LESSON 4: BACTERIOPHAGES

The history of the discovery of phages was briefly mentioned in our time line, and we'll give more of the story in the next lesson. In this lesson we will focus on just the anatomy and physiology of phages. (Scientists like to use "phage" as it is shorter than "bacteriophage.")

The T4 phage is about 200 nm tall, and belongs to a group of phages called the "tailed" pages. What looks to you like a stem is called the tail. The head is the capsid, and it does look like a head. Some phages have a collar right below the head, and some even have some whiskers coming out from the collar. (The whiskers do act like animal whiskers, somehow sensing the environment and pulling the tail fibers up if conditions are not right for successfully landing on a bacteria.) The stem part of the tail is called the "sheath." At the bottom of the sheath is a baseplate and attached to the baseplate are six tail fibers, which look very much like legs. The fibers have special shapes at their tips that match the shapes of certain parts on the surface of a bacteria, and this is what lets them find and latch on to the type of bacteria they can infect. Phages can't infect all bacteria, just one type. The receptors will only fit into one particular part in one species of bacteria. (Phage receptors <u>never</u> match any of the surface parts on human cells, nor any types of plant or animal.)

The capsid is packed full of DNA. It was packed under great pressure, so it is sort of "spring loaded" and ready to come streaming out when given a chance. The DNA is fairly long, but not the longest in the viral kingdom. The DNA has 169,000 "rungs" on its ladder. Each rung is called a **base pair** because it is made of two molecules called **bases**. The length of DNA is often written in bas pairs, like this: 169,000 bp, or even 169 kbp, where "k" stands for 1,000. The base pairs that make the rungs are [Adenine and Thymine] and [Cytosine, and Guanine]. They are arranged in a very particular order, so that they spell out a secret code that can be read by a little machine called a **ribosome**. (But wait-- T4 doesn't have any ribosomes, so what good is all that code? Hmm... it might have to borrow some ribosomes.)

Not all phages look like T4. Some have no tail or a very short one. Some have no tail fibers, or a long curly one. One phage is a long thin tube, looking more like the Tobacco Mosaic Virus than T4. All phages have names that are just letters and numbers. Besides T4 there's T2, T3, and so on up through T17. There's also a P series, an M series.

The T4 phage infects a very common bacteria called *E. coli*. ("E" is for "Escherichia." *ESH-er-RICK-ee-ah)* We have a type of *E. coli* living in our intestines and it is very helpful as long as the population doesn't get too large. However, there is also a type of *E. coli* that causes food poisoning. (By the way, did you notice that *E. coli* is always written in italic (slanty) letters? That's how scientists tell you that's their official classification name, using genus and species.)

E. coli is a rod-shaped bacteria that often has one or more tails called **flagella**. It has two membranes as a covering, and some poisonous strings of sugars sticking off the outside. These sugar chains have a very long name (lipopolysaccharides)so often they are called **endotoxins**. When a lot of *E. coli* die all at once and fall apart, these sugar chains can circulate in our bodies and make us sick. The T4 likes these toxic sugar chains, though, because that is one of the places it can get a grip on the bacteria.

Inside the bacteria we find: 1) a clump of DNA, 2) an almost invisible network of fine threads called the **cytoskeleton**, and, 3) most importantly, RIBOSOMES! Ribosomes are little machines that can read copies of DNA code. They are like factories can turn the DNA instructions into usable proteins that will become parts for the structure of a cell. Other types of proteins become additional machines, called enzymes. Enzymes are like little robots that only do one task. They might put two molecules together or take things apart.

After the T4's tail fibers latch on, the tail sheath contracts and out comes a protein needle to punch a hole in the bacteria's membranes, and also some packets of enzymes that will digest the "peptidoglycan" barrier in the middle, that is made of sugars and proteins. Then the DNA comes shooting out and goes inside the bacteria.

Once inside, the T4 DNA will follow the **lytic** cycle. The DNA will be read by little enzyme "robots" that will unzip the DNA and start making copies of one side. This copy of one side is called messenger RNA, mRNA. There will also be enzyme workers who will direct this process, telling the copier where to start and stop. The T4 DNA has 289 sections of code (called "genes") that each code for a different protein. There are even codes for making enzyme workers that will help very long protein strings fold up into their correct shapes. The shape of a protein is critical. Some enzymes are "inspectors" who find proteins that are folded wrong and get rid of them. And, most importantly, complete copies of the viral DNA are made.

When all the proteins have been made, they start to go together to make the virus parts: capsid, tail sheath, baseplate, tail fibers. Before the capsid is attached to the sheath, a little molecular motor on the bottom of the capsid pushes one of the DNA copies up into it. If we scaled up the motor to something we could see, this motor would be as powerful as a car engine! When about 100 to 150 new viruses have been assembled, the bacterial cell wall bursts open and all the viruses escape, ready to go off and infect 100 to 150 new cells. (This whole process takes only about 30 minutes.)

Other viruses follow a different path of infection, called the **lysogenic** cycle. The goal of this process is to have the viral genome hide for a long time, perhaps even years, but be ready to pop out at an opportune time, whenever that might be. The virus has instructions its DNA for how to fool the bacteria into adding the virus's DNA to its own DNA. A little enzyme machine cuts and stitches the two genomes to make one larger one. So when the bacteria begins to divide and make a copy of itself (the fission process), it copies that new version of the DNA with the viral genome in it. Presto, you then have two bacteria with viral genomes hiding inside. Then those two bacteria split, making four bacteria with viral genomes inside. And so on. At some point in the future, the viral DNA can come back out and start into the lytic cycle, where actual viruses are made.