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.

Finite neutralisation breadth of omicron after repeated vaccination

Exposure to SARS-CoV-2 antigens by vaccination or infection expands the breadth of neutralising antibodies to better recognise mutated variants,[1] which is part of the reason why ancestral SARS-CoV-2-based vaccines still protect against immune evasive variants like omicron.[2] However, since natural expansion of neutralisation breadth relies on antibody affinity maturation, a process consisting of somatic hypermutation and clonal selection of B cells, neutralisation breadth might be limited by the time since first antigen exposure.[3] We therefore wonder whether repeated vaccination in individuals with existing broad neutralisation breadth could trigger this limit, and if true, whether less frequent vaccination could maintain neutralisation breadth in those individuals.

We have reported that unvaccinated individuals at 12 months who were convalescent developed broader neutralisation breadth than individuals at 1 months who were convalescent and vaccination-only.[4] These convalescent individuals were followed-up at 24-month convalescence when they had received 1–3 doses of CoronaVac (appendix p 7), and compared with prevaccination 1-month and 12-month convalescent samples and uninfected healthcare workers (HCWs) at 1-month post-prime-boost or post-third-dose CoronaVac vaccination (appendix p 9). Vaccination and sample collection schedules were shown in the appendix (p 2). The 50% pseudovirus neutralisation titres ($pVNT_{50}$) of omicron sublineages BA.1, BA.2, and BA.4–BA.5 and ancestral Wuhan-Hu-1 were assessed by assays as described in the appendix (p 11), and neutralisation breadth was estimated as the geometric mean of $pVNT_{50}$ ratios between each omicron sublineage and ancestral Wuhan-Hu-1.

Both convalescent and HCW groups showed similar concentrations of durable neutralising antibodies against Wuhan-Hu-1 (appendix p 3). Interestingly, neutralisation of all omicron sublineages was enhanced by third vaccination among uninfected HCWs, whereas only neutralisation of BA.1 benefited from second or third vaccination among individuals who were convalescing (appendix p 3). Omicron versus Wuhan-Hu-1 $pVNT_{50}$ ratios suggested that repeated vaccination expanded neutralisation breadth only in individuals who were uninfected but not convalescent (appendix p 5). Notably, third vaccination at 6-month post-prime-boost improved neither neutralisation potency nor breadth among individuals who were convalescing (appendix pp 3, 5).

A unique strength of this study is avoiding variant-induced expansion of neutralisation breadth, which is independent of affinity maturation process,[5] by recruiting participants from a region without COVID-19 cases after ancestral SARS-CoV-2 outbreak. Without artifacts due to variant infection, our data provided preliminary evidence that neutralisation breadth of omicron sublineages was finite in individuals at 2 years who were convalescing with repeated vaccination. Individuals who are convalescing with broad baseline neutralisation breadth thus might not need frequent booster vaccination. In contrast, individuals who are uninfected might need timely boosters or ideally variant-based vaccines to acquire optimal neutralisation breadth against omicron and future variants.

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See **Online** for appendix