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Mini Review Open Access

# Poly (Lactic-Co-Glycolic) Acid (PLGA) Adjuvant for Immunotherapy

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## Mini Review

Nowadays, there are several efforts in immunotherapy especially biodegradable and biocompatible nano-polymers are using as immunomodulatory to induce cell mediated immune responses [1]. The advantages of nanoparticles have been proved to be potent immunomodulators in several kinds of vaccines to control a release of antigen, higher quality and quantity of immune responses and protect the integrity of antigens against degradation until delivered to the immune cell [1]. In particular, nanoparticle-based vaccines can demonstrate a critical role to CD8+ T-cell against viral infections by effective cross-present antigen MHC class I and MHC class II in pathways [1] Nanoparticles are potential carriers served as vaccine adjuvant for effective antigen delivery. Several materials of nanoparticles and liposomes have been proved to be safe and effective uses in modern vaccinology. Degradable polymers, for example polyesters (poly (lactic acid) and their copolymers), polyorthoesters, polyanhydrides and polycarbonates, are frequently used due to their properties are suitable for conjugation or loading with antigens, and can protect the antigen from degradation *in vivo.*

Nanoparticle-based vaccine delivery system could effectively encapsulate antigens to enhance and/or facilitate an uptake of antigens by antigen presenting cells (APCs) such as dendritic cells (DCs) or macrophages both *in vitro* and *in vivo* [1]. In particular, the antigen-delivery system targeting dendritic cells (DCs) as professional APCs would be mostly focused to be potential immunotherapy strategies. The nano-polymer particles targeting antigens to DC cell are new approaches to deliver the effective immunomodulators. An uptake of nanoparticles by DCs, facilitates the antigens are intracellular processed and antigen-presentation by MHC class I and II pathways to induce both CD4+ and CD8+ T-cell responses [2]. Nowadays, the biomaterial researches are focused intensively for immune-cell targeting continues to optimize the antigen delivery and adjuvant activity. The development of polymer chemistry and molecular immunology will help to be a successful DC-targeting system and might lead to the next generation of vaccines [2]. This review discusses the targeting biomaterials are considering as a promising strategy for the next generation of vaccines and immunotherapies and also particularly focused on the application of polymer-based nanoparticles as safety vaccine adjuvant, effective delivery system and potential immunomodulators. Therapeutic vaccines containing novel adjuvant formulations are increasingly reaching advanced development and licensing stages, providing new tools to fill previously unmet clinical needs. However, many adjuvants fail during product development owing to factors such as manufacturability, stability, lack of effectiveness, unacceptable levels of tolerability or safety concerns.

Poly (lactic-co-glycolic) acid (PLGA) has been the focus intensively for several decades in nanotechnology due to its desirable property as biodegradable synthetic polymers. PLGA has been approved in human and veterinary use by The American Food and Drug Administration (FDA) [3]. PLGA particles have been known to increase the potency of a vaccine formulation [4-6]. PLGA vaccinology is recently trendy to be considered as the one of the potential vaccine delivery system by its slow degradation rate before internalization in APCs [7,8]. In general, APCs mostly have been known to prefer uptake antigens and immunostimulators in particulate form more than soluble [7,8]. The particles could protect the antigen from proteolytic degradation [9], facilitate and enhance deposition after injection and oral delivery [10]. PLGA nanoparticles showed efficiently delivered the antigens *in vitro* to murine bone marrow-derived DCs, suggesting that PLGA nanoparticle is very effective and useful for immunotherapy targeted DCs. To prove the certain targeting function, DC-specific targeting antibodies on PEG-coated PLGA nanoparticles by Cruz et al. [11] shown that antigen dependent T-cell responses could be induced at 10-100 fold lower concentrations compared to non-targeted nanoparticles, and studied by Newman et al. [12] suggested that PLGA nanoparticles are able to induce and enhance immune responses for poor immunogens. There are several applications of PLGA particles in many kinds of therapeutic vaccines such as cancer-associated viral vaccine. The immunostimulators and antigens were encapsulated or adsorbed to PLGA particles including TLR agonists such as LPS [13], MPLA [11,14], β-glucan [15,16] and poly (I:C) [17]. PLGA particles are the good strategy for therapeutic vaccine to enhance the cytosolic delivery of antigens shown significantly increase the antigen-presentation to the MHC class I pathway and activate IL-2 secretion by T-cell compared to soluble antigens and antigen-coated latex beads, respectively [18]. Moreover, an uptake of particles rate has been shown more rapid and prolong for professional APCs. They possess the capacity to present antigens to both MHC classes I and II pathways, inducing both humoral and cellular responses due to HIV vaccines require the induction of both kinds of the immune system

For viral therapeutic vaccine, A very interesting work showed that HIV p24 protein adsorbed on the surface of surfactant-free anionic poly (D, L-lactide) (PLA) nanoparticles were efficiently taken-up by mouse DCs, inducing DC maturation [19], polylactide acid (PLA) or PLGA, not only provide a delivery system but also act as an adjuvant. Therefore, biodegradable nanoparticles vaccine carrying HIV antigens is the good strategy for HIV. For DNA vaccine, since DNA vaccines may not be promising and effective in humans as in animals. To increase the efficacy of DNA-based vaccines, PLGA has been used for encapsulating peptide [20]. Chitosan-modified PLGA microspheres could show an induction in both humoral and cellular immune responses by a single dose administered intranasal rout in rabbits. DNA-based vaccines can induce long-lasting immune responses. Recently, DNA encoding hepatitis B surface antigen (HBsAg)-encapsulated PLGA nanoparticles was shown an increasing immunity in mice. However, the successful clinical trials with the PLGA-encapsulated nanoparticle antigen have never been reported, suggesting that extensive experimental work is needed in this promising area.

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