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Can Bacteriophages be used as New Medicine in the Future?

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ABSTRACT

Bacteriophages have the potential to change the world. These small biological entities can change medicine in a big way. With a new wave of superbugs that have hit the Earth, antibiotics are falling behind as researchers need to make newer antibiotics to attack these new superbugs. These antibiotics take time to create, and in the long run, will become harder and harder to make. These drawbacks make antibiotics less favorable. Bacteriophages have the potential to be something new, and effective. With bacteriophages, that problem can be solved. Bacteriophages are small viruses that specifically target bacteria. They will not attack normal human cells, and that allows the immune system to also attack the bacteria with help from the Bacteriophage. They are organisms, so they can evolve, and since they are viruses, they can reproduce on their own. Bacteriophage research is still not 100% complete, but with the technology we have, we can start using phages in more severe cases of bacterial infections. Though it takes time to prepare, it only takes one or two doses to control an infection. A person can recover in a few days, with symptoms ceasing within 24 hours. The pros that bacteria bring to the table far outweigh the cons that come with phage therapy. With antibiotics falling behind in the modern world, it may turn out that bacteriophages can change the whole world of medicine. One of the only helpful viruses for mankind, there is almost nothing deadly about bacteriophages toward humans. Bacteriophages have the potential to become something big and change the antibacterial field forever.

Introduction

Most people in this world would know about the main medicine for fighting off bacterial infections, antibiotics. Antibiotics are generally effective in their task of killing bacteria, by attacking and breaking apart proteins in the bacteria's cell membrane. Even with the success of antibiotics, there may be a medicine better, bacteriophages. Bacteriophages are little viruses that target only bacteria. Bacteriophages only target a specific bacterium. This makes it so bacteriophages do not target human cells. This is a very targeted approach, killing only bacteria, and nothing else around it. This is still an experimental strategy, as many things can go wrong with bacteriophages. Looking into this further could revolutionize modern medicine. One big problem with antibiotics is that they kill everything around the bacteria. This includes friendly immune and tissue cells. Bacteriophages do target any other cells, other than their target. Bacteriophages could also be more effective than antibiotics when it comes to superbugs, bacteria like methicillin-resistant Staphylococcus aureus (MRSA). Also, the concentration of bacteriophages needed to fight off an infection would be way less than the concentration of antibiotics. It only takes one bacteriophage, or one dose, that would be enough to eliminate a threat. With antibiotics, since they do not reproduce or multiply, it takes multiple doses to eliminate the full threat. This brings up a new problem, antibiotic resistance. If antibiotics are used too much, then bacteria can build up resistance, and this can cause a patient to require hospitalization. Bacteriophages reproduce and multiply, allowing a single dose of phages able to eliminate an infection. It is hard for bacteria to build up resistance, as resistance is based on evolution. If the first dose is effective but slow, then a second dose can speed up the process. These superbugs have immunity to these antibiotics, so phage therapy would be more effective. There are limitations to phage therapy, especially since bacteriophages are still organisms. One major problem is that since bacteriophages have a narrow host range, it takes a bit more time to prepare and test a certain bacteriophage for

treatment. Another thing is that phages also have two mechanisms of invasion, lytic and lysogenic. Lytic is the pharmaceutical one, able to kill bacteria quicker, but since some are lysogenic, they are not able to kill bacteria quickly. Even with these limitations, bacteriophages are an almost perfect medicine to combat bacteria. With a few more years of research, bacteriophages could be the future, where they could work together with antibiotics or completely replace antibiotics.

Background on Bacteriophages

Bacteriophages are the most abundant organism on Earth, with about 10^31 viral particles in the population. They are very dynamic, with 10^23 phage infection every second. Bacteriophages are a fast-growing and active population, and they seem to not be slowing down as bacteria still exist in this world. Phages have been around for 3 billion years, which is about ¾ of Earth's history (Hatfull, 2011). They are continually evolving and changing to respond to new bacteria. Bacteriophages target only bacteria, and nothing else. They only target specific types of bacteria, and considering the vast number of bacteria, it's interesting how they do it. The structure of the bacteriophage is key to finding out how they infect their hosts. As seen in Figure 1, the capsid, or the head, is where DNA is held. The capsid is usually an icosahedral shape, which is 20 faces. There are many different types of shapes, but the majority have an icosahedral shape. The protein wall is made up of individual capsid proteins, about 60 of them. They are all monomers, which are attached in the icosahedral shape. The capsid is devoid of ribosomes on the protein wall, leaving just the individual capsid protein. The capsid is attached to the contractile sheath or the tail. This is when DNA passes through to get inside of a host. The tail can be found in many different types, and it is usually the shape of the tail and the type of DNA that classifies a bacteriophage. The bottom of the tail is called the baseplate hub. The baseplate hub is the part of the phage that locates its target. It controls the tail fibers, and when it recognizes a specific protein on a wall of bacteria (Harada et al., 2018).

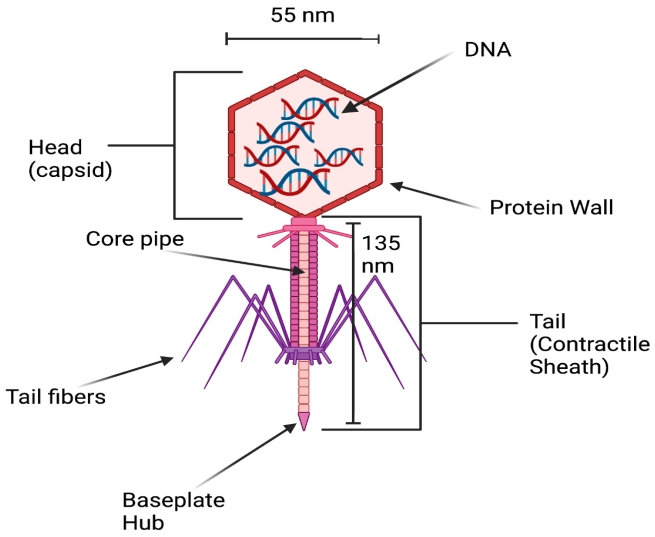


Figure 1. The structure of a bacteriophage shown above the tail is 135 nanometers and the head is about 60 nanometers. The molecular weight of the bacteriophage is 106 Da.

Viruses are basic, a protein membrane surrounding the virus's DNA. Bacteriophages are similar, but they do have an obvious difference. With the capsid being similar to viruses, the rest of the bacteriophage is not at all similar. It leads to a different way to build bacteriophages. As shown in Figure Two, the life cycle of a lytic bacteriophage has six steps: absorption, penetration, replication, maturation, release, and reinfection. A lysogenic bacteriophage has a different cycle, where absolution and penetration are the same, but instead of immediately hijacking the host, the bacteriophage DNA goes and sits among the host DNA, replicating and being passed on to daughter cells. Then the

DNA is in multiple bacteria and will start to be expressed and eventually lead to multiple bacteria being lysed at once. Absorption is when the bacteriophage attaches to the bacteria cell membrane. Sites on the phage attach to sites on the bacteria wall, like pili, flagella, proteins, specific receptors, or sugar transporters. Since each bacteria has different site shapes, a strain of bacteriophages can only attach one type of bacteria. Penetration is when the bacteriophage sends its DNA into the bacteria by drilling a hole in the wall. The drilling is done by enzymes, known as lysins. Then the phage's contractile sheath enters the bacteria and sends in some DNA. Replication is next, and this is when the genome of the phage and enzymes coded by the phage shut down the synthesis of macromolecules of bacteria, like DNA and RNA. The bacteria's metabolic machinery is then used to replicate and use the phage's genome to construct parts of phages. The enzymes used to break in and hijack the bacteria are also made by the bacteria. Then is maturation, when the parts that are made, proteins and enzymes, come together and build hundreds of phages. Monomers that are made are made into polymers of long protein chains. Release is when a lysogenic enzyme, made by the phage, is used to break the peptidoglycan and cause osmotic lysis, and the intact phages inside of bacteria are released. These lysins target the integrity of the cell wall and are designed to attack one of the four major bonds in the peptidoglycan. This activity can either be an endo-β-N-acetylglucosaminidase or N-acetylmuramidase, both of which act on the sugar bindings of the bacterial wall, an endopeptidase, which acts on the peptide bindings, or an N-acetylmuramoyl-L-alanine amidase, which hydrolyzes the amide bond connecting the glycan strand and peptide bindings (Fernandes & São-José, 2018). The last step is reinfection when all of the bacteriophages released go and infect other bacteria nearby. The average chance of reinfection is very high, nearly 80-90%, because of how bacteria live in colonies, so they are close to each other, and thus newly released phages have a high chance of reinfection.

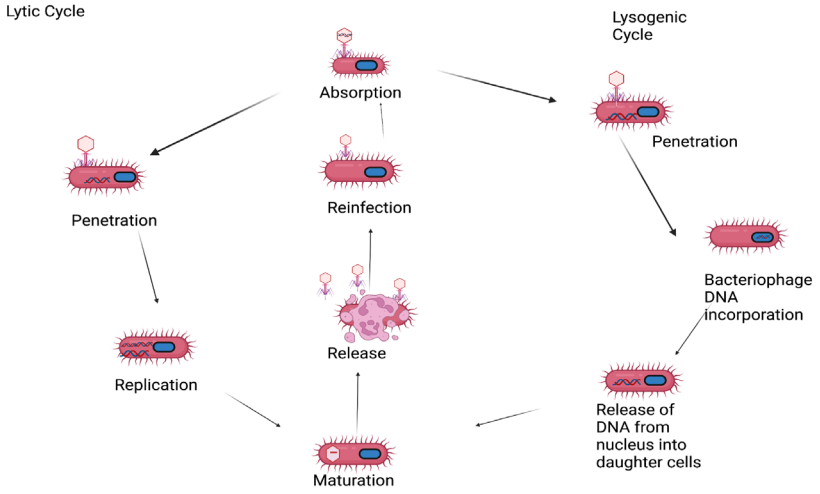


Figure 2. Life cycle, or update process, of a Bacteriophage. There are two processes shown in the life cycle. The faster, more pharmaceutical cycle is the Lytic Cycle.

Genome of Bacteriophages

As bacteriophages are the most abundant organism, they do have a very wide variety of genomes, they are also continually evolving, leading to a new change in DNA. One thing about bacteriophages is their size, and as they are really small, they can't carry a lot of DNA. Even though they are small it may be easy to split them apart, out of more than 5,000 lab phages, only about 750 of those phages have had their genomes sequences. About 70% of those phages correspond to about 12 bacterial hosts, howling how many individual phages target one. It shows how big their population truly is. With all their differences, they are split apart into different families. The biggest family is *Caudovirales*, with about 50% of the bacteriophage population. Other notable families include *Belfryvirales, Halopanivirales,*

Haloruvirales, Kalamavirales, Ligamenvirales, Tubulavirales, and *Norzivirales* (Contributors, 2019) All of the viruses in these families have some differences, whether it be a type of nucleic acid, morphology or corresponding bacteria. Some of these families only have one order of bacteriophage. The difference between a phage from *Ligamenvirales*, Acidianus filamentous virus 1, and a phage from *Norzivirales*,

MS2 is found in their morphology and nucleic acid. AFV1 is an enveloped, rod-shaped phage with Linear dsDNA, and MS2 is a nonenveloped, isometric phage with Linear ssRNA. Some have similarities, with the only difference being their target. A phage from *Belfryvirales,* Sulfolobus turreted icosahedral virus 1, and a phage from *Halopanivirales,* Haloarcula virus HCIV1, are pretty similar. Both are enveloped, icosahedral and both have Linear dsDNA. So, the nucleic acid does make a difference when classifying phages. There are differences between the different types, Linear dsDNA, Circular ssDNA, Circular dsDNA, Linear dsRNA, and Linear ssRNA. According to Figure 3, Linear and circular refers to the shape of the nucleic acid, it can be held in a circle or a linear shape inside of the capsid.

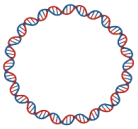
Types of Phage DNA	Image	Example of Phage
Linear dsDNA		Turriviridae
Circular ssDNA		Microviridae
Circular dsDNA		Corticoviridae
Linear ssRNA		Blumeviridae
Linear dsRNA		Picovirnaviridae

Figure 3. Types of nucleic acids within bacteriophages. There are 5 main types, and they work similarly. The most common types are Linear dsDNA and Circular dsDNA. Researchers can use these types of DNA to distinguish between types of bacteriophages.

The ds, or ss refers to double or single-stranded nucleic acids. Double-stranded DNA is the most common form of nucleic acid found in organisms and is the DNA found in humans. Single-stranded DNA is not as common, but it looks like RNA found in humans but has different nucleobases, with adenine, thymine, cytosine, and guanine. Single-stranded RNA is the same RNA found in humans, with the nucleobases adenine, uracil, cytosine, and guanine. Double-stranded RNA is not as common, as RNA is usually found single-stranded. Bacteriophages do organize the DNA they have in their body, as DNA is made up of genes and those genes are organized so they can be expressed when needed. This is where mosaicism comes into play. Mosaicism is the shape and how DNA can be switched around between different phages. Phages do take part in horizontal gene transfer, where genes are mixed around and placed into different places through different generations. Mosaicism is a big part of studying phage evolution, as it shows what genes have been replaced and what genes have been added. It's like a mosaic, where the entire picture is made up of little bits and pieces (Hatfull & Hendrix, 2011). Mosaicism shows the differences that bacteriophages have gone through, as shown in Figure 4. There are similarities shown between the 3 different phage genomes.

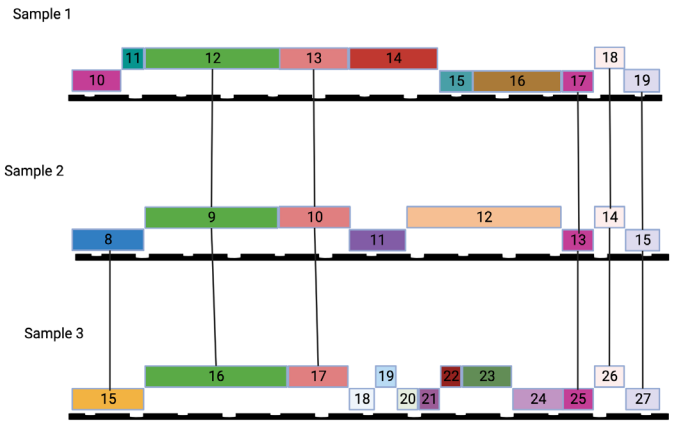


Figure 4. Mosaicism is shown between 3 different samples of bacteriophage genomes. The similarities are shown with the lines, and some genomes are the same throughout all three. They can be in different places of the genome but still express the same thing.

Mosaicism shows how bacteriophages have evolved over their 3 billion-year history. Bacteriophages came from early life forms, which at that time, were bacteria and other unicellular organisms. They have evolved alongside bacteria, constantly changing in response to their hosts. If phages want to be able to infect their hosts, they must keep evolving constantly, as bacteria evolve constantly, and some bacteria build resistance to phages. So phages have to evolve so that the bacteria that had a resistance doesn't anymore. It's kind of like how we have to constantly change our antibiotics in response to new superbugs, especially tuberculosis and MRSA.

The Spread of Information by Phages

Phages are a key player when it comes to bacterial evolution. This is because of horizontal gene transfer that takes place between phages and bacteria. Phages are thought to affect the evolution of 10-50% of bacteria and 50-100% of bacteria in areas unfriendly to protists. When phages put their DNA into a bacterial host, they sometimes take some out with them, like how bees get pollen on them when they drink nectar. Since lysogenic phages implant their DNA inside bacterial hosts, the bacteria can develop some virulent genes and express those traits. Some of the bacteria that were affected by the lysogenic will die, while some will incorporate it and express those virulent traits. The main method of spreading genes is endocytosis and exocytosis. Endocytosis is when a cell uses vesicles to take in an outside thing, like nutrients or pathogens, and brings it inside to either use or destroy. This can help bacteriophages because eukaryotic cells aren't affected by phages, and so phages can use these cells as a way to travel around an organism. Also, endocytosis is what allows bacteriophages to sometimes enter bacteria, and then exocytosis is how they get out. Exocytosis is when something is put into a vesicle, and it is taken out of the cell and sent out. This helps the bacteriophage move around eukaryotic cells. It allows them to spread more information to other bacteria. Bacteriophages can only target one type of bacteria. There are some phages that all target one similar strain of bacteria, but since each strain is different, phages usually target their type of bacteria. They have to identify their targets somehow, or else they won't be able to attack them. They locate their target by using their tail fibers. The tail fibers are the part that helps the bacteria move around and help feel for the necessary attachment points. As each bacteria is different, even if one protein is not correct, the phage can't stick and infect that bacteria. The fibers are feeling for points like lipopolysaccharide, porin transmembrane proteins, teichoic acids, organelles, or other things that are found on the cell membrane. As bacteria evolve, their main way of fighting off phages is to change those proteins or receptor sites found

on their cell membrane. If a phage that usually targets this type of bacteria comes across bacteria, then the phage wouldn't be able to do anything, as the shape of the capsid and the tail fibers would not allow the bacteriophage to attach. It has to be exact or else it would not work.

Bacteriophages and Antibiotics

Bacteriophages and antibiotics both play the same role, killing bacteria. They are different, one is made in a lab or by other microbes, while one is a living organism. Another difference is that once a phage is attached, it cannot be undone. When an antibiotic enters a bacterium, there are protein pumps, known as effluxes that can get rid of the antibiotic. They also kill their targets very differently. Bacteriophages are viruses, so they will inject their DNA and make the bacteria make more phages. Antibiotics do it differently. Some antibiotics enter the body, and disable the bacteria's cell membrane, lysing it. This type of death is done with DNA gyrase inhibitors, which target the production of gyrase within a bacterium, a necessary enzyme for ATP production. Treatment with rifamycins is next, which inhibits RNA synthesis, which is dependent on DNA. The cell wall synthesis inhibitors are next, which damage the structural integrity of the cell wall, making it looser and pretty weak. Damage to ribosomes, protein mistranslation, and damage to cellular energetics follow protein synthesis inhibitors. All of those steps are done in one medicine, or with multiple medicines and multiple doses (Kohanski et al., 2010). Another way of death is when a lethal amount of antibiotics are sent into the bacteria, which causes a harmful amount of hydroxyl radicals to be produced by an oxidative damage cellular death pathway, interfering with the TCA cycle and iron metabolism. Other antibiotics interfere with the bacteria's ability to reproduce and make nutrients. One example of an antibiotic that disables the cell wall is penicillin-type antibiotics like, amoxicillin and flucloxacillin. One example of the other type is tetracycline. Antibiotics kill in many different ways, but these are just two of the many ways. Some pros of antibiotics are that they are very easy to prepare and prescribe, instead of the long time it takes to prepare and test bacteriophages ready for human consumption. Another thing about antibiotics is that they are not specific to one strain of bacteria, as they target parts of the bacteria that are found in many different strains of bacteria. If the bacteria has a cell, then the cell wall protein is inhibited, leading to structural damage. Bacteria evolve fast, and that leads to a major problem with antibiotics. Many people think that they can just take more antibiotics so that their illness goes away, but when a person does that, it can lead to new "superbugs" that are immune to the antibiotics we have today. One common example of a superbug is Mycobacterium tuberculosis, which causes tuberculosis, and can evolve so much that TB can be immune to any antibiotics we have today. Another con is that antibiotics can affect our immune system and tissues. If antibiotics are used over a long period of time, antibiotics can damage someone's immune system. Since antibiotics don't have an off button till all the medicine is used up, they can go and target cells that are already fighting the bacteria, damaging anything around the site of infection. Phages don't have that problem, as phages can only attach to specific points on specific bacteria. Bacteria have also made ways to counteract bacteria, and there are seven different ways they can fight back. One is the efflux, which is a protein pump that is used to pump out any antibiotics that are inside of the bacteria. For the majority of bacteria with the pump, the pump transports the antibiotic out of the cytoplasm and into the periplasmic space using a transmembrane proton gradient. One major con of antibiotics is that they cannot adapt or change if reinfection occurs. Meanwhile, phages can readily adapt and evolve inside our own body and can be ready to fight off a new, evolved bacteria. As shown in Figure 5 below, antibiotics have a completely different structure than bacteriophages, since antibiotics are lab-made and are semisynthetic compounds.

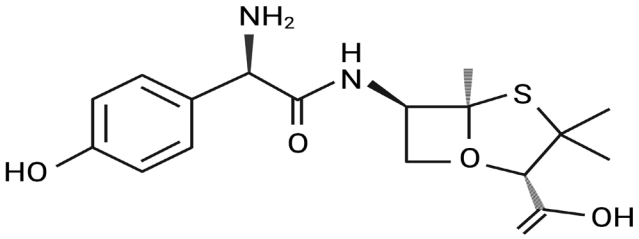


Figure 5. Structure of amoxicillin, an antibiotic. Antibiotics are chemical structures, far different from bacteriophages.

Pencillines, for example, are made naturally but the medical penicillin is made with natural compounds and other compounds. The beta-lactam antibiotic is made with natural penicillin, cephalosporins, and carbapenems. If an antibiotic is fully synthetic, then it is known as an antibacterial, such as sulfonamides, quinolones, and oxazolidinones. Since both antibiotics and bacteriophages kill bacteria, they can be put together and used as a combination to fight off a bacterial infection. When both are used, the treatment is known as Phage-Antibiotic Synergy (PAS) (Liu et al., 2020). This is highly experimental, and multiple outcomes can occur. One thing that could happen is that they act additively, where both of their efforts add up to the combinatorial efficacy. Another outcome would be that they work together, and their total efficacy is much greater than their individual efforts. The third result could be that nothing happens, due to a lack of action. A fourth outcome may be that there is antagonism, where the molecular action of one agent interferes with the other. These are all possibilities that can occur and must be taken into account. Now that antagonism could happen, before prescribing a synergetic treatment, *in vitro* assessments are taking place. This is to personalize the treatment and make it so that this patient can get treated with their special treatment. This does take a lot of time, as each patient prescribed this has to have their combination personalized, whereas antibiotics have a much wider range of hosts. There is still much work to be done on this topic of PAS, and it could become the next new prescription.

Phage Therapy

With bacteria becoming stronger and resistant to modern antibiotics, one possible solution is phage therapy. Phage therapy is the use of bacteriophages to fight off a bacterial infection. Bacteriophages Work pretty well against bacteria, and the success rate of phage therapy is very high. For the bacteria, *Staphylococcus, Pseudomonas, E. coli, Klebsiella, and Salmonella,* a total of 550 patients were treated, and the success rate was 92% (Sulakvelidze et al., 2001). Bacteriophage therapy is very successful, and there are very few side effects. Bacteriophages were somewhat discovered in 1896, with an English researcher named Ernest Hankin finding some sort of antibacterial agent in some rivers. The bacteriophage in that area was attacking the *Vibrio cholerae* and it was helping limit the spread of cholera. It took 20 years, in 1918, when bacteriophages were first used therapeutically. In 1919, a French scientist named Felix d'Herelle first used bacteriophages to fight off dysentery found in hospitalized patients. All the researchers who made the medicine ingested it to ensure it was safe, and then it was used on a 12-year-old boy with severe dysentery. All the symptoms ceased within one day, and the boy fully recovered in a few days. As shown by many Soviet experiments, bacteriophages were successful with most types of bacteria, and success rates were usually above the success rates for antibiotics (Sulakvelidze et al., 2001). There are many benefits to phage therapy, and one of those is the low dosage rate. (Loc-Carrillo & Abedon, 2011) As shown by d'Herelle, it only took one dose of phage therapy to fight off the disease. It was very fast to take out the bacteria too, as many patients felt symptoms ceasing within 24 hours and completely recovering within a few days. Many non-English papers were published all about phage therapy and how

effective it was. Even back then, when they didn't have the same technology, they were able to find a way to use these bacteriophages for their benefit. Now that we learned a lot more, it does take more time to prepare a phage therapy, but the longer preparation time comes with a faster, and easier way to recover from a disease. Even though phage therapy sounds great, there are a few drawbacks. One major drawback is that there may not be enough phages. Phages are foreign substances, and the immune system may target the phages. This is planned so that phages can get rid of the infection and then the immune system will get them. However, sometimes the immune system strikes fast and early, killing many of the phages, and then nothing happens. Evolution can also be a drawback, as phages also have to evolve to keep up with bacteria. Sometimes, phages do not keep up with bacteria, and then the body's immune system gets rid of the phages and what's left are bacteria that are now stronger. Phages can also pass information around, and some of that information can be used to combat phages or antibiotics. Usually, phages are used alone, but with new tests using PAS, phages may spread information that could lead to bacteria becoming resistant to antibiotics.

Research Techniques Using Phages

Phages are the most abundant organisms in the world, and they have been on this Earth for 3 billion years. Any organism that has been on Earth for that long has to have gone through evolution. Species change all the time, and that is evolution coming into play. We can use phages to learn more about the early organisms that were around during that time. Phages can also teach us a lot about proteins and how they work together within an organism. A technique called phage display shows us how the proteins and all the bonds in phages work together to build a bacteriophage. Phage display is an in vitro screening for identifying ligands for proteins and other macromolecules. This is super helpful, as we can now artificially make these ligands if we need a specific response from the cell. The whole point of phage display is the ability to express peptides and protein sequences as fusions to the coat proteins of a bacteriophage This is using different proteins to see which ones bacteriophages respond to. This can allow us to choose which page to use if we need to attack a certain bacteria. This method is also very useful to isolate and discover new phages. Since it's hard to tell the difference between phages with just your eyes, the phage display can be used to isolate and count new phages. Phage display was first found and used in 1985, and ever since, we have been improving on what the early researchers have done. With phage display being one of the ways for phage enumeration, there are multiple other ways phage enumeration can take place. One of the methods that is used is called Double Agar Overlay Assay (Ács, et al., 2020). This method is done with virulent phage particles. This method allows phage-host interactions in a confined environment. The environment is a double-layered Petri dish containing two layers of agar. The bottom is prepared with a medium supporting bacterial growth, for the *E. coli* bacteria where the common medium is lysogeny broth and brain heart infusion. This layer contains 1-1.5% agar. The top layer has the same medium, but with a lower concentration of agar, about 0.4-0.6%. This "soft agar" is mixed with the bacteria, and poured onto the bottom layer, creating a lawn. Since the top agar has a lower concentration, diffusion occurs and that allows the bacteria to go to the bottom and it allows phages to go through and bind to the bacterium. Samples containing bacteriophages are added to the top of the second layer, and dried or mixed in with the bacteria. Then the petri dish is incubated, for *E.coliI,* the incubation temperature is 37℃ overnight. If the phage is capable of infecting the bacteria, then little clear spots, known as plaques, will form containing lysed bacteria and phage particles. We are looking for single plaque zones, which are small. A single plaque zone is when a single phage infects a bacteria and the progeny phages infect nearby bacteria. Large clearing zones may be the result of other antimicrobial agents, and so the small plaques are the ones with phages. If a phage does not create a plaque, that area could be covered in even a smaller concentration of agar, as larger phages can move through a softer environment. Other divalent ions can also be added, like CaCl2 and MgCl2. These ions can help facilitate phage formation by aiding phages in absorbing themselves into the bacteria receptors. With the serial dilutions on a lawn, an ineffective phage can be spotted and the concentration of those phages can be determined. This concentration is expressed as a PFU, a plaque-forming unit, which is analogous to the colony-forming unit. This is one of the many methods that can be used to find out which bacteriophages would be helpful for medical uses.

Phages and Cancer

Phages attacking cancer cells is a really interesting topic, as bacteriophages attack bacteria. Cancer cells are eukaryotic cells, not bacteria. Eukaryotic cells also have very different protein markers on their cell membrane, which easily distinguish bacteria and eukaryotic cells. It is still very experimental, but it seems like it is possible. There was an experiment where bacteriophages, like the T4 phage, could express a KGD peptide with an affinity for the β3 integrin and can bring eukaryotic cells that carry this cellular marker with high specificity. This integrin is very common in cancer cells, and it could be one of the leading factors for metastasis. If phages can bind to this protein, then the phage might be able to lead to the inhibition of the tumor cell spread. The experiment was a success, and the T4 and HAP1 (a substrain of the T4) were able to bind to mouse and human melanoma and lung cancer cells. This experiment was able to show how the cancer cell metastasis was stopped. The binding was mediated by the GP24 capsid protein, which contains the KGD with the β3 interim, which is highly expressed on the surface of tumor cells (Bacteriophage Mediated). Another phage that could work would be the PK1A2 phage, which was shown to be able to penetrate kSK-N-SH human neuroblastoma cells (Petrov et al., 2022). The phage can bind to the polysialic acid that is secreted by the cell, and enter the bacteriophage. So, it seems that bacteriophages can go and attack certain cells, even if they are not bacteria. This could lead to the possibility of a cancer vaccine, which could revolutionize the medical world. As cancer is probably one of the leading causes of mortality in the world, a cancer vaccine could eliminate all of that. Using phage display, we can find out which phage could be suitable for a cancer vaccine. The best one so far is the T4 phage, but many others have been used. A cancer vaccine could be possible, and if it does come out, then it could change the whole world forever. Bacteriophages have that much of an impact on the world, and from just attacking small, simple bacteria, they can attack and maybe even eliminate one of the world's leading causes of mortality.

Conclusion

Even though bacteriophages are small, they can have a big impact on this world. They can change the entire medical field. Now that more superbugs are appearing, the need for bacteriophages and other alternatives is rising. Bacteriophages have risen to the occasion and they have shown that they can eliminate entire bacterial populations within the human body. Tests have already been done, and the effectiveness of bacteriophages over antibiotics cannot be underestimated. Bacteriophages are not fully ready yet, but they could replace antibiotics in the future. We could have them work together with PAS, but the outcomes are uncertain. A lot of different things could happen with PAS and with bacteriophages. Bacteriophages have pros, and one of the biggest pros is that they can evolve and keep up with bacteria, which means that there is a low chance that bacteriophages would ever get beat by bacteria. Another big pro is that phage therapy is quick, and an entire infection can be wiped out with one dose. There is a long way to go with bacteriophages, and more research can be done. If we focus our research on bacteriophages and learn more about them, we could have a very strong defense against bacteria. More research should be done toward learning about more and more phages, as we do not know a lot of phages, and we don't know what bacteria they are strong against. As more and more research is done in this field, we may have a massive change in the medical field when it comes to fighting off bacteria.

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