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INNOVATION IN SKIN CANCER VACCINES

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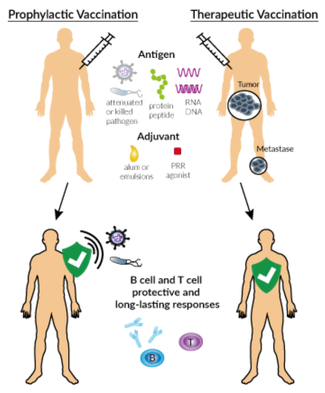
INTRODUCTION

Cancer vaccines are designed to induce specific and potent immune responses upon tumors, and consist of four classes: tumor lysate, dendritic cells, nucleic acids, and neoantigens.



The **prophylactic cancer vaccine** could be designate to **eliminate precancerous lesions** before they develop into invasive cancers.

Therapeutic cancer vaccines reprogram the body's immune system that previously tolerated tumor antigens and function as modulators against the tumor cells. In addition, they play a decisive role in **preventing tumor metastasis and recurrence.** Therapeutic cancer vaccines act on the innate immune system and **produce pools of cytotoxic T cells that directly kill tumor cells**.

Fig. 1 Prophylatic *vs* Therapeutic vaccination[1].

Conventional vaccines formulation typically include a tumor antigen(s) and immune adjuvant that are administered systemically. This activates effector T cells, which recognize the vaccine antigen(s).

***In situ* vaccines formulation typically includes an immune adjuvant** that is injected into the tumor directly. In response, T cells are recruited to the tumor microenvironment and activated against the antigens that are already present. This generates a more diverse pool of effector T cells that recognize diverse tumor antigens, helping to protect the patient from current and metastatic tumors that express the antigens found in the originally injected tumor.

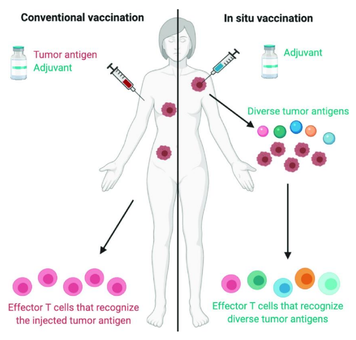


Fig. 2 Cancer vaccine formulations[2].

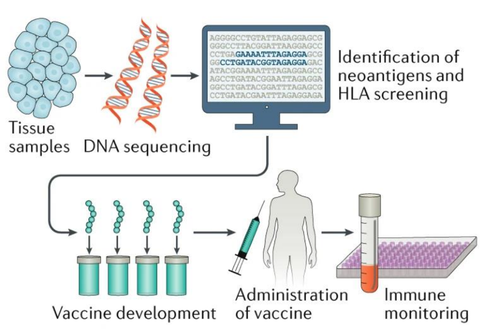


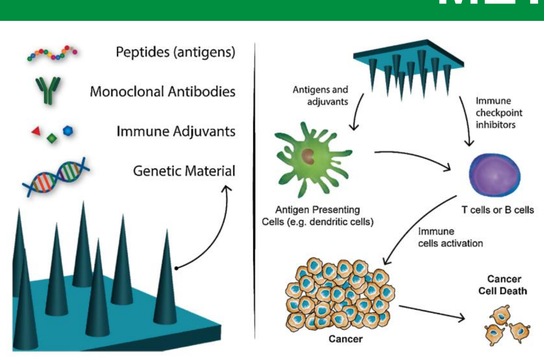
Fig. 3 Personalized cancer vaccines[3].

Personalized cancer vaccines can overcome interindividual differences and show great benefits for patients in the clinic due to the **highly tailored formulations**. **The personalized cancer vaccine contains patient-specific tumor derived epitopes, which have been proven to elicit a more specific cytotoxic T cell response than tumor-associated antigens**. They can be composed using various antigen forms, such as mRNA/DNA, peptides, cell fragments, whole tumor cells, immunogenic cell death related to lysates, and autologous dendritic cells. They exhibit advantages and deficiencies due to the various sources and properties of the antigens and the different immunologic mechanisms which are activate.

OBJECTIVES

Literature review about vaccine encapsulation into microneedles (MNs) carriers, to delineated method for improve the vaccine stability against degradation, increase cellular uptake, and target delivery to lymphoid organs. Literature scrutinize on MNs formulations focus on biomaterials for encapsulation of high quantities of vaccines and for increase the delivery to antigen-presenting cells (APCs).

METHOD



Bibliographic survey about the development of MN formulation for application as anticancer vaccines. **Concentrated on biomaterials and nanomaterials used in the MN vaccination.**

Fig. 4 MN development for application as anticancer vacines[4].

RESULTS

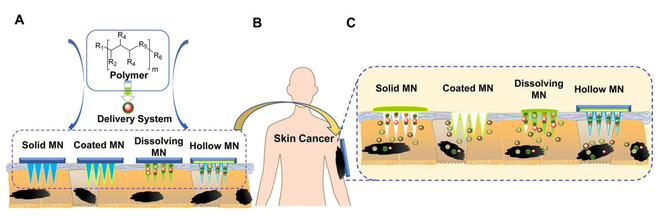


Fig. 5 MN-assisted vaccination in skin cancer treatment. (A) Vaccines combined with nanomaterials (such as liposomes, niosomes, polymers, or nanoparticles) in their formulation for application into MNs, such as solid, coated, dissolving, and hollow MNs. **(B) MNs are inserted near skin cancer cells for vaccination. (C) After MNs insertion, the vaccine is released into the tumor cells[5].**

Many materials have been studied as delivery vectors to enhance the therapeutic performance of cancer vaccines, including artificial materials, engineered microorganisms, cells and cell derivatives. These delivery vectors with distinct features are employed to **change antigen biodistributions and to facilitate antigen uptake, processing and presentation, improving the strength, velocity, and duration of the immune response when delivered by different strategies.**

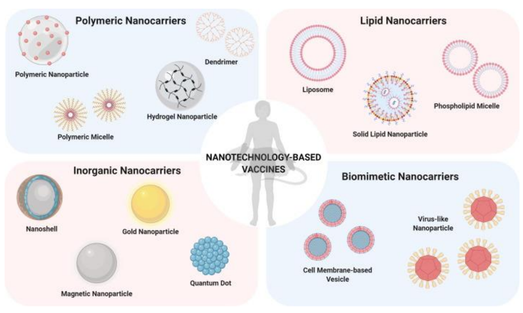
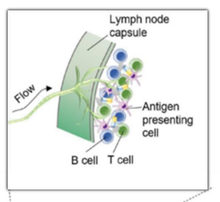


Fig. 6 Shows **types of nanoparticles carriers that have been exploited for cancer immunomodulation,** such as polymeric nanocarries, polymeric micelles, dendrimers , solid lipid nanoparticles, liposomes, phospholipid micelles, metal/inorganic systems (quantum dots, silica, magnetic and gold nanoparticle, and biomimetic-like nanocarriers, such as cell membrane-based vesicles and virus-like particles.

Fig. 6 Nanocarriers types for cancer vacines[6].

MNs for delivering cancer vaccines can accurately deliver antigens or immune adjuvants to specific skin layers, effectively target the immune cells residing in the skin, and induce a stronger immune response than the intradermal injection, thus improving the therapeutic effect on skin cancer. In addition, compared with intradermal injection, **MNs can decrease injection-related pain, and infected waste, allow self-administration, simplify vaccine cold-chain logistics, and reduce the risk of blood-borne pathogen transmission from repeated needle use** (Fig 7).



After 5 minutes application of dissolvable MNs into a dermis layer of the skin which is highly perfused with lymphatic capillary networks, released vaccines from dissolvable MNs bind and complex to endogenous albumin, and efficiently drain into draining lymph nodes, lead to enhanced lymphatic delivery[7].

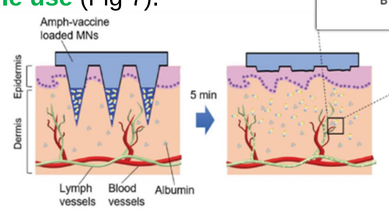


Fig. 7 Dissolvable MNs for cancer vacination[7].

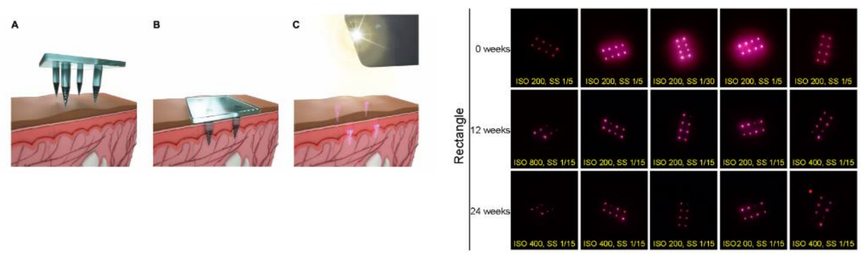


Fig. 8 (A) MNs with recording patient vaccination history (B) MNs are applied to the skin for 2 to 5 min, resulting in dissolution of the MN matrix and retention of fluorescent micro-particles. (C) An NIR LED and an adapted smartphone are used to image patterns of fluorescent microparticles retained within the skin. By selectively embedding microparticles within MNs used to deliver a vaccine, the resulting pattern of fluorescence detected in the skin can be used as an on-patient record of vaccination history [8].

CONCLUSIONS

It was presented a **review of MNs-based cancer vaccines** showing their design strategies, **aiming to develop safer, effective, and more stable MNs- based vaccines for skin cancer immunotherapy.** Specifically, was briefly outlined the advantages of using MNs in skin cancer vaccines, and introduced the types of cancer vaccines according to the antigen, including *in vitro, in-situ* treated tumor cells, or generated lysates, protein/peptide, and nucleic acid. Additionally, nanoparticles, including polymeric, lipid-based, and self-assembled peptide/protein, **were presented as carriers to integrate into MNs-based cancer vaccines, which could further enhance the immune response of vaccines** by increasing the uptake of antigens by immune cells and increasing the targeting of the vaccine to the lymph nodes (LNs). Finally, a promising design for recording patient's vaccination history was shown.

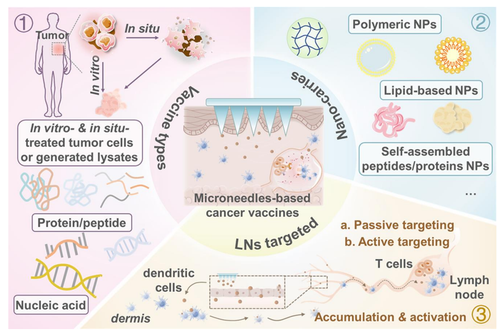


Fig. 9 Skin cancer vaccine compendium [9].

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