So, two bacteria walk into a grungy bar. The bartender says, "We don't serve bacteria here!" And, the bacteria says, "But, we work here. We're staph."

"Why did the mushroom get invited to the party?" "Because he's a fungi."

LOL, I didn't have a good bacteria song, so I Googled jokes about bacteria. So, you're welcome for the dad jokes to start this episode. If you haven't figured it out, we're going to be talking about bacteria, archaea, fungi, viruses, and prions in this episode.

Welcome to the Cellfie life. This is Nikaela, and I wanted to thank all of you for listening, and rating, and reviewing, and subscribing. If you are enjoying the podcast and want to help support the production of it, I have set up a Patreon page where you can support the podcast for as little as 25-cents an episode! Which is \$1 a month.

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If you have questions, comments, corrections, please let me know. The best way to reach me is on Instagram @t-h-i-s- c-e-l-l-f-i-e life or the website cellfielife.com. I post the script notes on the site, and I post MCAT review questions on my story just about every day.

Now, let's talk about those tiny little prokaryotes.

Question (**Q**): Do you remember the difference between prokaryotes and eukaryotes? Simple Answer (**A**): Prokaryotes do not have membrane-bound organelles; eukaryotes do have membrane-bound organelles.

Okay, let's meet the pro's, and by the pro's I mean those amazing prokaryotes that can: Survive in extreme environments, form symbiotic environments, replicate in many different ways... Some can survive with oxygen and without, meaning they can adjust their metabolism to meet the demands of their environment. They are pretty cool!

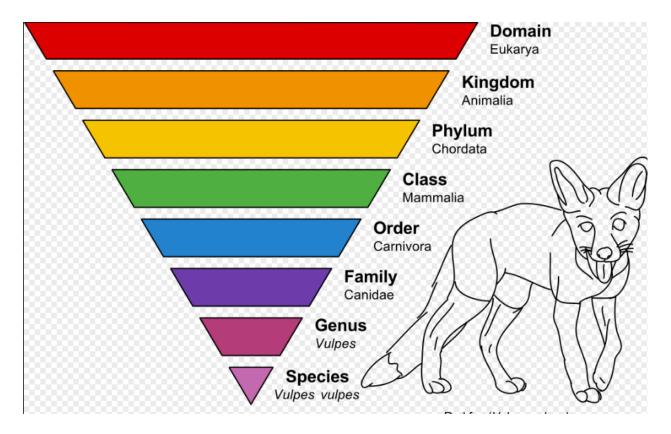
And, eukaryotes are the true nucleus, so are membrane-bound organelles—which is what our cells are—but we will talk about that next episode when we go into cells, specifically our cells.

So, prokaryotes are super simple: they don't have membrane-bound organelles, and their DNA is usually concentrated in an area called the nucleoid region.

We're going to talk about the pro's (the prokaryotes) but, first, let's do a quick rundown of taxonomic ranks.

So there are eight basic taxonomic categories; this doesn't include subspecies. Taxonomic ranks are just a way of classifying things in a step-down method where organisms are split into more specific groups.

The order from broadest to narrowest categorization **Domain Kingdom**, **Phylum**, **Class**, **Order**, **Family**, **Genus**, **Species**



How are we going to keep these taxonomic ranks in the correct order?

Obviously, we're gonna use a mnemonic device.

Dumb Kids Playing Cards On Freeway Get Smashed—I like this one because it sounds like a news headline.

There is also King Philip Came Over For Ginger Snaps! But, this one leaves out the domain.

Prokaryotes make up two of the three domains—and, remember, that domain is the first one listed on the taxonomic ranks. "Dumb kids playing cards on freeway get smashed..."

Domain, kingdom, phylum, class, order, family, genus, species.

- **Q**: Can you name the three different domains?
- A: Eukarya, Archaea, and Bacteria.

So, let's take a closer look at Archaea and Bacteria, both of which contain prokaryotes.

Actually, fun fact, there used to be only two domains: monera and eukarya. But, based on genetics, they separated into three domains.

Scientists looked at the 16s rRNA region, which is the region that I work with a lot for my research, so that's kinda cool. I'll go into more depth when we talk about genetics.

Archaea

So, archaea are similar to bacteria, but they are that badass aunt that rides a motorcycle, and travels the world, and makes friends wherever she goes. She helicopter-skis and swims with sharks. Some might even say she's a little extreme.

Archaea are archaic; they are ancient, and very well adapted, and can survive and thrive in extreme environments. They are extremophiles, thermophiles, [and] halophiles. Some are photosynthetic, but others can survive on things like methane gas and sulfur.

Archaea are in super harsh environments, high temps, cold temps, high salt, [and] low light. So, those hot springs in Yellowstone, and the Great Salt Lake in Salt Lake, and probably in the south pole—all these locations have archaea and have extreme environments.



https://gypsyguide.com/tour/yellowstone-grand-teton/

https://oceanwide-expeditions.com/blog/the-first-race-to-the-south-pole-in-50-years

Archaea are resistant to a lot of antibiotics and can be hard to target because of the similarities they have with eukarya.

Both archaea and eukarya start the translation with methionine and have similar RNA polymerases. But, archaea have circular DNA like bacteria and reproduce via budding or binary fission.

Both archaea and bacteria have flagella and come in different shapes and sizes. Basically, archaea and bacteria look similar which is why they have grouped the same origin and called archaebacteria.

Bacteria

Let us talk about bacteria. I will try not to get too excited or nerdy about it, but I really love the little guys.

What do you think of when you hear bacteria? Do you think germs and disease, antibacterial hand soap and gels? Maybe you're up on the current research that has really surged in the past ten years and think "microbiomes"? Specifically, [microbiomes] in your body. There are tons of bacteria in our bodies: about 10 times as many microbes in our bodies than human cells. And, the great thing about them is how helpful they actually are. Thus, all the studies on microbiomes.

The MCAT mostly focuses on human biology as opposed to microbiology, but there are some things we should be familiar with since they pertain to human health, disease, and treatment.

The first thing we brushed by is that bacterial DNA is circular and not membrane-bound; it just hangs out in a specific region. It can also have extra tiny circular non-chromosomal DNA called plasmids. We will talk more about that.

But, with bacteria, the basics are really with the shape. We still group bacteria based on shape. There are 3 categories to be familiar with:

Cocci is round. I think of this as a single grape. **Bacilli** are rod-shaped like a baguette. And, **spirilla** are spiraled like a corkscrew. It sounds like the makings of a lovely picnic.

Pop quiz time

Q: What was the spirochete that—we talked about in the *Embryogenesis II* episode—that can cross the placenta and hurt a fetus? Hint: Remember the T-O-R-C-H-E-S!
A: Here, we are talking about the S in the TORCHES acronym which is syphilis: *Treponema pallidum*.

And, while we're talking about spiral bacteria, I want to mention the big three spirochete bacteria are pathogenic.

Borrelia burgdorferi is Lyme disease.

Treponema pallidum—which is syphilis.

Leptospira interrogans: In humans, this bacteria is more of [an] accidental infection. It causes what is known as Weil's disease. It is contracted from coming in contact with infected animals, specifically their urine and blood, among other things.

How are we going to remember these...? **BLT**? **BLT** is not only for **b**acon, **l**ettuce, and **t**omato sandwiches. It's also for the spirochetes that are pathogenic in humans.

B: *Borrelia burgdorferi* - I remember this one because I think of the store Burgdorf's in NYC. Not that the two are not exactly related. But, Burgdorf's is in NYC, and Lyme disease is prevalent on the east coast, including New York.

Lyme Disease Maps: Historical Data | Lyme Disease

L: *Leptospira interrogans*. So, this spirochete looks like a question mark when viewed under the microscope. And, when you are interrogating someone, what are you doing—asking them a lot of questions? So, this interrogans looks like a question mark.

[T]: *Treponema pallidum*: I don't have a great one for remembering this one... I did some Googling and did not come up with anything significant. The best I have is that treponema sounds like a worm to me. I have no idea why, at some point, I decided that treponema sounds like a worm, and, a worm relates to syphilis. I don't know why my brain makes that connection.

If you have a great way to remember that *treponema pallidum* is syphilis, please let me know, so I can share it.

So, there we have our spirochete **BLT**. LOL, I hope you're hungry! Along with the shape of the bacteria, we look at how they cluster or group together.

Strepto means they are in a line or a twisted chain.

Staphylo is bunched up in a group like a bunch of grapes.

Diplo means they are partnered up. Diplo.

So, now we know that bacteria are prokaryotes that don't have complex membrane-bound organelles—but, rather, have circular DNA chromosomes—and are named after their shape and how they group. Now, let's talk about bacterial cell walls.

Bacterial Cell Walls

There are two types of bacterial cell walls: One has two membranes with a thin cell wall in-between them Two has a thick cell wall and then a membrane.

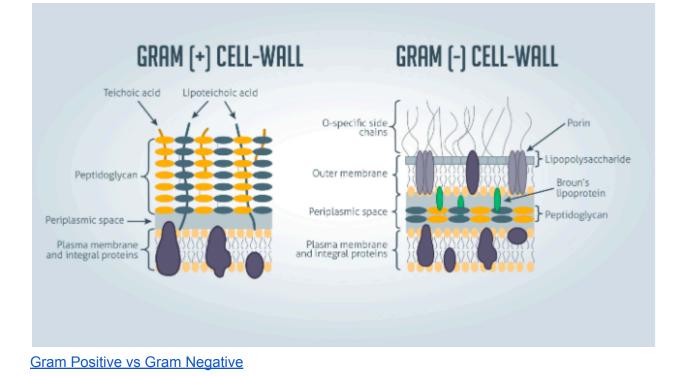
Cell walls are made of peptidoglycan; basically, a sugar and an amino acid that cross-bind together to form the cell wall. It's actually really cool, but I won't get into the details here because you don't need them for the MCAT. Just know that bacteria cell walls are made of peptidoglycan, and since humans don't have cell walls, this is a site for antibiotics to target.

The cell wall is responsible for the movement of solutes in and out of the bacteria. It also provides structure.

Let's start with the cell wall that is thick (and then has a membrane) since it's a bit simpler in that it doesn't have as many layers to its envelope. For clarification, the envelope is the cell wall and the membrane. This type of cellular envelope is gram-positive. We will go into the gram test in just a minute.

Gram-positive has two main layers in their envelopes with a space called the periplasmic space in between.

So, starting on the outside, working our way into the cytoplasm region of the bacteria, we have a very thick cell wall of peptidoglycans. Then, [there is a] periplasmic space and *then* a cellular membrane that is similar to our cell membranes.



The other type of cell wall is called gram-negative. This is the envelope that has a membrane, then a thin cell wall, then a periplasmic space, and then another membrane. Another difference in this bacterial envelope structure is that the outer membrane has lipopolysaccharides sticking out of it.

One more time: gram-negative bacteria have an outer membrane that has lipopolysaccharides sticking out of them. I think of the lipopolysaccharides like those air dancers; the tall, skinny, tube-like structures people put in front of stores to get people's attention. They dance and move around because of the fan.



Air Dancers | Image Rights

These lipopolysaccharides stick out of the outer membrane on gram-negative bacteria and are part of the reason gram-negative bacteria are so pathogenic in humans: the lipopolysaccharides can trigger an immune response.

Another reason gram-negative bacteria can be tricky to target with antibiotics is because they have that additional outer membrane—which makes it harder for antibiotics that target the cell wall to reach the wall and break it down—so that the bacteria can undergo osmotic rupture.

Now, let's talk about the gram-positive and -negative, specifically, where that name comes from. Basically, back in the day, a guy named *Hans Christian Gram* noticed when we were trying to satin some bacteria that some stained *blue-purple* while others stained *red-pink*. This difference in staining color came from the physiological differences in the bacteria we just discussed.

The gram-negative absorbed the safranin counterstain which makes the cell appear red-pink.

The gram-positive absorbs the crystal blue and appears a blue-purple. I remember the difference in this by saying: *red is dead*.

Red is dead: Gram-negative bacteria are usually much more worrisome and hard to kill. Gram-negative bacteria are harder to kill because they have three layers of defense.

Gram-negative stain[s] red-pink—red is dead.

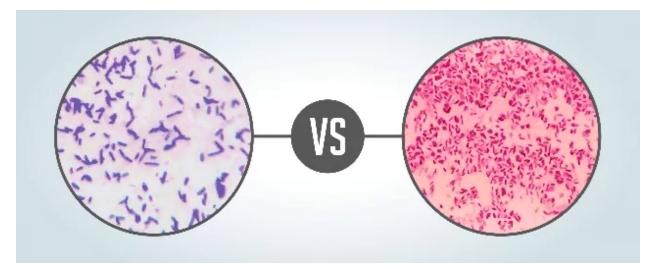
I also used to swear there was an Elvis Presley song that sang about being 'positively blue.' But, when I Googled that, nothing came up. But, it still sounds like a song Elvis would sing, right? "I'm positively blue over you."

Gram-positive—stain[s] blue-purple.

Before genetic identification was so prevalent, gram staining was used to help determine the type of antibiotics that would work on someone with a bacterial infection.

Red is dead—AKA—danger. When you think dangerous bacteria think gram-negative [bacteria] have an extra layer, so it makes them harder to kill with things like antibiotics.

Positively blue—gram-positive stain blue. They have a thicker cell wall with an inner membrane.



Gram Positive vs Gram Negative

I have linked some images and additional articles about gram staining if you're interested. They are in the script notes on the website.

Bacterial Environments & Characteristics

Moving on.

Just like humans like to live in different areas, I prefer dry heat, some people like snow, and some like humidity. I don't know why. Humidity and I aren't on the best of terms. Actually, I think bacteria are more like sea life. Some require coming up to the surface for air, some don't need to surface.

Bacteria have specific environments where they thrive.

Anaerobes don't require oxygen.

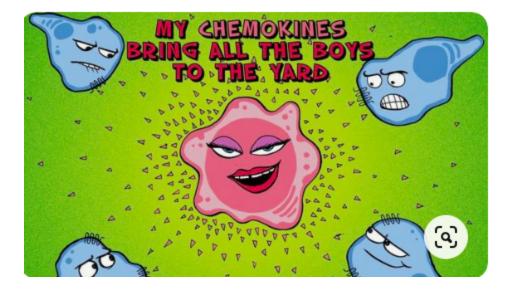
Obligate aerobes require oxygen for survival; they need oxygen to metabolize.

Facultative anaerobes are real little badasses because they can survive with oxygen or without oxygen.

Aerotolerant anaerobes are unable to use oxygen for metabolism, but the presence of oxygen doesn't harm them.

Bacteria get around by using *flagella*—which are basically long tails that they use to propel themselves around. Think propellers on a boat. They can use these flagella to move them towards or away from something.

An important vocab word to know is *chemotaxis*. You might have heard chemotaxis when you talked about the immune system in school. Your body uses chemotaxis for an immune response. Bacteria can also use chemotaxis. Chemotaxis is simply the ability to detect chemicals and move towards or away from them—which bacteria do by way of flagella or cilia.



You can also think of humans doing chemotaxis by smell. When you smell fresh bread, you might wander into the kitchen to see what's baking. If you smell something terrible coming from the bathroom, you'll probably walk the other way.

Okay, so bacteria have cytoplasm, and cell walls, and membranes. They have DNA in the nucleoid region and they don't have membrane-bound organelles, but what organelles *do* they have?

Some of the prep books mentioned that some bacteria have histone-like structures, but I think the most important thing to note is that the ribosomes are different in prokaryotes and eukaryotes. The reason [for] noting the differences between prokaryotes and eukaryotes is it gives us a place to target destruction via drugs. So, we mentioned that some drugs target the cell wall, particularly the peptidoglycan links. Another set of drugs target the ribosomes.

Bacterial ribosomes contain the 30s and 50s subunits, while eukaryotes contain 40 and 60s.

Now, how do I keep these sizes straight? So, my friend really likes a Korean singer named CL, and a few years ago, she was like, "Hey, want to go see her in concert in LA?"

And, I was like, "Sure." At the time, I didn't know who CL was, so on the way to LA, I learned one song, and it goes:

"I got myself a forty; I got myself a shorty." <u>CL - 'LIFTED' M/V</u>

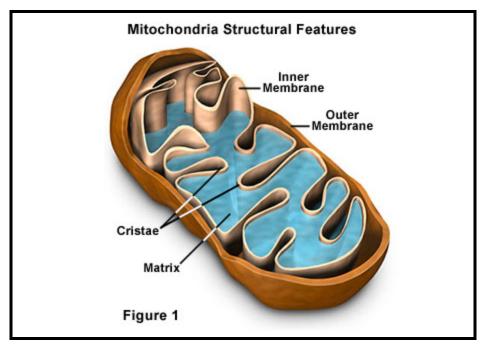
Bacteria can't get themselves a 40. Only we (humans) can pick up a 40, and then, I just remember for eukaryotes or prokaryotes, it's 20+ in size.

So, eukaryotes have the 40s and 60s: prokaryotes have the 30s and 50s.

Prokaryotes also don't have mitochondria: they use their cell membrane for the electron transport chain, which, if you think about, makes so much sense.

You've probably heard of the endosymbiotic hypothesis which suggests that our modern-day mitochondria are descendants of a specialized bacteria that survived endocytosis by another species, and, eventually, lead to them being incorporated into our cytoplasm.

So, if we believe that our mitochondria are the descendants of a bacteria being endocytosed, it makes sense that bacteria wouldn't have mitochondria and, instead, electron transport chain as part of their membrane.



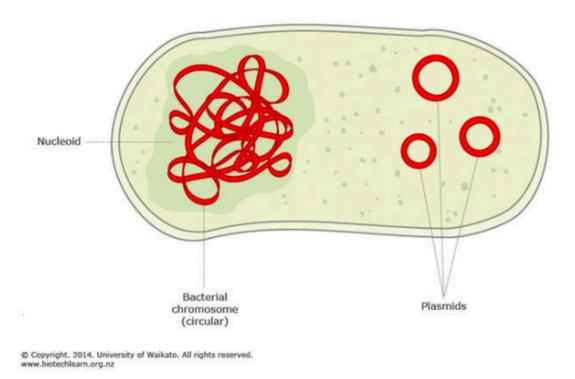
Mitochondria

Another interesting thing about bacteria is how they share their DNA and how they replicate.

At the beginning of this episode, we talked about how bacteria don't have membrane-bound organelles: they simply have an area called the nucleoid region where their circular DNA

resides. But, what is really cool is that bacteria don't have to have all their DNA contained in this region or one circle of DNA. There are these little sections of DNA that are smaller circles that are called *plasmids*.

Now, bacteria can take in plasmids from other bacteria. Plasmid DNA is not necessary for survival. The bacteria can get on fine without it, but the plasmid can carry extra genetic information, like antibiotic resistance. Plasmids are not required, so they are considered extrachromosomal DNA.



So, how do bacteria share genetic information and reproduce? Bacteria do not undergo mitosis or meiosis, but they still have ways of increasing their genetic variability. Distribution of extrasomal DNA is random, and daughter cells may or may not get a copy.

So, genetic variability can be increased one of three ways: *conjugation*, *transformation*, and *transduction*.

Conjugation: Conjugation is basically bacteria sex. One bacteria must have an F + plasmid. If it has the F+ plasmid, it is considered F+ if the bacteria is F+. It has the gene for a sex pilus, or a conjugation bridge, which is a one-way transfer of genetic material from the male F+ bacteria to the F- bacteria.

- 2) *Transformation* is pretty straight-forward. Transformation is when bacteria pick up DNA from the environment.
- 3) *Transduction* is when they incorporate genetic material via a vector, such as a virus, like a *bacteriophage*.

Bacteriophages are fascinating—they are viruses that infect bacteria. They look like weird, little spaceships that inject their genetic material.

Bacteriophages can carry genetic material from one bacterium to another. A bacteriophage can accidentally incorporate DNA from one bacteria, and then, when it goes and infects another bacteria, [it] can transfer this captured DNA.

So, these three methods are how bacteria can increase their genetic variability, but how do they reproduce?

It's not via mitosis or meiosis: it's by binary fission.

Bacteria reproduce via binary fission, which is asexual reproduction. The circular DNA replicates while the cell grows until it's large enough that it will pinch inward in the middle and produce two roughly identical daughter cells—I say "roughly" because remember that the plasmids are divided between the daughter cells randomly.

As you can see, binary fission is a lot less involved than mitosis, which means that it can happen a lot faster and can cause bacteria to grow exponentially, doubling each generation. The limiting factor for colonies is resources and waste accumulation.

Yay!! That wraps up our bacterial discussion.

Fungi

We are only going to cover a few things with fungus. Fungi isn't huge on the MCAT. We are just going to mention the barebones here. I do think that it will be more prevalent in medicine and on the MCAT as research advances into autoimmune disorders.

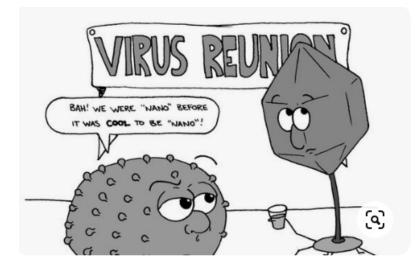
Fungi have cell walls made of *chitin*, which is the same thing lobster exoskeletons are made of... I always found that kinda freaky. Fungi are also heterotrophs meaning, they have to take in nutrition from their environment. Fungi can reproduce either sexually or asexually.

Fungi spend the majority of their lives as haploid and grow these long intertwining branches called *hyphae*.

Current research suggests that MS has a fungal component. I am going to link a few articles in the script notes if anyone is interested.

The Role of Fungi in the Etiology of Multiple Sclerosis

Viruses



Now, we are going to move on to viruses.

But, first, what is a virus, and is it alive?

If you want, you can go Google this very thing and see the different factions defending different positions. I don't have a super-strong opinion, so I'm just going to outline what I was taught.

Viruses have a lot of variabilities, as far as pathogenicity, but are pretty physiologically basic. They have a protein coat, called a *capsid*, and genetic material, which can be DNA or RNA. And, a few [viruses] have an envelope of proteins and lipids.

One more time. If a virus was a person, they would have on their coat, which is called a capsid, but some viruses are extra and like to layer, so on top of that capsid layer, they might have a massive fur coat. Think Macklemore here.



Now, the extra envelope, or fur coat, if you will. Actually, we're gonna go with a faux fur coat here. The faux fur is very sensitive; you can't just throw it in the washing machine with detergent and then move it to the dryer. No, the viral envelope is heat-sensitive and sensitive to detergents.

So, if you're wearing the beautiful faux fur coat that is super sensitive, you're gonna be easier to take-out—same with these viruses. The ones that have envelopes are easier to kill. The viruses that *don't* have the envelope are harder to kill because they aren't as sensitive.

Macklemore - Over It feat. Donna Missal - GEMINI Green Room Sessions

Also, this is one of my favorite Macklemore green room songs. I have listened to it *so* many times. I'm slightly obsessed. Donna Missal is so raw and, yes, listen to it.

Back to viruses. Viruses are tiny-smaller than bacteria.

Viruses have to infect a host cell and hijack the host cell's machinery in order to reproduce, which is the main argument for why viruses aren't considered living. Viruses can't replicate by themselves. They are deemed obligate intracellular parasites, which I think is just rather fantastic!

Viruses lack the ribosomes to carry out protein synthesis, which is why they need a host! So, once the alien invader has hijacked a cell—I think of viruses as alien invaders, I mean they even look alien, have you seen the structure of bacteriophages? If that is not an alien spaceship I don't know what is—*anyway*, once the virus has got into a host cell and taken over their computers and machines, it starts pumping out viral progeny, which are called *virions*. The little baby viruses, virions can now go forth and infect other cells.

Speaking of the bacteriophage spaceship, *bacteriophages* are viruses that target bacteria. I think this is a fascinating area of research. Bacteriophages that are targeted for specific pathogenic bacteria can be the next vast area of medicine. Instead of prescribing your patients an antibiotic, you could send a specimen to a lab that would program a targeted virus for that

bacteria which would be sent back and injected into your patient. The research I conduct hasn't been on viruses, but I do work with bacteria, and I would love to get into bacteriophages a little bit.

Something I think is pretty cool about viruses is that they can have RNA or DNA; single-stranded [or] double-stranded. They can have a lot of genes or only a few. So, humans and other animals have stringent regulations on what information we need in our genomes. Viruses are just like, *"Hey, I'll take anything."*

Important terms for viral genetic material include: *positive sense, negative sense, and retroviruses.*

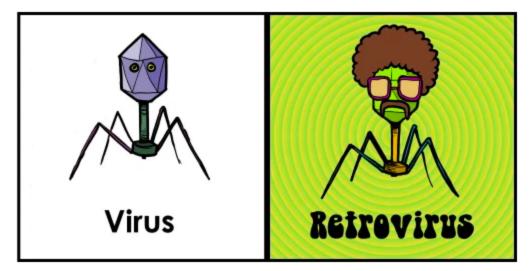
Positive sense: If a virus has RNA that can be directly translated to functional proteins it is said to be positive sense.

Negative sense means that the RNA strand is the template for a complementary strand. Once the complementary strand is made, the new strand can be used for protein synthesis. Negative sense RNA viruses must also carry an RNA replicase to help with this creation of the complementary strand.

So, to remember these, I just think, if someone is an optimist, they are positive, and they just go for it—like positive-sense RNA viruses can be directly translated.

If people are a little negative about a project, they may need to talk themselves into it before they get to work. It's more of a two-step process. Same with negative-sense RNA: it takes the two steps to get where it needs to go.

Retroviruses: Retroviruses work backward. They have an enzyme called *reverse transcriptase*, which takes the single strand of RNA and makes DNA. This DNA is then incorporated into the host's genome, and, then, the DNA is transcribed as if it was the host's own DNA. See how tricky these obligate intracellular parasites are? The only way to kill the virus once it's in the host is to kill the cell.



Note: This is a bacteriophage shape, just fyi. <u>Retrovirus by Velica</u>

Q: What is the most infamous retrovirus? **A**: Human immunodeficiency virus (HIV)

So, this is old science news like 2011—so, more than a *little* old, but when this came out, I was slightly obsessed. The headline in my brain was those who had family in Europe that lived through the plague have a 10% chance they are immune to HIV.

So, basically, viruses can only infect a specific set of cells, which is dictated by the receptors on the host's cells. HIV can only infect if the host has receptors called *CCR5*. The paper released talked about how the black death sweeping across the continent was a reason that Europeans, or those [of] European descent, have a higher chance of being immune to HIV. The frequent plague outbreaks occurred in tandem with the mutation frequency of CCR5. Others think that smallpox is the reason that Europeans have higher immunity to HIV. I'll link an article.

Did Black Death boost HIV immunity in Europe?

I mean, it's just cool. I love the idea of that hypothesis.

Also, I'm linking episodes of the podcast *This Podcast Will Kill You* not because this is an ad, but I love this podcast and their review of infectious agents. They have episodes on smallpox and the plague, so listen and enjoy.

<u>Ep 3 Gnarlypox - This Podcast Will Kill You | Podcast</u> <u>Ep 5 Plague Part 1: The GMOAT - This Podcast Will Kill You</u> <u>Ep 6 Plague Part 2: TGFA - This Podcast Will Kill You</u> Just as viruses have different genomes, viruses have different ways of getting into the cells. Some are endocytosed. Others inject their DNA like a needle. Others bind and become part of the cells membrane.

Okay, so the virus gets into the host, takes over, makes a bunch of baby viruses that now need to be released to the world.

So, the cell could just rupture and release the virions like a baby spiders hatching of my nightmares. But, if you kill the thing that you are using to reproduce, that is not the best life choice, because, then, you can't use the cell that you have taken over and already put in the energy to hijack.

Another way virions can escape is by doing a viral version of exocytosis called extrusion, which is where the virus binds to the plasma membrane and escapes in a membrane bubble. Escaping this way keeps the host cells alive and lets the virus keep using the cell as its puppet. When the virus is keeping the cell alive, the virus is said to be in the productive cycle.

Again, there are basically two phases of progeny release: *lytic* and productive.

Lytic: The cell lyses and releases all the progeny.

In the *productive phase*, the cell is kept alive, and the virions escape via extrusion.

Bacteriophages also have two cycles called *lytic* and *lysogenic cycles*. The lytic phase is basically the same. The virus hijacks the machinery, makes a bunch on viorins, and then ruptures the cell and releases the virions. If a virus is in the lytic phase, it's called *virulent*.

The lysogenic phase is when the virus integrates itself into the bacterial genome. The virus integrates as a provirus or prophage. The virus integrating into the bacterial genome is what initiates the lysogenic phase. The virus will be replicated along with the bacteria. However, if the bacteria are exposed to environmental factors, the virus can come out of the genome and enter a lytic phase.

As the virus leaves the bacterial genome, it can take part of the bacteria's DNA with it, which is what allows transduction between bacteria using a viral vector.

Prions

The last thing we are going to talk about in this episode is prions.

Prions are like proteins from hell. They are not alive. They are simply a protein that causes other proteins to misfold. They go from alpha-helical to a beta-pleated structure. Mad cow disease, Creutzfeldt Jakob disease, and fatal familial insomnia are all examples of prion disease, which

sounds like one of the most terrible ways to die. In fact, I'm going to start making a list of ways I don't want to die, and prions are going to be near the very top.

If you want to read a book about prion disease, check out *The Family That Couldn't Sleep: Medical Mystery*. (<u>The Family That Couldn't Sleep: A Medical Mystery</u>)

Final Thoughts

And, on that happy note, we are done! Thanks for listening. Ask me questions on Insta <u>@THISCELLFIELIFE</u>. Subscribe, rate, review.

Study hard, friends!