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PHAGE THERAPY

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Bacteriophages (phages) are the viruses of bacteria. Since immemorial times they have controlled the growth and spread of their bacterial hosts. Bacterial viruses are the ubiquitous lifelike entities in our biosphere. They can easily be found: in sewers, rivers, or patients urine and stool. When a strictly lytic phage adheres with its tail fibers to the surface of its target bacterium, it ejects the phage genome into the periplasm of the bacterial cell. The bacterial DNA and protein synthesis machinery is takeover to build copies of the phage. After a latent period, the newly formed phages burst out of their bacterial hosts, which are killed in the process. The phage progeny then go off to find new host bacteria to infect. Such phages can be considered as self-replicating antimicrobials. Phages have evolved only to infect certain bacteria and are harmless to mammalian cells.

Phages exhibit a number of properties that differ from antibiotics and hampered their development as pharmaceutical products. First, they tend to be specific about which bacteria they infect. Therapeutic phages can thus be selected to mainly kill one bacterial species or a clinically relevant subgroup, and spare the patient's beneficial bacteria. Most routinely employed antibiotics, in contrast, have a broad spectrum of activity, which can cause "collateral damage" to the patient's commensal microbiomes, which in turn can result in adverse effects such as the selection of antibiotic resistant bacteria species or antibiotic-associated diarrhea. Second, bacteria and phages are involved in a host-parasite relationship. Strictly lytic phages are ubiquitous in the environment and require the death of their bacterial host to complete their life cycle. Phages impose selection for resistant hosts, which in turn impose selection for effective phages. This results in what is called "antagonistic coevolution," an arms race between bacteria and phages, characterized by reciprocal evolution of bacterial resistance and phage infectivity. Bacteria can also become resistant to phages, but, in contrast to static antibiotics, phages have the capacity to overcome bacterial resistance.

In summary, phages have several characteristics that make potentially attractive therapeutic agents in clinical settings. Granted, many of these studies do not meet there current rigorous standards for clinical trials and remain many important questions that must be addressed before lytic phages can be widely endorsed for therapeutic use. However there is a sufficient part of data that need to find alternative treatment modalities against rapidly emerging, antibiotic-resistant bacteria – to warrant further studies in the field of phage therapy.