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Precision and Promise: Nanotechnology in the Treatment of Head and Neck Cancer and Autoimmune Diseases

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ABSTRACT: Nanotechnology has emerged as a transformative approach in the treatment of head and neck cancer (HNC) and autoimmune disorders, offering precise, targeted therapies with minimal systemic toxicity. In HNC, nanocarriers such as liposomes, dendrimers, and carbon nanotubes enable improved drug delivery, while theranostic nanoparticles and nanovaccines enhance immune activation and allow real-time monitoring. These innovations facilitate tumour microenvironment remodelling, overcome drug resistance, and optimize combination immunotherapy. In autoimmune disorders, nanotechnology overcomes the limitations of traditional therapies by enabling specific targeting, reducing long-term side effects, and improving therapeutic outcomes. Nanobiosensors, immunomodulatory nanoparticles, and gene therapy platforms offer advanced diagnostics and personalized treatment, while tolerogenic nanovaccines promote immune tolerance and tissue regeneration. The ability to tailor nanoparticles based on disease-specific markers and immune cell behaviour offers immense potential for personalized medicine. As clinical research advances, nanotechnology is poised to redefine the treatment landscape, improving patient outcomes, reducing toxicity, and enhancing therapeutic precision.

1. INTRODUCTION

Head and neck cancer (HNC) is the sixth most common cancer globally, with India bearing a significant burden, accounting for 30-40% of all cancer cases. The age-standardized incidence rate (ASIR) in India stands at 25.9 per 100,000 males and 8.0 per 100,000 females, with the highest prevalence in the northeastern region (31.7 per 100,000 males). The risk of developing HNC is 1 in 33 for males and 1 in 107 for females, with incidence surging after the age of 40, reaching 114.9 per 100,000 in males aged 60 and above. Major risk factors include tobacco and alcohol consumption, human papillomavirus (HPV) infection, and genetic predisposition, underscoring the need for advanced diagnostic and therapeutic approaches such as nanotechnology-based treatments. Similarly, autoimmune disorders, where the immune system attacks the body's own tissues, are on the rise in India, with conditions like systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and multiple sclerosis (MS) becoming increasingly prevalent [1]. A study estimated the prevalence of SLE at 3.2 per 100,000, while research in Delhi found that 18% of healthy individuals exhibited autoantibodies, with 9% testing positive for antinuclear antibodies (ANA), 6.6% for rheumatoid factor (RF), and 2.6% for anti-cyclic citrullinated peptide (CCP) antibodies. The COVID-19 pandemic further escalated autoimmune cases, with ANA positivity rates rising from 39.3% in 2019 to 69.6% in 2022 and a 9% increase in Nuclear Homogeneous patterns linked to SLE and RA, predominantly affecting individuals aged 31-60 [2]. These alarming trends highlight the need for innovative strategies, including nanotechnology-based drug delivery systems, to enhance targeted treatment efficacy while minimizing systemic toxicity in both HNC and autoimmune disorders.

Conventional cancer treatments such as chemotherapy and radiotherapy often lack specificity, damaging healthy tissues and causing severe systemic toxicity. Similarly, autoimmune disorders are largely managed through long-term immunosuppressive drugs, which reduce symptoms but increase vulnerability to infections, organ dysfunction, and relapse. In both cases, therapeutic resistance, poor bioavailability, and inadequate diagnostic precision further compromise treatment outcomes. These limitations highlight the urgent need for innovative therapeutic platforms that can deliver targeted, effective, and safer interventions. Although nanotechnology offers unique advantages including targeted drug delivery, theranostic applications, and immune modulation its translation into clinical practice remains limited. Most nanocarrier systems and immunomodulatory nanoparticles are still confined to preclinical studies or early clinical trials, with very few reaching regulatory approval. The long-term safety, biodistribution, and biodegradation of nanoparticles are not yet fully understood, raising concerns about potential toxicity. Moreover, there is a lack of standardized protocols for nanoparticle synthesis, characterization, and clinical evaluation, which hampers reproducibility and large-scale application. Importantly, while personalized nanomedicine shows promise, disease-specific tailoring of nanoparticles for HNC and autoimmune disorders is still at an experimental stage. Bridging these gaps is essential for establishing nanotechnology as a reliable and transformative therapeutic approach.

The need for targeted and efficient therapeutic strategies in cancer and autoimmune disorders has become increasingly critical due to the limitations of traditional treatment approaches. Cancer and autoimmune diseases represent two distinct yet interrelated areas of medical research, characterized by complex pathophysiologies that require nuanced therapeutic interventions [3]. As these conditions affect millions globally—over 18 million diagnosed with cancer in 2020 and approximately 50 million Americans suffering from autoimmune diseases—developing targeted therapies has emerged as a priority in improving patient outcomes and quality of life. Targeted therapies for cancer focus on specific genetic mutations and molecular pathways unique to tumour cells, allowing for personalized treatment plans that enhance drug efficacy while minimizing adverse effects. Similarly, in autoimmune disorders, targeted strategies aim to selectively inhibit aberrant immune responses, thereby reducing inflammation without compromising the overall immune system [4] Biologics and small molecules have revolutionized treatment options for conditions such as rheumatoid arthritis and lupus, significantly improving patient responses compared to traditional immunosuppressive therapies. Despite these advancements, both fields face challenges, including the development of therapeutic resistance in cancer and potential side effects associated with immunosuppression in autoimmune diseases. For instance, cancer therapies often struggle with resistance mechanisms, while autoimmune treatments may leave patients vulnerable to infections and malignancies due to their broad immune-modulating effects. Furthermore, issues such as high treatment costs and the need for biomarkers to predict patient responses underscore the complexity of tailoring therapies effectively [5]. Looking forward, the integration of innovative treatment modalities, such as combining targeted therapies with immunotherapies, holds promise for enhancing therapeutic efficacy in both cancer and autoimmune diseases. Ongoing research aims to refine these approaches, ultimately prioritizing personalized medicine strategies that are responsive to the unique biological characteristics of each patient, thereby fostering more effective and safer treatment outcomes.

Advances in nanotechnology have significantly impacted the treatment landscape for head and neck cancer (HNC) and autoimmune disorders, presenting novel strategies to enhance therapeutic efficacy and minimize side effects [6].By employing nanoscale materials, researchers have developed targeted drug delivery systems that improve the precision of treatments, offering hope for better patient outcomes in conditions often characterized by challenging treatment regimens and considerable adverse effects associated with traditional therapies [7]. The unique properties of nanomaterials, such as their ability to encapsulate drugs, enhance their bioavailability, and facilitate localized delivery, have garnered widespread interest in the medical community and beyond [8] . Nanocarriers are engineered to overcome biological barriers, improve drug stability, and increase the precision of drug targeting within the tumour microenvironment (TME). The use of smart nanocarriers, including liposomes, polymers, and metallic nanoparticles, has demonstrated promise in addressing challenges such as multidrug resistance and non-specific drug absorption, thus facilitating more personalized and effective treatment options.

2. NANOTECHNOLOGY IN HEAD AND NECK CANCER TREATMENT

The integration of nanotechnology into head and neck cancer treatment is poised to transform current therapeutic strategies, offering innovative solutions to long-standing challenges in oncology. One of the primary directions in this field involves the refinement and optimization of nanocarriers, which are engineered to deliver drugs directly to cancer cells while minimizing exposure to healthy tissue. This targeted delivery approach not only enhances drug efficacy but also reduces potential side effects associated with traditional treatments [9]. Dendrimers, which are macromolecules with highly branched and customizable structures, have been developed for cancer therapy. Their size typically ranges from 1 to 15 nm, allowing them to encapsulate therapeutic agents in a noncovalent manner, enhancing delivery to tumour sites. Notable examples include polyamidoamine (PAMAM) and polyethylene glycol (PEG) dendrimers, which have demonstrated promise in reducing tumour growth significantly compared to traditional methods, such as free systemic methotrexate [10]. Liposome can be classified into unilamellar and multilamellar vesicles, which differ in size and bilayer composition. Liposomes enhance the pharmacokinetics of drugs, allowing for sustained release and targeted action at tumour sites. The liposomal formulations containing doxorubicin have shown improved therapeutic effects against head and neck tumours, leveraging their ability to evade the immune system and reduce systemic toxicity [11]. Quantum dots, which are semiconductor nanoparticles, are being explored for their potential in biological imaging and as targeted therapy agents. Their unique optical properties allow for wavelength-tunable fluorescence, facilitating the real-time tracking of tumour-associated antigens [12] Carbon nanotubes have emerged as potential vehicles for delivering immune checkpoint inhibitors in cancer immunotherapy by enhancing the targeting of immune modulators [13]

Nanotechnology has emerged as a transformative approach in the treatment of head and neck cancers, with multiple platforms under active development. Liposomal cisplatin formulations have shown clinical promise by improving tumour delivery while reducing systemic toxicity (Table.1). Similarly, PLGA-based nanoparticles co-delivering chemotherapeutics and radiosensitizers enhance radiotherapy efficacy through controlled release and selective tumour sensitization. Gold nanoparticles enable photothermal therapy (PTT), producing localized tumour ablation upon near-infrared exposure and demonstrating synergy with immunotherapy in preclinical and early translational studies. Nanoparticle-mediated RNA interference (RNAi) provides another promising strategy, enabling oncogene silencing and resensitization to cisplatin in resistant tumour models through optimized lipid or polymeric carriers. Furthermore, theranostic nanoparticles that integrate imaging and therapeutic functions are advancing precision oncology by improving surgical margin visualization and enabling targeted postoperative therapy. Collectively, these nanotechnology-enabled interventions highlight the growing potential of multifunctional nano systems to overcome the limitations of conventional therapies and improve patient outcomes in head and neck cancers.

Table.1. Preclinical to clinical studies for head and neck cancer nanotherapies

Platform / study type	Mechanism / payload	Key result / translational status	References
Liposomal cisplatin variants	Encapsulation to reduce systemic toxicity and improve tumour delivery	Improved tumour control and reduced systemic toxicity in multiple studies; liposomal cisplatin formulations have progressed through clinical testing and show promise for ORL cancers	[1]

PLGA nanoparticles carrying chemo + radiosensitizer	Controlled release + radiosensitization to enhance radiotherapy	Preclinical HNSCC models show greater tumour regression vs free drug; active investigation in perioperative/adjuvant settings.	[2]
Gold nanoparticles (photothermal therapy, PTT)	Tumor-localized heating on NIR illumination to ablate tumour cells	Robust preclinical tumour ablation and synergy with immunotherapy in models; early translational studies support feasibility.	[3]
Nanoparticle-delivered siRNA / RNAi	Silence oncogenes or resistance pathways (e.g., for cisplatin resistance)	Effective gene knockdown in HNSCC models, resensitization to chemo; LNP/ polymeric carriers are being optimized for clinical use.	[4]
Theranostic NPs (imaging + therapy)	Combine imaging contrast and local therapy (drug + imaging)	Improved surgical margin visualization and targeted postoperative therapy in preclinical work — promising for precision surgery in HNC.	[5]

3. PASSIVE VERSES ACTIVE TARGETING OF NANOPARTICLES

Passive and active targeting of nanoparticles are two pivotal strategies employed in nanoparticle-based drug delivery systems, particularly in the context of treating diseases such as cancer. Passive targeting relies on the inherent physical and chemical properties of nanoparticles, leveraging physiological mechanisms such as the enhanced permeability and retention (EPR) effect to facilitate the accumulation of therapeutic agents in tumour tissues without the need for specific targeting ligands. This approach has garnered attention for its ability to improve drug delivery efficiency; however, it can result in non-specific distribution, leading to potential toxicity and variable efficacy depending on individual tumour characteristics [14]. Conversely, active targeting enhances delivery specificity by modifying the surfaces of nanoparticles with ligands that bind to specific receptors on target cells, tissues, or organs. This method aims to improve therapeutic outcomes by minimizing off-target effects, yet it introduces complexities related to ligand design and the biological interactions involved, which may compromise efficacy due to the presence of biological barriers[15].

4. ROLE OF NANOPARTICLES IN IMAGING AND DIAGNOSTICS

Nanoparticle-based contrast agents have significantly advanced medical imaging modalities such as Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), and Computed Tomography (CT)[16]. In MRI, superparamagnetic iron oxide nanoparticles (SPIONs) are utilized for their ability to enhance image contrast by altering local magnetic fields, thereby improving the visualization of anatomical structures and pathological conditions. Similarly, in PET imaging, radiolabelled nanoparticles, such as those tagged with positron-emitting isotopes, have been developed to improve the sensitivity and specificity of tumour detection[17]. For instance, radiolabelled iron oxide nanoparticles have been explored as dual-modality contrast agents for PET/MRI, combining the high sensitivity of PET with the superior spatial resolution of MRI. In CT imaging, nanoparticles containing high atomic number elements like gadolinium have been investigated to enhance contrast due to their strong X-ray attenuation properties[18]. These advancements underscore the potential of nanoparticle-based contrast agents in providing more accurate and detailed diagnostic information across various imaging platforms[19].

Theranostic nanoparticles represent a transformative approach in nanomedicine by integrating diagnostic and therapeutic functionalities into a single platform. These multifunctional nanoparticles are engineered to deliver therapeutic agents directly to diseased tissues while simultaneously enabling imaging of the delivery process and monitoring therapeutic responses[20]. For example, superparamagnetic iron oxide nanoparticles can be functionalized to carry chemotherapeutic drugs and serve as MRI contrast agents, allowing for real-time tracking of drug delivery and assessment of treatment efficacy. Additionally, radiolabelled nanoparticles have been developed for PET imaging to visualize biodistribution and target site accumulation, facilitating patient stratification and personalized treatment plans[21]. The dual capabilities of theranostic nanoparticles not only enhance the precision of therapy but also provide critical insights into the pharmacokinetics and biodistribution of therapeutic agents, thereby optimizing treatment outcomes[22].

The integration of nanoparticle-based contrast agents and theranostic nanoparticles into clinical practice holds the promise of revolutionizing disease diagnosis and treatment. By enabling high-resolution imaging and targeted therapy, these

nanotechnologies offer a more personalized and effective approach to patient care. Ongoing research and clinical trials continue to explore the full potential of these innovations, aiming to improve the specificity and efficacy of treatments while minimizing adverse effects[19]. As the field progresses, it is anticipated that nanoparticle-based strategies will become integral components of modern medical diagnostics and therapeutics, leading to better patient outcomes and more efficient healthcare delivery[22].

5. NANOVACCINES FOR IMMUNE ACTIVATION AND NANOPARTICLE-BASED CHECKPOINT INHIBITORS

Nanovaccines have emerged as a groundbreaking approach in cancer immunotherapy, offering a novel mechanism to enhance immune activation against tumours. Their unique ability to encapsulate antigens and adjuvants within nanocarriers significantly improves the stability and immunogenicity of vaccine components, allowing for controlled antigen release and prolonged immune system engagement. This strategy effectively primes the immune system to recognize and combat cancer cells more efficiently[23]

A notable advancement in this field is the development of personalized mRNA-based nanovaccines, such as mRNA-4157/V940. This vaccine incorporates mRNA sequences encoding neoantigens specific to an individual's tumour profile, identified through comprehensive genomic sequencing. Encapsulated within lipid nanoparticles, these mRNA sequences are delivered into the patient's cells, where they are translated into neoantigenic proteins[24]. This process stimulates a robust immune response, targeting cancer cells expressing these neoantigens. Clinical studies have demonstrated that combining mRNA-4157/V940 with immune checkpoint inhibitors, like pembrolizumab, significantly reduces the risk of cancer recurrence in patients with resected melanoma[25]

Another innovative example is autogene cevumeran, an individualized mRNA cancer vaccine developed for pancreatic ductal adenocarcinoma. This vaccine comprises multiple mRNA species encoding up to 20 neoantigens identified from the patient's resected tumour. Delivered via lipid nanoparticles, autogene cevumeran aims to elicit a personalized immune response against residual cancer cells. Phase I clinical trials have shown promising results, with patients exhibiting neoantigen-specific T cell responses and prolonged recurrence-free survival [26]

The novelty of these nanovaccine approaches lies in their capacity for personalization and precision. By tailoring the vaccine components to the unique mutational landscape of an individual's tumour, these therapies enhance the specificity and efficacy of the immune response. The integration of nanotechnology ensures efficient delivery and expression of neoantigens, while the combination with immune checkpoint inhibitors amplifies the anti-tumour effect[27]. These advancements represent a significant leap forward in the development of personalized cancer immunotherapies, offering hope for improved patient outcomes in various malignancies[24]

6. NANOTECHNOLOGY-BASED IMMUNOMODULATION IN AUTOIMMUNE DISEASES

Nanotechnology provides versatile strategies to modulate immune responses and restore tolerance in autoimmune and inflammatory disorders. Antigen-specific tolerance platforms, such as peptide-loaded nanoparticles, deliver autoantigens with tolerogenic adjuvants to promote regulatory T cell induction and immune tolerance, showing promise in type 1 diabetes, multiple sclerosis, and autoimmune myocarditis (Table. 2). Similarly, siRNA and RNA-based therapeutics delivered via lipid or polymeric nanoparticles can silence pro-inflammatory cytokines such as TNF-α and IL-6 at sites of inflammation, with applications in rheumatoid arthritis (RA) and inflammatory bowel disease (IBD). Nanoparticle-mediated macrophage targeting further enhances therapeutic precision by exploiting the preferential uptake of nanoparticles by inflammatory macrophages, thereby repurposing existing drugs for RA, systemic lupus erythematosus (SLE), and psoriatic arthritis with reduced systemic toxicity. In addition, tuning nanoparticle size and charge enables tolerogenic nanocarriers to bias antigen-presenting cell (APC) responses toward immune regulation across multiple immune-mediated inflammatory diseases. Finally, nanoparticle vaccines designed for immune reprogramming can present autoantigens or neo-epitopes in a non-inflammatory context, offering innovative therapeutic opportunities for autoimmune skin diseases and experimental autoimmune encephalomyelitis. Collectively, these approaches highlight how nanotechnology platforms can be tailored for disease-specific or broad-spectrum immunomodulation, advancing next-generation therapies for autoimmune disorders.

Table.2. Nanomedicine strategies & mechanisms for autoimmune disease therapy.

Strategy	Mechanism (how nanotech helps)	Disease applications	References
Antigen-specific tolerance (peptide-loaded NPs)	Targeted delivery of autoantigen + tolerogenic adjuvant to induce regulatory T cells (Tregs) and immune tolerance	Type 1 diabetes, multiple sclerosis, autoimmune myocarditis	[6]
siRNA / RNA therapeutics (LNPs, polymeric)	Silence disease-driving cytokines or costimulatory molecules (e.g., TNF-α, IL-6) at inflamed site	Rheumatoid arthritis (RA), inflammatory bowel disease (IBD)	[7]
Nanoparticle-mediated drug targeting to macrophages	Preferential uptake by inflammatory macrophages to repurpose old drugs with lower systemic exposure	RA, systemic lupus erythematosus (SLE), psoriatic arthritis.	[8]
Tolerogenic nanocarriers (size/charge tuned)	Physical properties steer uptake by tolerogenic antigen-presenting cells (APCs) to favor regulatory outcomes	General platform across multiple IMIDs (immune-mediated inflammatory diseases).	[9]
Nanoparticle vaccines / immune reprogramming	Re-educate immune system or present neo-epitopes in a non-inflammatory context	Autoimmune skin diseases, experimental autoimmune encephalomyelitis (EAE).	[10]

7. MULTIDRUG DELIVERY SYSTEMS USE OF NANOCARRIERS TO MODULATE TUMOUR MICROENVIRONMENT

Recent breakthroughs from 2023 to 2025 have revolutionized multidrug delivery systems using nanocarriers to modulate the tumour microenvironment (TME), significantly improving the efficacy of cancer treatments. These systems integrate chemotherapeutic drugs, immunotherapies, and gene therapies within a single nanocarrier, ensuring synergistic action while minimizing systemic toxicity. A major novelty in this approach is the development of multifunctional nanocarriers capable of co-delivering hydrophobic and hydrophilic drugs, overcoming solubility challenges and enhancing bioavailability. Additionally, the incorporation of nucleic acids, such as siRNA or CRISPR-Cas9 components, within nanocarriers allows for precise gene silencing and genome editing, targeting drug resistance pathways in cancer cells[28]. The ability to simultaneously modulate immune checkpoints, inhibit angiogenesis, and disrupt tumour stromal barriers makes these nanocarrier-based systems highly effective in overcoming the immunosuppressive nature of the TME[29].

The mechanism of action of these multidrug nanocarriers involves targeted delivery, controlled release, and TME remodelling. By functionalizing nanocarriers with ligands that recognize tumour-specific receptors, these systems ensure selective accumulation at the tumour site, reducing off-target effects and improving therapeutic efficacy. Stimuli-responsive nanocarriers, which release their payload in response to acidic pH, hypoxia, or enzymatic activity within the TME, enable precise drug activation at the tumour site[30]. This spatiotemporal control enhances the therapeutic index of anticancer agents while minimizing adverse effects. Furthermore, some advanced nanocarriers are engineered to actively reprogram immune cells, such as tumour-associated macrophages (TAMs) and dendritic cells, to shift the TME from an immunosuppressive state to a pro-inflammatory, tumour-attacking environment[31].

A particularly promising application of these nanocarrier-based multidrug delivery systems is in combination immunotherapy, where immune checkpoint inhibitors (ICIs) are co-delivered with immunostimulatory agents[32]. By effectively blocking inhibitory pathways like PD-1/PD-L1 while simultaneously activating cytotoxic T cells, these systems enhance immune surveillance and tumour eradication[33]. Moreover, nanocarriers targeting tumour vasculature and extracellular matrix components help normalize the blood supply and improve drug penetration into solid tumours, addressing one of the major challenges in cancer treatment as reported by the authors[34]. With continuous advancements, nanocarrier-based multidrug delivery holds immense potential to transform personalized cancer therapy, providing more effective, precise, and less toxic treatment strategies for various malignancies[35].

8. NANOTECHNOLOGY IN AUTOIMMUNE DISORDERS

Autoimmune diseases are a diverse group of disorders in which the immune system mistakenly attacks the body's own cells, leading to chronic inflammation and tissue damage. Common examples include multiple sclerosis, type 1 diabetes, and systemic lupus erythematosus. The etiology of these diseases is complex, often involving a combination of genetic susceptibility and environmental factors, making them a significant public health concern affecting millions worldwide[36]. Despite advances in medical science, current therapies primarily focus on symptom management and immune suppression, rather than offering curative solutions, which underscores the pressing need for more effective treatment strategies. The limitations of existing treatments for autoimmune diseases include significant side effects, lack of target specificity, and the necessity for long-term use, which can complicate patient care and diminish quality of life[37]. As traditional therapies do not address the underlying disease processes, patients may suffer from both disease-related complications and the adverse effects of their treatments. This situation highlights an urgent need for novel approaches that can provide targeted and sustainable therapeutic benefits while minimizing harmful side effects[38]

The integration of nanotechnology into autoimmune disease treatment not only offers hope for improved efficacy and reduced side effects but also presents opportunities for personalized medicine. By tailoring interventions to individual patient profiles and disease mechanisms, this approach could lead to more effective management strategies that enhance the overall quality of life for those affected by autoimmune disorders[39]. At the core of autoimmune diseases is the breakdown of autoimmune tolerance, which is essential for maintaining a balanced immune response. The immune system typically distinguishes between self and non-self entities, employing various immune cells such as macrophages, dendritic cells, T lymphocytes, and B lymphocytes to achieve this balance. However, in autoimmune conditions, this recognition process becomes impaired, leading to inappropriate immune activation against the body's own tissues[40].

9. NANOTECHNOLOGY IN DIAGNOSIS AND IMAGING

Nanobiosensors for early detection represent a cutting-edge area in biomedical technology that harnesses the unique properties of nanomaterials to diagnose diseases at unprecedented speeds and sensitivities. These devices play a crucial role in identifying specific biomarkers associated with various health conditions, including autoimmune diseases and infectious pathogens, thereby facilitating timely interventions that can significantly improve patient outcomes[41] For instance, electronic nanobiosensors utilize advanced detection methodologies, such as electrochemical and optical techniques, to enhance the sensitivity and specificity of biomarker detection. This has been particularly beneficial in diagnosing autoimmune disorders, where early detection can lead to better management strategies and reduced adverse effects from treatments[42]. There are different types of nanobiosensors which are as follows reported till now.

9.1 Electronic nanobiosensor

Electronic nanobiosensors are designed for the rapid detection of pathogen-specific biomarkers, significantly aiding in the early detection and prevention of infectious diseases. These sensors leverage nanotechnology to enhance sensitivity and specificity, allowing for timely diagnosis and intervention They often integrate various detection methodologies, including electrochemical and optical techniques, to provide real-time monitoring of biological signals[43]

9.2 Electrochemical biosensor

Electrochemical biosensors are a prominent type of electronic nanobiosensor that utilize bioelectrochemical phenomena to generate measurable outputs, such as current, potential, or conductivity changes[44] This type of sensor typically employs three electrodes: a reference electrode, an auxiliary electrode, and a working electrode, with silver/silver chloride (Ag/AgCl) being the most commonly used reference electrode. The advantages of electrochemical biosensors include high sensitivity, rapid response times, and the ability to detect multiple biomarkers simultaneously, making them suitable for various diagnostic applications, including autoimmune diseases and infectious pathogens[45] Numerous studies have documented the use of electrochemical techniques such as amperometry, impedimetry, and voltammetry for the detection of various disease-related biomarkers.

9.3 Nucleic Acid-Based Biosensors

Nucleic acid-based biosensors, including DNA and aptamer-based sensors, have emerged as powerful tools for detecting specific pathogens or biomarkers[46]. These biosensors exploit the hybridization of single-stranded DNA probes with complementary target sequences, providing a highly stable and adaptable platform for diagnostics. Their ability to transduce

hybridization events into measurable signals has led to their widespread use in detecting various conditions, including Helicobacter pylori infections and autoimmune disorders[47]

9.4 Microfluidics-Based Nanobiosensors

Microfluidics-based nanobiosensors represent another innovative approach to diagnostics, enabling the early diagnosis and real-time monitoring of disease progression. These sensors utilize miniaturized fluidic systems to manipulate small volumes of fluids, facilitating rapid biochemical reactions and analysis[48]. The integration of nanomaterials into microfluidic platforms enhances detection sensitivity and allows for multiplexing capabilities, making them ideal for point-of-care diagnostics[49].

In the context of systemic lupus erythematosus (SLE), research has shown that increased apoptosis and impaired clearance of apoptotic cells play critical roles in disease progression. Investigations into the clearance of cell-free DNA in SLE patients revealed that abnormalities in DNase activity and interactions with antibodies could activate inflammatory pathways, complicating the disease[49]. Additionally, the local administration of PAMAM dendrimers (PAMAM-G3) has shown promise in facilitating wound healing in cutaneous lupus erythematosus models by reducing extracellular nucleic acids and inhibiting inflammatory pathways associated with Toll-like receptors (TLR7 and TLR9)[42].

10. TARGETED DRUG DELIVERY SYSTEM

Nanocarriers are increasingly being explored for their potential applications in the treatment of autoimmune disorders, particularly through the controlled release of immunosuppressive drugs[50]. These advanced delivery systems aim to reduce systemic toxicity and improve the efficacy of therapies targeted at conditions such as systemic lupus erythematosus, systemic sclerosis, and rheumatoid arthritis[51]. Controlled drug release can be achieved through several strategies, including altering drug release kinetics and inducing drug release in physiological conditions specific to different tissues[52]. This tailored release mechanism is crucial for minimizing systemic toxicity and enhancing the therapeutic effect of immunosuppressive drugs. By carefully designing the drug loading methods and attachment strategies, researchers can significantly improve the precision of therapy while reducing adverse effects associated with conventional systemic drug delivery[52].

The primary advantage of using nanocarriers for drug delivery in autoimmune disorders lies in their ability to provide controlled release of immunosuppressive agents. This method allows for a more targeted approach, minimizing the risks associated with traditional systemic therapies that often lead to significant side effects[53]. By encapsulating drugs within nanocarriers, the release can be regulated based on environmental triggers, such as pH or specific enzymes present in the pathological tissue, ensuring that the drugs are activated only in the desired location[54]

By ensuring that higher concentrations of the drug are delivered directly to the site of action, nanocarriers limit the exposure of other organs to potentially harmful substances. This targeted delivery approach can significantly improve the safety profile of immunosuppressive therapies, which are often plagued by severe side effects due to their broad systemic action. Nanocarriers can encapsulate therapeutic agents and transport them directly to the target site, reducing systemic exposure and associated side effects[55]. This specificity not only enhances the therapeutic effect but also minimizes damage to healthy tissues, which is crucial in the treatment of autoimmune disorders where precise modulation of the immune response is required[56] Different types of nanocarriers, such as liposomes, micelles, and polymers, can be tailored to meet specific therapeutic needs, including modifications to their surface properties for enhanced cellular uptake and interaction with target cells[57]. This flexibility allows researchers to optimize formulations for individual patients or specific diseases, further enhancing treatment outcomes[58].

11. NANOPARTICLES IN IMMUNE MODULATION AND GENE THERAPY

The immunomodulatory effects of nanoparticles represent a transformative area of biomedical research, focusing on the ability of engineered particles to manipulate immune responses for therapeutic purposes[59]. These nanoparticles, which can be composed of various materials including polymers, lipids, and inorganic compounds, have shown promise in treating a range of immune-related conditions, particularly autoimmune diseases. Their significance lies in their potential to restore immune tolerance, deliver therapeutic agents effectively, and facilitate innovative approaches like gene editing and RNA-based therapies[60]. The application of nanoparticles in restoring immune tolerance has garnered attention due to the increasing prevalence of autoimmune disorders, where the immune system erroneously attacks the body's own tissues[61]. By promoting the activation of regulatory immune cells or inhibiting pathogenic responses, nanoparticles can help re-establish self-tolerance and ameliorate conditions like rheumatoid arthritis, diabetes, and multiple sclerosis[62].

Nanoparticles have emerged as a powerful tool in modulating immune responses, offering potential therapeutic strategies for various immune-related conditions, including autoimmune diseases. These particles can be designed to either deliver immunosuppressive drugs or directly interact with immune cells, thus altering the immune response in beneficial ways. Nanoparticles can modulate the immune response through various mechanisms[46]. The concentration of nanoparticles is crucial; while higher concentrations may lead to toxic effects and oxidative stress, lower concentrations can positively influence the immune response by activating specific immune cells. Furthermore, the shape of the nanoparticles influences their affinity for immune cells, which can affect both uptake and subsequent immune responses. Elongated or branched nanoparticles may be more efficiently internalized by certain cell types, enhancing their immunotherapeutic potential[63].

The dysregulation of self-tolerance can lead to autoimmune diseases, such as rheumatoid arthritis, diabetes, and multiple sclerosis. Nanoparticles can be engineered to restore immune tolerance by promoting the activation of regulatory immune cells or suppressing the activity of pathogenic ones[64]. For example, nanoparticles have been shown to modulate the secretion of inflammatory cytokines like IL-6 and TNF-α, which are crucial in the pathology of autoimmune diseases[65].

12. COMBINATION NANOTHERAPEUTICS FOR ENHANCED CANCER TREATMENT

Nanotechnology platforms enable rational combination therapies that integrate multiple treatment modalities within a single carrier system to maximize efficacy while minimizing toxicity. For example, gold nanorods have been employed to combine chemotherapy with photothermal therapy (PTT), where localized hyperthermia synergizes with cytotoxic agents to induce significant tumour regression at reduced chemotherapy doses (Table. 3). Similarly, PLGA nanoparticles loaded with radiosensitizers enhance radiotherapy effectiveness by amplifying DNA damage, thereby improving local tumour control. Liposomal nanocarriers delivering immune checkpoint inhibitors represent another strategy, offering targeted immune modulation that promotes T-cell infiltration and tumour clearance. In addition, lipid nanoparticles co-delivering cisplatin with siRNA provide a chemo-gene therapy platform capable of reversing drug resistance and restoring chemosensitivity. Finally, porphyrin-loaded polymeric nanoparticles demonstrate the promise of combining photodynamic therapy (PDT) with chemotherapy, leveraging reactive oxygen species-mediated apoptosis alongside cytotoxic drug action for strong synergistic effects. Collectively, these combination nanotherapeutic strategies highlight the power of nanoscale engineering to integrate multimodal treatments, offering new avenues for overcoming resistance and improving outcomes in cancer therapy. Probable mechanism involved while treating with nanoparticles for head and neck cancer and autoimmune disorder treatment (Fig.1).

Table.3. Combination nano therapies for head & neck cancer

Combination	Nanoplatform	Mechanism / rationale	Outcome (preclinical/clinical)	References
Chemo + Photothermal Therapy (PTT)	Gold nanorods	Heat + cytotoxic synergy	Tumour regression with reduced chemo dose.	[11]
Radiotherapy + Nanoparticles	PLGA NPs + radiosensitizer	Enhanced DNA damage	Greater local tumour control.	[12]
Immunotherapy + Nano-carriers	Liposomes delivering checkpoint inhibitors	Targeted immune modulation	Improved T-cell infiltration & tumour clearance.	[13]
Chemo + Gene therapy	LNPs delivering siRNA + cisplatin	Reverses drug resistance	Restored cisplatin sensitivity.	[14]
PDT + Chemo	Porphyrin-loaded polymeric NPs	ROS-mediated apoptosis + chemo	Strong synergistic cytotoxicity.	[15]

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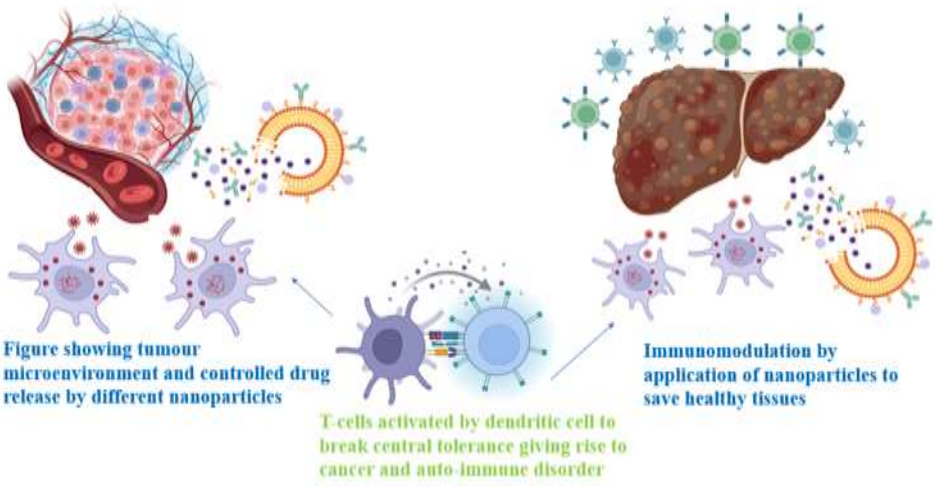


Fig.1. Probable mechanism involved while treating with nanoparticles for head and neck cancer and autoimmune disorder treatment.

13. NANO-BASED VACCINES AND TISSUE REGENERATION

Tolerogenic nanovaccines represent a cutting-edge therapeutic approach aimed at inducing antigen-specific immune tolerance to prevent or treat autoimmune diseases such as multiple sclerosis and rheumatoid arthritis[66]. Unlike conventional immunosuppressive therapies, which broadly suppress immune function and often lead to adverse side effects, tolerogenic nanovaccines seek to recalibrate the immune response—shifting it toward tolerance rather than inflammation[67]. These vaccines are typically designed to deliver self-antigens in combination with immunomodulatory agents via nanoparticle-based delivery systems. This strategy closely mimics the body's natural antigen presentation processes, where immune cells present antigens in a non-inflammatory context to induce tolerance. A key feature is the encapsulation of self-antigens with immunosuppressive compounds—such as cytokines, peptides, or immunosuppressive drugs—within a biodegradable nanoparticle matrix. One notable example includes abatacept-modified polydopamine nanoparticles, which have demonstrated enhanced targeting and delivery efficiency[68].

Preclinical studies show promising results—these nanovaccines not only alleviate autoimmune symptoms but may also reprogram the immune system's memory, offering a more durable solution with reduced dependence on lifelong immunosuppression. This is a significant advantage over existing treatments that often fail to address the root cause of immune dysregulation[69]. Using nanocarrier regenerating tissues after treatment of autoimmune disorder is shown in fig.2.

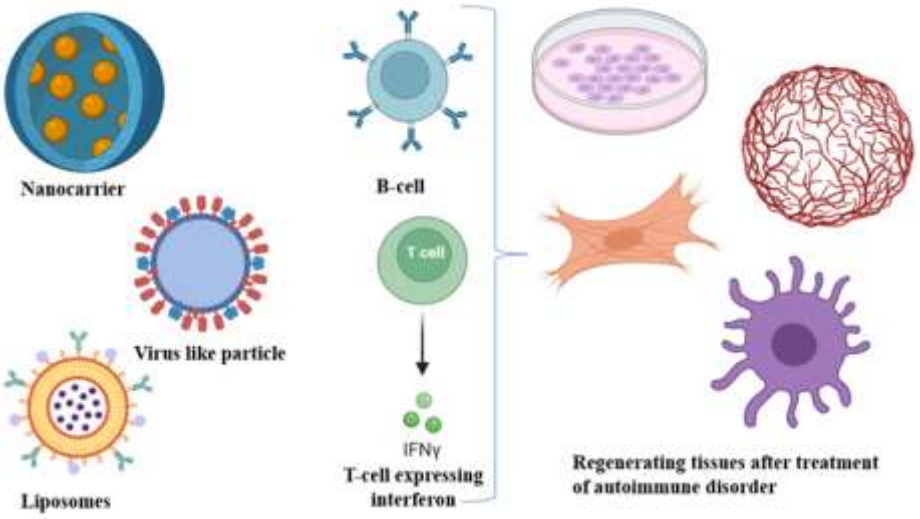


Fig.2. Using nanocarrier regenerating tissues after treatment of autoimmune disorder

The construction of a tolerogenic nanovaccine typically involves the encapsulation of a self-antigen alongside an immunosuppressive agent, such as dexamethasone, within a biocompatible nanoparticle matrix. This design is intended to facilitate targeted and controlled delivery of the therapeutic agents to immune cells[70]. A notable example of this strategy is the use of abatacept-modified polydopamine nanoparticles, which enhance the specificity and efficiency of delivery to antigen-presenting cells (APCs). By mimicking the natural antigen presentation pathways employed by APCs, such as dendritic cells, these nanovaccines help reestablish immune tolerance—a critical factor in maintaining immune homeostasis[71]. The precise and localized delivery reduces systemic exposure to immunosuppressive drugs, thereby minimizing side effects while promoting a tolerogenic immune response[72].

Peptide and protein-loaded nanoparticles (NPs) are emerging as pivotal tools in the realm of biomedical applications, particularly in the design of tolerogenic vaccines aimed at preventing autoimmune diseases. These advanced delivery systems can enhance the efficacy of therapeutic agents while minimizing adverse effects[73]. The strategic use of peptide-modified nanoparticles has demonstrated increased antibacterial efficacy, suggesting a potential for broader applications in immune modulation and therapeutic delivery[74].

The primary mechanism by which peptide-conjugated nanoparticles induce antigen-specific immune tolerance lies in their ability to protect biologically sensitive molecules, such as antigen-bearing peptides or nucleic acids, from enzymatic degradation[75]. This protective function ensures the efficient delivery of therapeutic agents to target immune cells, allowing for a controlled and sustained interaction with the immune system. Upon delivery, these nanoparticles facilitate an immune response that favours tolerance rather than activation, which is particularly critical in the treatment of autoimmune diseases[76]. In such conditions, the goal is to suppress harmful immune responses against self-antigens without compromising the body's ability to defend against pathogens, thus maintaining overall immune balance and functionality[77].

When designing peptide- and protein-loaded nanoparticles, several key factors must be considered, including morphology, size, surface charge, and composition, as these characteristics significantly influence how nanoparticles interact with the immune system[78]. These properties affect circulation time, cellular uptake, and immune recognition, ultimately determining the nanoparticle's efficacy as a drug delivery system. To improve therapeutic outcomes, it is crucial to engineer nanoparticles that can evade opsonization and phagocytosis by immune cells, thereby increasing their bioavailability[79]. Recent research highlights the use of naturally derived cell membranes to cloak nanoparticles, enhancing their biointerfacing capabilities and enabling more precise targeting, particularly beneficial in treating inflammatory and autoimmune diseases[80].

Nanomaterials have emerged as promising tools for the repair and regeneration of tissues damaged by autoimmune conditions, owing to their ability to modulate immune responses and promote tissue healing[81]. Various types of nanoparticles, including biodegradable polymers, cationic nanoparticles, and hybrid nanomaterials, have been extensively explored for their therapeutic potential. Biodegradable nanoparticles, such as those made from poly(lactic-co-glycolic acid) (PLGA), can encapsulate and deliver proteins, peptides, or immunomodulatory agents like rapamycin directly to inflamed or damaged tissues, creating a proregenerative microenvironment and reducing neutrophil infiltration. Cationic nanomaterials, synthesized from polymers like poly(amidoamine) (PAMAM) and polyphosphoramidate (PPA), exhibit bioactive properties such as anti-inflammatory and antimicrobial effects, facilitating targeted delivery and promoting tissue repair while minimizing systemic toxicity[82]. In parallel, hybrid nanomaterials, which combine metal cores with bioorganic coatings, offer multifunctional capabilities by enhancing tissue specificity and exerting anti-inflammatory actions, thereby overcoming limitations associated with conventional therapies[80]. Collectively, these nanotechnology-based strategies represent a transformative approach in the treatment of autoimmune diseases by not only regulating immune responses but also directly contributing to tissue regeneration and functional recovery. Innovations in nanomaterial technology are poised to significantly enhance the effectiveness of tolerogenic nanovaccines[78]. For example, abatacept-modified polydopamine nanoparticles have demonstrated improved targeting and cellular uptake of self-antigens, a crucial step for inducing a tolerogenic immune response. Future research is expected to focus on diverse nanoparticle formulations and surface modifications to fine-tune their immunogenic profiles, aiming for greater specificity and efficacy across a range of autoimmune conditions[72].

14. CONCLUSION

Nanotechnology has revolutionized the diagnosis and treatment of head and neck cancer (HNC) and autoimmune disorders, ushering in a new era of precision medicine. In HNC, nanocarriers like liposomes, dendrimers, and carbon nanotubes enable targeted drug delivery, enhancing therapeutic efficacy while minimizing systemic toxicity. Theranostic nanoparticles and

nanovaccines not only boost immune responses but also allow real-time monitoring of treatment, contributing to personalized care. Furthermore, multidrug-loaded nanocarriers remodel the tumor microenvironment, overcome drug resistance, and enhance the effectiveness of combination immunotherapy. Similarly, in autoimmune disorders, nanotechnology offers solutions to the limitations of traditional therapies, such as non-specific targeting and long-term side effects. Innovations like nanobiosensors, gene therapy platforms, and immunomodulatory nanoparticles provide precise diagnostics and targeted treatments. Tolerogenic nanovaccines, in particular, hold promise for restoring immune tolerance and reducing disease progression. These technologies support early detection, personalized therapy, and tissue regeneration. The adaptability of nanoparticles based on individual pathology and immune profiles underscores their transformative potential. As clinical research advances, nanotechnology stands poised to redefine the management of both cancer and autoimmune diseases, promising better outcomes, reduced toxicity, and a shift toward more effective, personalized, and regenerative therapeutic strategies.

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AUTHOR CONTRIBUTIONS

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Vijayakumar R: Data Curation, Validation, and Writing – Review and Editing.

S G Raman: Supervision, Resources, and Writing – Review and Editing.

Suresh Velayutham: Validation, Resources, and Writing – Review and Editing.

Sathyanathan Viswanathan: Supervision, Project Administration, and Writing – Review and Editing.

K Nithyakalyani: Methodology, Literature Review, Validation, and Writing – Review and Editing.

All authors reviewed and approved the final version of the manuscript.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ETHICS STATEMENT

Ethical approval was not required for this study.

DATA AVAILABILITY STATEMENT

Data supporting the findings of this study are available from the corresponding author upon reasonable request.

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