Characterization of B-cell receptor clonality and immunoglobulin gene usage at multiple time points during active SARS-CoV-2 infection

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Abstract

Purpose Although monoclonal antibodies specific to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are known, information about the B-cell receptor (BCR) repertoire and its change in patients during COVID-19 disease progression is underreported. **Methods** We used immunoglobulin heavy chain (IGH) variable region (IGHV) spectratyping and next-generation sequencing of peripheral blood B-cell genomic DNA collected at multiple time points during disease evolution to study B-cell response to SARS-CoV-2 infection in 14 individuals with acute COVID-19. **Results** We found a broad distribution of responding B-cell clones. The IGH gene usage was not significantly skewed but frequencies of individual IGH genes changed repeatedly. We found predominant usage of unmutated and low mutation-loaded IGHV rearrangements characterizing naïve and extrafollicular B-cells among the majority of expanded peripheral B-cell clonal lineages at most tested time points in most patients. IGH rearrangement usage showed no apparent relation to anti-SARS-CoV-2 antibody titers. Some patients demonstrated mono/oligoclonal populations carrying highly mutated IGHV rearrangements indicating antigen experience at some of the time points tested, including even before anti-SARS-CoV-2 antibodies were detected. **Conclusion** We present evidence demonstrating that the B-cell response to SARS-CoV-2 is individual and includes different lineages of B-cells at various time points during COVID-19 progression.

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