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EDITORIAL

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Editorial: Diverse responses to SARS-CoV-2 in the human population

SARS-CoV-2 has, of course, changed the global landscape, upending much of our lives over the last 2 years. Pandemic-related lockdowns and the crisis to our healthcare systems have driven a shift in how we conduct our daily lives. Even in the era of potent vaccines that can ably prevent severe COVID-19, the emergence of variants that evade immunity or are more infectious prevent a return to normalcy or at least understand how our lives will change for the foreseeable future.

A particularly vexing issue regarding SARS-CoV-2 is its heterogeneous nature in causing disease.: testing positive for SARS-CoV-2 does not regularly lead to symptomatic COVID-19. Testing issues at the beginning of the pandemic, that ultimately led into availability issues with testing supplies may have a role to play here, but it is now clear that testing positive, being infectious, and having symptomatic COVID-19 remain only weakly linked.

Of course, the human population has wide heterogeneity in the immune system, the most polymorphic genes being major histocompatibility antigens, most notably human leukocyte antigens (HLA), which represent the mechanism by which T cells are presented antigen. Polymorphisms in HLA may explain diverse responses to SARS-CoV-2.

In this issue of *Immunology*, we present work exploring how polymorphisms in antigen presentation machinery (HLA) can help define responses to coronaviruses, including susceptibility to severe disease. In one study, by Astbury et al, the authors report results from a longitudinal study of healthcare workers in the United Kingdom. They find a specific allele of HLA-DR associated with decreased T cell responses to SARS-CoV-2 and an increased risk of severe COVID-19 [1]. In a second study by Buckley et al, the authors explore how HLA polymorphisms may affect how patients may respond immunologically to SARS-CoV-2 versus other human coronaviruses [2]. Cross-reactivity between other coronaviruses, based on HLA, may ultimately define why some individuals respond robustly in response to SARS-CoV-2 infection and others may ultimately become more severely infected.

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