The role of selectivity of the SARS-CoV-2 virus for human genetic profiles in susceptibility and resistance to COVID-19

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Abstract

Recently observed similarities in COVID-19 susceptibility among genetically related individuals hints at a selectivity of the SARS-CoV-2 virus that hinges on the affinity for select genetic profiles prevalent in the human species. The selectivity determines susceptibility of clinical disease and extent of pathogenesis, including fatal lung and myocardial injury, and may be more cogent than the recently reported risk factors. The selectivity of the SARS-CoV-2 virus for human genetic profiles as a factor of the virulence appears to be a novel feature and was not previously noted in the epidemics of widespread viral respiratory illnesses in humans.

Keywords: COVID-19, Genetic profile, Pandemic, SARS-CoV-2, Susceptibility, Virulence

Original Submission: 30 April 2020; **Revised Submission:** 6 May 2020; **Accepted:** 11 May 2020

Article published online: 19 May 2020

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The transmission pattern of the COVID-19 disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) appears to exhibit unpredictable features [1,2]. Large variability in the clinical presentations of COVID-19 disease amongst close contacts and members of the same household have been observed in clinical practice. During my conversations with next of kin of several critically ill patients with COVID-19 at Ochsner Medical Center, New Orleans, LA, USA, similar narratives were brought to my attention—members of a genetically related family suffered similar severity of disease while non-genetically related individuals in direct contact were mildly affected or asymptomatic (for example: spouses). Following my observations of this occurrence in greater than half of the critically ill COVID-19 patients I encountered, a systematic study to investigate this phenomenon in the local population is in process.

A recent case of an 83-year-old male who died at home after 1 week of fever, cough, and delirium from COVID-19 further illustrates this phenomenon. At home close contacts included his daughter and her 3 adult children who tested positive for COVID-19 and suffered from self-limiting moderately severe symptoms around the same time; and his son-in-law who remained asymptomatic and later demonstrated IgG antibodies to the SARS-CoV-2 virus. These observations hint at a selectivity of the virus within the human species that is predictive of the induction of clinical disease and the extent of pathogenesis among individuals. Conceivably, such selectivity may be more cogent than the recently reported risk factors of older age ($\geq$65 years old) and comorbidities (diabetes, underlying heart diseases, hypertension) associated with the development of severe illness [3,4]. It can be hypothesized that the nature of this selectivity hinges on the affinity for select genetic profiles. Relevant to this hypothesis, the genetic underpinnings of the susceptibility to infection may be explained by the polymorphisms of functional receptors needed for the virus to enter host target cells. For instance, human angiotensin-converting enzyme 2 (ACE2) has shown to be involved in the viral genome replication process [5]. Susceptibility to organ injury, including fatal lung and myocardial injury, in COVID-19 is thought to be linked to variations in the distribution and functional attributes of ACE2 receptors in the population [6].

Several questions stem from this conceptual approach. These include: (a) Did the selectivity originate in a progenitor of SARS-CoV-2 that, after contact with humans, acquired favorable genetic modifications through adaptation during undetected human-to-human transmission; (b) is this selectivity a manifest of Darwin's theory of Evolution by Natural Selection; (c) is the selectivity fixed or evolving as the virus continues to spread during the pandemic; (d) what are the implications of this selectivity on the development of an effective vaccine.

https://doi.org/10.1016/j.nmni.2020.100697

The selectivity of the SARS-CoV-2 virus for human genetic profiles as a factor of the virulence appears to be a novel feature. There are no descriptions of a similar phenomenon associated with the 1918 influenza pandemic or the epidemics of widespread respiratory illnesses caused by other coronaviruses. Conceivably, this may have been underreported and not investigated systematically in the early to middle 20th century [7,8]. Among the non-respiratory viruses, susceptibility to human immunodeficiency virus-1 infection was reported to be associated with genetically determined variations in host chemokine receptors [9] suggesting that varied selectivity exists in the virulence behaviors of other viruses in nature.

Undoubtedly, the SARS-CoV-2 virus possesses advanced virulence with a tactical advantage—its ability to continue human-to-human transmission in asymptomatic vectors' [10]—thus allowing maximum infection. As a corollary, the selectivity of the virus for human genetic profiles as a prognosticating factor for the severity of clinical disease portends a disconcerting challenge ahead. In this race to save humanity, we can get ahead of the game by putting our scientific clout in the pursuit of understanding the virulence behaviors and stratagem of the SARS-CoV-2 virus and by uncovering the genetic differences that render natural virulence in humans.

Conflicts of interest

Fawad A. Khan has no conflicts of interest.

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