Journal of Clinical Research

Alsharabasy, J Clin Res 2017, 1:1

Editorial Open Access

Vaccine-Loaded Polymeric Vehicles in Cancer Immunotherapy

Amir Mohammed Alsharabasy*

Department of Radiation Biology, National Center for Radiation Research and Technology, Cairo, Egypt

***Corresponding author:** Alsharabasy AM, Department of Radiation Biology, National Center for Radiation Research and Technology, Cairo, Egypt, Tel: 00201004914998; E-mail: Alamier@Ymail.com

Received date: September 26, 2017; **Accepted date:** September 26, 2017; **Published date:** September 30, 2017.

Editorial

Immunostimulants are substances which enhance the ability of the immune system to fight the infection, disease or tumor. Examples include DNA, certain cytokines, monoclonal antibodies, immune system components, some hormones and vitamins as well as certain polymers. During chemotherapy, certain mechanisms are induced by such molecules for preventing the developed escape mechanisms by tumors. These can be through activating the host effector mechanism (e.g., phagocytes or the complement system), blocking the signaling of certain growth factors or inhibiting the angiogenesis of tumor. The systemic administration of the conventional vaccines, even at high doses, often results in poor efficacy due to the enzymatic degradation or fragmentation resulting from the applied shear stress during their administration by injection. This may be in combination with significant inflammatory cell infiltration with a rapid clearance in vivo before the sufficient expression of the antigen in the localized tissue [1]. Accordingly, multiple administrations are required.

The designing of certain polymeric delivery vehicles for the tumor antigens has gained the attention for guaranteed optimum immune response without causing any safety issues. These vehicles are to encapsulate different molecules and gene sequences with prolonged retention of the vector at the site of injection. This aims at increasing the probability of a more sustained expression and, subsequently enhanced immune response (Hong et al., 2007; Yang et al., 2008). For designing of a vehicle for immunostimulant, it as well as the candidate material should have special rheological properties for injection, and be bioresorbable, so the inflammation associated with the foreign body response can be eliminated. Moreover, the resorption rate should be in harmony with the rate of drug delivery to cause the minimal side effects. The different approaches in cancer immunotherapy based on the delivery of vaccines loaded in polymeric vehicles and the properties of such particles have been highlighted here.

Hossain and Wall [2] summarized the different carrier proteins for the tumor-specific antigen glycosylated mucin 1 (MUC1) which target the epithelial cell tumors. Moreover, the different mechanisms for the generation of effective anti-cancer responses by the delivered vaccine via targeting both humoral and cellular immunity were covered. Poly(4,4′-trimethylenedipiperdyl sulfide)-based micro particles were developed and loaded with ovalbumin (OVA) antigen and the adjuvant (CpG 1826) towards stimulating both the humoral and cellular immune responses in vivo using murine tumor model [3]. Following the subcutaneous injection of the cancer vaccine-loaded particles in mice, they demonstrated improved immune responses and increase in the levels of OVA-specific CD8+T lymphocytes.

As human papillomavirus (HPV) is the main cause of cervical cancer [4], the therapeutic HPV vaccine is used for the eradication of HPV infected cells. For instance, an antigen delivery system based on conjugates of 4-arm star poly (acrylic acid) (S4) and HPV-E7 protein-derived peptide antigen was designed and proved its efficiency as a robust therapeutic against E7-expressing TC-1 tumors in mice [5]. Moreover, a more developed macromolecular vaccine system of poly-tert-butyl acrylate conjugated to E6 and E7 peptide epitopes was generated towards stimulating the activity of the CD8+ cytotoxic T lymphocytes with eradicating the HPV-infected cells. The vaccine candidates were able to eliminate tumors in up to 50 % of the treated mice using a tumor model [6].

PC7A polymeric nanoparticles loaded with OVA as a model antigen were synthesized with a proved ability to induce the antigen-specific cytotoxic T lymphocyte (CTL) with a two-fold increase in response than certain conventional adjuvants [7]. Moreover, the loaded vehicles delivered OVA with higher efficiency than the antigen delivery alone. For instance, a 29-fold increase in the number of OVA-positive CD8α+ DCs was observed using the delivery system compared to the OVA alone, along with an improvement in the cross-presentation in antigen-presenting cells. Moreover, this nano-vaccine system eradicated the tumor growth in B16-OVA tumor cell-induced-tumor bearing mice with prolonging their survival.

Importantly, an interesting approach for the delivery of DNA vaccines depending on the invasive nature of bacteria was presented by Hu [8]. Self-assembled nanoparticles of the cationic polymer cross-linked β-cyclodextrin-PEI600 and plasmid DNA were synthesized, and used for the coating of Salmonellae. Through targeting the Vascular Endothelial Growth Factor Receptor-2 (VEGFR-2), the engineered non-viral delivery vector proved its ability to inhibit the tumor growth mediated by the activation of cytotoxic T-lymphocytes and secretion of certain cytokines. Moreover, this coating protected the bacteria from the phagosomes, and facilitated their dissemination into the blood after the oral administration of the polyplex nanoparticle-coated bacteria.

The delivery of antigens and vaccines loaded into liposomes has many advantages [9]; this guarantees the intracellular delivery of the antigen with ability to induce both the cellular and humoral immunity. However, due to the viral components of such delivery systems, these liposomes have been modified with pH sensitive polymers, especially in cancer immunotherapy. The two major approaches are: inclusion of pH-sensitive moieties, and the modification of the liposomes with pH-sensitive polymers. These approaches and their different applications in the immunotherapy have been reviewed by Yuba [10].

To summarize, with the development in the designing of polymeric vehicles for the delivery of different therapeutic molecules, the use of such vehicles, whether in the nano or micro scales for the antigen delivery has been improved as well. This resulted from the interaction between the polymer chemistry and immunology. However, focusing on cancer immunotherapy, these approaches are still in their primary

stages of development. The recent achievements aim at the conservation of the delivered vaccine and guaranteeing their targeted actions on the immune cells for inhibition of the growth of different tumors. Despite this limited number of achievements compared to the different types of cancers, there are now tremendous increasing efforts, hoping to find alternatives for the conventional delivery approaches for vaccines for treatment of different tumors.

References

1. Kim M, Park JY, Shon Y, Kim G, Shim G, et al. (2014) Nanotechnology and vaccine development. Asian J Pharm Sci 9: 227-235.
2. Hossain MK, Wall KA (2016) Immunological Evaluation of Recent MUC1 Glycopeptide Cancer Vaccines. Vaccines (Basel) 4: E25.
3. Geary SM, Hu Q, Joshi VB, Bowden NB, Salem AK (2015) Diaminosulfide based polymer microparticles as cancer vaccine delivery systems. J Control Release 220: 682-690.
4. Liu TY, Hussein WM, Toth I, Skwarczynski M (2012) Advances in peptide-based human papillomavirus therapeutic vaccines. Curr Top in Med Chem 12: 1581-1592.
5. Liu TY, Hussein WM, Jia Z, Ziora ZM, McMillan NA, et al. (2013) Self-Adjuvanting polymer-peptide conjugates as therapeutic vaccine candidates against cervical cancer. Biomacromolecules 14: 2798-806.
6. Hussein WM, Liu TY, Jia Z, McMillan NAJ, Monteiro MJ, et al. (2016) Multiantigenic peptide-polymer conjugates as therapeutic vaccines against cervical cancer. Bioorga and Med Chem 24: 4372-4380.
7. Luo M, Wang H, Wang Z, Cai H, Lu Z, et al. (2017) A STING-activating nanovaccine for cancer immunotherapy. Nature Nanotechnology 12: 648-654.
8. Hu Q, Wu M, Fang C, Cheng C, Zhao M, et al. (2015) Engineering nanoparticle-coated bacteria as oral DNA vaccines for cancer immunotherapy. Nano Lett 15: 2732-2739.
9. Nakanishi T, Hayashi A, Kunisawa J, Tsutsumi Y, Tanaka K, et al. (2000) Fusogenic liposomes efficiently deliver exogenous antigen through the cytoplasm into the MHC class I processing pathway. Eur J Immunol 30: 1740-1747.
10. Yuba E (2016) Design of pH-sensitive polymer-modified liposomes for antigen delivery and their application in cancer immunotherapy. Polym J 48: 761-771.