MEDICAL APPLICATIONS OF BACTERIAL VIRUS-BASED AND VIRUS-LIKE NANOPARTICLES

Kozlovska A., Konechna R.
Lviv Polytechnic National University, alisa.kozlovska.bt.2022@lpnu.ua

Introduction. The latest development in nanoscale engineering drastically increased the diversity of methods in medical diagnosis and treatment. The major role in the implementation of recent innovations belongs to viruses. These supermolecular structures possess unique properties, such as high stability, susceptibility to surface engineering of their capsids, innate biocompatibility, and an enormous range of shapes and sizes, which allow them to perform more precise and diverse functions than synthetically programmed nanomaterials.

To differentiate between viruses containing their native nucleic acid, which are referred to as viral nanoparticles (VNPs), viruses devoid of their nucleic acid are considered virus-like particles (VLPs). Both types of structures are already used in different therapeutic procedures or currently remain under clinical research, showing promising results. The mechanisms of their application are determined by the distinctive morphological and physiological characteristics of each nanoparticle class.

The coat proteins of VNPs are determined by their genetic code. Nucleic acid sequences of viruses are relatively small, and therefore many of their genomes have been sequenced and are well characterized. Using genetic engineering, insertion or replacement of residues can be performed to add functional groups [1, 2, 3].

On the contrary, the ability to empty the phage capsid of its genetic material opens up the opportunity to use these hollow phage heads of VLPS as cages for encapsulation of foreign materials [4].

The research aims to define the scope of application of bacterial virus-based and virus-like nanoparticles for medical purposes and determine promising directions for further research.

Materials and methods. Gathering and analysis of the scientific papers relevant to the topic.

Results and discussion. The ability of bacteriophages to enter mammalian cells without further replication makes them suitable as tools for therapeutic interventions. Genetically/chemically-modified viruses that display targeting peptides or synthetic functional molecules have been used as building blocks to design self-assembled nanostructures for drug delivery and the treatment of diseases. In particular, the reported ability of filamentous phages to penetrate to the central nervous system, which is difficult for most of the drug molecules and drug delivery systems due to the relative impermeability of blood-brain barrier, may contribute to making viruses promising drug delivery platforms [5].

Antibiotics are one of the group of drugs that have been loaded in viral-based drug carriers. It has been reported that the conjugation of many copies of the drug molecule onto the phage's major coat proteins increased potency by creating a microenvironment around bacterial cell with a locally high drug concentration. Treatment of gram-positive pathogenic bacteria *Staphylococcus aureus* with the low potency antibiotic chloramphenicol, well-known for its toxicity to blood cells, conjugated to the fd phage

retarded the growth of bacterial cells ~20-fold more efficiently than free chloramphenicol [6].

Viruses perform as carriers of therapeutic cargo for photothermal therapy (PTT), which employs gold nanoparticles as a heat source for inducing cell damage as a result of a light-to-heat conversion process. As gold nanoparticles generate local heating under light illumination, efficient delivery of gold nanoparticles to targeted cells is desirable for selective cell killing. Clusters of gold nanoparticles on T7 phage particles have been fabricated as a PTT delivery platform to treat prostate cancer cells in vitro. The assembly of gold nanoparticles on the capsid surface was achieved via the display of a gold-binding peptide and a prostate cancer cell-binding peptide, in tandem [7].

A potential vaccine against nicotine addiction has been recently developed using the 30-nm icosahedral capsid of bacteriophage Qβ chemically modified to display nicotine in a multivalent fashion. The multivalent and particulate nature of the Qβ-based vaccine boosts the production of anti-nicotine antibodies, thereby reducing blood nicotine levels and limiting transport across the blood-brain barrier [8,9].

A significant body of work has studied the use of VLPs for the development of improved contrast agents. By loading the standard NP-based contrast agents within VLPs, the new NPs gain improved relaxivities which then give higher-resolution images. Additionally, if the VLPs are further modified to target specific cells, the signal-to-noise ratio is increased even further giving clear images of, for example, tumors. To that end, HBVc and CPMV VLPs have been loaded with iron oxide NPs through coordination to the coat proteins or through passive encapsidation [10, 11].

Virus-like particles are used to load nucleic acids as well as drugs. MS2 VLPs are particularly suited to loading RNA. They require a short stem-loop RNA hairpin, which is typically part of their genomic RNA, to assemble into capsids [12]. This sequence has been easily extended to incorporate mRNAs, micro RNAs, and small interfering RNAs [12, 13]. P22 VLPs have been shown to load RNA through electrostatic interactions between the nucleic acid and the coat proteins. Qβ VLPs have also used similar principles to load DNA. These nucleic acid-loaded VLPs have been developed for various uses including vaccines and vaccine adjuvants [14], gene delivery systems [12], micro RNA delivery systems, gene knockdown systems [13], and gene replacement by delivering guide RNA for the CRISPR system [15]. Loading and retaining nucleic acids with VLPs is easier than for small molecules because the nucleic acids are usually much larger and the capsids have evolved to load and carry similar molecules, that is, their viral genomes.

Conclusions. Based on the information provided, it might be feasible that in the next few years, there could be several advances in the conventional drug delivery system, and it may not be a surprise that viral nanoparticles have been utilized as therapeutic carriers for selective drug targeting for inflammatory diseases and cancers, vaccine development, immunotherapy, and molecular imaging. Moreover, as engineering capabilities improve, even greater diversities of virus-based and virus-like particles can be created, expanding the possible applications of these materials.

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