The Second Immune System

Circulating around the planet is a variety of viruses that are constantly evolving and infecting individuals everyday. The most well known virus that is adamant about coming each and every winter is influenza, or also called flu for short. It is advised every year, by every physician, that individuals receive their flu shot between the months of August and September to help prevent infection from the flu in the colder months. It is important to receive the vaccination again every year because the flu virus alters itself and produces different strains throughout its course in which we are not protected against. Thankfully, we have our immune system to help fight against these illnesses and keep us safe from viruses invading our bodies. But what about wild animals that are unable to receive vaccines, and how can they prevent infection?

As human beings we tend to neglect the fact that other animals are susceptible to all different types of viruses and infections as well. Koalas, for example, are susceptible to chlamydia, leukemia, lymphoma, and in a more recently discovery KoRV; a virus specific to koalas that is a close relative to human immunodeficiency virus, aka HIV. KoRV is interesting because it is a retrovirus, meaning the virus injects its RNA into the cell and incorporates itself into the host's DNA, continuously interfering with the host's genes and creating chaos inside the body. Other viruses do not have the same effect and do not mess with our genes, whereas a human being's immune system is able to quickly defend itself and kill the pathogen. So then the question is, how do koalas protect themselves from a pathogen like a retrovirus once they become infected?

Although we can compare KoRV to HIV, its closest relatives are the gibbon ape leukemia virus (GaLV), feline leukemia virus (FeLV), and porcine endogenous retrovirus (PERV). All of these viruses are part of the genus Gammaretrovirus. It is understood that they are most likely a result from a relatively recent spillover from rodents and bats. There have been many KoRV's that have been discovered but the first to be isolated was KoRV-A. KoRV-A is heavily seen throughout the koala species in both integrated endogenous and infectious exogenous forms with provided evidence that it has been engaged with the population for over 150 years. Over time, additional subtypes of KoRV have been identified based on the difference in sequence and specificity of the host cell receptor. (Denner 2019)

As KoRV is being thoroughly researched, many scientists believe it is causing an evolutionary change in the species. Ancient retroviruses that became a part of the koalas genome millions of years ago were presumed to be deactivated but have recently been seen active. Dr. Theurkauf explains to the New York Times that it is believed KoRV is activating the ancient dormant viruses and allowing for deeper infection or possibly no infection at all. (Gorman 2019). This is a huge evolutionary change for the species as their DNA is being manipulated and mutated in modern time. It is very possible that these changes can result in positive adaptations to help the species prosper. Take the placenta for example; Endogenous retroviruses are the reason why mammals have placentas today. Perhaps koalas will find a way to withstand the viruses and cancers it currently carries or develop a new trait that is beneficial for them. Although it may not help with habitat destruction and car accidents, it is evolution in real time.

Koalas are special in that they are the only other mammals, other than human beings, that have an ongoing infection with a retrovirus. What is unique about KoRV is that it targets germ cells, or

more commonly known as the egg and sperm. This means that the virus is able to, and most definitely will, be passed on from parent to child. This is done through meiosis and sexual reproduction. The cells that carry the genetic material containing the infected DNA sequence copy this DNA and create daughter cells which later merge during sex and create the embryo that harvests the copied DNA from mother and father. Typically, other retroviruses infect our somatic cells, which compose the body and do not go through meiosis. So although HIV is capable of being passed along from mother to child during childbirth due to bleeding, it cannot be inherited the way our eye color and height are. As we know, there is no cure for HIV and therefore no cure for KoRV. Scientists have only recently begun to understand how we can treat patients carrying the virus with antiretroviral therapy and proper initiatives to take to prevent infection (Kean 2019).

Despite the fact that we do not have the medications readily available to us for these infections, our bodies are regimented to automatically attack a pathogen that enters our system and can fight against illnesses using antibodies. The immune system consists of two main parts; First, there is the innate immune system, which provides a general defense mechanism against foreign bodies and second comes the adaptive immune system. In the adaptive immune system, the body recognizes a pathogen, as it has come in contact with it before, and uses specific antibodies to target the invader. The adaptive immune system can also be referred to as, “a learned defense or a specific immune response. By constantly adapting and learning the body can also fight against bacteria or viruses that change over time” (National Center… 2019). While investigating this system in koalas, scientists uncovered what they believe to be a “second immune system”.

This second immune system behaves similarly to the one we already know and love. It is composed of the same parts using an innate and adaptive system. The innate system recognizes a specific feature shared by each retrovirus and therefore protects the koalas body from initially getting infected by the virus. If all fails, the adaptive immune system comes into play which allows the body to defend itself with its own “soldiers”. However, there are key differences in these two immune systems that stand out. As said previously, the first immune system works with antibodies that detect and fight against pathogens that enter the host. In the second immune system it is piRNA molecules that restrict the influence of DNA inserted by a previous retroviral infection.

piRNA molecules are apart of the small-noncoding RNA molecules that are present in animal cells. They work to make RNA-protein complexes used for transcription by interfering with piwi-subfamily Argonaute proteins (Piwi-interacting 2019). Astonishingly, the piRNA molecules are able to distinguish the difference between retroviral DNA and koala DNA. When a gene is to be expressed, a piece of RNA is read through a ribosome, which can be viewed as a “protein-manufacturing” system. We can think of the RNA as instructions for which proteins to build. The genetic pieces, that are not needed to complete the proteins, are typically spliced out before being read. Yet, when a piece of RNA that has originated from a virus is to be read, it does not do the splicing. This then alerts the cell of the virus’s presence and the cell then halts the transcription process so that the virus is unable to make the proteins that would cause harm to the individual (Joseph 2019). This second immune system is what is responsible for keeping koalas alive and prohibiting their mortality.

Scientists believe that this second immune system is potentially inside each and every one of us however, it has been clearly adapted and evolved through the koala species as they are

currently going through major genetic changes. Although the koalas are inheriting this KoRV retrovirus, they are also inheriting a unique immune system to help them fight the infection. Understanding this study can be extremely beneficial for human beings today. Although the medication created for HIV prevention does not involve residual DNA, scientists have opened a new door for researchers searching for a cure for HIV. We now have a better idea of controlling DNA to inhibit infection. Even though we are a ways away from finding a permanent solution for patients living with retroviruses, there are a couple strategies that have the potential to prevent the further spread of KoRV in the koala population.

The first strategy would be to isolate or quarantine any uninfected koalas to establish prevention of them interacting and contracting the infection. This most likely would only be possible for some groups of southern koala populations, since all populations in northern Australia are already carrying the virus. The second strategy would be an antiretroviral drug treatment for the infected koalas, just as we have for humans with HIV. This would be the most helpful scenario however it is unlikely due to limitations of drugs for retroviruses and even if a suitable treatment could be found, it would only help koalas in captivity and not in wild populations. The final strategy proposed is to produce a vaccination for KoRV. This vaccination could be given to animals in captivity and those who are taken into care throughout the year and released back to the wild in “catch and release” programs. All of which are great ideas but need further research (Denner 2019).

In conclusion, KoRV is being widely spread amongst the koala populations both wild and captive. It has affected the health of the species to a great extent and given rise to new genetic changes, causing rapid evolution. Koalas have adapted their immune system to help fight against the retrovirus and will continue to do so until the long term effects are seen. In the meantime, the koala species will be passing along their new genetic means from offspring to offspring until a possible solution is identified. As for humans, this new research has provided us with new puzzle pieces to fit into the grand scheme of how retroviruses work and how we can protect ourselves against them.

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(piRNA),with piwi-subfamily Argonaute proteins.