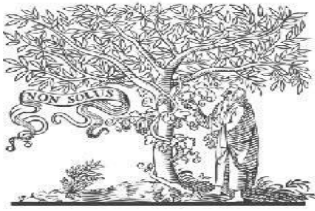


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Link : <https://ijiemr.org/downloads/Volume-12/Issue-05>

10.48047/IJIEMR/V12/ISSUE05/47

Title A Review of Bacteriophages and their Implications for Future Biotechnology

Pages: 475-483

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A Review of Bacteriophages and their Implications for Future Biotechnology

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Abstract

Bacteriophages, bacteria's natural predators, are now widely used in biotechnology. Their ability to fight antibiotic-resistant bacteria has garnered attention. Phages are also effective bio control agents in agriculture and petroleum. They also transport DNA and protein-based vaccines, helping create new vaccination methods. Phages exhibit proteins and antibodies and identify harmful germs. Bacteriophages have great promise in biotechnology, research, and medicines due to their diversity and manipulation. This thorough review article intends to help researchers, scientists, and biotechnologists working with phage-based applications promote biotechnology.

Keywords: Bacteriophage, Phage therapy, Antibiotics, Vaccine, Bio control

Introduction

Most bacteriophages have a polyhedral capsid and a tail with fibers to bind to bacterial cell receptors. Filamentous phages vary. The lytic and lysogenic life cycles of these phages infect bacteria. Phages proliferate within bacteria and

destroy them throughout the lytic life cycle. By integrating their genetic material into the host chromosome, temperate phages may lysogenically reproduce. This integration lets the phage reproduce with the host for generations. However, UV

light may cause the incorporated phage to lyse and exit the host chromosome[1].

Bacteriophages were first studied as antibacterial agents. After World War II, antibiotics made phages mostly research tools. Bacteriophages continue to advance molecular biology and biotechnology. They solved molecular biology puzzles. Bacteriophages have been revived as antibacterial agents, phage display devices, and vaccine delivery vehicles. Phage typing and other diagnostics use bacteriophages.

Phage therapy

Since 1919, phage treatment has employed bacteriophages to treat people. In 1896, Ernest Hankin discovered antibacterial action against *Vibrio cholera*, which causes cholera. Before Félix d'Hérelle discovered bacteriophages in 1917, Frederick Twort theorized that viruses (phages) were responsible for this antibacterial action. Phage therapy was popularized by d'Hérelle's 1925 plague treatment using antiplague phages. At Bombay's Haffkine Institute, he researched plague phage treatment. After antibiotics were popular in the 1940s, phage treatment was still used in the former Soviet Union[2]. Tbilisi's Eliava Institute pioneered phage treatment research and

use. Phage treatment has been resisted in the West owing to inaccurate early experiments and uneven outcomes. Phage treatment has succeeded in the US. William Smith and colleagues used phages to kill *E. coli* in mice. Phage biology and quality control concerns during therapeutic phage stock manufacturing were reasons many Western nations avoided phage treatment. Early phage treatment studies failed due to these problems. Phage treatment has been used in animals, plants, and people with mixed results. Phages outperform antibiotics. Targeting bacteria minimizes host flora harm. Targeting bacteria requires identification or phage cocktails. Phages self-limit because they need their bacterial hosts to develop. Phages cannot survive without the targeted bacterial infections. Phages may proliferate at infection sites, another benefit. Phages are usually harmless.

Phage display

Phage display, invented in 1985, synthesizes new polypeptides. Phage display involves fusing DNA encoding the desired polypeptide with phage coat protein genes to express the protein on the phage particle. Phage display typically uses the filamentous *E. coli* phage M13, however lambda and T7 may also be

utilized. Phage display libraries screen and isolate target-protein-specific peptides. Drug design uses these peptides as receptor mimics and molecular recognition reagents. Therapeutic drugs may decrease receptor-ligand interactions or serve as agonists. Phage display proteins may detect pathogens and environmental dangers. Phage display allows protein evolution to improve enzymatic activity and binding. Increase enzyme activity by randomly modifying its active site [3].

Phage display, especially on filamentous phages, may show Fab antibody fragment libraries. Research and cocaine addiction therapy utilize these libraries. Phages are nasally given and reach the CNS. Antibody fragments attach to cocaine molecules, blocking brain activity. Phage display is becoming a vital aspect of biotechnology. Phage antibodies have changed medication design and therapeutics. Phage display has illuminated protein-ligand and molecular evolution.

Type phage

Phage typing uses bacteriophages' selectivity for bacteria to type strains and identify pathogens. It includes identifying bacterial strains by their phage sensitivity patterns. Antibodies can detect phages attached to bacteria to boost detection

sensitivity. In phage typing, an unknown bacterial strain is exposed to various phages. Plaques (clear zones) show that the phages have developed and destroyed the bacterial cells, identifying the strain. Phages may identify harmful germs in other ways. Phages with reporter genes like lux genes can transport and express bacteria-specifically. Phages with fluorescent dyes covalently linked may also detect particular adsorption. Adenylate kinase may be detected following particular bacterial lysis. Moreover, phage antibodies and peptides may bind to poisons and bacterial infections. Dual phage technique detects antibody-antigen interaction in bacterial detection. Phage amplification tests may identify harmful microorganisms. These methods are used to detect Mycobacterium TB, E. coli, Pseudomonas, Salmonella, Listeria, and Campylobacter. Phage typing helps diagnose and investigate harmful germs by identifying and characterizing bacterial strains[4].

Phage-targeted gene delivery

Phages may deliver therapeutic genes. The phage coat protects the DNA following injection in DNA vaccine delivery and targeted gene delivery. These apps have different ideas. Phages may target certain

cell types by displaying foreign proteins on their surfaces, which is essential for gene therapy. Phage display and artificial covalent conjugation show targeting and processing chemicals on phages. Fibroblast growth factor targeting sequences target receptor-expressing cells. Protein sequences like the adenovirus penton base, which mediates entrance, attachment, and endosomal release, promote phage absorption and release. The protein transduction region of the HIV tat protein and the SV40 T antigen nuclear localization signal have also been used to improve lambda phage uptake and nuclear targeting. Integrin binding peptides improve gene transport via binding and up taking, whereas DNase II inhibitor peptides prevent DNA degradation.

Phage display libraries test phages' cell and tissue targeting. After inoculation with phage display libraries, phages were isolated from removed tissues in mice. In vitro methods have isolated phage-displayed peptides that improve mammalian cell cytoplasmic absorption. Through phage display library screening or rational design, phages may target particular tissues. Phages can carry genes to particular cells and organs, enabling gene therapy. Phage-based gene delivery research has medicinal potential[5].

Vaccines by phages

Phages deliver vaccines. Phage particles may directly contain vaccination antigens. In DNA vaccines, phage genomes include antigen synthesis sequences, making them delivery vehicles. Phage display may create phages with specified antigenic peptides. Novel antigens and mimotopes (peptides that imitate protective compounds) may be found by screening phage display libraries with particular antiserum. Phage display libraries may be tested against convalescent serum to find disease vaccines. Animal vaccinations have employed entire phage particles with antigenic peptides. After growth, chemicals may be chemically attached to the phage surface to show more antigens. Phages contain antigens on their coat proteins, which naturally combine adjuvant action. This removes protein purification and conjugation to a carrier protein before vaccination [6].

Intact phages can deliver DNA vaccines better than plasmids. Purified phage particles containing the vaccine gene are introduced into the host. The virus-like phage coat protects DNA and directs the vaccination to antigen-presenting cells. Compared to normal DNA immunization, mice and rabbits had better antibody

responses. A hybrid phage vaccination has a DNA vaccine under a eukaryotic promoter and a phage display version of the same antigen on its surface. This vaccine would efficiently target the humeral and cellular immune systems. Adding protein sequences to the phage vaccine's surface may target certain immune cell types, such as liver galactose-recognizing hepatic receptors. Isolating

phage display library peptides targets dendritic and Langerhans cells. These methods show how phages may boost immune responses and target particular immune cells in vaccine delivery. Phage-based vaccination research might improve vaccine technology. (Figure 1) shows immunization methods using phage delivery.

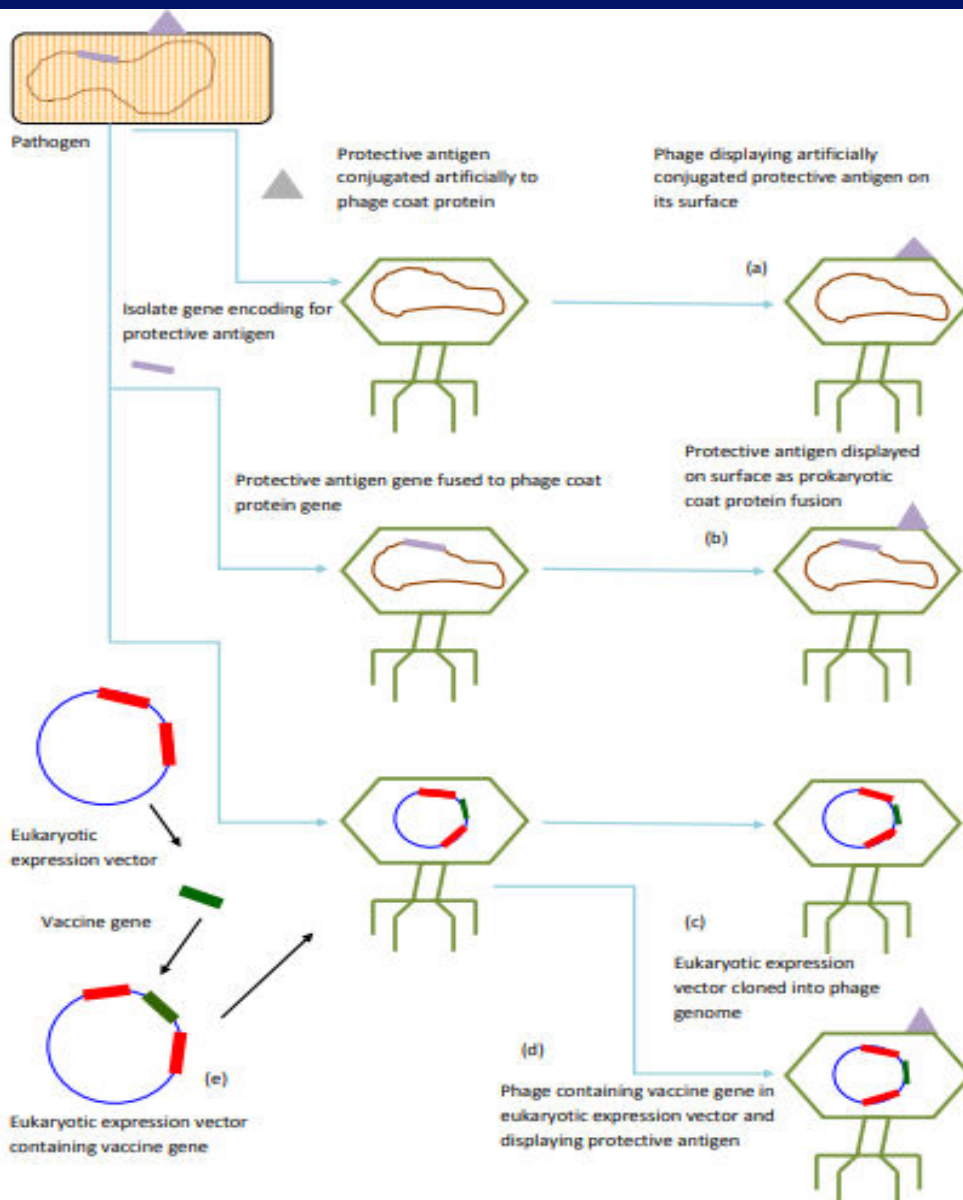


Figure 1 Phage-delivered vaccination techniques. Phage-delivered protein vaccine might inoculate host. (b) The host is injected with phage-delivered protein vaccine, but the protective antigen is prokaryotic coat protein fusion. Phage-mediated DNA vaccination of host. Hybrid phage vaccination delivers protein and DNA vaccinations to the host. Standard DNA vaccine host injection.

Bacteriophage bioprocessing and bio control

Phages may kill plant, fungal, and product-associated bacterial pests. Many plant pathogens have been controlled using

phages. Phages inhibit *Xanthomonas pruni*, which causes bacterial spot diseases in peaches, cabbage, and peppers. They also fight *Ralstonia solanacearum* in tobacco and *Xanthomonas campestris*, which stains tomatoes. Phages cure *Pseudomonas tolaasii*-caused mushroom bacterial blotch [7].

Phages may eliminate microorganisms in thermal power plant condenser tubes, preventing bio fouling. Bacteriophages minimize bacterial contamination in food, especially minimally processed foods where heat treatments may alter taste or texture. Controlling pathogens in fruits and vegetables is essential since processing may compromise their quality [8]. Phages prevent pathogens like Salmonella and Campylobacter on chicken skin, Salmonella enteritidis in cheese, Listeria monocytogenes on meat, and fresh-cut fruits without heat. Phage bioprocessing may prolong animal product shelf life. Phages decrease germs, improving food safety and preservation. Phages can manage pests, bio fouling, and bacterial contamination in bioprocessing. This study may lead to new microbial solutions for agricultural and food sectors [9,10].

Conclusion

Phages have several biotechnology and medicinal uses, as seen above. Phages may aid disease diagnostics, phage typing, phage vaccinations, and phage therapy. Phage mixtures may treat antibiotic-resistant microorganisms. Phages may show antibodies against bacteria and target and lyse bacterial cells individually. They can also deliver DNA or phage display vaccines. Phages can cure plant and fruit bacterial diseases and food spoiling. Phage usage has drawbacks. Phages must be safe, effective, and immune-responsive. Optimize phage growth and purification procedures. However, recent advances in biotechnology and molecular biology suggest that biosphere-abundant phages may solve many human problems.

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