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Study shows COVID-19 vulnerability is highly dependent on host genetic architecture

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By Dr. Tomislav Meštrović, MD, Ph.D. (/medical/authors/tomislav-mestrovic)

May 10 2020

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A new US study available on the preprint server *medRxiv* (<https://www.medrxiv.org/content/10.1101/2020.05.01.20088054v1>)* reveals certain genetic variations that are associated with infection susceptibility and diverse clinical presentation of coronavirus disease (COVID-19) – including asymptomatic cases and severe forms of the disease in younger patients.

The ongoing pandemic of severe acute respiratory syndrome (SARS-CoV-2) brought to the attention the pressing public health demand to adequately understand human genetic variation in response to the viral challenges.

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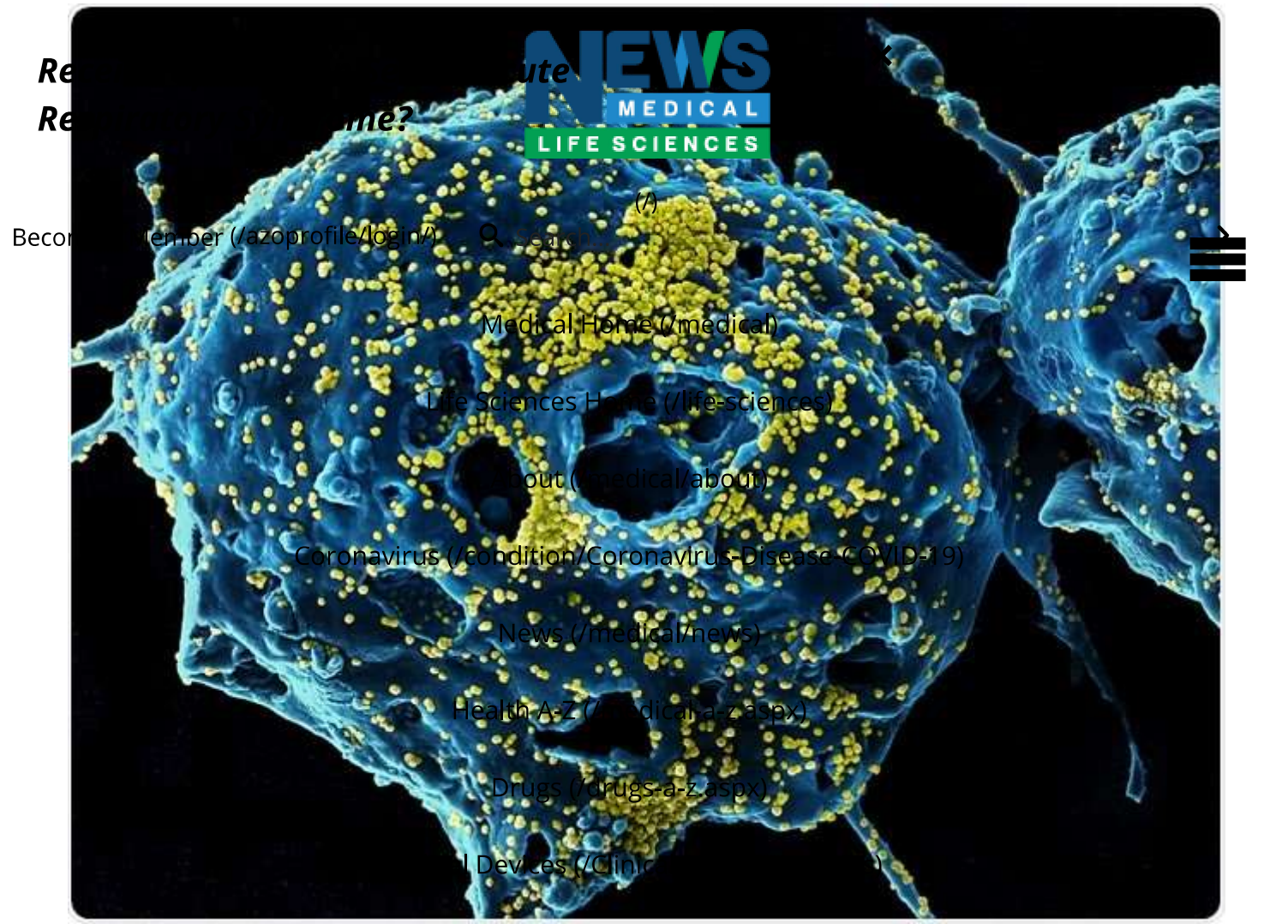
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MERS Virus Particles Colorized Scanning Electron Micrograph of Middle East Respiratory Syndrome virus particles (yellow) attached to the surface of an infected VERO E6 cell (blue). Image captured and color-enhanced at the NIAID Integrated Research Facility in Fort Detrick, Maryland. Credit: NIAID MediKnowledge (/mediknowledge)

Humans and viruses have evolved together for millennia, resulting in genetic polymorphisms that guide the host responses to viral infection. Consequently, clinical variation in COVID-19 severity and symptomatic presentation may be a result of differences in host genetic factors related to the immune response.

This is why researchers from the University of California San Francisco, the University of Texas at Austin, and St. Jude Children's Hospital in Memphis (United States) decided to appraise the genetic architecture of host response to viral infection, especially taking

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In-depth exploration of the host viral response

In this new study, the researchers utilized the data from the UK Biobank population-based study to identify genetic variants that create a protective environment for host genetics and its viral response. They have analyzed the data of 7,924 participants (predominantly of European ancestry).



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The study was to appraise 28 antigens for 16 viruses that have been linked to neurodegenerative diseases and malignancies but also to put the emphasis on the SARS-CoV-2 test in a separate subset of MedBank (medical).



Accordingly, they have conducted integrative genome-wide and transcriptome-wide analyses of antibody response and positivity to viral antigens. Pleiotropic associations between lead variants affecting antibody levels and several chronic diseases with viral risk factors were explored in depth.

Symptom span explained by HLA genetic variations

Study findings confirm that human leukocyte antigen (HLA) class II and III genes are pivotal host genetic factors implicated in regulating the immune response to diverse viral antigens, with potential implications for complex diseases.

Furthermore, the researchers have also discovered that specific HLA alleles linked to multiple common infections are associated with SARS-CoV-2 positive tests. More specifically, based on 1028 subjects tested for SARS-CoV-2, they have identified seven class II HLA susceptibility alleles (five associated with other viruses).

"Considering genetic variation within the HLA region, our results not only confirm its pivotal role at the interface of host-pathogen interactions, but also highlight the overlap in variants, classical alleles, and genes that mediate these interactions across virus families and antigens, emphasizing study authors."

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Associations between HLA alleles and SARS-CoV-2 status may indicate a different clinical course with milder infection or asymptomatic status, which is linked to lower COVID-19 exposure.

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Influencing the viral receptor

The research also pointed towards the inverse
relationship between genetically predicted
angiotensin-converting enzyme 2 (ACE2) gene
expressions and a positive SARS-CoV-2 testing
result. Albeit ACE2 plays a critical role in enabling
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"We suspect that decreased ACE2 expression may reduce viral infection by limiting available receptors for viral entry, and once a cell is infected, the reduced expression may aid SARS-CoV-2", explain study authors.

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SARS-CoV-2 viruses are binding to ACE-2 receptors on a human cell, the initial stage of COVID-19 infection. Conceptual 3D Illustration Credit: Ralena Kon / Shutterstock

Research implications

"Understanding the interplay between host genetic factors and immune response has implications for public health and may facilitate the discovery of novel therapeutics including vaccines," said study authors.

"Upon further elucidation of the risk of infection and COVID-19 severity, our results suggest that HLA typing may be a feasible tool in the SARS-CoV-2 response for identifying at-risk populations and prioritizing vaccine distribution", they conclude.

Naturally, further research is needed to understand the viability of this approach in diverse populations, whereas therapeutic research on ACE2 inhibitors will elucidate what is happening behind the downregulation of SARS-CoV-2 receptors after infection.

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Respiratory Syndrome?

Dr. Tomislav Meštrović is a medical doctor, M.D. in biomedical and health sciences, specialist in the field of clinical microbiology, and an Assistant Professor at Croatia's youngest university - University North. In addition to his interest in clinical, research and lecturing activities, his immense passion for medical writing and scientific communication goes back to his student days. He enjoys contributing back to the community. In his spare time, Tomislav is a movie buff and an avid traveler.

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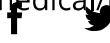


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