Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Antigenic mapping of emerging SARS-CoV-2 omicron variants BM.1.1.1, BQ.1.1, and XBB.1

Novel SARS-CoV-2 omicron variants, including BM.1.1.1, BQ.1.1, and XBB.1, continue to emerge at an unprecedented rate, evading pre-existing immunity from vaccination and previous infection. Quantifying the antigenic diversity of variants might assist in selecting future vaccine strains. To determine the antigenic relationships between emerging SARS-CoV-2 omicron variants, we and others[1–4] used antigenic cartography, whereby multidimensional scaling is used to generate antigenic maps in which the positions of antigens and antiserum samples directly correspond to neutralising titres. This method allows for the quantification and visualisation of antigenic properties of different variants simultaneously.

Previously, we used the hamster model for SARS-CoV-2 to generate an antigenic map.[4] We now inoculated hamsters with the currently dominant omicron BA.5 variant, which is genetically close to BA.2, differing in the spike amino acid sequence by only three substitutions and two deletions (appendix p 1). Neutralising titres were determined using all serum samples and variants grown previously, along with omicron BA.5 and the omicron BQ.1.1, BM.1.1.1, and XBB.1 variants, which emerged in late 2022 (appendix p 2). Omicron BA.5 antiserum samples neutralised the homologous virus, BA.2, and BQ.1.1 efficiently, whereas omicron BM.1.1.1 was poorly neutralised. None of the serum samples were able to substantially neutralise XBB.1.

Next, we generated an updated antigenic map using all available antiserum samples and viral variants (appendix p 3). In this map, all omicron variants were positioned distantly from the pre-omicron cluster. Omicron BA.5 was positioned within one antigenic unit from BA.2, with an antigenic unit representing a two-fold dilution in neutralisation titrations. All remaining omicron variants were positioned 2·3 to 7·0 antigenic units from each other. Omicron BQ.1.1, BM.1.1.1, and XBB.1 mapped the furthest from the pre-omicron variants. Similar results were observed in a map generated in three dimensions (appendix p 4). The data were well represented in two and three dimensions, with no substantial improvement at a higher number of dimensions (appendix p 5). Two dimensional and three dimensional map distances correlated well with neutralisation titres and overall there was good coordination and accuracy in the placement of the antigens and serum samples. Despite the lower certainty in the positioning of BQ.1.1, BM.1.1.1, and XBB.1, the reactive heterologous serum samples present in the map, which are well spaced, allow for a good approximation of the antigenic position of new variants (without their respective homologous serum samples). We observed that human post-vaccination neutralisation titres reflected the antigenic map, as the largest reduction in neutralising titres compared with the D614G variant is against omicron BQ.1.1, BM.1.1.1, and XBB.1, followed by omicron BA.1, BA.2, and BA.5 to similar levels (appendix p 6).

Our data reveal substantial cross-neutralisation of BA.5 antiserum samples against BQ.1.1 but little cross-neutralisation against XBB.1 and BM.1.1.1. Despite the antigenic similarities between BA.5 and BQ.1.1, thus far there is little evidence for increased neutralisation of BQ.1.1 by BA.5 bivalent vaccines, potentially due to immunological imprinting.[5–7] In addition, these newly emerging variants do not cluster close to each other, therefore a vaccine based on any of these variants might poorly cross-neutralise new, emerging variants, which could be equally antigenically distant. Continuous mapping of new variants and a greater understanding of the evolutionary trajectory of SARS-CoV-2 could indicate potential vaccine candidates.

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See **Online** for appendix

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