Impact of intra-host immune adaptations on the evolution of SARS-CoV-2 S protein among individuals with SARS-CoV-2 infections in South Africa, 2020 to 2022

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Abstract

Background Intra-host diversity studies are used to characterise mutational heterogeneity of SARS-CoV-2 infections to understand the impact of virus-host adaptations. This study investigated the frequency and diversity of the spike (S) protein mutations within SARS-CoV-2 infected South African individuals. Methods Single nucleotide polymorphism (SNP) assays and whole genome sequencing were performed on SARS-CoV-2 positive samples. Allele frequency (AF) was determined using TaqMan Genotyper software for SNP analysis and galaxy.eu for analysis of FASTQ reads. Results The SNP assays identified 5.3% (50/948) Delta cases with heterogeneity at delY144 (4%; 2/50), E484Q (6%; 3/50), N501Y (2%; 1/50) and P681H (88%; 44/50). Sequencing identified 9% (210/2381) cases with Beta, Delta, Omicron BA.1, BA.2.15, and BA.4 lineages with heterogeneity in the S protein. Heterogeneity was primarily identified at positions 19 (1.4%) with T19IR (AF 0.2-0.7), 371 (92.3%) with S371FP (AF 0.1-1.0), and 484 (1.9%) with E484AK (0.2-0.7), E484AQ (AF 0.4-0.5) and E484KQ (AF 0.1-0.4). Conclusion Mutations at heterozygous amino acid positions 19, 371 and 484 reduce recognition of neutralising antibodies, however the impact of the multiple substitutions at the same position is unknown. Therefore, we hypothesise that intra-host SARS-CoV-2 quasispecies with heterogeneity in the S protein facilitate competitive advantage of variants that can completely/partially evade host's natural and vaccine-induced immune responses.

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