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Title: Nanomedicines and Nanovaccines: from bench to clinic

Abstract

In Pharmaceutics and Medicine, nanoparticles (i.e., liposomes, lipid nanoparticles, micelles, dendrimers) belong to the class of innovative excipients and have been used as such in many biomedical applications for both diagnostic and therapeutic purposes. They offer many important advantages, including non-toxicity, biocompatibility, biodegradability, increased efficacy, and reduced toxicity of the encapsulated bioactive molecules, through targeted and controlled release. Their great versatility in structure enables their functionalization and active targeting to specific tissues and cells. Currently, there are several medicinal products in the clinic and market, in which nanoparticles are components and serve as drug delivery nanosystems.

The first-ever approved nanomedicinal formulation was Doxil[®], which incorporates the drug molecule doxorubicin (an anthracycline antibiotic) inside PEGylated liposomes, also known as Stealth[®], and is administered in various types of cancer. There are additionally nanomedicines for infections, pain management, hepatitis, influenza, anemia and other pathological conditions, some of which are in the market, while numerous others are currently in clinical trials. Other nanomedicines that have been approved are Myocet[®], which also incorporates doxorubicin, Abelcet[®], Ambisome[®] and Amphotec[®], which were developed to deliver the drug amphotericin B to fungal infections, while Epaxal[®] and Inflexal[®] V are indicated for Hepatitis A and Influenza, respectively. Recently, Onivyde[™] was approved for the delivery of irinotecan to metastatic adenocarcinoma of the pancreas. All these formulations share the common trait of having particles in the nanoscale, however, the lyotropism and as a result, the morphology of the system (internal or external) is in most cases quite different, resulting in different surface properties and interactions with biological components, which can lead to altered pharmacokinetic profiles and final treatment efficacy and safety.

While classic vaccines have proved greatly efficacious in eliminating serious infectious diseases, innovative vaccine platforms open a new pathway to overcome dangerous pandemics via the development of safe and effective formulations. Such platforms play a key role either as antigen delivery systems or as immunostimulators that induce both innate and adaptive immune responses. Liposomes or lipid nanoparticles, virus-like particles, nanoemulsions, polymeric or inorganic nanoparticles, as well as viral vectors, all belong to the nanoscale and are the main categories of innovative vaccines that are currently on the market or in clinical and preclinical phases.

At this point, it is important to note that many of the aforementioned innovative technologies follow the physicochemical principles of nanotechnology. In the last decades, nanomedicine has boosted progress and some impressive results have been achieved in its short-term history. In vaccinology, nanoparticles (NPs) have a dual role, as their action includes both antigen delivery and adjuvanticity. Functional platforms, consisting of stimuli-responsive biomaterials that can be



administrated by alternative routes result in decrease of the cost, time and effort needed for the design and development of effective vaccines. Nanovaccinology allowed the development of a smart-vaccine against COVID-19 in less than a year.