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Review Article

Theranostics: A Boon in Cancer Diagnosis and Therapy

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ABSTRACT

Modern approaches in improvement of new nanomaterials have gained enormous attention due to various biomedical application, along with cancer theranostics. The characteristic physico-chemical feature of these materials, including their small size and wide-range surface-to-volume ratio provide potentiality for cancer theranostics that combine diagnosis , biosensing , imaging detection and immune therapy.Recent procurement for cancer immunotherapy have gained considerable attention in controlling the body's immune system to fight against cancer.In this abstract , nanomedicine with inherent immunomodulatory properties presents interesting window(of opportunity) which can stimulate the function of immune cell. The goal is to cover broad range of information about the immunomodulation properties of nanomedicine in cancer theranostics i.e factors like pH, hypoxia, tumor angiogenesis, tumor extracellular matrix which have a huge role in the immunomodulation of nanomedicine and also strategies to enhance cancer theranostics applications. According to recent studies, cancer therapy can be potentially improved through nanoparticle based immunotherapy.

Keywords: Nanoscience; Immunomodulatory nanomaterial; Cancertheranostics; Bio sensing; Imaging detection

INTRODUCTION

Recent outcome in cancer immunotherapy has brought about significant interest in tackling the body's immune system to fight cancer [1]. A lot of strategies have been scrutinized to improve the effectiveness reducing toxicities of cancer immunotherapy. Successes in cancer immunotherapy have significant interest in tackling the body's immune system to fight cancer [1]. Numerous approaches have been investigated to improve the efficacy while reducing toxicities of cancer immunotherapy [2]. Distinct Nano formulation of antigens, cytokines, chemokine's, nucleotides show various immune cells which have been successfully exhibitied in many preclinical settings, producing promising results [3]. However, in these, Nano medicine mostly assist as a vechicle to enable the more-productive transport of immunostimulatory agents to scale up antitumor immune response. This new category of immune nanomedicine by selection regulate vital signal pathways inside distinctive immune cell population through their material compositions, geometrics, or surface modification to come up with potent growth effects. Thus by planning of more efficient delivery devices for immunomodulating agents or the handling of refined nanoconstructs which will by choice regulate immune system. In this way nanomedicine can progress by providing delivery platform for immune therapy and the way nanomaterial is designed to possess intrinsic immunomodulatory properties itmay mount anticancer immune response. Cancer treatment using immunotherapeutics mainly rely on three important components the first component deals with an efficacious transfer of cancer antigens to immune cells such as dendritic cells. The investiture of anticancer immune response after delivery ofadjunct and cancer antigen to immune cells is the second component of this treatment. The third component involves IDTM to induce a response to the anticancer immunotherapeutics. Thus this is obtained by nanoparticle system which can be used for the triggering of immune system against cancer.

IMMUNOMODULATORY NANOMEDICINE

One of the developing area of research in immune cancer nanomedicine is the recognition or building of nanoconstructs that can regulate explicit steps along the immune activation cascade For instance, Ferumoxytol , an iron oxide nanoparticle formulation approved by United States Food and Drug Administration for the treatment of anemia shown to cause the polarization of tumor-associated macrophages towards the pro-inflammatory M1-like phenotype and promote reactive oxygen species [4]. Intrinsic injection of ferumoxytol intensely reduce tumor growth of orthotopically implanted MMTV-PyMT breast

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tumors and inhibits the formation of metastatic lesions in the liver and lung(4). Nanoparticles can also be used to enhance both tumor delivery and to produce antitumor immune response. Magnetic nanoparticles comprise of therapeutic fucoidan-dextran which were modified with PD-L1 inhibitors and T-cell activators to bring about a multifunctional complex [5]. As cancer immunotherapies like immune checkpoint inhibitors are progressively getting used for localized cancers in the frontline settings with alternative therapeutic modalities, these studies demonstrate nanomedicine potential for combinational therapy for cancer treatment.

Fabrication of Nanoparticle for Cancer Immune-Therapy

A significant development is the field of cancer immunotherapy has been initiated durning the last few years. However, clinical trials of cancer vaccines could not obtain significant success. In recent year, new opportunities , especially fabricated nanoparticle based technique , have been scrutinize for treatment ofcancer [6]. Specifically, cancer vaccines have been favorably delivered using multifunctional nanoparticle, which shows several benefits, including targeted delivery of immunotherapeutics using stimuli-sensitive materials which results increase in drug efficiency. Other benefit of nanoparticle system is the concurrent delivery of multiple therapeutic component , where treatment and imaging agents can be incorporated in the core and on the surface of multifunctional nanoparticle for cancer targeting [7]. Ongoing studies have explained that nanoparticles have multifaceted function for (1) working as an efficacious substitute for generation and transduction of CAR-(chinemric antigen receptor T-cell, (2) imparting tumor-suppressing activity to TAM (tumor associated macrophages) [8].In addition , nanoparticle platform cam be used for the improvement of cancer therapy.

Cancer Theranostics Applications of Immunomodulatory Nanomaterials

Vaccine

A broad range of cancer vaccines has been analysed for a variety of human malignancies and the aim is to deliver tumor-associated antigens to professional antigen presenting cells to bring out adaptive immune responses mediated by tumor-specific cytotoxic T cells and antibodies. The vaccine in the form of nanoparticles not only antigen cohesion and immunogenicity , but also targets delivery and control release.The vaccine in the form of nanoparticles is not only for antigen constancy or immunogenicity , but also assists delivery and control release. Apart from vaccination, co-delivery of tumour antigens and adjunct is also important.

Multi-clone antibody

Hindrance of receptor with antibodies is an important function of molecular targetedtherapy , involving the hindrance of VEGF human epidermal growth factor receptor.The perishable poly(di-lactide-co-glycolide) nanoparticle carrying anti-OX 40 antibody will induce cytoxic lymph cell proliferation and tumor specific toxicity [9]. The antibody could raise anti-tumor immunity for cancer immunotherapy in association with nano-vaccines. The merger of simple physical combination of an antigen with a synthetic polymeric nanoparticle called PC7A and anti- PD-1 shows extra-ordinary synergy with 100% survival over 60 days in TC-1 model [10].

Artificial antigen presenting cells

Antigens presenting cells (APCs), having macrophages and dendritic cells, seize foreign pathogens and show peptides to T cells in the forms of antigen-major histocompatibility and active immune response. Synthetic artificial APCs are particles that use protein for T cell activation, such as MHC-epitope or agonist anti-CD28 which have been joined [11]. The first generation a APCs were made of solid, small-sized polystyrene beads with iron oxide cores and used for ex vivo expansion of T cells As compare to first generation, the second generation of a APCs were smaller at nanometre size scale for in vivo showing beneficial distribution to T-cell-rich region [12].

Nanomedicine as Immune-Modulating Agents

Though most of the research on nanomaterial-immune cell interactions has been carried out for studying the noxious effects of nanoparticles [13], an area of enormous concern is to tackle the immunomodulating properties of nanomaterials to treat patient with cancer or autoimmune disease. Polymeric nanomaterial can be set up to imitate the biological interactions between antigen-presenting cells and T cells to act as distinct subcellular granules to encourage antitumor immunity [14]. Likewise, nanomedicine can be set up to depend on immune cells to particularly target and attack different types of tumors. Nanoparticles filled with chemotherapeutic agents were carried into neutrophils, which are then listed to resection bed of brain tumors by postsurgical inflammatory cytokines to let out the drugs that reduce recurrences [15]. This immune cell depended tumor targeting plan also applies to another innate immune cell types. For example combining anti-PD-L1 antibodies onto plasma membrane of platelets, which gets collected in the resection cavity after tumorsurgery which can lead to reduce local and distant recurrence risks and survival in tumour-bearing mice [16]. Nano and small particles are also designed to imitate the function of immune cell subsets. Likewise, multivalent synthetic dendritic cells designed by polymeric nanoparticles which increases efficacy of T cell activation [17].

Nanomedicines as Delivery Platforms for Immunomodulating Agents

Synthetic and naturally acquired nanoparticle possessdistinctive physical and chemical properties that make them well-suited as drug-delivery platforms. Nanoformulations of traditional chemotherapeutic agents lay out ways to modify the pharmacokinetics and pharmacodynamics components of cytotoxic drugs without altering their turmoricidalactivities [18]. Nanoparticles incorporated using different material composition which can be capsulate anticancer drugs within their inner core. The surface of nanoparticle can be developed to dock targeting entity such as antibodies, peptides or recombinant proteins that further enhance the selective accession of drugs without tumourtissues [19]. These distinctive advantages of nanomaterial have also been used for immuno-oncology application. Nanoparticles can be used give particular cytokines , growth factor , or cocktail of immune stimulators to increase immune cell function [20]. With recent modification in genome editing there have been interest in using nanomaterial to give nucleic acids such as siRNA for development of cas9 mRNA to restore specific disease associated genes in vivo. Nanoparticles have an advantage for immune targeting because of their associated uptake by innate immune cells, like monocytes,macrophages, and dendritic cells in the body [21-22]. Nanoparticles made with unique composition and surface charge profiles can particularly homes to lymphoid organs such as the spleen and produce immunomodulatory effects. These distinctive

properties make nanoparticle an ideal contender for antitumor vaccine delivery.

Effects of Immunomodulatory Nanomedicine on the Tumor Microenvironment (TME)

Tumors can make immunosuppressive tumor microenvironment which can increase cancer growth and metastasis. Thus, cancer can be treated by immunomodulation of tumorenvironment [23]. Tumourmicro environment carry a high level of TAMs. These are the immune cells which give rise to excess of immunoregulatory cytokines such as TGF-(transforming growth factor).In inclusion, TAMs fabricate inflammatory cytokines like IL-6 heading to the repression of anticancer immune responses. Thus, effective cancer immunotherapy requires targeting and killing TAMs in the tumor environment utilizing surface developed nanoparticles. Hepatic,lung, breast cancer show overexpression of many cytokines including TGF repressactivation, maturation and the differentiation of immune cells. So an immune response in cancer might be brought by suppression of the TGF in the tumor microenvironment. Tumor microenvironment of hepatic , gastrointestinal and breast cancer have high levels of tumor-suppressor cells like MDSCs which produce different kind of cytokines like IL-10 for starting of Tregs and inhibition of another immune cells. In this review, efficacious cancer immunotherapy requires MDSC eradication in the tumor microenvironment. Nanoparticle-mediated delivery of immunomodulatory to the tumor microenvironment can be achieved via active or passive transport. Recent studies combine many therapeutic approaches like (checkpoint, blockade, immunotherapy, Nano scale etc.) with nanotechnology to overcome the immunosuppressant microenvironment of tumor-assisting effective treatment of tumour [24-28].

CONCLUSION

The current studies show the application of biomaterial-based nanoparticles in the enhancement of anticancer immunity. Nanoparticles can improve antigen presentation viz structured delivery of cancer antigens and therapeutic supplements to APCs in immunological organs for ex. Lymph, nodes. So, a vaccine like extended and broader immune effect can be relent by utilizing nanoparticle-filled cancer immunotherapeutics as compared with free immunotherapeutic agents. The above mentioned review disclose the interdisciplinary research, specially the group of various biomedical approaches, has generated into current cancer immunotherapy. However the expansion of biomaterial-based anticancer immunotherapy requires a detail information of how biomaterial interact with immune system. For cancer immunotherapy nanoparticle has interaction with immune system. For cancer immunotherapy, nanoparticle growth by using biomaterial has played an important role is getting therapeutic efficacy at relatively low dose and avoiding toxicity. In short, cancer patient's life condition and span can be ameliorate by evolving cancer vaccines based on nanoparticle. Regardless of all challenges, it is ascertainable that immune nanomedicine will play a dominant role in developing of cancer medicine. A better knowledge of how immune system interacts with engineered nanomaterials will enable researchers to make optimal immune nanomedicines that are both safe and efficient in treatment.

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