



Living with Coronavirus in Peace and No Panic

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Abstract

The new coronavirus that is now popular with the title of COVID-19 around the world and boasting in spreading at a pandemic level, causing more panic than killings, is the seventh in the line of the class of coronaviruses. This family of viruses headed by the common cold or flu virus has lived in symbiosis with humans for long. Viruses such as Coronaviruses that have lived for millions of years, much longer than any other beings on the earth keep evolving for survival. Coronaviruses on the path of their evolution for survival have evolved into different types of SARS (Severe Acute Respiratory Syndrome), MERS (Middle East Respiratory Syndrome) and now COVID-19 targeting specifically us human beings. In fact, the outbreak of Coronaviruses in different forms over the past several years is a good indicator that these viruses are pushing for survival and co-evolution within the human hosts.

The symbiotic and ecological option of living with Coronaviruses in peace with no panic and resistance that might be surprising is not new in the nature as living in peace or "symbiosis" among the living creatures from plants, animals, bacteria and viruses to us humans have been a rule and part of the law of survival than exception. The symbiosis between coronaviruses and their hosts that is obligatory and not optional on part of the viruses could be in fact beneficial and evolutionary for us.

The universal entry of the coronaviruses in the recent years and now with the virulence pandemic of COVID-19 is a strong evidence of the natural selection obligation that the virus has for maintenance of our longer-term survival.

Introduction

Viruses such as Coronaviruses have lived for millions of years, much longer than any other beings on the earth and keep evolving for survival. This is more true for RNA viruses such as Coronaviruses that depend on their hosts to survive, due to lack of DNA for independent living. So on the path of their evolution for survival; they evolve in different types invading the hosts like

humans. SARS (Severe Acute Respiratory Syndrome) and MERS (Middle East Respiratory Syndrome) that hit humans' population a few years ago before COVID-19 are the other types of Coronaviruses. In fact, the outbreak of Coronaviruses in different forms over the past several years is a good indicator that these viruses are pushing for survival and co-evolution now within the human hosts [1-7].



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In this article, I discuss the wise option of living with Corona-viruses in peace with no panic and resistance. This contention that might surprise many is not new in the nature as living in peace or “symbiosis” among the living creatures from plants, animals, bacteria and viruses to us humans have been a rule and part of the law of survival than exception. The symbiosis between two livings could be obligatory or facultative (optional) that could be different on each side of the equation or relationship. For example in the case of microbes and viruses, the symbiosis on their parts is obligatory as they cannot survive without the hosts, but is optional on the hosts part to let them in or fight back and being destroyed.

Symbiosis and endosymbiosis

Symbiosis, a Greek word meaning, “living together”, is any type of close and long-term biological relationship, interaction and dependency between two biological organisms in a mutualistic, commensalistic or parasitic manner. Endosymbiosis or living inside of the tissues of the hosts that most microbes, such as bacteria and viruses do, including many bacteria already living in peace within us, e.g. in our digestive system, assists with our normal living. A peaceful and healthy endosymbiosis in fact leads over time to reduction of the genome size and power of the invader or endosymbiont and lower its fatality due to the adaptation with the host.

This has been a vital part of “co-evolution” in nature on earth since its living inception. In fact, eukaryotes, the origin of plants, fungi and animals like us all have evolved through this symbiogenesis. Mitochondria, chloroplasts and other cellular organelles that divide and replicate independent of the cells in living creatures like us are the obvious examples of such evolutionary endosymbiosis. In fact, the notion of Darwinism based on competitive survival has been replaced in the modern scientific arena to the cooperative and symbiotic evolutionary survival [8-10]. One of the most impressive example of endosymbiosis indeed is the microbiota living in the mammalian guts including 100 trillion microbes living in one human’s gut. The gut microbiota is so vital for the maintenance of our immune system in fight against infections and diseases for our survival that when disrupted and not cooperated with, e.g. in the case of slow bowel movements and constipation, they could turn to pathogens and causing diseases such as colon cancers. In endosymbiosis, e.g. our guts microbiota, the relationship is not static but dynamic and plastic or flexible on both sides. Any disruption of this equilibrium takes long and many processes of negotiations, commensalism and mutualism on both parts for the sake of peace and survival, unless the terms of homeostasis is broken repeatedly or continually by one side that is mostly by the hosts. This indeed is a major lesson observed diligently in molecular biology that needs to be expanded to other symbioses and endosymbiosis around and within us. In fact, the survival of our ecosystem outward and inward is heavily dependent on a full cooperation between the partners of symbiosis and endosymbiosis that hinges mostly on the hosts part like us [11-16]. Another impressive well know example of endosymbiosis between us and the microbes is the bacterial communities present in the vagina of reproductive-aged women as a cornerstone of a multifaceted antimicrobial defense system. The vaginal microbiota play a significant role in the prevention of bacterial vaginosis, yeast and sexually transmitted infections, urinary tract and HIV infections among others. The lactic acid-producing bacteria (mainly *Lactobacillus* sp.), common colonizing bacteria in the human vagina, are the key players in maintaining homeostasis

of this microbiota endosymbiosis. Like the gut, depending on the sexual activity, menstrual cycle, and other environmental factors, there are periods of community-wide stability as well as periods of extreme variability. The stability or healthy symbiosis and instability or dysbiosis in vagina depends heavily on the host and her sexual/hygienic/reproductive behaviours [17-20].

Viruses are not antagonistic but essentials

While the roles of bacteria have been known for long in endosymbiosis of the hosts well-being like us, the role of viruses traditionally and still out of scientific arena in endosymbiosis has not been appreciated until about a decade ago. Indeed viruses due to their much minute sizes and its cellular structures, particularly RNA or particle viruses that cannot survive independently have much more endosymbiotic roles not only in the large size beings like us, but even within bacteria. This mutualistic relationship has been explored in detail recently pointing to the vitality of viral endosymbiosis not for short-term survival but for long-terms and in the hosts’ evolution, as they are the major partners in the hosts’ genomes. In fact, the viral symbiogenesis seems to be the most important factor in the evolution of all forms of life on earth [21-24].

Viruses that have been until recently associated with diseases and studied as such, are the most abundant and diverse biological entities on the planet. Recent biodiversity surveys in desert, ocean, soil, animals and plants have revealed the vital roles of viruses in every ecosystem. Due to their obligatory existence as endosymbiont within all other beings larger than themselves, the viruses have to possess evolutionary plasticity to form and maintain the most excellent models of symbiotic relationships. Moreover and most importantly, the viruses are the main force behind the genome diversities and genetic evolutions across all species. Indeed the majority of virus-host interactions all around are commensal or friendly. But even in the case of antagonistic interactions, when there is resistance from the host by fighting the virus through its immune armamentarium, the plasticity and obligation of the virus for endosymbiosis living and evolutionary genetic diversification, assists the survival of the host at the end of the arm race, as the end of life of the host would be the end of life of the virus [25-34]. A great example of such co-evolution and assistance in survival is the “interferon”, a master regulator of the immune system and cell metabolism found in nearly all cell types that has evolved within lives through viral interactions. Another impressive example observed in the interaction between a bacterium and lytic virus and also in the killer viruses of yeast by the virus protection against the lytic phage (virus fighting against its own killing machine) for the survival of the host, ultimately leading to the endosymbiosis or dependency of the host onto the virus for living.

Studies on plants that were first to appreciate the importance of viral interactions and symbiosis in ecosystem, diversity and evolution of the plants, have also shown how viruses assist the plants in coping with their adverse environments such as drought, thermal tolerance and adversarial invasions [34-43].

In human studies, GB virus C has been shown to fight against HIV through down-regulation of cell receptors for entry, reduced replication, promoting interferon and interactions with interleukin immune pathways. Latent herpes virus and cytomegalovirus have also been shown to enhance the T cells immune response to influenza and other fatal microbial invasions. Endogenous retroviruses that make up at least 8% of human genomes and non-retroviral endogenous viruses have been revealed in recent

years that have been contributing for millions of years to the genetic evolution and diversities of all living forms on earth. This so-called endogenization of viral elements has sculpted the evolution of extant genomes in all domains of life. The significance of the contribution of viral interactions in the evolution of their hosts' genetic make-up, diversity and survival became possible only since the sequencing and analysis of hosts genomes such as humans in the recent years. In brief, viruses that have until recently been considered fatal and antagonistic to life, at least in the field of virology, genetics, evolution, ecosystem and biodiversity, have been appreciated as the most important vital elements of life on the planet [44-63].

What about the aggressive viruses?

As early as mid-80s, it has been argued that the virulence of a microbial invasion such as viral infections could be favored by the natural selection and lead more to co-evolution, when pathology enhances genetic transmission, better adaptation and evolution [64]. This has also been shown in the case of coronavirus as early as mid-90s, when it was shown that mouse hepatitis virus strain A59 (MHV-A59) a member of the family of coronaviruses, containing a single-stranded positive-polarity RNA genome, similar to other coronaviruses, e.g. SARS and COVID-19, that the co-evolution between the mouse and the virus favors virulence. In a *vitro* (lab study), Wan Chen and Ralph Baric in 1996 showed the resistant host cells of the mouse that impede the vertical transmission of the virus created a genetic bottleneck for the subsequent selection of a more virulent variants viruses [65].

The virulent coronaviruses such as SARS, MERS and now COVID-19 that once long ago were circumlocated to the wild life mostly bats and one genu have rapidly spread intra-species (e.g. between different genu of bats) and recently inter-species even to humans.

This rapid spread of this class of virus with its high virulence is a hallmark of the coronavirus rapid evolution [66]. Most recently, Letko and colleagues in 2018 have shown that how MERS-CoV by altering the surface charge of its spike (or crown where the name of Corona derives from) surpasses the host cell receptor resistance for entry [67]. Koonpaew et al., [68] in 2019 have also shown another coronavirus, Enteropathogenic Porcine Epidemic Diarrhea Virus (PEDV) and Porcine Delta Coronavirus (PDCoV) that cause diarrhea in neonatal pigs in the past decade circumvent or subvert the host's first line of defense for entry.

The evolutionary pathway of Coronavirus

Most impressive Wertheim and colleagues in 2013 argued and showed that coronaviruses infecting mammals (alpha-and-beta coronaviruses) and gamma-and-delta coronaviruses infecting birds have co-existed and evolved with these ancient species between 190 to 489 million years ago [69]. By analysis of the nucleotide sequences of these coronaviruses at the non-recombinant regions of their genomes and estimation of the branch length of the inferred maximum likelihood of their phylogenies, these researchers were able to extrapolate the lineage of Coronaviruses being as ancient as their hosts, back to an average of 300 million years ago. More recently it has also been shown that the human coronavirus OC43 involved in the common cold or flu, that's a beta coronavirus type 1, similar to the one infecting cattle (BCoV) has been spilled over from bovine to our homo sapiens ancestor after the first contact with

their respiratory tracts [70].

The coronavirus spillover once again has emerged in the recent years with full force of the new types of beta coronavirus infections such as SARS, MERS and now COVID-19. Such pathogen emergence is driven by ecological, genetic factors and codon usage at the service of adaptation of the virus to the hosts, through natural selection based on translation efficiency and drift according to the genomic mutation pressure. On the path of its evolution and adaptation to its host and breaking any resistance, the human coronavirus OC43 has evolved and changed to many genotypes and variants that had already been shown in the human samples in France and China among other places. What we have seen and suffered by the novel coronaviruses of SARS, MERS and now COVID-19 in the recent years are all the tips of an iceberg of biodiversity and power of co-evolution of the coronaviruses deep down in the ocean of a universal ecosystem on earth [71-81].

An Enemy that was never

The human coronaviruses that evolved almost a million year ago with our Homo sapiens ancestor and lived with us since as a peaceful common cold or flu in our respiratory system has been striking back in the recent years. Our current knowledge despite the vast and fast progress in the field of virology and bridging with genetics, evolution and ecosystem, is still in its infancy, lest to resist the entry of our own coronavirus with its diversity and unbreakable armamentarium. Despite our current and ongoing all global panic over COVID-19, the virus has been fatal only in the elderly and individuals with underlying severe medical conditions with poor immune system to adapt to the virus. According to the recent WHO data on COVID-19 mortality, almost 20% of the fatalities have been in the age group of over 80 years old with decreasing drastically by decade down the ladder of life, so 10% in the age group of 70-79, less than 5% in the age group of 60-69 and just over 1% in the age group of 50-59 with rare to almost no mortality in any age group under 50 years old (less than 1% in all age groups of 0-49). The above factual data is an evidence that the virus is not antagonistic and against our survival, but an endosymbiont and a part of the co-evolution and ecosystem that needs to be with us. While the interaction or invasion of the coronavirus on the surface seems to be unilateral and opportunist with no benefit for us, our scarce knowledge in the very field cautions us to the contrary. Unlike the antagonistic and destructive viruses such as HIV and HPV, the corona viruses like many so other good viruses have never caused the extinction of their bovine and avian hosts and not even our own humans' CoV-OC43 over million years of cohabitation has not harmed us seriously. Therefore, it is obvious that our human coronavirus in its different variants, even the current ongoing COVID-19 is a mutual partner that most probably is on the mission of evolving us or helping us to adapt to the current and the future environment. The virulence of the new variants of the human coronavirus as detailed in other viral cases is not a sign against mutual cohabitation or symbiosis and co-evolution but it speaks of the urgency for the need of entry at the service of genomic diversity and evolution. The fatalities of elderly and immune compromised population are due to their lack of defense, notwithstanding this entry and adaptation for a healthier future, and they might not be fit candidate hosts for the virus. Any resistance to the virus entry, specially at the current time of its utmost urgent virulence for entry could lead to another later more aggressive entry through another more fatal pandemic outbreak.

Conclusion

The current universal panic about the COVID-19 has been so far the worst pandemic event befalling on the humans globally. Although there have been epidemics and pandemics across the human history such as plague and Spanish Flu, none has been this extensive crossing all the waters and lands. While at the onset, the virus outbreak appeared as an epidemic and limited to China and its Wuhan province where the outbreak started, there has been rarely any place on the face of earth to have skipped this microbial invasion. This universal entry of the coronavirus, after the recent SARS and MERS with its powerful virulence is a strong evidence of the natural selection obligation that the virus has for maintenance of our longer-term survival.

The lack of knowledge in the public about the significance of symbiosis with other beings such as viruses that have been the backbones of life like other vital elements making this planet, has been the cause of our world-wide panic never seen before. While even in the scientific arena viruses until recently were thought as antagonistic and pathogens, we need to come to the realization and appreciation of the role of viruses in every single life form from plants to bacteria and larger animals like us. Symbiosis and endosymbiosis is a vital part of life and has existed from the inception of life on the planet with no exceptions, even for us. In summary the human coronavirus OC43 that has spilled over almost a million year ago from bovines to our homo, sapiens ancestor has been living with us in peaceful endosymbiosis causing only a mild flu or common cold since. The recent aggressive invasion of the virulent variants of the virus, e.g. SARS, MERS and now COVID-19 does not mean that the virus agenda has changed from a peaceful cohabitation and co-evolution to wipe us out! In fact the current understanding and appreciation in the field is that the virulence and aggression of the virus for entry is not antagonistic to life, but at the service of an urgent entry for maintaining survival, natural selection and evolution on both sides of the equation, the virus and the host. Any resistance and fighting back would lead to the future more aggressive and fatal entry of the virus as history has repeated itself with the outbreak of the current and ongoing COVID-19 that has been much more virulent than his sisters SARS & MERS.

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