

The Perfect Storm and A Global Call to Reason: An Evolutionary Perspective on The Existential Threat of Covid-19 to Humanity

Procunier William*

Nipissing University, Ontario, Canada.

*Correspondence:

Procunier William, Department of Psychology, Nipissing University, 100 College Avenue, North Bay, Ontario, Canada P1B 8L7.

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ABSTRACT

The Covid-19 pandemic has put us at a generational cross roads in human evolution as a result of our accumulated impact on the planet during the Anthropocene. People/governments in positions of power and influence need to address this threat in a much more concerted and efficient manner. We need to think at a species level in evolutionary terms for our collective survival as a result of this confluence of public health, socio-economic and geopolitical forces being brought to bear. The article discusses and provides some evolutionary insights into aspects of the epidemiology, genetics, genomics and clinical outcomes of Covid-19 in relation to these threats.

Keywords

Evolution, Genetics, Genomics, Covid-19, Humanity.

Introduction

Primates of the genus homo can be dated back some 2.1 million to 200,000 years ago before present [1] with modern day origins of extant humans occurring between 100,00 to 50,000 years ago based on fossil record as well as molecular data [2]. Comparative genomics studies through the identification of human accelerated regions (HARs) and other human-specific genome sequences would seem to support these findings [3], although there is also a consensus in part that hypotheses on the origins and population dispersal of these taxonomic entities out of Africa through Eurasia and Oceania maybe more complex than originally hypothesized [4]. By contrast, virus's have existed on earth during the earliest stages of life some 3.8-4.0 billion years ago [5] and have a history of co-evolution with cells [6].

Virus's can be found in multiple species from all three super kingdoms of the tree of life; the Archea, Bacteria and Eukarya and are fundamental agents of change at the most basic molecular genomic and proteomic structural levels. They can move vertically through a species and horizontally across species. Generally scientists/clinicians talk about mutations that may affect the viral genome like Sars Cov-2 with respect to pathogenicity

and transmission. These changes can refer to single nucleotide DNA/RNA polymorphisms that may affect structural gene protein product. These non-synonomous changes can potentially modulate both quantity/quality of binding of the viral protein to its host receptor like the spike protein/and/or efficacy of viral replication through the enzymes DNA/RNA dependent DNA/RNA polymerases. However, virus's can also recombine/re-assort their genes consistent with structural rearrangements such as inversions that can impact their gene regulation/protein production similar to that seen for chromosomal DNA with the much larger genomes of higher organisms (eukaryotes) [7,8].

Viral genomes/proteomes also have different types of 3D structural folds (FSF) comprised of amino acid (a.a) motifs. One type are histone chaperones (jelly roll folds) [6] that can potentially interact with chromatin remodelling complexes; central machinery for how the epigenome works in regulating protein production during cell metabolism.

Covid-19-Genetics/genomics/clinical observations

The etiological agent(s) of this Covid-19 pandemic are SARS-CoV-2/variants within the family coronaviridae [9]. During infection as these RNA virus's replicate, they can exchange genetic material by recombination/reassortment in the process of virion

production as they disseminate through our body systems and attack various cell surface receptors on different human organs which can lead to eventual external viral shedding and/or transmission. There may also be potential genetic/genomic exchanges through co-infections with other strains and possibly other viral species and/or host DNA. Notwithstanding ethnicity, race, population density and pre-existing conditions, a significant portion of the clinical phenotypic symptoms from Covid-19 in humans are probably due to underlying genetics of the person and their interaction with the specific viral strains/variants e.g. the spike protein of the SARS-CoV-2 enters the cell through the ACE-2 gene product (receptor) [10,11].

This receptor product is found on cells (epithelial/endothelial) of most organs throughout the body and the central nervous system (CNS). ACE-2 can interact with multiple genes and signalling pathways that impact the innate immune system /cardio vascular system, renal system-kidneys, muscles and gastro-intestinal tract through their up and down gene regulation of protein product [12-14].

The ACE-2 gene has been around for sometime with homologs/variants in multiple species that have a common origin in worm like ancestors [15]. Variants of human ACE-2 also occur that impact cardiovascular function; ACE pharmaceutical inhibitors [16] (potential use for Covid-19? e.g. catopril) have been developed for the treatment of cardiovascular disease/hypertension. Genome wide DNA sequencing association studies (GWAS) have found people with variants for the gene that can affect the efficacy of the inhibitor [17,18].

There also appears to be reported gender differences in clinical outcomes of some populations. A simple explanation may be based on Mendelian genetics. The ACE-2 gene is found on the X chromosome in humans; therefore males are hemizygous (have an either /or response) where as females have 2 copies and can have a more graded response based on their potential allelic combinations of at least 3 different classes of response. Yet, another significant case for globalized personalized genomic healthcare [19] in trying to understand individual/population variation with respect to new and emerging infectious/zoonotic diseases.

Covid-19 is not going away. As a result of the virus's global seeding and reseeding through migration/travel in such a short time and because of a lack of a unified overall coherent global strategy, a generational effort will be required to abate and control SARS CoV-2 and its evolving variants through multi-omic approaches for vaccine and therapeutic development [20]. At least 3 strains of the virus have already been documented as has been shown through phylogenetic analysis from various geographically distinct populations [21]. Nevertheless, bioinformatic approaches/screening using highly genetically characterised populations like those from Iceland (deCode Genetics) may prove useful to look for individuals/sub groups that show resistance to infection similar

to that seen for AIDS where a deletion in the CCR5 gene receptor tends to blocks HIV viral entry into T cells [22,23].

Covid 19; evolutionary implication(s) for global sustainability

In the current epicentre of the pandemic, the USA, there is already ongoing spiking waves of Covid-19 from the early opening of states in the mid west/southwest/southeast and it was only a matter of time before the gains on the coasts from social distancing and stay at home requirements were nullified.

This fluid situation was further exacerbated by lawful civil protests against racial injustice. These super spreader events along with too early openings have now led to internal implosion amongst the states which will impact migration/travel/commerce/supply chains. As containment measures have relaxed, the purported fall 2nd southern hemisphere wave is already coming through migration patterns/air travel; hotspots around the world continue to explode in India, Pakistan, Brasil, Ecuador, Peru,Russia, Africa (South Africa), Sweden,UK, Europe, middle east and China/SE Asia (in reality the virus spread represents an ongoing continuum).

In addition to the growing mid term to longer term effects of morbidity on quality of life/economic impact in adults, children/adolescents need to be monitored for neural/cognitive development given the increasing incidence of infection in children and because the virus has now been shown to cross the placenta and cause neurological damage in a newborn [24]. Further, one of the more troubling aspects of the virus's properties that has not been adequately explained/ investigated are the reports of the virus's longevity and associated morbidity; people having it, getting better and then retesting positive later.

One interpretation over and above potential faulty testing [25] and /or reinfection in these individuals is that the virus maybe demonstrating some form of latency/senescence. It is an RNA virus that enters the cell cytoplasm and sequesters the host's DNA machinery in the nucleus. It maybe signalling the nucleus to stop full virion production so as not to immediately burst the cell (apoptosis) and shed in the body somewhat similar to that of DNA viruses under stress. Such virus's can form episomes (encapsulated viral DNA) in the nucleus like herpes simplex (cold sores) or herpes zoster (shingles) and /or insert into host DNA like human papilloma virus (HPV- cervical cancer causing).The uniqueness the virus cannot be underscored as it has been shown most recently to develop filopodia that enhance binding to cell membranes and can be correlated to an up- regulation of host genes associated with the cytoskeleton, cell cycle (apoptosis) and inflammation [26].

Further, glycan molecules found within the spike protein appear to shield the effect of host immune produced neutralizing antibodies [27]. Taken together and with respect to latency if true, these findings would impact the successful development of vaccines/therapeutics and effect frequency of transmission of the virus in relation to clinical outcomes /abatment/control/reinfection and

immune response (memory/ hypersensitivity).

The evolution of homeostasis through the control and regulation of metabolic processes has been a marvel of higher life forms. Although these systems are governed by dynamic equilibriums from the cell to the organ to the individual to the population and can be perturbed and recover, they can also reach breaking points that lead to unpredictable chaos and destruction.

Humans are not exempt from Darwinian evolution through natural selection; the culling of humanity [28] and the reverse of globalization. Populations [28], races [29] and species do and have gone extinct such that the “domination of global ecosystems by people” (the Anthropocene era) “has caused a sharp rise in the rate of extinctions to far above pre-human levels where the loss of biodiversity affects the functioning of natural ecosystems and threatens human well-being” [30,31].

We need to think at a species level in evolutionary terms for our collective survival as a result of this confluence of public health, socio-economic and ongoing geopolitical forces being brought to bear that continue to affect the stability of western/eastern democracies. The clock is ticking on the species we call “homo sapiens”-wise humans???

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