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Emerging theranostic gold nanostructures to combat cancer: Novel probes for Combinatorial Immunotherapy and Photothermal Therapy

Sanjay Kumar [a], Ayush Mongia [a], Shikha Gulati [a,*], Parinita Singh [a], Anchita Diwan [a], Shefali Shukla [a]

[a] Department of Chemistry, Sri Venkateswara College, University of Delhi, Delhi, 110021

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ABSTRACT

The application of gold nanoparticles in immunotherapy has emerged as one of the most effective therapeutic strategy for eradicating cancer by releasing antigens, oligonucleotides, adjuvants, immune-stimulating agents into the body. Gold nanoparticles are found to be a superior choice, for generating attack on oncogenic cells, due to their low toxicity, better target specificity, diagnostic capabilities, and enhanced cellular uptake rate. This review focuses on the efficiency of several functionalized gold nanoparticles of diverse shapes and sizes as delivery vehicles to desired target cells through effective immunotherapy, along with a brief discussion about photothermal therapy.

1. Introduction

According to the World Health Organization (WHO), cancer is the second foremost cause of death globally and is responsible for an estimated 9.6 million deaths in 2018. Globally, about 1 in 6 deaths is due to cancer [1]. In spite of extensive research in the cancer treatment, it is still a challenge for humankind. Conventional therapies such as chemotherapy, radiotherapy, and surgery cannot eradicate cancer effectively as they are unable to generate specific attack against tumor cells without harming healthy cells. Nanotechnology has emerged as a field of research where the materials of nanometer range (1–100 nm) have the potential to increase the selectivity and potency of biological chemical, and physical methodologies for eliciting cancer death at a cellular level owing to their minimal size while reducing collateral toxicity to healthy human cells. Nanomaterials are increasingly being utilized to target cancer cells with pronounced specificity via both active and passive targeting. From the past several years, various investigations have been carried out in applications of gold nanoparticles (AuNPs) mediated immunotherapy for cancer treatment, which has proven to better than conventional therapies. With continuous advancements in the synthesis techniques over the last two decades, gold nanoparticles can now be manufactured with a well-controlled size distribution, giving rise to a variety of shapes namely sphere shape, rod shape, triangle shape, hexagonal shape, and many more [2]. Owing to their adaptable shape (such as nanospheres, nanorods, etc.), size, surface-chemistry, bio-inertness and low toxicity, AuNPs provide an effective pathway for cancer treatment. In particular, these particles have been employed for delivering various anti-cancer drugs (doxorubicin [3], 6-mercaptopurine [3]) immuno-adjuvants (imiquimod (R837) [4]) & (CpG (cytosine-phosphate-guanine) oligonucleotides [5-7]) and also for sensing anticancer agents [8].

As a novel platform in biomedicine and nanotechnology, gold

Abbreviations: WHO, World Health Organization; NPs, Nanoparticles; CpG, cytosine-phosphate-guanine.; MHC, Major Histocompatibility Complex.; DC, Dendritic Cells.; TNBC, Triple negative breast cancer cells.; PDL1, Programmed death ligand 1.; EGFR, Epidermal growth factor receptor.; DTNB, 5,5-dithio-bis-(2-nitrobenzoic acid); pMBA, Para-mercaptobenzoic acid; DOX, Doxorubicin; MP, 6-mercaptopurine; IC, Inhibitory concentration.; ICP-MS, Inductively coupled mass spectrometry; TLR, Toll like receptor; ODN, Oligodeoxynucleotides; HAuNs, Hollow gold nanospheres; AuNP, Gold nanoparticles; TF_{ag}, Thomsen Friedenreich antigen; TACA, Tumor associated carbohydrate antigen.; Thr, Threonine; Ser, Serine; Amph, Amphiphilic; GLP, Ganodermalucidum polysaccharide; TGF, Transforming growth factor; MPLA, Monophosphoryl lipid A; BMDC, Bone marrow derived dendritic cells.; RLN, Regional lymph nodes; HSP, Heat shock proteins; AuNS, Gold nanospheres; AuNR, Gold nanorods; BSA, Bovine serum albumin; HA, Hyaluronic acid; NSC, Neural stem cells; MMP2, Matrix metalloproteinase-2; Treg, Regulatory T cell; SEM, Scanning electron microscopy; SC-ICP-MS, Single cell inductively coupled mass spectrometry; EPR, Enhanced permeability and retention effect; PTT, Photothermal therapy; SPR, Surface plasmon resonance; OT, Octanethiol; MUS, Mercaptoundecanesulfonic acid; ALL, Acute Lymphoblastic Leukemia; PEG, Polyethylene glycol; MSN, Mesoporous silica nanoparticles; CTL, Cytotoxic T Lymphocytes; NK Cells, Natural Killer cells; MDSCs, Myeloid-derived suppressor cells; NIR, Near Infrared region; AuNDs, Gold nanodumbbells; MEH-PPV, poly(2-methoxy-5-(2ethylhexyloxy)−1,4-phenylenevinylene); AuNCs, Gold nanoclusters.

* Corresponding author.

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