Antibody repertoire diversity correlates with neutralization breadth in COVID-19 convalescent individuals

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Abstract:
Identifying features of development of an effective antigen-specific B cell repertoire could aid in understanding of the infection and/or vaccine driven affinity maturation of B cells and the resulting humoral immune responses. In the present study, through Fluorescence activated cell sorting followed by sequencing, antigen specific B cell repertoire was correlated with neutralization breadth of the monoclonal antibodies isolated from a COVID-19 convalescent individual (C-03-0020). Briefly, spike Recotor bunding domain specific B cells were sorted from PBMCs, followed by isolation, cloning, sequencing and generation of dual antigen-positive IgG as complete antibodies. We confirmed their binding to the receptpr binding domain by ELISA and then observed their neutralization profile against the circulating/evolving SARS-CoV-2 variants through *in vitro* neutralization assays. Two novel neutralizing monoclonal antibodies (MAbs), THSC20.HVTR11 and THSC20.HVTR55, representing unique B cell lineages, were isolated from an unvaccinated donor C-03-0020 and compared to five Mabs previously reported from the same individual with distinct epitope specificities and B cell lineages. THSC20.HVTR11 was found to neutralize Omicron BA.1 and BA.2 potently THSC20.HVTR55 neutralize most of the pre Omicron wave variants but fail to neutralize all Omicron variants. In conclusion, antibodies isolated from C-03-0020 donor who was infected with ancestral SARS-CoV-2 in early 2020 were found to be varied in terms of both epitope specificities, B cell lineages of origin as well as their capability to neutralize all known variants of concern. Establishment of unique lineages leading to diverse B cell repertoire immediately following infection may have contributed to the broad polyclonal humoral immune response.