Emerging Bioengineering Approaches for Cancer and Tumor Therapy

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Abstract: Cancer has become a significant socioeconomic burden globally, with millions of new cases and deaths each year. The promising field of bioengineering has recently undergone significant advancements, providing new methods for combating cancer. Increasing attention has been directed toward understanding the molecular mechanisms of human diseases, supported by the availability of various genetic tools and rapid technological advancements. These developments have enabled the use of the latest gene therapy techniques for cancer treatment, including gene editing, gene deletion, and correcting defective genes through methods such as TALENs, Zinc fingers, RNAi, CRISPR, site-directed mutagenesis (SDM), and enzyme therapy to modulate catalytic activity. In addition, bioengineering vaccines like mRNA vaccines, bioinformatics, computational tools, artificial intelligence (AI), nanotechnology, and chemotherapy are emerging as significant cancer treatment strategies. Among these, gene editing and gene therapy have gained particular attention in recent years and are often used in combination with other therapeutic approaches. The engineering of enzymes and advancements in nanotechnology have also significantly progressed. AI and bioinformatics have contributed to more precise diagnosis, prediction, and prognosis, enabling tailored treatment of cancer and tumors. Imaging and radiotherapy, enhanced by AI, have improved surgical outcomes, even from remote locations. Precision oncology has emerged, using bacteria and viruses to target tumors directly. In this review, we discuss recent advancements and challenges in various cancer therapies.

Keywords: Bioengineering, Gene therapy, CRISPR-Cas9, RNAi, Enzyme therapy, Chemotherapy, Bioinformatics, Computational tools, Artificial Intelligence, Cancer and Tumor

Introduction

Cancer has a long historical presence in humanity, with the earliest known cases dating back to around 1500 BCE (Beg and Parveen, 2021). The incidence and mortality rates of cancer have continued to rise globally, with approximately 19.3 million new cases and 10 million deaths recorded in 2020, as per Global Cancer Statistics (Sung et al., 2020). Despite the availability of conventional cancer treatments like radiation, chemotherapy, and surgery, these approaches often prove insufficient and fail to fully eradicate the disease, as evidenced by the increasing cancer incidence and mortality rates (Qian et al., 2021). While significant research has focused on understanding molecular mechanisms, immunotherapy, and signaling pathways such as PI3K/AKT/mTOR, many cancers remain resistant to treatment, necessitating the development of new therapeutic strategies (Hosseini et al., 2019; Zahoor et al., 2019); however, the drug resistance and cancer recurrence necessitate new therapeutic approaches (Schirrmacher, 2019).

Cancer is now one of the greatest threats to human health globally. The International Agency for Research on Cancer (IARC), under the World Health Organization (WHO), reports that many countries lack adequate resources to properly

manage the disease, with only 39% of countries having basic cancer management services. Cancer is currently the second leading cause of death worldwide, accounting for approximately 9.3 million deaths annually, with one in six deaths attributed to the disease. It is predicted that by 2030, 26 million new cancer cases will emerge, leading to 17 million probable deaths. By 2050, the number is expected to increase significantly, particularly in low- to middle-income countries, where 61% of all new cancer cases are projected to occur. In the United States alone, 611,720 cancer-related deaths have been reported in 2024, with over two million new cases expected this year (Hobbs, 2024). These alarming statistics highlight the urgent need to improve clinical treatments, enhance bioengineering of enzymes and drugs, develop advanced drug delivery systems, and refine therapeutic techniques such as nanotechnology and chemotherapy to combat cancer more effectively worldwide (Binns and Low, 2024).

1. Gene Therapy

Recent studies have shown that gene therapy holds significant promise for correcting defective genes responsible for cancer. Techniques such as ribonucleic acid interference (RNA i) and clustered regularly interspaced short palindromic repeat/CRISPR-associated nuclease 9 (CRISPR/Cas9) genome editing system have garnered considerable attention globally.

I. DNA based Gene Therapy

Unlike traditional cancer treatments, DNA-based gene therapy focuses on editing the genetic material of cancer patients by replacing defective genes with functional ones or modifying existing sequences.

a. Gene Editing through CRISPR/Cas9 and Cancer

The CRISPR/Cas9 system has emerged as a powerful genetic engineering tool, widely applied to manipulate nucleases for editing specific genes in cancer cells. Oncoproteins such as Myc, CycE, and their regulator archipelago (ago) are known to control cellular growth through the polyubiquitination-mediated protein degradation pathway. Mutations in the archipelago (ago) gene have been linked to breast and ovarian cancers in humans (Zahoor et al., 2019; Vo et al., 2018). The CRISPR-Cas9 technique enables precise gene editing in oncogenes and the restoration of tumor suppressor genes, presenting a promising strategy for cancer treatment (Hosseini et al., 2019a; Gemayel et al., 2024; Carrera-Pacheco et al., 2024).

Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) and CRISPR-associated protein 9 (CRISPR/Cas9) is a cutting-edge genetic technique considered one of the most advanced tools for cancer treatment (Ma et al., 2024; Guo et al., 2022). This system allows for the editing of genes for a range of purposes, including both knock-out and knock-in operations. The CRISPR/Cas9 system originates from the bacterial adaptive immune response against invading bacteriophages, first discovered in *E. coli* in 1987 (Li et al., 2022). It operates via a single-guide RNA (sgRNA), which is specifically designed to complement the target site of interest. This guide RNA directs the Cas9 endonuclease to create a double-stranded break (DSB) at the precise location within the DNA sequence (Ruan et al., 2022). CRISPR-Cas9 offers highly efficient, site-specific gene correction and editing (Ma et al., 2024).

Unlike earlier techniques such as Zinc-Finger Nucleases (ZFN) and Transcription Activator-Like Effector Nucleases (TALEN), which require modification of the endonucleases for each specific target, the CRISPR/Cas9 system only requires altering the guide RNA (gRNA) for different target sites. This distinctive feature of CRISPR/Cas9, where the endonucleases remain unchanged, makes it more cost-effective compared to conventional methods like TALEN and ZFN (Jiang et al., 2019). Furthermore, the ability to design specific gRNAs for various target sites enhances both the accuracy and target specificity of the system, making it more precise than previous approaches (Jiang et al., 2019).

The scope of the CRISPR/Cas9 system has significantly expanded in the medical field, particularly in cancer treatment. The American Society for Cancer reports that breast cancer is the leading cause of death in the U.S. (Binns and Low, 2024) and other parts of the world (Siegel et al., 2024). CRISPR/Cas9 has been employed to modify T cells, enhancing their ability to inhibit tumors (Zhao et al., 2018; Guo et al., 2018; Choi et al., 2019). Moreover, CRISPR/Cas9 targeting the *Ptch1* gene has shown success in treating brain tumors (Vo et al., 2018). In vertebrate models, such as mice, CRISPR/Cas9 has been applied to target tumorigenesis-related genes (Ratan et al., 2018). A notable application includes

treating tyrosinemia type I in mouse hepatocytes caused by *Fah* mutation, which was corrected using CRISPR/Cas9 (Xu et al., 2020). Furthermore, multiplexed gene-editing techniques using CRISPR/Cas9 have been employed in mouse models to inhibit tumor growth by targeting multiple genes, achieving high accuracy without significant off-target effects (Liang et al., 2023).

The deactivated protein variant of Cas9 (dCas9) is utilized by the CRISPR-Cas system to bind DNA without causing double-strand breaks, blocking transcriptional initiation and thereby downregulating genes. This technique, known as CRISPR interference (CRISPRi), has been applied in cancer research to induce gene loss-of-function. For instance, *CASP8AP2* has been identified as an essential viability factor in lung cancer, while synergistic effects of *ITGB5*, *TIMP1*, and *TMEM176B* genes on prostate cancer cell proliferation have been observed. Activation of *TMEM176B* and *TIMP1*, coupled with inhibition of *ITGB5*, has shown potential in suppressing prostate cancer growth (Yang et al., 2021; Myacheva et al., 2023). CRISPRi has also been widely used for screening various cancer-related factors across different organs, helping to identify and improve cancer therapies (Handly et al., 2020; Davies et al., 2021; Ahmed et al., 2021; Cui et al., 2022). Thus, CRISPR/Cas9 has proven highly effective in cancer and tumor research (Ma et al., 2024).

b. RNA based Cancer Treatment

MicroRNAs (miRNAs) and small interfering RNAs (siRNAs) represent short nucleic acid molecule-based techniques with significant potential in cancer treatment. siRNAs facilitate mRNA degradation in the cytoplasm by binding to RNA-induced silencing complexes (RISC), which use siRNA or miRNA as templates to locate and degrade target mRNA via RNase activity. Both miRNAs and siRNAs have shown inhibitory effects on tumors and cancer cells (Guan et al., 2019; Xiong et al., 2010). miRNAs have the ability to block translation, exhibiting anticancer effects against liver, pancreatic, and breast cancers. In vivo delivery of siRNAs has demonstrated significant control over cancer metastasis (Parvani et al., 2015). Notably, miRNA delivery using a three-helix structure has been effective in reducing the size of malignant tumors in mice by disrupting cancer-related gene expression. This approach simultaneously activates tumor-inhibiting miRNAs while suppressing tumor-promoting miRNAs (Conde et al., 2016). RNA-based therapy, especially in combination with chemotherapy, has shown remarkable specificity, targeting cancer cells without affecting normal cells—a common issue in chemotherapy alone. Such approaches, including RNA-RNA co-delivery and drug combination therapies, are gaining attention as promising cancer treatment strategies (Beck et al., 2021; Cao et al., 2024; Erdoğan et al., 2023; Espinoza et al., 2021; Liang et al., 2023; Naseri et al., 2025).

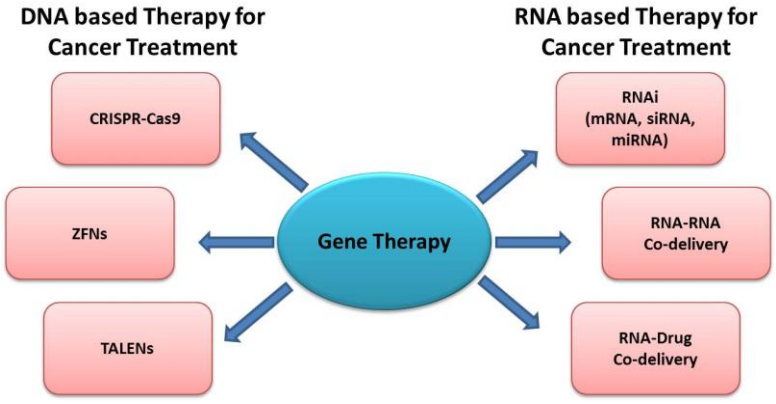

Figure 1: *Different Gene Therapy Approaches for Cancer Treatment*

II. Site-Directed Mutagenesis

Site-directed mutagenesis (SDM) has emerged as a crucial genetic tool for molecularly characterizing gene products, such as enzymes or proteins. It plays an essential role in modulating specificity, activity, solubility, and stability of enzymes, as well as elucidating their biochemical properties and dissecting their roles in signal transduction (Pommier et al., 2003; Majeed et al., 2015;

Zeymer and Hilvert, 2018; Fu et al., 2024; Majeed et al., 2024). The selection and identification of the specific site for SDM is critical to the process. Various bioinformatics tools and software not only help in identifying the precise mutagenesis site but also in reproducing 3D structures before and after mutagenesis (Majeed et al., 2024a; Steiner et al., 2012). Databases like Swiss-model or NCBI can be used to generate amino acid sequences for drawing 3D structures. Through UCSF Chimera, the activity and stability of enzymes, both in wild-type and mutant forms, can be comprehensively studied. SDM in glycosyltransferases, a family of enzymes responsible for glycosylation, has been suggested to assist in the development of cancer drugs (Majeed et al., 2024).

SDM is widely used for enzyme modification to enhance catalytic efficiency. For example, terpenoids, known for their anti-inflammatory and antitumor properties, and α-galactosidase, an enzyme used in cancer diagnosis and therapy, have both been improved through SDM to increase their catalytic efficacy (Xu et al., 2014; Sarkar et al., 2022). Additionally, a mutant superantigen, SEC2(T20L/G22E), developed via SDM, has demonstrated enhanced antitumor activity compared to its native form in vitro (Wang et al., 2009). A promising approach in cancer therapy, amino acid deprivation therapy (AADT), inhibits cancer cell proliferation by limiting amino acid availability without affecting normal cells, which have lower amino acid requirements. This makes AADT selective and non-toxic (Pokrovsky et al., 2022; Kumar et al., 2022; Zhang et al., 2024).

Among targets for AADT, asparagine has shown promise. L-asparaginase, an enzyme that hydrolyzes L-asparagine into L-aspartate and ammonia, inhibits the availability of essential amino acids in cancer cells, leading to cell death and reduced proliferation (Butler et al., 2021). However, L-asparaginase also accepts L-glutamine as a substrate, which can lead to side effects like cerebral hemorrhage and neurological disorders due to decreased glutamine levels (Van Trimpont et al., 2022; Fengmin et al., 2023). Recent SDM efforts have improved L-asparaginase's activity, reducing its L-glutaminase activity and minimizing these side effects (Zhang et al., 2024). Another recent breakthrough includes the production of the anticancer compound dehydroabietic acid through heterologous expression in *Saccharomyces cerevisiae* via SDM (Ma et al., 2024a). Nanobodies, traditionally produced from camelid immune libraries, are widely used in diagnostics and immunotherapy. However, due to the complexity of animal-based procedures, recent studies have utilized CDR grafting and SDM to prepare genetically engineered nanobodies, such as anti-CD20 nanobodies, for leukemia treatment. SDM, when combined with other therapeutic techniques, holds potential in treating cancer and tumors (Gu et al., 2023; Heidari et al., 2024).

2. Enzyme Engineering/Therapy

Enzymes are essential biochemical catalysts, facilitating specific reactions due to their protein-based nature, which grants them high specificity to distinguish substrates of similar structures. Their catalytic efficiency is closely tied to the integrity of their protein conformation (Tandon et al., 2021). Mutations can compromise this efficiency, leading to dysfunction in enzyme-related diseases, prompting the development of drugs targeting these compromised enzymes. In recent years, enzymes have emerged as valuable tools for investigating and treating various pathological conditions, including cancer and metabolic deficiencies (Majeed et al., 2024; Wang et al., 2024; Tvaroška, 2022). By utilizing genetic engineering, enzymes can be modified to activate under specific conditions, such as the hypoxic or acidic environments found in tumor cells. Besides creating new enzymes, existing enzymes can be optimized for better activity through recombinant DNA technology. This includes manipulating molecular structures, altering amino acid sequences, and introducing mutations via genetic engineering (Majeed et al., 2024; Wang et al., 2024). These techniques are crucial for enhancing desirable enzyme traits, such as improving kinetic properties, increasing thermal stability, adjusting optimal temperatures, enhancing specificity, and eliminating allosteric regulations (Tandon et al., 2021).

Clinically and medically important compounds are being produced by genetically introducing the gene encoding the desired product into various organisms, using genetic engineering techniques (Fig. 2). This process has enabled the development of several natural anticancer drugs through enzyme engineering (Majeed et al., 2024; Wang et al., 2024; Tvaroška, 2022). By bioengineering enzymes, researchers can assess the presence or absence of critical amino acids at catalytic sites, an approach made possible through methods such as domain swapping or site-directed mutagenesis (SDM). These engineered enzymes are designed to target and bind to specific structures and molecules found

in cancer cells, enabling the precise delivery of therapeutic agents directly to the cancerous tissues for more effective treatment.

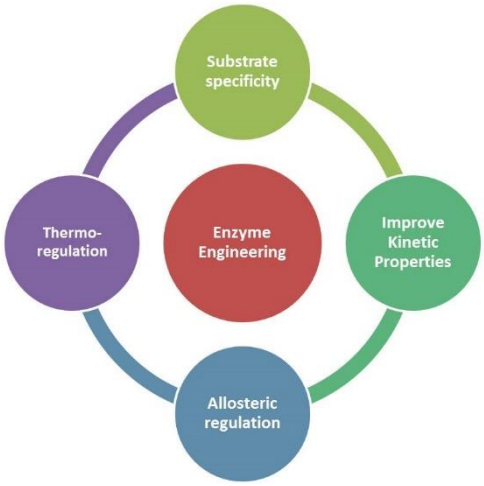

Figure 2: *A brief summary of Enzyme Engineering*

Genetic modifications in enzymes enable them to restore target molecules for proper physiological metabolism. While these treatments offer significant advantages over previously established therapeutic approaches due to their specificity, enzyme therapies also present several challenges. One major issue is their short in vivo half-life, which can lead to decreased specificity due to enzyme degradation in the body. Additionally, the patient's immune system may recognize the administered recombinant enzyme as a foreign neo-antigen, triggering an immune response. This immune reaction reduces therapeutic efficacy by generating anti-drug antibodies, which either inhibit enzyme activity by binding to its catalytic site or block substrate access. Such immune responses have been observed in several studies. For example, glucocerebrosidase treatments in Gaucher's disease patients (Rosenberg et al., 1999), α-L-iduronidase therapy in Hurler's syndrome (Kakavanos et al., 2003), α-glucosidase in Pompe's disease, and α-galactosidase in Fabry's disease have all shown immune responses against these enzymes (Amalfitano et al., 2001; Eng et al., 2001). Despite these issues, ongoing research is focused on developing novel biotechnological strategies to enhance the efficacy and application of enzyme therapies in the future (Radadiya et al., 2020; Jadhav et al., 2020; Liu et al., 2021).

3. Bioengineering of Vaccines

mRNA-based therapies are emerging as a highly effective approach for disease treatment. The success of mRNA vaccines during the COVID-19 pandemic has laid the foundation for further advancements in this field, particularly in cancer immunotherapy (Cao et al., 2024a; Mir et al., 2024). mRNA vaccines work by stimulating the innate immune system, which then triggers an adaptive immune response, targeting the disease (Cao et al., 2024a; Mir et al., 2024). In recent developments, mRNA vaccines have shown significant promise for cancer treatment by expressing tumor antigens in antigen-presenting cells (APCs), which subsequently activates both the innate and adaptive immune systems (Li et al., 2023; Miao et al., 2021).

mRNA vaccines are gaining recognition for their safety, potency, and cost-effectiveness, despite certain limitations such as instability, in vivo inefficiency, and immunogenicity issues (Li et al., 2023; Miao et al., 2021). Structural modifications of mRNA are being explored to overcome these limitations. The emergency authorization of COVID-19 mRNA vaccines, such as Comirnaty (BNT162b2) and Spikevax (mRNA-1273), by the US FDA has opened new possibilities for using mRNA technology in cancer immunotherapy (Miao et al., 2021). Over the past two years, mRNA vaccines have significantly contributed to combatting SARS-CoV-2

and have provided a platform for ongoing research into cancer vaccines (Li et al., 2023).

The key to mRNA vaccine success lies in its practical mechanism—unlike traditional vaccines or viral vectors, mRNA vaccines prompt the body to produce the necessary proteins directly after injection. However, to maximize their efficacy against cancer, improving mRNA vaccine delivery systems in terms of safety and handling is crucial. Combination therapies have been suggested to enhance efficacy (Tan et al., 2023; Duan et al., 2022).

mRNA vaccines are being increasingly studied as an alternative approach for cancer prevention and treatment (Beck et al., 2021). Large-scale production of mRNA vaccines has helped reduce costs, but clinical trials for cancer treatments remain focused on non-replicating mRNAs (Lu and Robbins, 2016; Li et al., 2019). Self-amplifying mRNAs (SAM), a more cost-effective approach, are advancing to the clinical trial stage for cancer treatment (Tan et al., 2020; Liu et al., 2021). These vaccines can stimulate a robust immune response by encoding specific tumor-associated antigens, utilizing self-amplifying RNA vectors, or combining mRNA with adjuvants. Other strategies include gene editing tools, immune checkpoint inhibitors, and novel delivery systems aimed at enhancing the immune response against cancer cells (Beck et al., 2021).

Although preclinical studies of mRNA cancer vaccines show promise, their efficacy in early clinical trials remains limited. Additional challenges include manufacturing complexity, immunogenicity, and stability. Nonetheless, with further development, mRNA cancer vaccines hold significant potential as a breakthrough in cancer treatment (Tan et al., 2020; Liu et al., 2021; Li et al., 2019).

4. Chemotherapy

Traditional cancer treatment has predominantly focused on systemic therapies like chemotherapy, where drugs circulate through the bloodstream to block or slow down the growth of cancer cells. Chemotherapy is primarily employed in two ways: to treat cancer by inhibiting its progression or to reduce tumor size, often relieving painful symptoms (Sharma et al., 2024). However, the cytotoxic nature of chemotherapy impacts healthy organ systems, particularly the kidneys and liver, and can lead to irreversible side effects on the skin, heart, and nerves, sometimes with fatal consequences (Gustafson et al., 2013; Aslam et al., 2014; Sharma et al., 2024). While some side effects are reversible over time, chemotherapy also poses challenges such as drug resistance, limited target specificity, and reduced efficacy against certain tumor cells. Combining chemotherapy with gene therapy has been suggested as a way to enhance its success in cancer treatment, with the addition of ultrasound technology further improving outcomes (Peng et al., 2023; Sharma et al., 2024).

Recent advances have explored using nanoparticles, specifically designed to target DNase, to inhibit cancer cell proliferation and metastasis. This approach has shown promise in controlling tumor metastasis and improving chemotherapy outcomes (Peng et al., 2023; Sharma et al., 2024). Despite the drawbacks, significant progress has been made to optimize chemotherapy, including the development of next-generation black hole algorithms that have shown potential in effectively managing and treating cancer. While new state-of-the-art techniques continue to emerge, the combination of chemotherapy with other modern approaches offers a cost-effective and efficient treatment strategy (Dos Santos et al., 2024).

5. Nanotechnology

Nanomedicine has emerged as a rapidly advancing field in cancer treatment. Although chemotherapy remains a key option, its limitations have spurred interest in alternative methods. Depending on the type, stage, and nature of the cancer, different strategies are employed. The rising incidence of skin cancer, in particular, has prompted the exploration of nanocarriers as an efficient therapeutic approach (Mongia et al., 2024).

Nanoparticles, which are less than 100 nanometers in diameter, are increasingly being recognized for their potential in cancer treatment. Their favorable properties, including a high surface-to-volume ratio, heterogeneous nature, and enhanced site specificity, make them suitable for standalone treatments or in combination with other therapeutic options. Various modifications have enabled the development of versatile nanoparticles, including coated, magnetic, metal, and silica variants. In addition, nanocarriers such as polyplexes, exosomes, liposomes, and polymersomes are being employed

to induce tumor cell death and stimulate an immune response (Peer et al., 2020; Gavas et al., 2021).

Recent breakthroughs in nanotechnology have led to the development of DNA nanostructures for the targeted delivery of cancer drugs. These nanosystems are bioengineered for precision, ensuring accurate delivery to specific tissues or locations. Engineered to recognize and bind to cancer cells, these nanostructures represent a significant advancement in targeted cancer therapy (Yadav et al., 2024).

6. Cancer Therapy through Viral and Bacterial Pathogens

Under challenging and often unavoidable circumstances, chemotherapy and radiotherapy remain the primary options for cancer treatment. However, drug resistance has emerged as a significant obstacle, with certain tumor tissues proving difficult for drugs to penetrate deeply (Duong et al., 2019). This has created a growing demand for alternative treatment options that demonstrate effectiveness under specific conditions. Recently, bacterial-based therapies and oncolytic viruses (OVs) have been employed with success in combating cancer. The principle behind this is that the tumor microenvironment is susceptible to bacterial colonization, which in turn induces an immune response against the tumor. Many bacteria can infiltrate and colonize tumors, aiding in their eradication. Additionally, OVs have shown the ability to specifically target cancer cells, inducing apoptosis (Shalhout et al., 2023).

Historically, bacteria such as *Streptococci* and *Clostridia* were among the first employed in cancer therapy. Today, advancements in genetic engineering have led to the use of genetically modified bacteria in cancer treatments (Yarahmadi et al., 2024). Bacterial species like *Salmonella*, *Listeria*, and *Clostridium* are particularly promising because of their natural ability to penetrate tumors, replicate, and shrink them through various mechanisms (Duong et al., 2019). Research has shown that *Salmonella typhimurium* can directly attack and kill tumor cells, proliferating within the tumor until the cells undergo apoptosis, necrosis, or rupture (Sarotra et al., 2016). Numerous bacteria and viruses, including *Bifidobacteria*, *Clostridium*, *Listeria monocytogenes*, *Salmonella typhimurium*, *Bacillus*, as well as oncolytic viruses like vaccinia viruses, adenoviruses, reoviruses, herpesviruses, and coxsackieviruses, have been tested in various therapeutic strategies with remarkable outcomes. These findings position them as key players in the potential eradication of malignant tumors (Kiaheyrati et al., 2024). Consequently, there is increasing support for the development of strategies that incorporate these specific bacteria and viruses, either alone or in combination, to treat cancer in humans (Kiaheyrati et al., 2024; Ijaz et al., 2024; Cao et al., 2024a).

7. Bioinformatics and Computational Tools

Bioinformatics tools have been extensively applied in a broad range of research areas, particularly in genomics and proteomics, to advance our understanding of human cancers (Anashkina et al., 2021). Long non-coding RNAs (lncRNAs), endogenous RNA molecules of approximately 200 nucleotide base pairs, have gained attention due to their prominent role in humans, especially in embryonic development and cancer progression (Gu et al., 2021; Zhang et al., 2021). Research has demonstrated that lncRNAs are significantly associated with carcinogenesis (Chen et al., 2023; Statello, 2021; Xu et al., 2022). Thanks to advances in bioinformatics, new therapeutic tools, such as SINEUPs, are emerging for RNA-based therapies (Stransky & Galante, 2010; Espinoza et al., 2021). These developments have helped elucidate the precise mechanisms of lncRNA-regulated gene expression, shedding light on key processes in cancer, including metastasis, cell invasion, proliferation, and apoptosis (Xu et al., 2020; Zhang et al., 2021; Erdoğan et al., 2023).

More recently, dysregulation of lncRNAs has been linked to gastric cancer (Naseri et al., 2025). The use of high-throughput techniques has generated vast amounts of data, stored in databases and repositories, such as the Stanford Microarray Database and the Gene Expression Omnibus, which are crucial for advancing cancer research (Hanauer et al., 2007). Other tools, including Module Maps, SLAMS (Stepwise Linkage Analysis of Microarray Signatures), and COPA (Cancer Outlier Profile Analysis), have also greatly contributed to this field (Hanauer et al., 2007; Stransky & Galante, 2010). Following the year 2000, The Cancer Genome Atlas (TCGA) project emerged as an extension of the Human Genome Project, with the goal of developing a comprehensive atlas of genetic changes associated

with cancer (Tomczak et al., 2015). Moreover, the Cancer Biomedical Informatics Grid (caBIG™), an initiative of the National Cancer Institute (NCI), has greatly enhanced the biological research community's access to data, contributing significantly to cancer research and the development of precision medicine (Fenstermacher et al., 2006).

Substantial advancements have been made using in silico techniques, especially in genomics and proteomics (Anashkina et al., 2021; Beg & Parveen, 2021). Recently, predictive models for protein structures have been developed to assist in site-directed mutagenesis (SDM). For instance, the use of BLAST tools and the SWISS-Model Template Library (SMTL) allows for protein model building, and visualization through UCSF Chimera has been reported (Majeed et al., 2024a). Majeed and colleagues (2024a) performed SDM on the glycosyltransferase enzyme UGT71B8, comparing wild-type and mutant forms, which opens new possibilities for cancer treatment. Glycosyltransferases have also been identified as promising targets in gastric cancer therapy (Wang et al., 2024). In addition, bioinformatics tools like PrDOS (http://prdos.hgc.jp/cgi-bin/top.cgi) enable researchers to determine enzyme disorder probabilities, further enhancing cancer research (de Brevern, 2020).

Any gene or gene product associated with cancer can be analyzed using bioinformatics tools, and 3D structural validation can be achieved through methods such as the Ramachandran plot. In summary, bioinformatics and computational tools have revolutionized cancer research by integrating vast datasets, advanced software, and algorithms, driving cancer research toward more targeted and effective treatments (Altschul et al., 1997; Waterhouse et al., 2018; Chauhan et al., 2020; Majeed et al., 2015; Anashkina et al., 2021; Beg & Parveen, 2021).

8. Artificial Intelligence

Over the past decade, artificial intelligence (AI) has undergone significant evolution, now offering advanced and innovative approaches for the diagnosis and treatment of cancer. AI has revolutionized early detection, enabling the prediction of cancer onset and progression even in the earliest stages, a development often referred to as precision oncology. Through AI-enhanced imaging and radiotherapy, healthcare professionals are now able to more precisely delineate tumor boundaries and cancerous cells. This precise targeting has led to significant improvements in therapeutic outcomes (Weerarathna et al., 2023). While human expertise remains crucial, AI surpasses traditional methods in several areas, particularly in cancer and tumor treatment.

It has been suggested that an integrated approach combining multiple strategies such as radiodiagnosis, radiotherapy, ophthalmology, dermatology, pharmacology, chemotherapy, immunotherapy, nanotechnology, targeted therapy, and surgery could provide even more effective cancer treatments (Cabral et al., 2023; Weerarathna et al., 2023).

Cancer is a complex disease caused by genetic mutations, often resulting in uncontrolled cell proliferation. Even among similar tumor types, characteristics can vary greatly, making accurate predictions challenging. AI, however, leverages genomics and proteomics data to develop personalized medicine approaches. For instance, the HER2 biomarker has been effectively used in breast cancer patients, illustrating the utility of AI-based precision medicine (Binns & Low, 2024). AI has made significant strides in enhancing cancer detection accuracy, reducing risk, improving prognosis and prediction at early stages, and characterizing tumors. The use of AI algorithms and sophisticated computing software continues to push the boundaries of what is possible in cancer diagnosis and treatment (Binns & Low, 2024; Weerarathna et al., 2023).

Challenges and Future Perspectives

Cancer continues to pose a significant threat to global health, currently standing as the second leading cause of death worldwide. The rising global cancer burden demands a focus on developing precise, effective, and cost-efficient treatment strategies. Significant progress has been made in understanding the molecular mechanisms underlying cancer, with gene therapy emerging as a promising tool for its treatment. However, despite the progress, several invisible risks remain under-examined. Off-target effects and side effects of nucleic acid-based drugs—such as complications in the blood and digestive systems—along with the non-targeted delivery of nanoparticles, bacterial strains, and viruses,

need thorough investigation to ensure safety and efficacy.

Drugs like doxorubicin, widely used against various cancer types, are known to cause several side effects that warrant further research into safer alternatives. Integrating bioinformatics tools and artificial intelligence into cancer diagnosis and treatment stages can offer significant advancements in precision medicine. These tools can help process large datasets from genomics and proteomics, ensuring more accurate predictions of cancer progression and improving patient outcomes. However, careful consideration must be given to optimizing algorithms and software before moving forward with personalized oncology.

To ensure success, there is a pressing need for the optimization of emerging techniques for safe, affordable, and precise cancer treatment. Furthermore, potential unforeseen issues, including ethical concerns, must be carefully addressed as new therapeutic technologies and methodologies continue to evolve. The balance between innovation and patient safety should remain a top priority as we move toward the future of cancer treatment.

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