Nanotechnology for infectious diseases

To achieve the biggest impact, nanotechnology-based strategies developed to manage infectious diseases in resourced-limited settings need to take into account the local context.

As demonstrated during the current COVID-19 pandemic, nanotechnology can play a major role in global health. From better screening and diagnostics, to therapeutics and vaccines, as well as health monitoring devices, nanotechnology-enabled approaches have the potential of making a tangible impact in the field of infectious diseases. Moreover, as discussed by Friedrichs and Bowman in a Comment in this issue, the fast-tracked approval of the two messenger RNA (mRNA) vaccines against SARS-CoV-2, though justified by the urgency of the situation, represents a 'first' in terms of regulations that might set a precedent for future approval of similar nano-enabled formulations.

The potential impact of nanotechnology on global health has long been recognised by bioengineers working in the field, and resulted in the development of numerous strategies for pathogens tracking and monitoring, drug delivery and disease prevention. And yet, the majority of these strategies have been limited to pre-clinical demonstrations; those that have progressed to a clinical stage, have often been suspended or, in the case of many diagnostics and monitoring devices, failed to reach broad distribution and implementation.

The reasons for this are multiple, ranging from scientific to economic and socio-cultural ones. The two Reviews published in this issue are mainly centered on the scientific challenges. They analyse how nanotechnology can contribute to the treatment and prevention of infectious diseases, with specific focus on 'the big three', that is, human immunodeficiency virus (HIV) infection, tuberculosis (TB) and malaria. In their Review in this issue, Kirtane and colleagues overview the nano-based approaches that might improve treatment of these diseases, considering the basic scientific aspects typically linked to infectious diseases (such as the rise of drug resistant pathogens and poor drug availability on infection sites) and those that are associated with their management. Specifically, it has been observed that the long and complex drug administration regimens needed for treatment, might lead to low patient adherence and eventually to treatment failure, especially in remote areas with limited access to health infrastructures. Engineered formulations for sustained or pulsatile drug release, such as cabotegravir and rilpivirine (the only nano-enabled therapeutics that progressed to the clinic and are now in phase III clinical trials for the treatment of HIV), and rationally designed delivery systems that can efficiently deliver multiple drugs to infection sites, improving drug solubility and intracellular targeting, are some examples of what nanotechnology can offer to address the above issues.

Parallel to the advances in designing nanotechnology-based systems for the treatment of HIV infection, TB and malaria, substantial efforts have been put in developing prevention strategies. In their Review in this issue, Fries and co-workers examine the common challenges that these otherwise very different diseases present with respect to developing efficient vaccines against them, and how nanotechnology can address them. In these pathologies, infection does not tend to generate protective immunity, which complicates antigen identification and vaccine optimization. An ideal vaccine against these three diseases should generate both humoral and cellular immunity, interacting with multiple cells in different tissue locations. In this context, the flexibility afforded by nanomaterials allows iterative modulation and precise control of specific features, including: number, type and spatial arrangement of carried antigens; co-delivery of adjuvants; and surface functionalization. Modulating material type, shape, size and flexibility might extend vaccine durability in vivo and improve trafficking to the right biological tissues and cellular compartments.

As mentioned in both Reviews, the storage, distribution and administration of nanotechnologies need to be considered when designing strategies for global health, especially for diseases that predominantly impact resource-limited areas of the globe with a hot and humid climate. Some devices might simply not work in those conditions, vaccines and therapeutics might need storage at low temperature, requiring infrastructures that are not readily available everywhere (a glaring examples are the mRNA vaccines against COVID-19). However other factors prevent the successful implementation of (nano)technology health solutions in low and middle-income countries (LMICs). Their cost, for example. And more generally the 'trickle down' approach to global health technologies, which sees their research and development process being carried out in high-income countries before being exported to countries in the Global South[1,2]. This approach is problematic as it often fails to take into account what Salamanca-Buentello and Daar define in their Comment in this issue, E^{3}LSC (for ethical, environmental, economic, legal, social and cultural) considerations. These principles, which the authors relate to the concept of 'nanoequity', should guide the development and implementation of nanotechnology strategies for global health problems. Among them: an equitable distribution of the innovations (the recent rise of 'vaccine nationalism' being a sobering negative example, although partially offset by the COVAX initiative (https://www.who.int/initiatives/act-accelerator/covax)); waive of intellectual properties, which would make most innovations more affordable; increased appreciation of the socio-cultural-environmental context where nanotech innovations should be applied. Developing nanotechnology-based medical platforms in the countries that most need them before scaling them up would likely solve several of the problems related to the E^{3}LSC challenges. Along the same lines, Hamad-Schifferli and Gomez-Marquez advocate in their Comment a home-grown approach that involves end users in the design, development and optimization of nanotechnology innovations, as opposed to the use of black box technologies that create dependency from the manufacturing lab, with associated costs and lack of flexibility. Specifically referring to diagnostics, the authors propose that sharing protocols might enhance the impact of nanotechnology in global health; in particular, they argue that that diagnostic middleware workers, who generally run clinical laboratories in LMICs, should be able to freely access nanotechnology protocols, and modify them, using locally sourced materials and instrumentations, to adapt them to the needs of the local population. ❐

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