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Infectious disease susceptibility in the context of African genetic diversity

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During late 2019, the world saw the emergence of the Coronavirus Disease 2019 (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). To date, more than 242 million infections have been observed in 223 countries/territories across the globe, with a staggering 4.9 million individuals losing their lives to COVID-19. South Africa has not remained unscathed by the pandemic, having more than 2.9 million COVID-19 cases and over 88 000 COVID-19 deaths. Significant inter-individual variability has been observed in host responses to COVID-19, with host genetic factors being proposed as a contributor to SARS-CoV-2 susceptibility and disease severity. This observation echoes that of the ancient disease of tuberculosis (TB), still a chief cause of death in many areas, with Africa home to most high burden countries. To find the genetic underpinnings of TB in South Africa, we have studied the complete susceptibility spectrum, from individuals with rare susceptibility mutations to common genetic variants in the general population. We used association studies, genome wide linkage studies and genome-wide association studies and incorporated population genetics and computational analyses to identify genes and loci that inform the variation in disease outcome between individuals. We are establishing a large COVID-19 cohort representative of South African populations, including individuals that have tested both positive and negative for SARS-CoV-2 to elucidate the underlying genetic markers that are associated with both infection and severe/critical COVID-19. This includes whole genome sequencing of younger individuals diagnosed with a rare Multisystem Inflammatory Syndrome in Children (MIS-C) that is directly related to a previous SARS-CoV-2 infection, which is often very mild or asymptomatic in children. Our findings could assist with the management of infectious diseases in resource-poor African settings, where an overburdened healthcare system in the past has not been able to accommodate infection surges.

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