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S1E1: Is Coronavirus Alive?

Hello, I'm Phil Gibson and welcome to BioTA. The name of this podcast comes from the Greek word meaning life. It's also an acronym for the full name of the podcast, Biology Through Audio. My goal is to introduce listeners to biology in a way that helps them understand, explain, compare, and evaluate different biological phenomena that we encounter every day. To do this, I'll draw from current events, past events, and what I think are some really interesting biological examples. At the end of each episode, you'll find supporting references and additional resources in case you want to explore further.

So, let's get started with the question that is the topic of this first episode: What does it mean to be alive? To answer this question, let's look at something that is on everyone's mind right now, the novel coronavirus. Its official name is Severe Acute Respiratory Syndrome Coronavirus 2, and it causes coronavirus disease 2019. To make things easier, I'll refer to them as SARS-CoV-2 for the virus and COVID-19 for the disease throughout the remainder of this episode.

And as we are all well aware, in late 2019, reports began to come out of Wuhan, China that there was an outbreak of a new respiratory disease. This mysterious disease was spreading rapidly and having serious, often lethal consequences for some of its victims. Scientists identified the virus causing the disease as a new strain of coronavirus, a large group of viruses that contains at *least* eight viruses known to affect humans.[1] Some of these coronaviruses are fairly common and cause only mild respiratory illnesses, such as the one responsible for 15-30% of the common colds many of us experience each year[2]. Others are less common and more serious such as SARS-CoV, the virus responsible for the Severe Acute Respiratory Syndrome (SARS) pandemic in 2002 and 2003, or MERS-CoV that caused the Middle East Respiratory Syndrome (MERS) epidemic in 2015.

Samples of the virus from the first group of individuals infected with this new or “novel” coronavirus out of Wuhan provided undeniable evidence that it had done what many other viruses and diseases had done before. That is, it made the jump from a population of wild animals into humans. And that’s when a chain of events began to occur that would have incredible and, in some instances, devastating effects on each and every human population that would encounter this new virus—probably for years to come.

Like a lot of folks, I watched news reports about the pandemic on TV, and I saw questions scroll across the bottom of the screen: What is this new virus? What even is a virus? Where did it come from? How could this happen? How do we stop the virus and the pandemic? Is all of this as unprecedented as it seems to be? These are all excellent questions and we can find the answers to them by considering some fundamental biological concepts and principles.

[Music main section and fade]

OK, so first up is an incredibly important question, is the virus SARS-CoV-2 alive? To answer that, let’s begin by thinking about what it means to be alive. What are the features that all living things share?

There are some traits that probably come to mind quickly such as the fact that living things use energy and resources. Living things maintain homeostasis, their internal balance of conditions to support life We can put those features in a catch-all of metabolism. Living things have organization in their body. That is, they aren’t just a collection of parts, those parts are put together in a certain way in order to function. Living things respond to stimuli and the input of information from their environment. Living things have adaptations that help them survive in their environment. And in those adaptations, we can again see examples of the important relationship between structure and function (what parts are present, how they’re put together, and how they function). For example, a bird’s wing has to have certain features, and those features have to be put together in a certain way for a bird to be able to fly. Although all bird wings have feathers, feathers on different species have different properties, which are adaptations for how those species live. Owls have feathers that muffle sound and provide stealth as they swoop in to feed on unsuspecting prey. Vultures, who feed on carrion (you know, dead things), have no need for such sound-buffering feathers since the food they eat doesn't respond to sound and can't run away[3].

Another trait of living things is that they reproduce. They make more of themselves through asexual reproduction, which makes what you can generally think of as "clones". Or they combine gametes (sperm and eggs) through sexual reproduction. Either way, multicellular organisms typically start out simple with a few cells, and then go through processes of specializing, building, assembling, however you want to think about it, but it's basically growing and developing to making the different parts of the body as the organism develops. Living things get bigger and mature.

It's through reproduction that living things pass on their DNA, the chemical threads that contain the instructions for life. They hand their DNA down from generation to generation, either through asexual or sexual reproduction, as a molecular legacy of their lineage from ancestors to descendants. Now, that's a huge topic in and of itself, and we'll definitely address it in a later episode, but for now, just realize and appreciate that ***genetic material is inherited from our ancestors, and passed on to our offspring***. The information in that DNA is read and used, or as biologists would say it, the information in the genes containing the DNA molecules is ***expressed***, to build and operate the organism. Gene expression and how the information in DNA is used by the cell is called the Central Dogma of Biology and it explains the flow of information within a cell as that cell reads and follows the instructions for life.

Okay, let's get back on track. Another defining feature of all organisms, and this is a really big one for determining what a majority of biologists consider to be *alive*, is that all living things are made of one or more cells. Got that? Living organisms are made of cells.

Cells, regardless of how complex they may be, are made of the same three basic parts: a cell membrane that forms the outer boundary of the cell and delimits the cell as a unit separate from the rest of the universe. You can think of it as a sac that contains the next two parts, an inner fluid called cytoplasm, and DNA, the genetic material. The cytoplasm is where metabolic reactions occur. The cytoplasm also provides the place for DNA to be expressed.
So, to make a quick summary here, life as most biologists define it, is a condition in which a system has all of the features or does all of the things we just listed. The cell is the smallest organizational level where all of those processes can happen.

So, given those criteria, are viruses like SARS-CoV-2 alive? The simple answer to that is no. But let’s think about that a little bit more.

Viruses are a piece of genetic material (nucleic acid), either single or double stranded RNA or DNA. There is no cell. These pieces of DNA or RNA may or may not be surrounded by a protective protein shell called a **capsid**. The virus can’t do anything on its own without a cell. But, you see, a virus does its dirty deeds by invading host cells. Viruses use structures on their capsid to target, identify, and get past the defenses of host cells. Once inside the cell, the virus then takes over the cellular machinery that is part of the host cell’s normal operations. Now that it is under the control of new genetic management, the cell has a new job: make more virus. Instead of reading its own host DNA, the cell starts reading the virus’s DNA (or RNA). These new instructions now direct the activity of the cell. This can lead to a ton of problems in the cells that are unique to the virus, unique to the different types of cells it affects, or unique to how the body overall responds or fails to respond to the viral invasion.

A virus can act directly on cells or tissue or by breaking down the normal orderly function of the host’s body. They can ~~also~~ act immediately or play a stealthier game, reactivating later in the host’s life. For example, chickenpox, which used to be almost a rite of passage for preschool aged children, generally causes mild illness with fever and an itchy, blistery rash that lasts about a week. No big deal, right? Well, not so fast. The virus that causes chickenpox, Varicella-zoster, has a nasty habit of lying dormant in host cell DNA until something triggers it to express again, decades later. This is what's known as shingles, and it comes with a rash that can last for weeks and sometimes pain that can last for months. In stark contrast, the Ebola virus wastes no time infecting, disrupting, and destroying different tissues throughout the host's body until they die or recover from the disease.

Scientists are still trying to figure out these and other important features of the novel coronavirus we are currently facing. Like other coronaviruses, SARS-CoV-2 is a specialist in affecting host respiratory systems. It has greater ease of transmission and infection, but lower fatality rates than SARS and MERS. COVID-19 also appears to be affect other parts of the body such as the feet in some individuals. In others, it affects taste and smell. And then in still some other individuals it causes severe inflammations throughout the body. Some researchers are investigating whether a type of proteins on the surface of many cells in the respiratory system called ACE2 is related to these symptoms and how the virus invades cells. All of these are pieces of a puzzle that scientists are trying to unravel as they try to understand the pathology of this disease.

So, to wrap up the answer to our first question, is the virus alive? No, not in the normal sense. Viruses exist at the fuzzy borderline, the grey twilight zone between chemistry and life. It's more accurate to think of a viral particle as being active DNA or RNA that is capable of taking over a cell [4]. Which if you think about it, kind of makes them even scarier because now they are just pieces of nucleic acid out there in the environment waiting on a host.

In the interest of full disclosure and fairness, I should note that some scientists disagree with the requirement that living systems require cells and think that viruses should be considered living. They argue that viruses have genetic material, organization, specialization, replicate asexually, evolve, and show adaptations which they consider to be the essential traits for being considered living[5]. I agree that these are all important traits and in no way would I ever suggest that viruses and their cousins the viroids and prions are not biologically important, but as far as being living, having some form of cellular structure is for many biologists, myself included, an essential defining feature for living systems.

Quick timeout for an important FYI here: Handwashing inactivates a virus when soap molecules break apart the covering surrounding the virus's genetic material and can affect the DNA or RNA itself. Soap also helps remove viruses and other disease-causing organisms from the skin, making it easier for the water to wash them away. So, let's remember, pandemic or not, basic hygiene is incredibly important to fight disease, so keep washing your hands. Remember, it's the little things that can make a big difference.

OK, question number two: where did this new virus SARS-CoV-2 come from to start infecting humans anyway? The answer to this one is a little more straight forward than our first question. It was a combination of evolution and chance. This new virus evolved from another coronavirus that already existed in an animal population in nature. Somehow a human became infected with this virus by coming into contact with an animal that was also infected with this virus. And that, my friends, began a chain of virus transmission to other humans, other cities, other countries, and other continents.

Let me explain further about how we know this. . .

Scientists learned a lot about the new disease just from pictures of the virus[6]. SARS-CoV-2 has some telltale features showing it's built like other viruses we've seen before. Remember that protein coat, the capsid? Because it kind of looks like a spikey crown, biologists named viruses with this unique type of capsid "corona" viruses (corona is Latin for crown). So, when virologists got a look at this new virus, the appearance of the capsid indicated the group of viruses it belongs to and, consequently, the way it affects infected individuals. The new virus also functions like other coronaviruses we have encountered previously. On the tip of the spikes on the capsid is what virologists call a spike protein. That protein coat allows these viruses to attack and infect cells in the respiratory system and some other places in the body where the ACE 2 protein I mentioned previously is found. SARS-COV-2 is also genetically similar to other coronaviruses. In the same way that you can take one of the various DNA tests to figure out your genetic similarity to different people, you know, get the big picture perspective on your ancestry, scientists compare DNA and RNA among species to determine how genetically similar they are and figure out their ancestry and relationships.

It’s possible to trace ancestry through genetic material because DNA in most things and also RNA in viruses, was passed from ancestors to descendants over generations through asexual or sexual reproduction. This genetic legacy can be used to trace the history of different lineages. The more similar the genetic material is, the more closely related two species, individuals, or viruses are. Scientists have sequenced the SARS-CoV-2 RNA (what scientists call its genome), and confirmed that it is without a doubt related to coronaviruses that commonly affect animal respiratory systems. And in many instances, if a virus will infect other mammals, it can potentially infect us.

Now, let’s take a little side trip here and talk about that.

SARS-CoV-2, H1N1 Swine Flu virus, Rabies virus, Nipah virus, and many, other viruses, as well as some bacteria and parasites cause what epidemiologists call zoonotic diseases. Zoonotic diseases are caused by pathogens that can be transferred from an animal population to a human population. This event when a disease moves into a new host is sometimes called a host jump, or spillover.

Epidemiologists who study host jumps have found that in some instances one or more mutations can change a virus just enough, allowing it to do something a little bit different, so that it not only persists in the original host, but also infects humans as a new host. This new mutation may have little or no consequences for the original host, but it can potentially be devastating to the new host species that has no defenses for the novel disease.

Scientists are collecting data to shed light on how the spillover of SARS-CoV-2 event likely happened. So far, we have learned that SARS-CoV-2 is 96% similar to a virus named RATG13 that is particularly common in some wild bat populations in Asia[7]. This does not mean that they are exactly the same virus, but it is valuable evidence about the history of the novel coronavirus. Their high genetic similarity tells us that the two coronavirus strains both share a common origin in some virus in a population of animals, probably bats. Mutations occurred in one strain which appear to have given it the ability to infect humans. Using computational tools to determine how long it would take for the 4% differences in the RATG13 and SARS-CoV-2 genomes to accumulate, researchers have estimated that they split from one another about 50 years ago. What that means is way back in the late 1960’s or early 1970’s a lineage of virus in a population of bats began to differ from an existing virus and eventually that lineage gave rise to what we now know as SARS-CoV-2. It’s been in one or more bat populations along with a number of other coronaviruses as just a normal part of their viral environment. After that, you could say that it was just a matter of time and chance before an intermediate host picked up this new virus and maybe even transmitted it though several other host species before an immensely consequential crossing of paths with a human.

Researchers are currently searching for other coronaviruses that may be even more similar to SARS-CoV-2 because data are also indicating that SARS-CoV-2 may have moved through an intermediate host animal between bats and humans. Epidemiologists are narrowing down their list of potential intermediate hosts which include a range of mammals from wild macaques to pangolins, and even domesticated livestock, but exactly how the novel coronavirus spilled over into the human population may never be known. One thing we do know is that as human populations spread into new areas, there is a chance that we will be encountering animals and most importantly the viruses they carry that we haven't met before. Each time that happens, there is a possibility that these encounters will be the beginning of a new outbreak.

And that brings us to our final question: Will this virus go away?

If by asking this, you mean will the pandemic end, the answer is almost certainly yes. A pandemic is just a new disease that is spreading rapidly over a large geographic region. It doesn't have to be a deadly disease, it's just a new disease. Pandemics start as a local outbreak, and then spread throughout a population, becoming an epidemic, and then a pandemic as the disease begins to infect people worldwide. Right now, as I am preparing this, SARS-CoV-2 is still spreading rapidly. We are still in the pandemic stage. At some point, the rapid rate of spread will taper off and this stage will end. We just don't know how long that will take. We don't know how many lives will be lost. And we don't know how many people will recover, but have to endure lifelong consequences of their infection.

Although we can't say what the future holds with 100% accuracy about what will happen to this specific virus, we can use our understanding of viruses in general and coronaviruses in particular in addition to our knowledge of previous pandemics to get an idea of what the virus might do and how we can act to minimize its impacts on people. To be sure, it won't just magically disappear someday. We won't just wake up one morning and it will all be gone, and the world will be just like it was in the years BC, you know, before coronavirus. Based on what we have observed and the data so far, it is reasonable to expect that this is a virus that will persist in human populations at some, low level. So, it's very likely to be here for a while. What does that mean for us?

One thing is clear above all else. To stop the virus, we have to isolate the virus. Although we use new terminology like self-quarantine or social distancing, these are old techniques humans have used before as effective methods to get control over the spread of a disease as much as possible.

Whether it was during the Black Death, the Influenza outbreak of 1918, or any of the many others, the ability to contain the spread by isolating infected and contagious individuals is an effective tool that humans have used before, long before viruses were even discovered. The effectiveness of this approach, however, depends on how and how easily the virus is transmitted from an infected person to a new host.

Viruses such as Epstein-Barr virus require direct contact with contaminated bodily fluids making them more difficult to transfer and easier to contain. Nipah virus spreads from animal to person, person to person, and through contaminated food. Respiratory viruses like colds, flus, and coronavirus are notorious for their ease of transport in the tiny droplets and aerosols we form when we breathe, talk, sneeze, or cough making them much more difficult to contain. But one thing's for certain all of them: if the virus can't infect new individuals, the spread can be slowed and maybe stopped. It's that simple. That's part of how masks work. They contain the droplets we breathe out and reduce the amount of virus in the air. That helps because if someone is asymptomatic or shedding virus before they feel sick, the mask can make it harder for the particles to get in the air and infect someone else. Maybe it can even stop you from breathing one in. The main point is that if we wear masks to protect each other, we also protect ourselves.

Another thing that could happen which can slow the spread of the virus, is herd immunity. If a virus causes a person to develop antibodies against it—antibodies that linger in the body, the immune system protects that person from being re-infected. Herd immunity for that virus occurs in a population when so many individuals have become infected, recovered, and afterwards are immune to reinfection that the virus does not come into contact with any new potential hosts. Another way to think of it is that if an infected individual comes into a population with herd immunity, there is a very low probability of the infected individual coming into contact with an individual that is not already immune. I'll cover herd immunity in more detail in an upcoming podcast. What is important to think about now is that we don't know enough about how human immune systems will respond to SARS-Cov-2 infection in the long term to know if herd immunity is even a possibility. But one thing we do know is that letting the disease spread unchecked and hoping herd immunity happens will come with an outrageously high level of mortality and suffering that is neither morally nor ethically acceptable, especially when something as simple as wearing masks and socially distancing can help prevent others from getting sick.

Vaccines can be a highway to herd immunity that will dramatically slow the spread of a virus in a population. Fundamentally, vaccines work the same way as described above except rather than having to suffer through the disease, we use either inactivated or weakened forms of viruses to trigger the body's immune system and prepare it to fight off infection. Herd immunity through vaccines also helps protect individuals who can't be vaccinated by surrounding them with immune individuals. Immunocompromised and unvaccinated individuals are protected because the virus can't gain a foothold in the population and get to them.

As for the current pandemic, the race is on right now in a worldwide scientific effort to develop a vaccine and other therapies that work with the immune system in much the same way, including antibodies or other protein particles to halt this virus. On that front, all we can do now is wait and hope there are scientists working right now who are on the right track. There are promising results coming in, but only time will tell.

I realize some of you are probably saying to yourself, ok, so let's say we do slow down transmission, what happens to the virus?

Remember what I mentioned before, that the current virus is the product of evolution. Although they are not alive, they experience mutations in their genetic material that can change them in some way. With viral diseases, the speed of evolution is critical. Let's briefly look into that.

In some instances, like measles, the virus evolves so slowly that one-time exposure or vaccination can provide long-term protection. Even if the virus changes a little, the body still recognizes it. Others, like seasonal influenza, evolve so rapidly that they require a new vaccine annually to keep up with the changing virus in a kind of epidemiological arms race. In these instances where the virus cannot be completely eradicated, it just becomes part of the host populations where it is persistent at low levels or shows seasonal peaks and valleys[8]. It becomes what we call an endemic virus. It's becomes something that we live with and try to contain to the best of our ability to protect public health.

OK, so what about SARS-CoV-2?
We know this virus is mutating, changing, evolving. New genetically distinct strains have already been identified. How fast and where those mutations occur will be a big part of how we are able to respond through vaccines and other measures. Coronaviruses tend to evolve more slowly than viruses like the flu, so there may be hope for an effective vaccine to be developed eventually that wouldn't require an annual booster. That's one of the big known unknowns right now. Just a heads up, I will specifically talk about mutations and novel coronavirus evolution in an upcoming episode.

Alright, let's wrap this up and summarize the three main points.

ONE: Are viruses like SARS-Cov-2 alive? No, although viruses share many traits with living systems they are not alive because they are not composed of cells. However, they are biologically important entities because they can invade and take over living cells. We can't kill a virus *per se*, but we can take steps to neutralize its ability to infect cells and reduce its ability to spread and/or infect individuals.

TWO: Where did the novel coronavirus come from? It evolved from an existing strain of coronavirus. Data clearly indicate SARS-CoV-2 is a zoonotic disease that crossed from a wild animal population into humans. Researchers are currently investigating how this happened and what changes in this viral strain are responsible for its unique effects. Similar to other coronaviruses it causes predominantly respiratory disease that are, as you would expect, easily transmitted through the air, so social distancing and masks are essential for containment. SARS-CoV-2 can also be transmitted through contact if someone say coughs in their hand, shakes your hand, and then you scratch your eyes or nose. Remember, we know that soap and water help kill the virus. So keep washing your hands!

AND THREE: Will it go away? Probably not. At least not any time soon. There is still a lot to figure out, but we do know that other coronaviruses have shown correlation with seasonal temperature cycles like influenzas. It is not known for sure whether declines in infections that ended the SARS pandemic and MERS epidemic were directly due to warm, humid conditions inactivating the virus or changes in social behaviors by humans during the summer that limited transmission. Influenza outbreaks occur most often in the winter, but it doesn't disappear during the summer, it just persists in very low levels in susceptible individuals during warm seasons and peaks in the other hemisphere where it is the cold part of the year. We know that coronaviruses and influenza viruses have greater success infecting individuals in cold dry conditions, so a seasonal increase is not unexpected in the fall and winter. And it is clear from current data, it doesn't go away in the summer. SARS-CoV-2 is something that we will likely be dealing with in some form or another for years to some as a virus that is endemic in human populations.

Exit Music fade in low

In the past, plagues were often considered some type of divine punishment or even a curse cast to seek vengeance and balance the cosmic scales. Science, however, tells us that new diseases and the outbreaks they cause are all just a pretty common part of life. And although this current pandemic and its consequences seem unprecedented to us now, the occurrence of new diseases caused by the spillover of a virus from the population of one host into a new one is nothing new.

It would be great to think that this pandemic will be the last we will have to deal with. Maybe for us, right now or for a little while, but definitely not for humans forever into the future. I'm not meaning to be alarmist here, but there is a very real possibility that a virus capable of starting the next pandemic is already out there, somewhere. In order to prepare for our next encounter, we need to give science the attention it deserves, and maybe take a few lessons from history as well.

As much as we may hate to admit it, viruses, these pieces of non-living RNA and DNA have always been here and always will be. I saw an article recently[9] that reminded me of a quote by immunologists Jean and Peter Medwar[10] who described viruses as "bad news wrapped in protein". Surveying the well-established record of destruction that many viruses have left in their wake, it is hard to disagree with that conclusion. But remember that there is no malicious intent, c'mon these are just strands of nucleic acid. As one of the characters in Jurassic Park said about *T. rex*, or was it the velociraptors? They "just do what they do."
[ROAR]

So, even with all of our abilities as possibly the most creative and clever species Earth has ever seen, we can't make viruses go away. But what we can do, what we must do is take the tremendous power these tiny, non-living entities can have in our lives very seriously. We must learn from our past experiences with them, prepare for future encounters with them, and figure out how to live with them in a world that is as much theirs as ours.

I’m Phil Gibson and this has been BioTA.

Terri Gibson helped me with co-writing and editing duties for this episode.
A lot of other folks, too many to name here, contributed greatly appreciated feedback along the way.

Thanks for listening, have a great day, and take very good care of your genetic material.

References and other resources to support this episode can be found on my website.

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