practical medical applications, which could impede the timely access of theranostics to patients who require them.

Gene Editing and Gene Therapy

CRISPR/Cas9 Applications in Cancer Treatment

CRISPR/Cas9 provides scientists with a potent tool to specifically target cancer cells, alter genetic material, and fundamentally transform the field of cancer therapy.

An important utilization of CRISPR/Cas9 in the field of cancer treatment is its capacity to accurately pinpoint cancer-causing mutations. CRISPR/Cas9 exploits the inherent defense mechanism of bacteria to selectively recognize and attach to DNA sequences inside the genome of cancer cells (55). This technique streamlines the process of identifying and altering oncogenic genes that are responsible for the genesis and advancement of cancer. It empowers scientists to deactivate these genes and impedes the growth of tumors.

Furthermore, CRISPR/Cas9 has demonstrated immense promise in the advancement of individualized cancer immunotherapies. Through the manipulation of immune cells, specifically T cells, researchers can augment their capacity to identify and selectively attack cancerous cells (56). The CAR-T cell therapy, which is recognized for its efficacy, has demonstrated exceptional outcomes in the treatment of specific forms of leukemia and lymphoma, providing optimism to patients who were previously considered untreatable.

CRISPR/Cas9 also shows potential in cancer treatment by enhancing the sensitivity of cancer cells to chemotherapy. Scientists can enhance the susceptibility of cancer cells to routinely used chemotherapy drugs by modifying certain genes responsible for chemotherapy resistance using gene editing (57). This technique has the capacity to transform cancer treatment by diminishing drug resistance and enhancing the efficacy of chemotherapy, thereby enhancing patient outcomes.

CRISPR/Cas9 can be utilized to manipulate tumor-specific viruses for the purpose of cancer treatment. Scientists can utilize CRISPR/Cas9 to alter the genetic material of oncolytic viruses, resulting in the creation of viruses that specifically target and reproduce within cancer cells without harming healthy cells (28). This technique has demonstrated potential in preclinical investigations and presents a possible pathway for precise and effective cancer therapy. CRISPR/Cas9 can be employed to create animal models of cancer for the purpose of scientific investigation. By incorporating precise gene abnormalities linked to human tumors into animal models, researchers can gain a deeper understanding of the molecular pathways behind the onset and advancement of cancer. This can result in the creation of more efficient remedies and therapies.

CRISPR/Cas9 has a significant role in cancer treatment via its ability to identify cancer-associated mutations. Scientists are employing the gene-editing abilities of CRISPR/Cas9 to create precise and effective diagnostic tools for the early diagnosis of tumors (59). These technologies identify specific mutations in DNA or RNA, enabling the detection of cancers in their initial stages. Timely identification of this condition has the potential to significantly enhance survival rates with prompt therapies.

Moreover, CRISPR/Cas9 presents the potential to provide innovative, precise treatments for cancer. By utilizing this technology to ascertain pivotal oncogenes or tumor suppressor genes, scientists can devise medicines to specifically target these genes and impede their function, resulting in tumor regression (60). This method has the capacity to limit off-target effects, therefore decreasing side effects and enhancing patient results. CRISPR/Cas9 can be used as a research instrument to screen extensive collections of genes to pinpoint prospective therapeutic targets. Through a methodical process of modifying many genes in cancer cells, scientists can pinpoint the specific genes that are essential for the survival or rapid growth of cancer cells. This understanding can inform the advancement of precise therapeutic interventions that capitalize on the weaknesses of cancer cells, resulting in enhanced efficacy of treatments.

CRISPR/Cas9 has the capacity to unravel the enigmas behind cancer metastasis, a phenomenon that accounts for the bulk of fatalities associated with cancer. Through the manipulation of genes associated with metastasis, researchers can acquire a deeper understanding of the mechanisms that drive the dissemination of cancer cells and potentially create interventions to impede or stop the spread of cancer.

Oncolytic Viruses and Gene Therapy Approaches

Oncolytic viruses are genetically engineered viruses that are specifically engineered to infect and reproduce within cancer cells (61). These viruses can be modified to specifically cause the death of cancer cells, either by triggering cell death or by stimulating an immune response against the tumor. The adeno-

virus is a frequently employed oncolytic virus that has undergone substantial research and modifications for therapeutic purposes. These viruses can be additionally altered to transport genes that increase their ability to destroy cancer cells or to directly produce therapeutic genes inside the tumor.

Gene therapy methods, however, consist of introducing therapeutic genes into cancer cells to rectify a genetic anomaly or to amplify the immune system's anti-cancer properties (62). There are multiple approaches to accomplishing this, including the administration of viral vectors or the utilization of non-viral vectors like liposomes or nanoparticles. Therapeutic genes can be engineered to specifically eliminate cancer cells, impede the growth of tumors, or bolster the immune system's ability to target the tumor.

The processes by which oncolytic viruses and gene therapy approaches work can differ based on the virus or gene employed. Oncolytic viruses could eliminate cancer cells by either activating the production of harmful genes within the tumor or by triggering apoptosis, a controlled cell death mechanism (63). Moreover, these viruses can activate the immune system to identify and combat cancerous cells. Gene therapy methods, however, can stimulate anti-cancer effects by impeding tumor growth, triggering cell death, or augmenting the immune response against the tumor.

An instance showcasing the capacity of oncolytic viruses is the utilization of the herpes simplex virus (HSV) for the therapeutic intervention of melanoma. HSV has the capacity to selectively invade and reproduce within melanoma cells, resulting in their eradication (64). Furthermore, the virus can be manipulated to generate a protein known as granulocyte-macrophage colony-stimulating factor (GM-CSF), which can augment the immune response against the tumor. Trials involving the use of oncolytic HSV in a clinical setting have demonstrated encouraging outcomes, as several patients have displayed either complete or partial remission of tumors.

Likewise, gene therapy methods have demonstrated significant promise in the treatment of cancer. CAR T-cell therapy is a revolutionary gene therapy method that has been developed to treat specific types of blood malignancies. This treatment involves the genetic modification of a patient's T cells to express CARs that specifically target tumor antigens (65). This modification enhances the immune system's capacity to identify and eliminate cancer cells. The efficacy of CAR T-cell therapy in treating patients with relapsed or refractory leukemia and lymphoma has been remarkable, resulting in its approval by regulatory agencies.

Given these encouraging outcomes, oncolytic viruses and gene therapy techniques are accompanied by hurdles and limits. A significant obstacle lies in the transportation of these treatments to the specific location of the tumor. The immune system and other physiological barriers within the body can impede the efficient administration of oncolytic viruses and gene treatments, consequently diminishing their therapeutic effectiveness. Furthermore, there is a lingering concern regarding the possibility of unintended effects on non-targeted areas and the activation of immune responses against the therapeutic vectors or genes.

Conclusions

Cancer therapy encompasses a variety of interventions aimed at specifically targeting and eradicating malignant cells within the human body. The field is broad and includes multiple treatment methods like as surgery, radiation therapy, chemotherapy, immunotherapy, targeted therapy, and hormonal therapy. Every method is customized to address the specific requirements of individual patients, considering characteristics such as tumor type, stage, and overall health state. Surgery is the excision of malignant tissues via surgical interventions, whereas radiation therapy employs high-energy beams to eradicate cancer cells or impede their proliferation. Chemotherapy utilizes systemic administration of medicines to eradicate proliferating cancer cells. Immunotherapy seeks to enhance the patient's immune system's ability to combat cancer cells by utilizing chemicals produced endogenously or synthesized in a controlled environment. Targeted therapy aims to inhibit the activity of specific molecules that play a role in the growth and dissemination of tumors. Hormonal therapy is typically employed for hormone-dependent malignancies, such as breast and prostate cancer. As continuous research efforts have resulted in enhanced results and higher rates of survival for several individuals, the field of cancer therapy has made substantial advancements in recent decades, resulting in notable enhancements in both the survival rates and the quality of life for individuals diagnosed with cancer. Nevertheless, the domain of cancer therapy is perpetually advancing, with scientists consistently investigating novel methodologies and technology to enhance therapies.

Targeted therapies are a promising approach in the field of cancer therapy. Conventional chemotherapy is designed to eliminate cells that divide quickly, but it frequently impacts healthy cells too, resulting in significant adverse effects. Targeted therapies specifically target chemicals or genetic defects that are seen in cancer cells. Through targeted assault on cancer cells, these medicines have the potential to diminish adverse effects and enhance efficacy. An instance of this is the significant impact made by the advancement of tyrosine kinase inhibitors on the therapy of specific cancer types, such as chronic myeloid leukemia. Scientists are currently investigating further objectives and developing customized medicines for various types of cancer, which have the potential to result in more individualized and efficient treatments.

Immunotherapy represents a promising avenue for future advancements. Immunotherapy utilizes the body's immune system to combat cancer cells. This method has significant potential as it harnesses the body's innate immune system to specifically target and eliminate cancer cells. Immunotherapies, such as immune checkpoint inhibitors, have demonstrated exceptional efficacy in some cancer forms, notably melanoma and lung cancer. Researchers are advancing their comprehension of the immune system and its interactions with cancer cells, leading to the development of innovative strategies to augment immune responses against malignancies. Researchers are currently investigating the use of combination immunotherapies and immune therapies that target many components of the immune response. The goal is to enhance the efficacy and longevity of treatment.

Nanotechnology is a highly promising field in the realm of cancer treatment. Nanoparticles can be designed to transport medications directly to cancerous cells, thereby reducing harm to healthy tissue. These particles can specifically target tumors

by either attaching specific receptors on cancer cells or exploiting the distinct characteristics of tumor blood vessels. In addition, nanoparticles can be engineered to deliver medications in a regulated fashion, guaranteeing extended contact between cancer cells and therapeutic substances. Nanotechnology facilitates the utilization of sophisticated imaging methods for the detection and surveillance of cancer, while also offering vital insights into therapy efficacy.

Gene therapy employs many methods to deliver therapeutic genes into cancer cells to augment their capacity to combat the disease. Viral vectors are frequently employed as a means of introducing genes into cancer cells by utilizing genetically engineered viruses. Therapeutic genes can be engineered to generate targeted proteins that hinder the growth of tumors or trigger programmed cell death. For example, including genes that encode immune checkpoint inhibitors can facilitate the removal of restrictions on the immune system, enabling it to identify and eradicate cancer cells more efficiently. Gene editing technologies, such as CRISPR-Cas9, are demonstrating potential in the field of cancer therapy. These technologies enable accurate manipulation of genes, providing the ability to rectify genetic defects, repress cancer-causing genes, or augment the production of tumor-suppressor genes. Gene editing has the potential to be beneficial for creating cancer treatments that are customized to each patient's unique genetic composition. Nevertheless, much scientific investigation and ethical deliberations over gene editing must be resolved prior to its extensive implementation in cancer treatment.■

References

1. Mukherjee AG, Wanjari UR, Namachivayam A, Murali R, Prabakaran DS, Ganesan R, Renu K, Dey A, Vellingiri B, Ramanathan G, Doss C GP, Gopalakrishnan AV. Role of immune cells and receptors in cancer treatment: An immunotherapeutic approach. Vaccines (Basel) 2022; 10(9):1493. DOI: https://doi.org/10.3390/vaccines10091493
2. Nassar SF, Raddassi K, Ubhi B, Doktorski J, Abulaban A. Precision medicine: Steps along the road to combat human cancer. Cells 2020; 9(9):2056. DOI: https://doi.org/10.3390/cells9092056
3. Gonçalves GAR, Paiva RMA. Gene therapy: advances, challenges and perspectives. Einstein (Sao Paulo) 2017; 15(3):369-375. DOI: https://doi.org/10.1590/S1679-45082017RB4024
4. Strianese O, Rizzo F, Ciccarelli M, Galasso G, D'Agostino Y, Salvati A, Del Giudice C, Tesorio P, Rusciano MR. Precision and personalized medicine: How genomic approach improves the management of cardiovascular and neurodegenerative disease. Genes (Basel) 2020; 11(7):747. DOI: https://doi.org/10.3390/genes11070747
5. Baranwal J, Barse B, Di Petrillo A, Gatto G, Pilia L, Kumar A. Nanoparticles in cancer diagnosis and treatment. Materials (Basel) 2023; 16(15):5354. DOI: https://doi.org/10.3390/ma16155354
6. Chehelgerdi M, Chehelgerdi M, Allela OQB, Pecho RDC, Jayasankar N, Rao DP, Thamaraikani T, Vasanthan M, Viktor P, Lakshmaiya N, Saadh MJ, Amajd A, Abo-Zaid MA, Castillo-Acobo RY, Ismail AH, Amin AH, Akhavan-Sigari R. Progressing nanotechnology to improve targeted cancer treatment: Overcoming hurdles in its clinical implementation. Mol Cancer 2023; 22(1):169. DOI: https://doi.org/10.1186/s12943-023-01865-0
7. Shiravand Y, Khodadadi F, Kashani SMA, Hosseini-Fard SR, Hosseini S, Sadeghirad H, Ladwa R, O'Byrne K, Kulasinghe A. Immune checkpoint inhibitors in cancer therapy. Curr Oncol 2022; 29(5):3044-3060. DOI: https://doi.org/10.3390/curroncol29050247
8. Riella LV, Paterson AM, Sharpe AH, Chandraker A. Role of the PD-1 pathway in the immune response. Am J Transplant 2012; 12(10):2575-2587. DOI: https://doi.org/10.1111/j.1600-6143.2012.04224.x
9. Alsaab HO, Sau S, Alzhrani R, Tatiparti K, Bhise K, Kashaw SK, Iyer AK. PD-1 and PD-L1 checkpoint signaling inhibition for cancer immunotherapy: Mechanism, combinations, and clinical outcome. Front Pharmacol 2017; 8:561. DOI: https://doi.org/10.3389/fphar.2017.00561
10. Buchbinder EI, Desai A. CTLA-4 and PD-1 pathways: Similarities, differences, and implications of their inhibition. Am J Clin Oncol 2016; 39(1):98-106. DOI: https://doi.org/10.1097/COC.0000000000000239
11. Okobi TJ, Uhomoibhi TO, Akahara DE, Odoma VA, Sanusi IA, Okobi OE, Umana I, Okobi E, Okonkwo CC, Harry NM. Immune checkpoint inhibitors as a treatment option for bladder cancer: Current evidence. Cureus 2023; 15(6):e40031. DOI: https://doi.org/10.7759/cureus.40031
12. Brahmer JR, Lacchetti C, Schneider BJ, Atkins MB, Brassil KJ, Caterino JM, Chau I, Ernstoff MS, Gardner JM, Ginex P, Hallmeyer S, Holter Chakrabarty J, Leighl NB, Mammen JS, McDermott DF, Naing A, Nastoupil LJ, Phillips T, Porter LD, Puzanov I, Reichner CA, Santomasso BD, Seigel C, Spira A, Suarez-Almazor ME, Wang Y, Weber JS, Wolchok JD, Thompson JA; National comprehensive cancer network. management of immune-related adverse events in patients treated with immune checkpoint inhibitor therapy: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol 2018; 36(17):1714-1768. DOI: https://doi.org/10.1200/JCO.2017.77.6385
13. Basudan AM. The role of immune checkpoint inhibitors in cancer therapy. Clin Pract 2022; 13(1):22-40. DOI: https://doi.org/10.3390/clinpract13010003

14. Hernández-López A, Téllez-González MA, Mondragón-Terán P, Meneses-Acosta A. Chimeric antigen receptor-t cells: A pharmaceutical scope. Front Pharmacol 2021; 12:720692. DOI: https://doi.org/10.3389/fphar.2021.720692
15. Dotti G, Gottschalk S, Savoldo B, Brenner MK. Design and development of therapies using chimeric antigen receptor-expressing T cells. Immunol Rev 2014; 257(1):107-126. DOI: https://doi.org/10.1111/imr.12131
16. Cappell KM, Kochenderfer JN. Long-term outcomes following CAR T cell therapy: What we know so far. Nat Rev Clin Oncol 2023; 20(6):359-371. DOI: https://doi.org/10.1038/s41571-023-00754-1
17. Messmer AS, Que YA, Schankin C, Banz Y, Bacher U, Novak U, Pabst T. CAR T-cell therapy and critical care: A survival guide for medical emergency teams. Wien Klin Wochenschr 2021; 133(23-24):1318-1325. DOI: https://doi.org/10.1007/s00508-021-01948-2
18. Levine BL, Miskin J, Wonnacott K, Keir C. Global manufacturing of CAR T Cell therapy. Mol Ther Methods Clin Dev 2016; 4:92-101. DOI: https://doi.org/10.1016/j.omtm.2016.12.006
19. Fesnak AD. The challenge of variability in chimeric antigen receptor T cell manufacturing. Regen Eng Transl Med 2020; 6(3):322-329. DOI: https://doi.org/10.1007/s40883-019-00124-3
20. Liu Z, Zhou Z, Dang Q, Xu H, Lv J, Li H, Han X. Immunosuppression in tumor immune microenvironment and its optimization from CAR-T cell therapy. Theranostics 2022; 12(14):6273-6290. DOI: https://doi.org/10.7150/thno.76854
21. Zhang C, Liu J, Zhong JF, Zhang X. Engineering CAR-T cells. Biomark Res 2017; 5:22. DOI: https://doi.org/10.1186/s40364-017-0102-y
22. Kumar AR, Devan AR, Nair B, Vinod BS, Nath LR. Harnessing the immune system against cancer: Current immunotherapy approaches and therapeutic targets. Mol Biol Rep 2021; 48(12):8075-8095. DOI: https://doi.org/10.1007/s11033-021-06752-9
23. Liu D, Che X, Wang X, Ma C, Wu G. tumor vaccines: Unleashing the power of the immune system to fight cancer. Pharmaceuticals (Basel) 2023; 16(10):1384. DOI: https://doi.org/10.3390/ph16101384
24. Enokida T, Moreira A, Bhardwaj N. Vaccines for immunoprevention of cancer. J Clin Invest 2021; 131(9):e146956. DOI: https://doi.org/10.1172/JCI146956
25. Le I, Dhandayuthapani S, Chacon J, Eiring AM, Gadad SS. Harnessing the immune system with cancer vaccines: From prevention to therapeutics. Vaccines (Basel) 2022; 10(5):816. DOI: https://doi.org/10.3390/vaccines10050816
26. Cheever MA, Higano CS. PROVENGE (Sipuleucel-T) in prostate cancer: The first FDA-approved therapeutic cancer vaccine. Clin Cancer Res 2011; 17(11):3520-3526. DOI: https://doi.org/10.1158/1078-0432.CCR-10-3126
27. Kantoff PW, Higano CS, Shore ND, Berger ER, Small EJ, Penson DF, Redfern CH, Ferrari AC, Dreicer R, Sims RB, Xu Y, Frohlich MW, Schellhammer PF; IMPACT Study Investigators. Sipuleucel-T immunotherapy for castration-resistant prostate cancer. N Engl J Med 2010; 363(5):411-422. DOI: https://doi.org/10.1056/NEJMoa1001294
28. Fan T, Zhang M, Yang J, Zhu Z, Cao W, Dong C. Therapeutic cancer vaccines: Advancements, challenges, and prospects. Signal Transduct Target Ther 2023; 8(1):450. DOI: https://doi.org/10.1038/s41392-023-01674-3
29. Liu J, Fu M, Wang M, Wan D, Wei Y, Wei X. Cancer vaccines as promising immuno-therapeutics: Platforms and current progress. J Hematol Oncol 2022; 15(1):28. DOI: https://doi.org/10.1186/s13045-022-01247-x
30. Berger MF, Mardis ER. The emerging clinical relevance of genomics in cancer medicine. Nat Rev Clin Oncol 2018; 15(6):353-365. DOI: https://doi.org/10.1038/s41571-018-0002-6
31. Wang M, Yu L, Wei X, Wei Y. Role of tumor gene mutations in treatment response to immune checkpoint blockades. Precis Clin Med 2019; 2(2):100-109. DOI: https://doi.org/10.1093/pcmedi/pbz006
32. Jardim DL, Goodman A, de Melo Gagliato D, Kurzrock R. The challenges of tumor mutational burden as an immunotherapy biomarker. Cancer Cell 2021; 39(2):154-173. DOI: https://doi.org/10.1016/j.ccell.2020.10.001
33. Nagahashi M, Shimada Y, Ichikawa H, Kameyama H, Takabe K, Okuda S, Wakai T. Next generation sequencing-based gene panel tests for the management of solid tumors. Cancer Sci 2019; 110(1):6-15. DOI: https://doi.org/10.1111/cas.13837
34. Bai R, Chen N, Li L, Du N, Bai L, Lv Z, Tian H, Cui J. Mechanisms of cancer resistance to immunotherapy. Front Oncol 2020; 10:1290. DOI: https://doi.org/10.3389/fonc.2020.01290
35. Hicks JK, Dunnenberger HM, Gumpper KF, Haidar CE, Hoffman JM. Integrating pharmacogenomics into electronic health records with clinical decision support. Am J Health Syst Pharm 2016; 73(23):1967-1976. DOI: https://doi.org/10.2146/ajhp160030
36. Pottier C, Fresnais M, Gilon M, Jérusalem G, Longuespée R, Sounni NE. Tyrosine kinase inhibitors in cancer: Breakthrough and challenges of targeted therapy. Cancers (Basel) 2020; 12(3):731. DOI: https://doi.org/10.3390/cancers12030731
37. Kim M, Baek M, Kim DJ. Protein tyrosine signaling and its potential therapeutic implications in carcinogenesis. Curr Pharm Des 2017; 23(29):4226-4246. DOI: https://doi.org/10.2174/1381612823666170616082125
38. Kang ZJ, Liu YF, Xu LZ, Long ZJ, Huang D, Yang Y, Liu B, Feng JX, Pan YJ, Yan JS, Liu Q. The Philadelphia chromosome in leukemogenesis. Chin J Cancer 2016; 35:48. DOI: https://doi.org/10.1186/s40880-016-0108-0
39. Kirschner J, Cathomen T. Gene therapy for monogenic inherited disorders. Dtsch Arztebl Int 2020; 117(51-52):878-885. DOI: https://doi.org/10.3238/arztebl.2020.0878

40. Kole R, Krainer AR, Altman S. RNA therapeutics: Beyond RNA interference and antisense oligonucleotides. Nat Rev Drug Discov 2012; 11(2):125-140. DOI: https://doi.org/10.1038/nrd3625
41. Theodoridis PR, Bokros M, Marijan D, Balukoff NC, Wang D, Kirk CC, Budine TD, Goldsmith HD, Wang M, Audas TE, Lee S. Local translation in nuclear condensate amyloid bodies. Proc Natl Acad Sci U S A 2021; 118(7):e2014457118. DOI: https://doi.org/10.1073/pnas.2014457118
42. Waarts MR, Stonestrom AJ, Park YC, Levine RL. Targeting mutations in cancer. J Clin Invest 2022; 132(8):e154943. DOI: https://doi.org/10.1172/JCI154943
43. Mahdieh N, Rabbani B. An overview of mutation detection methods in genetic disorders. Iran J Pediatr 2013; 23(4):375-388.
44. Yip HYK, Papa A. Signaling pathways in cancer: Therapeutic targets, combinatorial treatments, and new developments. Cells 2021; 10(3):659. DOI: https://doi.org/10.3390/cells10030659
45. Tewabe A, Abate A, Tamrie M, Seyfu A, Abdela Siraj E. Targeted drug delivery - from magic bullet to nanomedicine: Principles, challenges, and future perspectives. J Multidiscip Healthc 2021; 14:1711-1724. DOI: https://doi.org/10.2147/JMDH.S313968
46. Wang EC, Wang AZ. Nanoparticles and their applications in cell and molecular biology. Integr Biol (Camb) 2014; 6(1):9-26. DOI: https://doi.org/10.1039/c3ib40165k
47. Nakamura Y, Mochida A, Choyke PL, Kobayashi H. Nanodrug delivery: Is the enhanced permeability and retention effect sufficient for curing cancer? Bioconjug Chem 2016; 27(10):2225-2238. DOI: https://doi.org/10.1021/acs.bioconjchem.6b00437
48. Yao Y, Zhou Y, Liu L, Xu Y, Chen Q, Wang Y, Wu S, Deng Y, Zhang J, Shao A. Nanoparticle-based drug delivery in cancer therapy and its role in overcoming drug resistance. Front Mol Biosci 2020; 7:193. DOI: https://doi.org/10.3389/fmolb.2020.00193
49. Ezike TC, Okpala US, Onoja UL, Nwike CP, Ezeako EC, Okpara OJ, Okoroafor CC, Eze SC, Kalu OL, Odoh EC, Nwadike UG, Ogbodo JO, Umeh BU, Ossai EC, Nwanguma BC. Advances in drug delivery systems, challenges and future directions. Heliyon 2023; 9(6):e17488. DOI: https://doi.org/10.1016/j.heliyon.2023.e17488
50. Jeelani S, Reddy RC, Maheswaran T, Asokan GS, Dany A, Anand B. Theranostics: A treasured tailor for tomorrow. J Pharm Bioallied Sci 2014; 6(Suppl 1):S6-S8. DOI: https://doi.org/10.4103/0975-7406.137249
51. Janib SM, Moses AS, MacKay JA. Imaging and drug delivery using theranostic nanoparticles. Adv Drug Deliv Rev 2010; 62(11):1052-1063. DOI: https://doi.org/10.1016/j.addr.2010.08.004
52. Cescon DW, Kalinsky K, Parsons HA, Smith KL, Spears PA, Thomas A, Zhao F, DeMichele A. Therapeutic targeting of minimal residual disease to prevent late recurrence in hormone-receptor positive breast cancer: Challenges and new approaches. Front Oncol 2022; 11:667397. DOI: https://doi.org/10.3389/fonc.2021.667397
53. Abyzova E, Dogadina E, Rodriguez RD, Petrov I, Kolesnikova Y, Zhou M, Liu C, Sheremet E. Beyond Tissue replacement: The Emerging role of smart implants in healthcare. Mater Today Bio 2023; 22:100784. DOI: https://doi.org/10.1016/j.mtbio.2023.100784
54. Alghamdi MA, Fallica AN, Virzì N, Kesharwani P, Pittalà V, Greish K. The promise of nanotechnology in personalized medicine. J Pers Med 2022; 12(5):673. DOI: https://doi.org/10.3390/jpm12050673
55. Stefanoudakis D, Kathuria-Prakash N, Sun AW, Abel M, Drolen CE, Ashbaugh C, Zhang S, Hui G, Tabatabaei YA, Zektser Y, Lopez LP, Pantuck A, Drakaki A. The potential revolution of cancer treatment with CRISPR technology. Cancers (Basel) 2023; 15(6):1813. DOI: https://doi.org/10.3390/cancers15061813
56. Lee HM. Strategies for manipulating T cells in cancer immunotherapy. Biomol Ther (Seoul) 2022; 30(4):299-308. DOI: https://doi.org/10.4062/biomolther.2021.180
57. Vaghari-Tabari M, Hassanpour P, Sadeghsoltani F, Malakoti F, Alemi F, Qujeq D, Asemi Z, Yousefi B. CRISPR/Cas9 gene editing: A new approach for overcoming drug resistance in cancer. Cell Mol Biol Lett 2022; 27(1):49. DOI: https://doi.org/10.1186/s11658-022-00348-2
58. Yuan M, Webb E, Lemoine NR, Wang Y. CRISPR-Cas9 as a powerful tool for efficient creation of oncolytic viruses. Viruses 2016; 8(3):72. DOI: https://doi.org/10.3390/v8030072
59. Akram F, Haq IU, Sahreen S, Nasir N, Naseem W, Imitaz M, Aqeel A. CRISPR/Cas9: A revolutionary genome editing tool for human cancers treatment. Technol Cancer Res Treat 2022; 21:15330338221132078. DOI: https://doi.org/10.1177/15330338221132078
60. Azangou-Khyavy M, Ghasemi M, Khanali J, Boroomand-Saboor M, Jamalkhah M, Soleimani M, Kiani J. CRISPR/Cas: From tumor gene editing to T cell-based immunotherapy of cancer. Front Immunol 2020; 11:2062. DOI: https://doi.org/10.3389/fimmu.2020.02062
61. Jhawar SR, Thandoni A, Bommareddy PK, Hassan S, Kohlhapp FJ, Goyal S, Schenkel JM, Silk AW, Zloza A. Oncolytic viruses-natural and genetically engineered cancer immunotherapies. Front Oncol 2017; 7:202. DOI: https://doi.org/10.3389/fonc.2017.00202
62. Das SK, Menezes ME, Bhatia S, Wang XY, Emdad L, Sarkar D, Fisher PB. Gene therapies for cancer: Strategies, challenges and successes. J Cell Physiol 2015; 230(2):259-71. DOI: https://doi.org/10.1002/jcp.24791
63. Kaufman HL, Kohlhapp FJ, Zloza A. Oncolytic viruses: A new class of immunotherapy drugs. Nat Rev Drug Discov 2015;14(9):642-662. DOI: https://doi.org/10.1038/nrd4663. Erratum in: Nat Rev Drug Discov 2016; 15(9):660.
64. Scanlan H, Coffman Z, Bettencourt J, Shipley T, Bramblett DE. Herpes simplex virus 1 as an oncolytic

viral therapy for refractory cancers. Front Oncol 2022; 12:940019. DOI: https://doi.org/10.3389/fonc.2022.940019

65. Jogalekar MP, Rajendran RL, Khan F, Dmello C, Gangadaran P, Ahn BC. CAR T-Cell-Based gene therapy for cancers: New perspectives, challenges, and clinical developments. Front Immunol 2022; 13:925985. DOI: https://doi.org/10.3389/fimmu.2022.925985

Received: October 06, 2023 | Revised: November 15, 2023 | Accepted: November 22, 2023