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Phages- a novel remedy for future.

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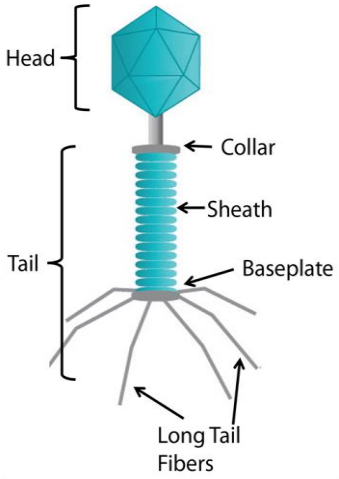
Introduction

Bacteriophages are the bacteria killers of normal flora with the diverse range of potential therapeutic actions. They were found to be highly host specific with self-replicating property and spread through bacteriolysis. It was first discovered in 1914 by Felix d' Herelle as potent agent to combat bacterial infections and diseases caused by them. But soon after the discovery of antibiotics and their highly effective action of curing any disease condition, phages therapeutic study was interrupted. Unnecessary usage of antibiotics in human, veterinary, agricultural and industrial practices has led to the serious problem of antibiotic resistance that we are facing today. Thus, this is the need of the hour to look for other alternatives to combat disease conditions in future like predatory bacteria, bacteriophages, herbal medicines, etc.

Properties of phages as the therapeutic agent-

- They have the ability to divide themselves in a way that they can determine their own dosage.
- Broad spectrum range of lytic phages that are highly specific in nature.
- They have the tendency to disappear after the elimination of host body.
- Diversified mechanism of action utilized to treat multi drug resistance bacterial strains.
- They can be coupled with proteins, antibiotics, etc and can be used for developing therapies.
- Shows efficacies towards biofilm producing agents.
- Modify themselves with respect to their host strains.



Mechanism of action :

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- Mutation-example-bacillus phages inhibiting recognition sites and cleaves phage genome by mutation in thymic containing restriction sites.
- Attaches to bacterial cell surface by recognition of specific receptors
- Co-evolution of phages and bacteria to modify lipopolysaccharide layer
- Phages evolution with respect to the hydrolysis of bacteria exopolysaccharide or capsules.
- Phages may alter or bypass epithelial cell layer permeability to enter the host body and provides antibacterial immunity.
- They sometimes even activate the antimicrobial response by reacting with the RNA and DNA sensors for mutation and several other pathways.

Different applications of phage therapy-

- Bacteria biosensing
- Gene transfer
- Vaccine adjuvants- induces both humoral and cell mediated type but are proved less immunogenic till date.
- Nanocarriers of vaccines-phages particles like genome or empty capsids are packed with the therapeutic agents to alter the eukaryotic cellular machinery
- Drugs and therapeutics
- Therapy for cancer and tumors-by using recombinant technologies by bioconjugation in which capsid of phages are conjugated and act as the carrier molecule.
- Treatment of degenerative diseases- it has seen that the bacteriophages crosses the blood brain barrier that provides immunity against microbial infection. Example- M13 filamentous phages used for Parkinson and Alzheimer disease diagnosis.
- Anti-biofilm agents
- Surface disfectant
- Food preservation

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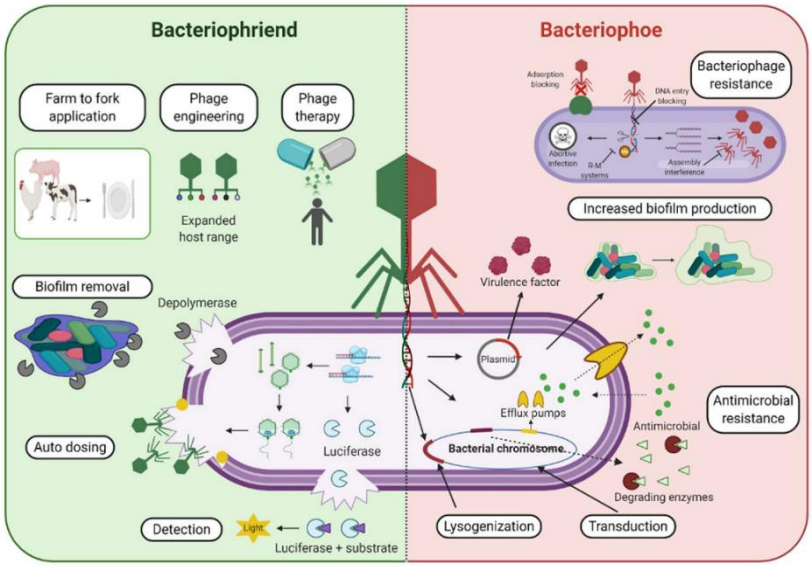

Phages therapy developed for animal pathogens-

Phage	***Host***	***Infection***	***Description***
vB_EcoM-UFV13	Biofilm forming *Trueperella pyogenes*	Mastitis, metritis, and endometritis in cows leading to economic losses.	Effective biofilm disruption was observed using UFV13
vB_VspP_pVa5	*Vibrio splendidus*	Disease and mortality in fish and bivalves.	In aquaculture *V.splendidus* can be efficiently controlled by using lytic vB_VspP_pVa5
Phage preparation FBL1	*Bacillus licheniforis*	Mortality of the pacific white shrimp (*Litopenaeus vannamei)*	Inhibit growth of the host and also the biofilm formation.
A cocktail of 4 lytic phages of E.coli	*E. coli*	Mastitis in cows reducing milk yield	Broad spectrum and hinders the growth in raw milk

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Phages therapy developed for foodborne pathogens-

Phage	Host	Infection	Description
SE07	*Salmonella enteritidis*	Foodborne infections	Reduction in pathogen colonies in food like eggs, juice and meat
Campylobacter jejuni lytic phages	*C. jejuni*	Contaminated poultry meat	Effective reduction of organism in low temperature.
phiLLS	MDR E. coli	Foodborne diseases	Shows lytic action against the strain
phiE142(Myoviridae)	MDR E. coli O157:H7 and *S.enterica*	Foodborne diseases	Successfully lyse both the strains.
Vpp1	*V.parahaemolyticus*	Causative agent for gastroenteritis in human via consuming infected sea food	Effectively used in oyster depuration to reduce the infection in infected oyster.

Future prospects-

Bacteriophage biocontrol stratergies are more natural and traditional approach to safety and preservation of food, animal and human body. But unfortunately, the technology is still limited to the laboratory trials, animals or horticultural crops. There is considerable commercial interest in phages related to human medicine and animal disease control. More value is given in the foreign countries like biophage company of north America and intralytix involved in food preservation. Intralyix has food additive petition (FAP) pending with U.S. food and drug administrator to allow *Listeria monocytogenes* specific phages on food to reduce risk associated with foodborne condition.

The best thing about phages is that they have restricted host range in respect to diversified bacterial susceptibility. The more advance approach is being made using cocktail therapy to widen the host range with complementary activities. It can be used as a hurdle approach.

As Campbell said-

"Bacteriophages research is now undergoing a renaissance in which the primary focus is the pheges themselves rather then the molecular mechanism.