Journal of Virology®

GENETIC DIVERSITY AND EVOLUTION

Human Leukocyte Antigen Susceptibility Map for Severe Acute Respiratory Syndrome Coronavirus 2

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ABSTRACT Genetic variability across the three major histocompatibility complex (MHC) class I genes (human leukocyte antigen A [HLA-A], -B, and -C genes) may affect susceptibility to and severity of the disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus responsible for coronavirus disease 2019 (COVID-19). We performed a comprehensive *in silico* analysis of viral peptide-MHC class I binding affinity across 145 HLA-A, -B, and -C genotypes for all SARS-CoV-2 peptides. We further explored the potential for cross-protective immunity conferred by prior exposure to four common human coronaviruses. The SARS-CoV-2 proteome was successfully sampled and was represented by a diversity of HLA alleles. However, we found that HLA-B*46:01 had the fewest predicted binding peptides for SARS-CoV-2, suggesting that individuals with this allele may be particularly vulnerable to COVID-19, as they were previously shown to be for SARS (M. Lin, H.-T. Tseng, J. A. Trejaut, H.-L. Lee, et al., BMC Med Genet 4:9, 2003, https://bmcmedgenet.biomedcentral.com/articles/10.1186/1471-2350-4-9). Conversely, we found that HLA-B*15:03 showed the greatest capacity to present highly conserved SARS-CoV-2 peptides that are shared among common human coronaviruses, suggesting that it could enable cross-protective T-cell-based immunity. Finally, we reported global distributions of HLA types with potential epidemiological ramifications in the setting of the current pandemic.

IMPORTANCE Individual genetic variation may help to explain different immune responses to a virus across a population. In particular, understanding how variation in HLA may affect the course of COVID-19 could help identify individuals at higher risk from the disease. HLA typing can be fast and inexpensive. Pairing HLA typing with COVID-19 testing where feasible could improve assessment of severity of viral disease in the population. Following the development of a vaccine against SARS-CoV-2, the virus that causes COVID-19, individuals with high-risk HLA types could be prioritized for vaccination.

KEYWORDS COVID-19, HLA, MHC class I, SARS-CoV-2, coronavirus

Recently, a new strain of betacoronavirus (severe acute respiratory syndrome coronavirus 2, or SARS-CoV-2) emerged as a global pathogen, prompting the World Health Organization in January 2020 to declare an international public health emergency (1). In the large coronavirus family, comprising enveloped positive-strand RNA viruses, SARS-CoV-2 is the seventh encountered strain that causes respiratory disease in

Citation Nguyen A, David JK, Maden SK, Wood MA, Weeder BR, Nellore A, Thompson RF. 2020. Human leukocyte antigen susceptibility map for severe acute respiratory syndrome coronavirus 2. J Virol 94:e00510-20. https://doi.org/10.1128/JVI.00510-20.

Editor Tom Gallagher, Loyola University Chicago

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Received 23 March 2020
Accepted 14 April 2020
Accepted manuscript posted online 17 April 2020
Published 16 June 2020